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Proteon Therapeutics, Inc.

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As submitted confidentially with the Securities and Exchange Commission on August 5, 2014 as Amendment No. 1 to the confidential submission. This draft registration statement has not been publicly filed with the Securities and Exchange Commission and all information herein remains strictly confidential.

Registration No. 333-

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM S-1

REGISTRATION STATEMENT
Under
The Securities Act of 1933

Proteon Therapeutics, Inc.

(Exact name of Registrant as specified in its charter)

Delaware	**2836**	**20-4580525**
(State or Other Jurisdiction of Incorporation or Organization)	(Primary Standard Industrial Classification Code Number)	(I.R.S. Employer Identification Number)

200 West Street
Waltham, MA 02451
(781) 890-0102
(Address, including zip code, and telephone number, including area code, of Registrant's principal executive offices)

Timothy P. Noyes
Chief Executive Officer
Proteon Therapeutics, Inc.
200 West Street
Waltham, MA 02451
(781) 890-0102 x1021
(Name, address, including zip code, and telephone number, including area code, of agent for service)

Please send copies of all communications to:

Julio E. Vega, Esq. **William S. Perkins, Esq.** **Bingham McCutchen LLP** **One Federal Street** **Boston, MA 02110** **(617) 951-8000**	**Patrick O'Brien, Esq.** **Ropes & Gray LLP** **Prudential Tower** **800 Boylston Street** **Boston, MA 02199-3600** **(617) 951-7527**

Approximate date of commencement of the proposed sale to the public: As soon as practicable after the effective date of this Registration Statement.

If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act, check the following box. o

If this Form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. o

If this Form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. o

If this Form is a post-effective amendment filed pursuant to Rule 462(d) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. o

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, or a smaller reporting company. See the definitions of "large accelerated filer," "accelerated filer" and "smaller reporting company" in Rule 12b-2 of the Exchange Act. (Check one):

Large accelerated filer o	Accelerated filer o	Non-accelerated filer ☒ (Do not check if a smaller reporting company)	Smaller reporting company o

CALCULATION OF REGISTRATION FEE

Title of Each Class of Securities to be Registered	**Proposed Maximum Aggregate Offering Price(1)(2)**	**Amount of Registration Fee**
Common Stock, $0.001 par value per share	$	$

(1) Includes additional shares of common stock that the underwriters have the option to purchase.

(2) Estimated solely for the purpose of calculating the registration fee pursuant to Rule 457(o) under the Securities Act of 1933, as amended.

The Registrant hereby amends this Registration Statement on such date or dates as may be necessary to delay its effective date until the Registrant shall file a further amendment which specifically states that this Registration Statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act of 1933, as amended, or until the Registration Statement shall become effective on such date as the Securities and Exchange Commission, acting pursuant to said Section 8(a), may determine.

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The information in this preliminary prospectus is not complete and may be changed. These securities may not be sold until the registration statement filed with the Securities and Exchange Commission is effective. This preliminary prospectus is not an offer to sell these securities and we are not soliciting offers to buy these securities in any jurisdiction where the offer or sale is not permitted.

SUBJECT TO COMPLETION, DATED AUGUST 5, 2014

PRELIMINARY PROSPECTUS

PROTEON Therapeutics

Shares

Common Stock

$ per share

This is the initial public offering of Proteon Therapeutics, Inc. We are offering shares of our common stock. Prior to this offering, there has been no public market for our common stock. We estimate that the initial public offering price of our common stock will be between $ and $ per share.

We intend to apply to have our common stock listed on The NASDAQ Global Market under the symbol "PRTO."

We are an "emerging growth company" as that term is used in the Jumpstart Our Business Startups Act of 2012 and, as such, we have elected to comply with certain reduced public company reporting requirements for this prospectus and future filings.

Investing in our common stock involves risks. See "Risk Factors" beginning on page 12.

	Per Share	Total
Initial public offering price	$	$
Underwriting discount and commissions(1)	$	$
Proceeds, before expenses, to us	$	$

(1) We have agreed to reimburse the underwriters for certain expenses. See "Underwriting."

We have granted the underwriters a 30-day option to purchase up to a total of additional shares of common stock on the same terms and conditions set forth above.

The underwriters expect to deliver the shares of common stock to purchasers on , 2014.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

Stifel **JMP Securities**

Baird **Oppenheimer & Co.**

The date of this prospectus is , 2014

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Unless the context requires otherwise, references in this prospectus to "Proteon," "the Company," "we," "us" and "our" refer to Proteon Therapeutics, Inc.

In this prospectus, we refer to our subsidiary Proteon Therapeutics Limited as "Proteon UK."

You should rely only on the information contained in this prospectus or contained in any free writing prospectus filed with the Securities and Exchange Commission. Neither we nor the underwriters have authorized anyone to provide you with additional information or information different from that contained in this prospectus or in any free writing prospectus filed with the Securities and Exchange Commission. We are offering to sell, and seeking offers to buy, our common stock only in jurisdictions where offers and sales are permitted. The information contained in this prospectus is accurate only as of the date of this prospectus, regardless of the time of delivery of this prospectus, or of any sale of our common stock.

Through and including , 2014 (the 25th day after the date of this prospectus), all dealers that effect transactions in these securities, whether or not participating in this offering, may be required to deliver a prospectus. This is in addition to the dealers' obligation to deliver a prospectus when acting as underwriters and with respect to their unsold allotments or subscriptions.

For investors outside the United States: Neither we nor any of the underwriters have done anything that would permit this offering or possession or distribution of this prospectus in any jurisdiction where action for that purpose is required, other than in the United States. You are required to inform yourselves about and to observe any restrictions relating to this offering and the distribution of this prospectus outside of the United States.

PROSPECTUS SUMMARY

This summary highlights information contained elsewhere in this prospectus and does not contain all the information that you should consider in making your investment decisio You should read the entire prospectus, including our financial statements and related notes and the information set forth in the sections titled "Risk Factors," "Special Note Regardi Forward-Looking Statements" and "Management's Discussion and Analysis of Financial Condition and Results of Operations" before deciding whether to purchase shares of ou common stock. Unless the context otherwise requires, we use the terms "Proteon," "our company," "we," "us" and "our" in this prospectus to refer to Proteon Therapeutics, Inc.

Company Overview

We are a late-stage biopharmaceutical company focused on the development of novel, first-in-class pharmaceuticals to address the needs of patients with renal and vascular diseas Our product candidate, PRT-201, is a recombinant human elastase that we are developing to reduce vascular access failure in patients with chronic kidney disease undergoing preparing for hemodialysis, a lifesaving treatment that cannot be conducted without a functioning vascular access. We believe the data from our completed Phase 2 trial of PRT-201 patients undergoing creation of an arteriovenous fistula, or AVF, support that a one-time, local application of PRT-201 during AVF surgical placement reduces AVF failure, thereb improving patient outcomes and reducing the burden on patients and the healthcare system. We are not aware of any approved preventative treatments to reduce the failure rate of AVF

In May 2014, following the results from our Phase 2 trial and to fund our first Phase 3 trial, we closed on the $25.0 million first tranche of a $45.0 million total financing. Th financing was led by Abingworth, Deerfield and Pharmstandard and included investments from our existing venture investors. We expect to initiate the first of two Phase 3 trials fo PRT-201 in radiocephalic AVFs, our initial indication, in the third quarter of 2014 and initiate the second Phase 3 trial in the first half of 2015. PRT-201 has received fast trac designation which is designed to facilitate the development and expedite the review of drugs to treat serious conditions and fill an unmet medical need, from the United States Food an Drug Administration, or FDA, and orphan drug designation in the United States and European Union, for hemodialysis vascular access indications.

We retain worldwide commercial rights to PRT-201. If approved by regulatory authorities, we intend to commercialize this product in the United States ourselves with a specialt hospital sales force, focused primarily on vascular surgeons, and intend to seek one or more collaborators to commercialize the product in additional markets. Our patents include clain covering formulations, methods of manufacturing and uses of elastases, providing protection in the United States through mid 2029 and the European Union through 2028, and wi potential extension through 2032 in the United States and the European Union.

Established Medical Need

The need to improve vascular access outcomes is well established in the hemodialysis community. A 2014 publication estimated the total cost of managing hemodialysis vascul access dysfunction in the United States to be approximately $2.9 billion annually. AVFs are the gold standard of vascular access for hemodialysis, as they are associated with few complications and reduced rates of hospitalization. However AVFs have a greater than 50% failure rate in their first year after surgical placement, resulting in frequent surgical interventional procedures and a high rate of abandonment, leading to increased morbidity, mortality and costs of care.

We estimate there are approximately 130,000 AVFs created in the United States annually. In an AVF procedure a surgeon transects a vein and sutures it to the side of a nearb artery, typically in the arm. There are a limited number of potential artery-vein combinations in the arm that can be used by surgeons to create an AVF. The medical community endors radiocephalic AVFs, in which the cephalic vein is sutured to the radial artery in the wrist, as the optimal form of vascular access and the recommended first

choice for new hemodialysis patients. A radiocephalic AVF as compared to other forms of vascular access preserves the potential future use of other access further up in the arm, simpler to create and is less likely to result in serious complications, including heart failure, central stenosis, which is the narrowing of blood vessels in shoulder or chest, and reduce blood flow to the hand. Unfortunately, radiocephalic AVFs suffer from high failure rates, with up to 70% failing within 12 months after their surgical placement. We estima approximately 40% of all AVF placements are radiocephalic.

While AVF failure can usually be restored via an intervention such as balloon angioplasty, which is dilation of a blood vessel with a balloon, or a surgical revision. However, thes procedures are costly, invasive, painful, and associated with a number of complications and often need to be repeated. AVF patients in the United States on average require greater tha 1.5 procedures per year. Procedures to restore function typically cost Medicare between $5,000 and $13,000 per procedure. A recent publication indicates that maintaining radiocephalic AVF can cost on average more than $17,000 in the first year after surgical placement.

PRT-201

We demonstrated that PRT-201, a recombinant human elastase, generates fragments of elastin, a protein present in blood vessel walls. We believe the fragments of elastin inhib formation of neointimal hyperplasia, which is the growth of tissue inside vessels that narrows AVFs and reduces blood flow. We believe that a one-time, local application of PRT-201 the external surface of the vessels during AVF surgical placement can modify the injury response, or scarring, resulting from surgery and thereby reduce the severity of neointim hyperplasia and AVF failure following surgery. During the AVF placement surgery, the surgeon administers drops of PRT-201 onto the surface of the artery and vein of the AVF for 1 minutes followed by a saline irrigation. We believe that, if our Phase 3 clinical program is successful, PRT-201 will potentially become the standard of care for patients with chron kidney disease who are undergoing surgical placement of a radiocephalic AVF.

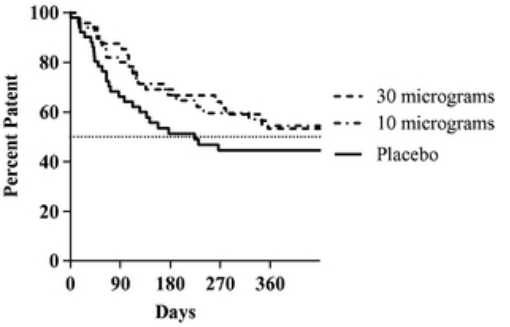
Phase 2 AVF Trial Results

In 2013, we completed a multicenter, randomized, double-blind, placebo-controlled Phase 2 trial of PRT-201, which treated 151 patients with chronic kidney disease undergoi surgical creation of a radiocephalic AVF (n=67) or brachiocephalic AVF (n=84), which is performed by suturing the brachial artery to the cephalic vein at the elbow. Of these 15 patients, 51 patients received placebo, 51 patients received a dose of 10 micrograms of PRT-201, and 49 patients received a dose of 30 micrograms of PRT-201. The primary efficac endpoint was AVF primary unassisted patency, defined as the time from surgical creation of the AVF to occurrence of a thrombosis or an intervention, such as angioplasty to restore maintain patency, or function. Other efficacy endpoints included unassisted maturation, which is defined as increased vessel diameter and blood flow at the AVF without the need for a intervention such as angioplasty, average rate of procedures to restore or maintain AVF patency, secondary patency, which is defined as abandonment of the AVF and the need fo creation of a new vascular access, use for hemodialysis and hemodynamically significant stenosis, or narrowing of blood vessels.

Primary Endpoint

Both doses of PRT-201 showed a trend toward efficacy, although neither dose met the primary endpoint with statistical significance. Median patency, the time at which 50% patients in a group lost primary unassisted patency, was 224 days in the placebo group and greater than 365 days in each of the PRT-201 treatment groups indicating that PRT-20 prolonged primary unassisted patency. The following Kaplan-Meier curves display primary unassisted patency.

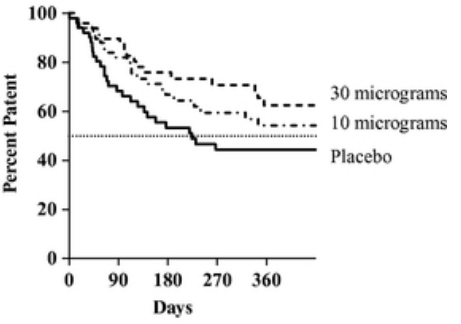
Primary Unassisted Patency—All AVFs



Note: Prespecified analysis.

An analysis of the primary endpoint data revealed an uneven distribution in primary unassisted patency loss events due to central stenosis, which occur remote from the site of a AVF. Central stenoses commonly exist prior to AVF placement and are unmasked following placement of brachiocephalic AVFs, which have higher blood flow than radiocephal AVFs. These stenoses are unrelated to treatment with PRT-201. To correct for this uneven distribution, we conducted a non-prespecified analysis of the primary endpoint that exclude patency loss events due to central stenoses. The following Kaplan-Meier curves display primary unassisted patency for all AVFs (excluding central stenoses), suggesting a reduction the risk of primary unassisted patency loss for the 30 microgram dose versus placebo that was significant from a statistical point of view.

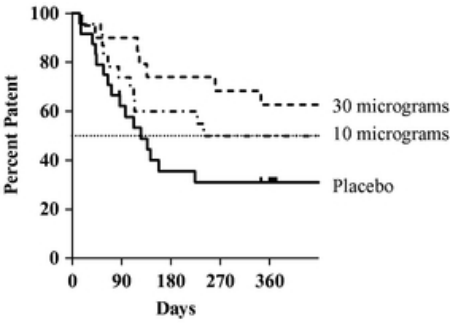
Primary Unassisted Patency—All AVFs
(Excluding Central Stenoses)



Note: Not prespecified analysis.

The benefit of PRT-201 on primary unassisted patency was most pronounced in the subset of patients undergoing placement of a radiocephalic AVF. Recent publications indica that radiocephalic AVFs suffer from higher rates of patency loss and maturation failure, with up to 70% of AVFs in the wrist being subject to patency loss within 12 months after the surgical placement. The subset analysis of this endpoint was not prespecified. The following Kaplan-Meier curves display the reduction in risk of primary unassisted patency loss in th subset of patients with radiocephalic AVFs. Median patency was 125 days in the placebo group and 377 days in the 30 microgram group (in some cases the 12 month follow up occure after day 365 due to patient schedules), indicating an improvement in primary unassisted patency that was significant from a statistical point of view.

Primary Unassisted Patency—Radiocephalic AVFs



Note: Not prespecified analysis.

Secondary Endpoints

In one of our prespecified secondary endpoints, unassisted maturation, which is defined as adequate vessel diameter and blood flow without the need for an intervention such a angioplasty, PRT-201 showed a significant benefit from a statistical point of view at three months in the 30 microgram dose using the two commonly accepted measures of maturatio namely, the Robbin criteria and the Kidney Disease Outcomes Quality Initiative, or KDOQI, criteria.

The effect of PRT-201 on maturation was more pronounced in the subset of patients who underwent creation of a radiocephalic AVF. For the 30 microgram dose of PRT-20 unassisted maturation of the radiocephalic AVFs, a prespecified analysis, showed an increase in the percentage of patients with mature AVFs compared with placebo using the Robb criteria (93% versus 47%) which is significant from a statistical point of view and a trend toward improvement using the KDOQI criteria (57% versus 24%).

Safety and Tolerability

In the trial, patients treated with PRT-201 reported adverse events comparable to placebo. These events were consistent with the medical events experienced by chronic kidne disease patients undergoing AVF placement surgery. The most common adverse events were AVF incision pain, venous stenosis, AVF thrombosis, steal syndrome and hypoesthesi Serious adverse events, or SAEs, reported by the investigator as possibly drug-related occurred in two 10 microgram PRT-201 patients, both AVF thrombosis, and two 30 microgra patients (one chest pain and one swelling at the surgical incision). There were no SAEs reported by the investigator as possibly drug-related in the placebo group. There was one SA reported by the investigator to be drug-related in the 10 microgram PRT-201 group, AVF maturation failure, and there were none in the other treatment groups.

Phase 3 Trial Design

In April 2013, we held an end of Phase 2 meeting with the FDA during which we confirmed elements of our Phase 3 development plan, including the primary endpoint. We plan perform two Phase 3 trials of PRT-201 using a 30 microgram dose, enrolling patients undergoing surgical placement of a radiocephalic AVF. In our Phase 2 trial, PRT-201 showed th greatest benefit in radiocephalic AVFs.

The Phase 3 trials will use the same primary endpoint, primary unassisted patency over 12 months, used in our Phase 2 trial. In our end of Phase 2 meeting with the FDA, the FD agreed that primary unassisted patency could be used as the primary endpoint. Our secondary endpoint, secondary patency over 12 months, and tertiary endpoints, unassiste maturation, use for hemodialysis and average procedure rates, in our Phase 3 trials were all endpoints in our Phase 2 trial.

We began enrolling patients in our first 300 patient Phase 3 clinical trial in the third quarter of 2014, and anticipate that results will be available in 2017. This Phase 3 clinical tri will include two groups, one receiving PRT-201 (n=200) and the other receiving placebo (n=100). We expect to initiate the second, substantially similar, Phase 3 clinical trial in the fir half of 2015. If the results of the first Phase 3 trial are sufficiently compelling, we intend to meet with the FDA to discuss the possibility of submitting a Biologics License Applicatio or BLA, supported by the single Phase 3 trial and may decide to submit a BLA to the FDA prior to completing the second Phase 3 trial.

Additional PRT-201 Indications

We believe that PRT-201 has potential benefits for hemodialysis patients undergoing other types of vascular access procedures. In 2013, we completed a successful Phase 1/2 tri in patients undergoing surgical placement of an arteriovenous graft, or AVG, which is a synthetic tube a surgeon uses to connect a vein and an artery. We may develop PRT-201 f additional hemodialysis indications including AVGs or brachiocephalic AVFs.

We believe PRT-201 also has the potential to treat a number of renal and vascular diseases for which therapeutic options are limited. We are currently enrolling patients wi symptomatic peripheral artery disease, or PAD, in a Phase 1 dose-escalation trial in which patients are treated with PRT-201 via a drug delivery catheter following balloon angioplasty.

Commercial Opportunity

We estimate approximately 130,000 AVFs are created in the United States annually, of which 40% are radiocephalic. We believe that the number of radiocephalic AVFs create annually may rise significantly if PRT-201 gains FDA approval, as this would allow surgeons to place radiocephalic AVFs in patients that they previously considered at an unacceptab high risk of AVF failure.

If approved, PRT-201 will be administered primarily by vascular surgeons, who we believe are acutely aware of the clinical need and are receptive to new therapies. We believ PRT-201 will be reimbursed appropriately as costs related to AVF surgical placement, which is typically performed in the hospital outpatient setting, are not included in the ESR bundle, the single bundled payment from Medicare for a number of the costs of hemodialysis treatments, medications, labs and supplies for patients with end stage renal disease. W believe that PRT-201 adoption will be supported by key stakeholders, including referring nephrologists, patient advocacy groups, large dialysis organizations and payors. We plan t target our marketing and sales efforts to vascular surgeons who create AVFs. There are approximately 2,800 vascular surgeons in the United States. We believe a specialty hospital sal force of approximately 75-100 representatives will enable us to call on the approximately 1,300 hospitals that account for more than 90% of the AVF surgical placements performed the United States annually.

Our Strengths

We believe our company and PRT-201 possess the following attributes that increase the likelihood that we will be successful in developing and commercializing PRT-201:

- *Entering Phase 3 trials for radiocephalic AVF placement.* We plan to conduct our Phase 3 clinical trials in radiocephalic AVFs using a 30 microgram dose of PRT-20 the population and dose in which, in a non-prespecified analysis, we observed an improvement in primary unassisted patency with PRT-201 in our Phase 2 trial.
- *Phase 3 endpoints same as our Phase 2 trial.* The primary endpoint in our Phase 3 trial, primary unassisted patency, will be the same as that used in our Phase 2 trial. I April 2013, we held an end of Phase 2 meeting with the FDA during which we confirmed elements of our Phase 3 development plan including the primary endpoint.

- *Safety profile supports approval.* Based on results from our clinical trials and preclinical studies, we believe PRT-201, which is administered once and only acts locall has demonstrated a safety profile that will support approval if our planned Phase 3 clinical program is successful. At our end of Phase 2 meeting with the FDA, w confirmed that we do not need to conduct any additional preclinical studies to support a BLA filing.
- *Unmet medical need.* A 2014 publication estimated the total cost of managing hemodialysis vascular access dysfunction in the United States to be approximatel $2.9 billion annually. We are not aware of any approved preventative treatments to reduce the AVF failure rate. PRT-201 has received fast track designation from th FDA, which is designed to facilitate the development and expedite the review of drugs to treat serious conditions and fill an unmet medical need.
- *Substantial and readily-addressable market opportunity.* We estimate a sales force of approximately 75-100 representatives will enable us to call on the approximate 1,300 hospitals that account for more than 90% of the AVF surgical placements performed in the United States annually. We believe PRT-201 will be reimburse adequately as costs related to AVF surgical placement, which is typically performed in the hospital outpatient setting, are not included in the ESRD bundle.
- *Experienced team.* Both our Chief Executive Officer and Chief Medical Officer were senior executives at GelTex, a biopharmaceutical company, where they playe leading roles in the development and commercialization of Renagel, a treatment for hemodialysis patients that led to Genzyme's acquisition of GelTex for more tha $1 billion.

Our Strategy

Our strategy is to develop and commercialize PRT-201 for patients suffering from renal and vascular diseases, beginning with patients undergoing surgical creation of radiocephalic AVF. Key elements of our strategy include our plans to:

- complete clinical development of PRT-201 and seek regulatory approval in its lead indication in the United States;
- commercialize PRT-201 directly in the United States;
- undertake clinical development of PRT-201 in Europe and establish partnerships for commercialization of PRT-201 in all or parts of Europe;
- pursue additional indications for PRT-201;
- establish partnerships for development and commercialization of PRT-201 in Japan and other Asian countries; and
- in-license or acquire additional product opportunities.

Risks Associated with Our Business

Our business is subject to numerous risks and uncertainties, including those highlighted in the section entitled "Risk Factors" immediately following this prospectus summar These risks include, among others, the following:

- we have a limited operating history and have incurred significant losses since our inception and we anticipate that we will continue to incur losses for the foreseeab future;
- we will require substantial additional financing to achieve our goals, and failure to obtain this necessary capital when needed on acceptable terms, or at all, could force u to delay, limit, reduce or terminate our product development, any commercialization efforts or other operations;
- we are substantially dependent on the success of our current product candidate, PRT-201, and cannot guarantee that this product candidate will successfully comple Phase 3 clinical trials, receive regulatory approval or be successfully commercialized;
- in our Phase 2 AVF trial neither dose of PRT-201 met the primary endpoint with statistical significance;
- PRT-201 may not have favorable results in later clinical trials or receive regulatory approval;

- the denial or delay of regulatory approval of PRT-201 or any additional product candidates would prevent or delay commercialization and have a material adverse effe on our potential to generate revenue, our business and our results of operations;
- if we are unable to establish effective marketing and sales capabilities or enter into agreements with third parties to market and sell our product candidates, if they ar approved, we may be unable to generate product revenues;
- even if PRT-201 or any additional product candidates receive regulatory approval, they may fail to achieve the broad degree of physician adoption necessary fo commercial success;
- PRT-201 or any additional product candidates, if approved, may face significant competition and our failure to effectively compete may prevent us from achievin significant market penetration and expansion;
- we and our contract manufacturers are subject to significant regulation with respect to manufacturing our product candidates. The manufacturing facilities on which w rely may not continue to meet regulatory requirements and have limited capacity; and
- if our efforts to protect our intellectual property related to PRT-201 or any additional product candidates are not adequate, we may not be able to compete effectively our market.

Corporate Information

Proteon was incorporated under the laws of the State of Delaware in March 2006, and at that time, acquired Proteon Therapeutics, LLC, our predecessor, which was formed in Jun 2001. Our executive offices are located at 200 West Street, Waltham, Massachusetts 02451, and our telephone number is (781) 890-0102. Our website address www.ProteonTherapeutics.com. The information contained on, or accessible through, our website does not constitute part of this prospectus. We have included our website address this prospectus solely as an inactive textual reference.

Implications of Being an Emerging Growth Company

We are an "emerging growth company" as defined in the Jumpstart Our Business Startups Act of 2012. We will remain an emerging growth company until the earlier of (1) the la day of the fiscal year (a) following the fifth anniversary of the completion of this offering, (b) in which we have total annual gross revenue of at least $1.0 billion, or (c) in which we ar deemed to be a large accelerated filer, which means the market value of our common stock that is held by non-affiliates exceeds $700 million as of the prior June 30th, and (2) the da on which we have issued more than $1.0 billion in non-convertible debt securities during the prior three-year period. We refer to the Jumpstart Our Business Startups Act of 2012 in th prospectus as the "JOBS Act," and references in this prospectus to "emerging growth company" shall have the meaning ascribed to it in the JOBS Act.

As an emerging growth company, we may take advantage of specified reduced disclosure and other requirements that are otherwise applicable, in general, to public companies th are not emerging growth companies. These provisions include:

- reduced disclosure about our executive compensation arrangements;
- exemption from the non-binding shareholder advisory votes on executive compensation or golden parachute arrangements;
- exemption from the auditor attestation requirement in the assessment of our internal control over financial reporting; and
- reduced disclosure of financial information in this prospectus, such as being permitted to include only two years of audited financial information and two years o selected financial information in addition to any required unaudited interim financial statements, with correspondingly reduced "Management's Discussion and Analys of Financial Condition and Results of Operations" disclosure.

We may choose to take advantage of some, but not all, of the available exemptions. We have taken advantage of some reduced reporting burdens in this prospectus. Accordingl the information contained herein may be different than the information you receive from other public companies in which you hold stock. The JOBS Act permits an emerging growt company to take advantage of an extended transition period to comply with new or revised accounting standards applicable to public companies. We have irrevocably elected not t avail ourselves of this extended transition period and, as a result, we will adopt new or revised accounting standards on the relevant dates on which adoption of such standards required for non-emerging growth companies.

THE OFFERING

Common stock we are offering	shares
Common stock outstanding after giving effect to this offering	shares
Option to purchase additional shares	The underwriters have a 30-day option to purchase a total of additional shares of common stock.
Use of proceeds	We estimate that our net proceeds from this offering will be approximately $ million at an assumed initial public offering price of $ per share, which is the midpoint of the price range set forth on the cover page of this prospectus, after deducting estimated underwriting discounts and commissions and estimated offerin expenses payable by us. We expect to use the net proceeds of this offering to accelerate the commencement of our second Phase 3 clinical trial of PRT-201, to accelerate our chemistry and manufacturing controls activities, to fund additional research and development activities and for other general corporate purposes. See "Use of Proceeds."
Risk factors	See "Risk Factors" beginning on page 12 and the other information included in this prospectus for a discussion of factors you should carefully consider before decidin to invest in our common stock.
Proposed NASDAQ Global Market Symbol	"PRTO"

In this prospectus, unless otherwise indicated, the number of shares of common stock outstanding and the other information based thereon is based on share of common stock outstanding as of June 30, 2014 and does not reflect:

- 17,982,120 shares of common stock issuable upon exercise of stock options outstanding as of June 30, 2014 at a weighted-average exercise price of $0.22 per share;
- 10,471,282 shares of our common stock issuable upon exercise of warrants with a weighted-average exercise price of $0.29 per share that we expect to be exercised pri to the closing of this offering;
- 18,361 shares of common stock reserved for issuance pursuant to future equity awards under our 2006 Equity Incentive Plan; and
- shares of common stock reserved for future issuance under our 2014 Equity Incentive Plan, which will become effective immediately prior to the closing of this offerin (including shares of common stock reserved for issuance under our 2006 Equity Incentive Plan, which will be added to the shares reserved under the 2014 Equi Incentive Plan upon its effectiveness).

Unless otherwise indicated, all information in this prospectus reflects or assumes the following:

- the amendment and restatement of our certificate of incorporation and bylaws, which will occur immediately prior to the closing of this offering;
- the conversion of all of our outstanding shares of our preferred stock into 134,918,694 shares of common stock, including the conversion of our Series D convertib preferred stock on an assumed one-for-one basis which will occur automatically upon the closing of this offering. See

"Capitalization—Series D Convertible Preferred Stock" for applicable conversion price adjustments;

- a one-for- reverse stock split of our common stock to be effected on , 2014 prior to completion of this offering;
- no exercise of stock options on or after June 30, 2014; and
- no exercise by the underwriters of their option to purchase up to a total of additional shares of common stock in this offering.

SUMMARY FINANCIAL DATA

The following summary financial data for the years ended December 31, 2012 and 2013 have been derived from our audited financial statements included elsewhere in th prospectus. The selected statement of operations data for the six months ended June 30, 2013 and 2014 and the selected balance sheet data as of June 30, 2014 were derived from ou unaudited financial statements appearing elsewhere in this prospectus. These unaudited financial statements have been prepared on a basis consistent with our financial statements and in our opinion, contain all adjustments, consisting only of normal and recurring adjustments, necessary for a fair presentation of such financial data. You should read this data togethe with our audited financial statements and related notes included elsewhere in this prospectus and the information under the captions "Selected Financial Data" and "Management Discussion and Analysis of Financial Condition and Results of Operations." Our historical results are not necessarily indicative of our future results, and our operating results for th six-month period ended June 30, 2014 are not necessarily indicative of the results that may be expected for the fiscal year ending December 31, 2014 or any other interim periods or an future year or period.

	Proteon Therapeutics, Inc.			
	Years Ended December 31,		Six Months Ended June 30,	
	2012	2013	2013	2014
			(Unaudited)	
	(in thousands except share and per share data)			
Operating expenses:				
Research and development	$ 5,907	$ 3,994	$ 2,003	$ 2,785
General and administrative	2,089	3,128	1,417	1,656
Acquired in-process research and development	—	—	—	—
Total operating expenses	7,996	7,122	3,420	4,441
Loss from operations	(7,996)	(7,122)	(3,420)	(4,441)
Other income (expense):				
Investment income	20	4	3	3
Interest expense	—	(861)	—	(857)
Other income (expense)	6	67	5	(99)
Total other income (expense)	26	(790)	8	(953)
Net loss	$ (7,970)	$ (7,912)	$ (3,412)	$ (5,394)
Unrealized loss on available-for-sale investments	(5)	(1)	—	(23)
Comprehensive loss	$ (7,975)	$ (7,913)	$ (3,412)	$ (5,417)
Reconciliation of net loss to net loss attributable to common stockholders				
Net loss	$ (7,970)	$ (7,912)	$ (3,412)	$ (5,394)
Accretion of redeemable convertible preferred stock to redemption value	(6,133)	(6,119)	(3,039)	(3,409)
Extinguishment of Series B redeemable convertible preferred stock	—	—	—	—
Net loss attributable to common stockholders	$ (14,103)	$ (14,031)	$ (6,451)	$ (8,803)
Net loss per share attributable to common stockholders—basic and diluted	$ (3.85)	$ (3.76)	$ (1.76)	$ (2.31)
Weighted-average number of common shares used in net loss per share attributable to common stockholders—basic and diluted	3,659,790	3,732,436	3,659,790	3,812,904
Pro forma net loss per share attributable to common stockholders—basic and diluted (unaudited)		$ (0.10)		$ (0.04)
Pro forma weighted-average number of common shares used in net loss per share attributable to common stockholders—basic and diluted (unaudited)		72,457,068		107,333,127

	As of June 30, 2014		
	Actual	Pro Forma(2)	Pro Forma As Adjusted(3)(4)(5)
		(unaudited) (in thousands)	
Balance Sheet Data:			
Cash and cash equivalents	$ 8,646	$ 8,646	$
Working capital	19,915	19,915	
Total assets	27,142	27,142	
Preferred stock	123,904	—	
Common stock and additional paid in capital	4	123,908	
Total stockholders' deficit	(109,290)	21,194	

(1) See Note 2 within the notes to our financial statements appearing elsewhere in this prospectus for a description of the method used to calculate basic and diluted net loss per common share and pro forr basic and diluted net loss per common share.

(2) Pro forma to reflect the conversion of all outstanding shares of our preferred stock into shares of common stock upon the closing of this offering.

(3) Pro forma as adjusted to reflect the pro forma adjustments described in (2) above, and to further reflect (i) the filing and effectiveness of our amended and restated certificate of incorporation, which w occur immediately prior to the closing of this offering and (ii) the sale of shares of our common stock offered in this offering, assuming an initial public offering price of $ per share, the midpoint the price range set forth on the cover page of this prospectus, after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

(4) A $1.00 increase (decrease) in the assumed initial public offering price of $ per share, the midpoint of the price range set forth on the cover of this prospectus, would increase (decrease) the pro forn as adjusted amount of each of cash and cash equivalents, working capital, total assets, common stock and additional paid-in-capital and total stockholders' (deficit) equity by approximately $ millio assuming that the number of shares offered by us, as set forth on the cover of this prospectus, remains the same and after deducting underwriting discounts and commissions and estimated offering expens payable by us.

(5) A 1,000,000 share increase in the number of shares offered by us together with a concomitant $1.00 increase in the assumed initial public offering price of $ per share, the midpoint of the price ran set forth on the cover of this prospectus, would increase the pro forma as adjusted amount of each of cash and cash equivalents, and total stockholders' (deficit) equity by approximately $ millio after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

RISK FACTORS

Investing in our common stock involves a high degree of risk. You should carefully consider the risks and uncertainties described below, together with all of the other information in this prospectus, including our financial statements and related notes, before deciding whether to purchase shares of our common stock. If any of the following risks are realized, our business, operating results and prospects could be materially and adversely affected. In that event, the price of our common stock could decline, and you could lose part or all of your investment. The risks and uncertainties described below are not the only ones we face. Additional risks and uncertainties not presently known to us or that we currently believe to be immaterial may also adversely affect our business.

Risks Related to Our Financial Condition and Need for Additional Capital

We have a limited operating history and have incurred significant losses since our inception and we anticipate that we will continue to incur losses for the foreseeable future.

We are a clinical-stage biotechnology company, and we have not commercialized any products or generated any revenues from the sale of products. We have incurred losses from operations in each year since our inception, and our net losses were $8.0 million and $7.9 million for the years ended December 31, 2012 and 2013, respectively, and $3.4 million and $5.4 million for the six months ended June 30, 2013 and 2014, respectively. As of June 30, 2014, we had an accumulated deficit of $109.3 million. We do not expect to generate any product revenues in the foreseeable future. We do not know whether or when we will generate revenue or become profitable.

We have devoted most of our financial resources to research and development, including our clinical and preclinical development activities. To date, we have financed our operations primarily through the sale of equity securities and convertible debt. Our current product candidate, PRT-201, is in clinical trials and we have no commercial sales, which, together with our limited operating history, make it difficult to assess our future viability. The amount of our future net losses will depend, in part, on the rate of our future expenditures and our ability to obtain funding through equity or debt financings or strategic collaborations. We have not completed pivotal clinical trials for any product candidate and it will be several years, if ever, before we have PRT-201 or any future product candidates ready for commercialization. Even if we obtain regulatory approval to market PRT-201 or any additional product candidates, our future revenues will depend upon the size of any markets in which PRT-201 or any additional product candidates have received approval, our ability to achieve sufficient market acceptance, reimbursement from third-party payors and other factors.

We expect to continue to incur significant expenses and increasing operating losses for the foreseeable future. We anticipate that our expenses will increase substantially if and as we:

- continue our clinical development and seek regulatory approval of PRT-201, particularly with respect to its lead indication of radiocephalic AVFs;
- commercialize PRT-201 directly in the United States;
- undertake clinical development of PRT-201 in Europe and establish partnerships for commercialization of PRT-201 in all or parts of Europe;
- pursue additional indications for PRT-201 including clinical development of PRT-201 for brachiocephalic AVFs, patients requiring placement of an AVG and peripheral artery disease, or PAD;
- in-license or acquire additional product opportunities and make milestone or other payments under any in-license agreements;
- establish a sales, marketing and distribution infrastructure to commercialize any products for which we may obtain marketing approval;
- maintain, protect and expand our intellectual property portfolio;
- attract and retain skilled personnel;

- create additional infrastructure to support our operations as a public company and our product development and planned future; and
- experience any delays or encounter issues with any of the above.

The net losses we incur may fluctuate significantly from quarter to quarter and year to year, such that a period-to-period comparison of our results of operations may not be a good indication of our future performance. In any particular quarter or quarters, our operating results could be below the expectations of securities analysts or investors, which could cause our stock price to decline.

We will require substantial additional financing to achieve our goals, and a failure to obtain this necessary capital when needed on acceptable terms, or at all, could force us to delay, limit, reduce or terminate our product development, any commercialization efforts or other operations.

Our operations have consumed substantial amounts of cash since inception. As of June 30, 2014, our cash, cash equivalents and investments were $25.4 million. Our research and development expenses were $5.9 million and $4.0 million for the fiscal years ended December 31, 2012 and December 31, 2013, respectively, and $2.0 million and $2.8 million for the six-months ended June 30, 2013 and June 30, 2014, respectively. We believe that we will continue to expend substantial resources for the foreseeable future developing PRT-201 and any additional product candidates. These expenditures will include costs associated with research and development, potentially acquiring new technologies, potentially obtaining regulatory approvals and manufacturing products, as well as marketing and selling products approved for sale, if any. In addition, other unanticipated costs may arise. Because the outcome of our planned and anticipated clinical trials is highly uncertain, we cannot reasonably estimate the actual amounts necessary to successfully complete the development and commercialization of PRT-201 or any additional product candidates.

We began enrolling patients in our first Phase 3 clinical trial of PRT-201 during the third quarter of 2014 for patients undergoing placement of radiocephalic AVFs. Prior to completing enrollment in our first Phase 3 trial, we expect to initiate the second Phase 3 trial. Based on our current operating plan, and absent any future financings or strategic partnerships, we believe that the net proceeds we receive from this offering, and our existing cash and cash equivalents and investments will be sufficient to fund our projected operating expenses and capital expenditure requirements through , allowing us to obtain results from our first Phase 3 clinical trial of PRT-201 in radiocephalic AVFs. This period could be shortened if there are any significant increases beyond our expectations in spending on development programs or more rapid progress of development programs than anticipated. We do not expect our existing capital resources, including the net proceeds from this offering, to be sufficient to enable us to complete our second Phase 3 trial. Moreover, we do not expect to be able to initiate any other trials, including those for other indications of PRT-201, prior to receiving and reviewing data from our first Phase 3 clinical trial. Furthermore, our operating plan may change as a result of many factors currently unknown to us, and we may need to seek additional funds sooner than planned, through public or private equity or debt financings, government or other third-party funding, marketing and distribution arrangements and other collaborations, strategic alliances and licensing arrangements, or a combination of these approaches. Even if we believe we have sufficient funds for our current or future operating plans, we may seek additional capital if market conditions are favorable or if we have specific strategic considerations.

Any additional fundraising efforts may divert our management from their day-to-day activities, which may adversely affect our ability to develop and commercialize PRT-201 or any additional product candidates. In addition, we cannot guarantee that future financing will be available in sufficient amounts or on terms acceptable to us, or at all. We could also be required to seek funds through arrangements with collaborative partners or otherwise at an earlier stage than would otherwise be ideal and we may be required to relinquish rights to PRT-201 or any additional product candidates, or otherwise agree to terms unfavorable to us, any of which may have a material adverse effect on our business, operating results and prospects.

If we are unable to obtain funding on a timely basis, we may be required to significantly curtail, delay or discontinue one or more of our research or development programs or the commercialization of any approved products or be unable to expand our operations or otherwise capitalize on our business opportunities, as desired, which could materially adversely affect our business, financial condition and results of operations.

We have never generated any revenue from product sales and may never be profitable.

As a company, we have never obtained regulatory approval for, or commercialized, any product candidate. Our ability to generate substantial revenue and achieve profitability depends on our ability, alone or with strategic collaboration partners, to successfully complete the development of, and obtain the regulatory approvals necessary to commercialize PRT-201 or any additional product candidates. We do not anticipate generating revenues from product sales for at least the next several years, if ever. If PRT-201 or any additional product candidates fail in clinical trials or do not gain regulatory approval, or if PRT-201 or any additional product candidates, if approved, fail to achieve market acceptance, we may never become profitable. Even if we achieve profitability in the future, we may not be able to sustain profitability in subsequent periods. Our ability to generate future revenues from product sales depends heavily on our success in:

- completing clinical development of PRT-201 for one or more indications and research and preclinical and clinical development of any additional product candidates;
- seeking and obtaining regulatory and marketing approvals for PRT-201 if and when we complete clinical trials;
- establishing and maintaining supply and manufacturing relationships with third parties that can provide adequate (in amount and quality) products and services to support clinical development and the market demand for PRT-201, if approved;
- launching and commercializing PRT-201 if we obtain regulatory and marketing approval, either by collaborating with a partner or, if launched independently, by establishing a sales, marketing and distribution infrastructure;
- obtaining and maintaining adequate coverage and reimbursement from third-party payors for PRT-201;
- obtaining market acceptance of PRT-201 as a viable treatment option;
- addressing any competing technological and market developments;
- implementing additional internal systems and infrastructure, as needed;
- identifying and validating new product candidates;
- negotiating favorable terms in any collaboration, licensing or other arrangements into which we may enter;
- maintaining, protecting and expanding our portfolio of intellectual property rights, including patents and know-how;
- developing PRT-201 such that, if approved, it can be commercialized without infringing the intellectual property rights of third parties; and
- attracting, hiring and retaining qualified personnel.

Even if PRT-201 or any additional product candidates that we may develop is approved for commercial sale, we anticipate incurring significant costs associated with commercializing any approved product candidate. Our expenses could increase beyond expectations if we are required by the FDA, the European Medicines Agency, or EMA, or other regulatory agencies, domestic or foreign, to perform clinical trials and other studies in addition to those that we currently anticipate. Even if we are able to generate revenues from the sale of any approved products, we may not become profitable and may need to obtain additional funding to continue operations. Our failure to become and remain profitable would depress the market price of our common stock and could impair our ability to raise capital, expand our

business, diversify our product offerings or continue our operations. A decline in the value of our company could also cause you to lose all or part of your investment.

Risks Related to Clinical Development, Regulatory Review and Approval of Our Product

We are substantially dependent on the success of our current product candidate, PRT-201, and cannot guarantee that this product candidate will successfully complete Phase 3 clinical trials, receive regulatory approval or be successfully commercialized.

We currently have no products approved for commercial distribution. We have invested substantially all of our efforts and financial resources in the development of our current product candidate, PRT-201. Our business depends entirely on the successful development and commercialization of PRT-201, in vascular access or additional indications, which may never occur. Our ability to generate revenues in the near term is substantially dependent on our ability to develop, obtain regulatory approval for, and then successfully commercialize PRT-201. We currently generate no revenues from sales of any products, and we may never be able to develop or commercialize a marketable product.

PRT-201 will require additional clinical development, regulatory approval, commercial manufacturing arrangements, establishment of a commercial organization, significant marketing efforts and further investment before we generate any revenues from product sales. We are not permitted to market or promote PRT-201 for any indication before we receive regulatory approval from the FDA or comparable foreign regulatory authorities, and we may never receive such regulatory approval for any of our product candidates. If we do not receive FDA approval for, and successfully commercialize, PRT-201, we will not be able to generate revenue from PRT-201 in the United States in the foreseeable future, or at all. Any significant delays in obtaining approval for and commercializing PRT-201 will have a substantial adverse impact on our business and financial condition.

We have not previously submitted a BLA to the FDA, or similar drug approval filings to comparable foreign authorities, for any product candidate, and we cannot be certain that PRT-201 or any additional product candidates will be successful in clinical trials or receive regulatory approval. In our Phase 2 clinical trial, our primary efficacy endpoint of primary unassisted patency did not show statistically significant benefit for the 30 microgram dose versus placebo with regard to primary unassisted patency. While statistical analyses of the subset of patients with radiocephalic AVFs suggested a clinically significant benefit over placebo for that patient subset, those analyses were not prespecified, and we cannot assure you that these results will be repeated in our Phase 3 trials. Following completion of the trial we analyzed the data in a number of ways in addition to the analysis specified in the protocol for the Phase 2 clinical trial of PRT-201. For example, we analyzed the data from the subset of patients undergoing placement of a radiocephalic AVF. Analysis of data in a manner or from subsets that were not prespecified in the protocol is typically not sufficient to serve as the basis for regulatory approval and is generally not considered as reliable as analyses which were prespecified in the protocol. Even though our Phase 3 trials will enroll patients undergoing a surgical procedure to create a radiocephalic AVF (i.e., that subset of patients in which PRT-201 showed a greater benefit in our Phase 2 clinical trial), there are risks of failure inherent at any stage of product development, and we may not demonstrate efficacy with regard to the primary endpoint of our planned Phase 3 clinical trials, or unexpected adverse events may appear. Further, PRT-201 or any additional product candidates, may not receive regulatory approval even if they are successful in clinical trials. If approved for marketing by applicable regulatory authorities, our ability to generate revenues from PRT-201 will depend on our ability to:

- create market demand for PRT-201 through our own marketing and sales organization, and any other arrangements to promote this product candidate we may otherwise establish;
- hire, train and deploy a specialty hospital sales force, focused primarily on vascular surgeons, to commercialize PRT-201 in the United States;

- manufacture PRT-201 in sufficient quantities and at acceptable quality and manufacturing cost to meet commercial demand at launch and thereafter and establish and maintain agreements with wholesalers, distributors and group purchasing organizations on commercially reasonable terms;
- create partnerships with third parties to promote and sell PRT-201 in any foreign markets where we receive marketing approval;
- maintain patent protection and regulatory exclusivity for PRT-201;
- launch commercial sales of PRT-201, whether alone or in collaboration with others;
- achieve appropriate reimbursement for PRT-201;
- effectively compete with other products; and
- maintain a continued acceptable safety profile of PRT-201 following launch.

As we continue to develop PRT-201 for other indications, including AVG, brachiocephalic AVF and PAD, or additional product candidates, we will face similar risks and challenges.

Clinical development is a lengthy and expensive process with an uncertain outcome due to many factors. Because the results of early clinical trials are not necessarily predictive of future results, PRT-201 may not have favorable results in later clinical trials or receive regulatory approval.

Clinical development is expensive, difficult to design and implement, takes many years to complete and its outcome is inherently uncertain. Failure can occur at any time during the clinical trial process and PRT-201 is subject to the risks of failure inherent in drug and biological development, including failure to demonstrate efficacy in a pivotal clinical trial or in the patient population we intend to enroll, the occurrence of severe or medically or commercially unacceptable adverse events, failure to comply with protocols or applicable regulatory requirements and determination by the FDA or any comparable foreign regulatory authority that a drug and biological product is not approvable. Trends and results observed in earlier stage clinical trials, particularly trends and results observed through analysis of the data which was not prespecified in the protocol, may not be replicated in later stage clinical trials. For example, as is common with Phase 2 trials, we explored a number of endpoints and analyzed the data from our Phase 2 clinical trial of PRT-201 in a number of ways, some of which were not prespecified. Product candidates such as PRT-201 in Phase 3 clinical trials may fail to demonstrate sufficient efficacy despite having progressed through initial clinical trials, even if certain non-prespecified analyses of primary or secondary endpoints in those early trials showed trends toward efficacy or, in some analyses, statistical significance. Companies frequently suffer significant setbacks in late-stage clinical trials due to lack of efficacy, manufacturing or formulation changes or adverse safety profiles, even after earlier clinical trials have shown promising results. During the course of our clinical development, we modified our PRT-201 finished product formulation for our Phase 3 trials and commercial launch in order to facilitate ease of administration and fill and finish of vials at our 30 microgram dose. Our formulation changes could adversely affect results in our clinical trials, requiring us to make further formulation changes. Additional changes could cause us to delay or repeat clinical trials, and we could incur unexpected costs that would have an adverse effect on our business, operating results and prospects.

The design of a clinical trial can determine whether its results will support approval of a product, and flaws in the design of a clinical trial may not become apparent until the clinical trial is well advanced or completed. Proteon has limited experience in designing clinical trials and may be unable to design and execute a clinical trial to support marketing approval. In addition, preclinical and clinical data are often susceptible to varying interpretations and analyses. Many companies that believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval for the product candidates. Even if we believe that the results of clinical trials for our product candidates warrant marketing approval, the FDA or comparable non-United States regulatory authorities may disagree and may not grant marketing approval of PRT-201 or any additional product candidates.

In some instances, there can be significant variability in safety or efficacy results between different clinical trials of the same product candidate due to numerous factors, including changes in trial procedures

set forth in protocols, differences in the size and type of the patient populations, changes in and adherence to the clinical trial protocols and the rate of dropout among clinical trial participants. Any Phase 3 or other clinical trial that we may conduct may not demonstrate the efficacy and safety necessary to obtain regulatory approval to market PRT-201 or any additional product candidate.

Any delay or failure in our clinical trials would delay our obtaining, or make us unable to obtain, applicable regulatory approvals, which would prevent us from commercializing PRT-201 or any additional product candidates, generating revenues and achieving and sustaining profitability.

If clinical trials of PRT-201 or any additional product candidates fail to demonstrate safety and efficacy to the satisfaction of the FDA and comparable non-United States regulators, we may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of PRT-201 or any additional product candidates.

We are not permitted to commercialize, market, promote or sell any product candidate in the United States without obtaining marketing approval from the FDA. Comparable non-United States regulatory authorities, such as the EMA, impose similar restrictions. We may never receive such approvals. We must have completed extensive preclinical development and clinical trials to demonstrate the safety and efficacy of the product candidate in humans before we will be able to obtain these approvals. Clinical testing is expensive, difficult to design and implement, can take many years to complete and is inherently uncertain as to outcome.

Any inability to successfully complete clinical development could result in additional costs to us and impair our ability to generate revenues from product sales, regulatory and commercialization milestones and royalties. In addition, if (1) we are required to conduct additional clinical trials or other testing of PRT-201 beyond the trials and testing that we contemplate, (2) we are unable to successfully complete clinical trials of PRT-201 or any additional product candidates or other testing, (3) the results of these trials or tests are unfavorable, uncertain or are only modestly favorable or (4) there are unacceptable safety concerns associated with PRT-201 or any additional product candidates, we, in addition to incurring additional costs, may:

- be delayed in obtaining marketing approval for PRT-201 or any additional product candidates;
- not obtain marketing approval at all;
- obtain approval for indications or patient populations that are not as broad as we intended or desired;
- obtain approval with labeling that includes significant use or distribution restrictions or significant safety warnings, including boxed warnings;
- be subject to additional post-marketing testing or other requirements; or
- be required to remove the product from the market after obtaining marketing approval.

In general, the FDA requires two adequate and well-controlled clinical trials to demonstrate the effectiveness of a product candidate. If the results of our first Phase 3 clinical trial are sufficiently compelling, we intend to meet with the FDA to discuss the possibility of submitting a BLA supported by the single Phase 3 trial and may decide to submit a BLA to the FDA prior to completing the second Phase 3 trial. If we attempt to rely on a single Phase 3 trial to demonstrate the effectiveness of PRT-201, the usual demonstration of the statistical significance in the primary efficacy endpoint (p=0.05) is unlikely to be sufficient to obtain approval of PRT-201, and we would likely be required to demonstrate more robust statistical significance. Even with a robust p-value, the FDA may not consider the results of the single Phase 3 trial to be sufficient for BLA filing or approval, and may require that we conduct additional trials.

We may be unable to obtain regulatory approval for PRT-201 or any additional product candidates under applicable regulatory requirements. The denial or delay of any approvals would prevent or delay commercialization and have a material adverse effect on our potential to generate revenue, our business and our results of operations.

PRT-201 and any additional product candidates are subject to extensive governmental regulations relating to, among other things, research, clinical trials, approval, manufacturing, recordkeeping, labeling, storage, advertising, promotion, distribution, import, export and commercialization. In order to obtain regulatory approval for the commercial sale of any product candidate, we must demonstrate through extensive preclinical studies and clinical trials that the product candidate is safe and effective for use in each target indication. Failure to obtain marketing approval for a product candidate will prevent us from commercializing the product candidate. PRT-201 is still in development and is subject to the risks of failure inherent in drug or biologic development. We have not received approval to market any product candidate from regulatory authorities in any jurisdiction. Proteon has only limited experience in conducting and managing the clinical trials, and in submitting and supporting the applications necessary to gain marketing approvals and expect to rely on third-party clinical research organizations to assist us in this process. Securing marketing approval also requires the submission of information about the product manufacturing process to, and inspection of manufacturing facilities by, the regulatory authorities. PRT-201 may not be effective, may be only moderately effective or may prove to have undesirable or unintended side effects, toxicities or other characteristics that may preclude our obtaining marketing approval or prevent or limit commercial use. We may gain regulatory approval for PRT-201 or any additional product candidates in some but not all of the territories available or some but not all of the target indications, resulting in limited commercial opportunity for the product, or we may never obtain regulatory approval for PRT-201 or any additional product candidates in any jurisdiction.

The process of obtaining marketing approvals, both in the United States and abroad, is expensive, may take many years if additional clinical trials are required, if approval is obtained at all, and can vary substantially based upon a variety of factors, including the type, complexity and novelty of the product candidates involved. Changes in marketing approval policies during the development period, changes in or the enactment of additional statutes or regulations, or changes in regulatory review for each submitted product application, may cause delays in the approval or rejection of an application. The FDA and foreign regulatory authorities also have substantial discretion in the drug and biologics approval process. The number and types of preclinical studies and clinical trials that will be required for regulatory approval varies depending on the product candidate, the disease or condition that the product candidate is designed to address, and the regulations applicable to any particular product candidate. Approval policies, regulations or the type and amount of clinical data necessary to gain approval may change during the course of a product candidate's clinical development and may vary among jurisdictions, and there may be varying interpretations of data obtained from preclinical studies or clinical trials, either of which may cause delays or limitations in the approval or the decision not to approve an application. Regulatory agencies can delay, limit or deny approval of a product candidate for many reasons, including:

- the FDA or comparable foreign regulatory authorities may disagree with the design or implementation of our clinical trials;
- we may be unable to demonstrate to the satisfaction of the FDA or comparable foreign regulatory authorities that a product candidate is safe and effective for its proposed indications;
- the results of later-stage clinical trials may not meet the level of statistical or clinical significance required by the FDA or comparable foreign regulatory authorities for approval;
- the results of later-stage clinical trials may not confirm the positive results from earlier preclinical studies or clinical trials;
- we may be unable to demonstrate that a product candidate's clinical and other benefits outweigh its safety risks;
- the FDA or comparable foreign regulatory authorities may disagree with our interpretation of data from preclinical studies or clinical trials;

- the data collected from clinical trials of PRT-201 or any additional product candidate may not be sufficient to the satisfaction of the FDA or comparable foreign regulatory authorities to support the submission of a BLA, or other comparable submission in foreign jurisdictions or to obtain regulatory approval in the United States or elsewhere;
- our manufacturing processes or facilities may not be adequate to support approval of our product candidates; or
- regulatory agencies may change their approval policies or adopt new regulations in a manner rendering our clinical data insufficient for approval.

It is possible that neither PRT-201 nor any product candidates we may seek to develop in the future will ever obtain the appropriate regulatory approvals necessary for us or any future collaborators to commence product sales. Any delay in obtaining, or failure to obtain, required approvals would materially adversely affect our ability to generate revenue from the particular product candidate, which likely would result in significant harm to our financial position and adversely impact our stock price.

We may face difficulty in enrolling patients for clinical trials.

We may find it difficult to enroll patients in our clinical trials, which could delay or prevent clinical trials of PRT-201 or any additional product candidates. We have never previously limited a trial to patients undergoing a surgical procedure to create a radiocephalic AVF, as we will do for our Phase 3 trials. Identifying and qualifying patients to participate in clinical trials of PRT-201 or any additional product candidates are critical to our success. The timing of our clinical trials depends on the speed at which we can recruit patients to participate in testing product candidates. The enrollment timeline for radiocephalic AVF patients is lengthy and there are limited numbers of sites from which we can enroll pre-hemodialysis or hemodialysis patients. If patients are unwilling to participate in our trials because of negative publicity from adverse events or for other reasons, including competitive clinical trials for similar patient populations, the timeline for recruiting patients, conducting trials and obtaining regulatory approval of potential products may be delayed or prevented. These delays could result in increased costs, delays in advancing our product development, delays in testing the effectiveness of our technology or termination of the clinical trials altogether. We may not be able to identify, recruit and enroll a sufficient number of patients, or those with required or desired characteristics to achieve diversity in a trial, to complete our clinical trials in a timely manner. Patient enrollment is affected by factors including:

- severity of the disease under investigation;
- design of the trial protocol;
- size of the patient population;
- eligibility criteria for the trial in question;
- perceived risks and benefits of the product candidate under study;
- proximity and availability of clinical trial sites for prospective patients;
- availability of competing therapies and clinical trials;
- efforts to facilitate timely enrollment in clinical trials;
- patient referral practices of physicians; and
- ability to monitor patients adequately during and after treatment.

We may not be able to initiate or continue clinical trials if we cannot enroll a sufficient number of eligible patients to participate in the clinical trials required by regulatory agencies. If we have difficulty enrolling a sufficient number of patients to conduct our clinical trials as planned, we may need to delay, limit or terminate ongoing or planned clinical trials, any of which would have an adverse effect on our business.

If we experience any of a number of possible unforeseen events in connection with clinical trials of PRT-201 or any additional product candidates, potential marketing approval or commercialization of PRT-201 or any additional product candidates could be delayed or prevented.

We may experience numerous unforeseen events during, or as a result of, clinical trials that could delay or prevent marketing approval of PRT-201 or any additional product candidates, including:

- trials of PRT-201 or any additional product candidates may produce unfavorable or inconclusive results;
- we may decide, or regulators may require us, to conduct additional clinical trials or abandon product development programs;
- our third party contractors, including those manufacturing PRT-201 or any additional product candidates or components for commercial use or ingredients thereof or conducting clinical trials on our behalf, may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner or at all;
- regulators or institutional review boards may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;
- we may have to suspend or terminate clinical trials of PRT-201 or any additional product candidates for various reasons, including a finding that the participants are being exposed to unacceptable health risks, undesirable side effects or other unexpected characteristics of a product candidate;
- regulators or institutional review boards may require that we or our investigators suspend or terminate clinical research for various reasons, including noncompliance with regulatory requirements or their respective standards of conduct, a finding that the participants are being exposed to unacceptable health risks, undesirable side effects or other unexpected characteristics of the product candidate or findings of undesirable effects caused by a chemically or mechanistically similar biologic or biologic candidate;
- we may experience delays in reaching or fail to reach agreement on acceptable clinical trial contracts or clinical trial protocols with prospective trial sites;
- patient enrollment in these clinical trials may be slower than we anticipate and is limited to a select number of sites, which could cause significant delays given the prolonged enrollment period;
- participants may drop out of these clinical trials at a higher rate than we anticipate and we may not be able to obtain the follow up data for the 12 month period planned in our Phase 3 trial;
- patients who enroll in a clinical trial may misrepresent their eligibility to do so or may otherwise not comply with the clinical trial protocol, resulting in the need to drop the patients from the clinical trial, increase the needed enrollment size for the clinical trial beyond the 300 proposed for each Phase 3 trial or may extend the clinical trial's duration;
- the FDA or comparable foreign regulatory authorities may disagree with our clinical trial design or our interpretation of data from preclinical studies and clinical trials;
- the FDA or comparable foreign regulatory authorities may fail to approve or subsequently find fault with the manufacturing processes or facilities of third party manufacturers with which we enter into agreements for clinical and commercial supplies;
- our finished product that has been manufactured for the PRT-201 Phase 3 trials many be inadequate, or the materials or manufactured product candidates necessary to conduct future clinical trials of PRT-201 or any additional product candidates may be insufficient, inadequate or not available at an acceptable cost, or we may experience interruptions in supply; and
- the approval policies or regulations of the FDA or comparable foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient to obtain marketing approval.

Product development costs for us will increase if we experience delays in testing or pursuing marketing approvals and we may be required to obtain additional funds to complete clinical trials and prepare for possible commercialization of PRT-201 or any additional product candidates. We do not know whether any

clinical trials will begin as planned, will need to be restructured or will be completed on schedule, or at all. Significant clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize PRT-201 or any additional product candidates or allow our competitors to bring products to market before we do and impair our ability to successfully commercialize PRT-201 or any additional product candidates and may harm our business and results of operations. In addition, many of the factors that cause, or lead to, clinical trial delays may ultimately lead to the denial of marketing approval of PRT-201 or any additional product candidates.

Any product for which we obtain FDA approval will be subject to extensive ongoing regulatory requirements, and Proteon may be subject to penalties if it fails to comply with regulatory requirements or if it experiences unanticipated problems with its products, when and if any of them are approved.

Any product for which we obtain marketing approval, along with the manufacturing processes, post-approval clinical research, labeling, advertising and promotional activities for such product, will be subject to continual requirements of and review by, the FDA and comparable regulatory authorities. These requirements include submissions of safety and other post-marketing information and reports, registration and listing requirements, current good manufacturing practices, or cGMP requirements relating to manufacturing, quality control, quality assurance and corresponding maintenance of records and documents, requirements regarding the distribution of samples to physicians and recordkeeping. We must also comply with requirements concerning advertising and promotion for PRT-201 or any additional product candidates for which we obtain marketing approval. Promotional communications with respect to prescription drugs, including biologics, are subject to a variety of legal and regulatory restrictions and must be consistent with the information in the product's approved labeling. Thus, we will not be able to promote any products we develop for indications or uses for which they are not approved.

Even if regulatory approval of a product is granted, the approval will be subject to limitations on the indicated uses for which the product may be marketed and may be subject to other conditions of approval. We and our contract manufacturers could be subject to periodic unannounced inspections by the FDA to monitor and ensure compliance with cGMPs. In addition, approval may contain requirements for costly post-marketing testing and surveillance to monitor the safety or efficacy of the product. Discovery after approval of previously unknown problems with any such products, manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may result in actions such as:

- restrictions on our ability to conduct clinical trials, including full or partial clinical holds on ongoing or planned trials;
- restrictions on such products' manufacturing processes;
- restrictions on the marketing of a product;
- restrictions on product distribution;
- requirements to conduct post-marketing clinical trials;
- untitled or Warning Letters;
- withdrawal of the products from the market;
- refusal to approve pending applications or supplements to approved applications that we submit;
- recall of products;
- fines, restitution or disgorgement of profits or revenue;
- suspension or withdrawal of regulatory approvals;
- refusal to permit the import or export of our products;
- product seizure;
- injunctions; or
- imposition of civil or criminal penalties.

Accordingly, assuming we receive marketing approval for PRT-201 or any additional product candidates, we and our contract manufacturers will continue to expend time, money and effort in all areas of regulatory compliance, including manufacturing, production, product surveillance, post-marketing studies and quality control.

PRT-201 may cause undesirable side effects or have other properties that could delay or prevent their regulatory approval, limit the commercial profile of approved labeling, or result in significant negative consequences following any potential marketing approval.

As with many pharmaceutical and biological products, treatment with PRT-201 or any additional product candidates may produce undesirable side effects or adverse reactions or events. These adverse events may occur despite our belief, based on our preclinical and clinical trials to date, that our PRT-201 has a safety profile that will support approval if we successfully complete of our planned Phase 3 clinical program. For instance, PRT-201 shows a high degree of structural similarity with other human serine proteases, and it is theoretically possible that if anti-PRT-201 antibodies developed that they could cross-react with one or more of those other proteases because of the structural similarity, and prompt an adverse reaction. However, we have not seen any evidence of such cross-reactivity in our preclinical or clinical trials to date.

Based on our Phase 2 trial, adverse side effects that could occur with treatment with PRT-201 include AVF surgical incision pain, venous stenosis, AVF thrombosis, steal syndrome and hypoesthesia. If any of these adverse events occur in rates or severity exceeding placebo and unacceptable to regulatory authorities, if anti-PRT-201 antibodies develop and are associated with cross-reactivity to other proteases, or unknown serious events emerge, our clinical trials could be suspended or terminated and the FDA, the EMA or other foreign regulatory authorities could order us to cease further development of, or deny approval of, PRT-201 or any additional product candidates for any or all targeted indications, or they could require limitations or onerous warnings on the product label. The product-related side effects could affect patient recruitment or the ability of enrolled patients to complete the trial. If we elect or are required to delay, suspend or terminate any clinical trial of PRT-201 or any additional product candidates, the commercial prospects of such product candidates will be harmed and our ability to generate product revenues from any of these product candidates will be delayed or eliminated. Any of these occurrences may harm our business, financial condition and prospects significantly.

We may not be able to maintain orphan drug designation or obtain or maintain orphan drug exclusivity for PRT-201

We have obtained orphan drug designation from the FDA for PRT-201. In the United States, under the Orphan Drug Act, the FDA may designate a product as an orphan drug if it is intended to treat a rare disease or condition, which is generally defined as a patient population of fewer than 200,000 individuals in the United States.

Orphan drug exclusivity may be lost if the FDA determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the product to meet the needs of patients with the rare disease or condition.

Even if we obtain orphan drug exclusivity for PRT-201, that exclusivity may not effectively protect the product from competition because different products can be approved for the same condition. Even after an orphan product is approved, the FDA can subsequently approve the same product for the same condition if the FDA concludes that the later product is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care.

We may expend our limited resources to pursue a particular product candidate or indication and fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success.

Because we have limited financial and managerial resources, we have focused on developing one product candidate, PRT-201, and have focused on developing this product candidate for specific indications that we identify as most likely to succeed, in terms of both its regulatory approval and commercialization. As such, we are currently primarily focused on the development of PRT-201 for vascular access, and our Phase 3 trials will be limited to the application of PRT-201 in radiocephalic AVFs.

In the future we intend to pursue additional indications such as the application of PRT-201 in brachiocephalic AVF placement and/or patients undergoing placement of an AVG. As a result, we may forego or delay pursuit of opportunities with other product candidates or for other indications that may prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs and product candidates for specific indications may not yield any commercially viable products. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate.

Even if we obtain and maintain approval for PRT-201 or additional product candidates from the FDA, we may never obtain approval for PRT-201 or additional product candidates outside of the United States, which would limit our market opportunities and adversely affect our business.

Even if we obtain approval of a product candidate in the United States by the FDA, such approval does not ensure approval of such product candidate by regulatory authorities in other countries or jurisdictions, and approval by one foreign regulatory authority does not ensure approval by regulatory authorities in other foreign countries or by the FDA. Sales of PRT-201 or any additional product candidates outside of the United States will be subject to foreign regulatory requirements governing clinical trials and marketing approval. Even if the FDA grants marketing approval for a product candidate, comparable regulatory authorities of foreign countries must also approve the manufacturing and marketing of the product candidate in those countries. Approval procedures vary among jurisdictions and can involve requirements and administrative review periods different from, and greater than, those in the United States, including additional preclinical studies or clinical trials. In many countries outside the United States, a product candidate must be approved for reimbursement before it can be approved for sale in that country. In some cases, the price that we intend to charge for our products, if approved, is also subject to approval.

Based on additional data including the data from our Phase 3 clinical trials and assuming sufficient funds become available, we plan to commence a clinical trial of PRT-201 in Europe for patients undergoing placement of radiocephalic AVFs. Prior to enrolling our first patient in Europe, we plan to formally seek guidance from the EMA regarding its requirements for regulatory approval. We expect results from this trial to be available two to three years after the first patient is enrolled. If results of this European trial successfully meet its primary endpoint and depending on the guidance obtained from the EMA, we would expect to submit a Marketing Authorization Application, or MAA, following our receipt of the trial results. Obtaining an approval is a lengthy and expensive process and the EMA has its own procedures for approval of product candidates. Even if a product candidate is approved, the EMA may limit the indications for which the product may be marketed, require extensive warnings on the product labeling or require expensive and time-consuming clinical trials or reporting as conditions of approval. Regulatory authorities in countries outside of the United States and Europe also have requirements for approval of product candidates with which we must comply prior to marketing in those countries. Obtaining foreign regulatory approvals and compliance with foreign regulatory requirements could result in significant delays, difficulties and costs for us and could delay or prevent the introduction of PRT-201 or any additional product candidates in certain countries.

If we are found in violation of federal or state "fraud and abuse" laws or other healthcare laws and regulations, we may be required to pay a penalty and/or be suspended from participation in federal or state healthcare programs, which may adversely affect our business, financial condition and results of operation.

We may also be subject to various federal and state laws pertaining to healthcare "fraud and abuse," including anti-kickback laws and false claims laws. Anti-kickback laws make it illegal for a prescription

drug or biologic manufacturer to solicit, offer, receive or pay any remuneration in exchange for, or to induce, the referral of business, including the purchase or prescription of a particular drug or biologic. Due to the breadth of the statutory provisions, it is possible that our practices might be challenged under anti-kickback or other fraud and abuse laws. Moreover, recent healthcare reform legislation has strengthened these laws. For example, the recently enacted Patient Protection and Affordable Care Act, or ACA, among other things, amends the intent requirement of the federal anti-kickback and criminal healthcare fraud statutes to clarify that a person or entity does not need to have actual knowledge of this statute or specific intent to violate it. In addition, the ACA clarifies that the government may assert that a claim that includes items or services resulting from a violation of the federal anti-kickback statute constitutes a false or fraudulent claim for purposes of the false claims statutes. False claims laws prohibit anyone from knowingly and willingly presenting, or causing to be presented for payment, to government third-party payors (including Medicare and Medicaid) claims for reimbursed drugs, or biologics or services that are false or fraudulent, claims for items or services not provided as claimed, or claims for medically unnecessary items or services. Our activities relating to the sale and marketing of our products may be subject to scrutiny under these laws. Violations of fraud and abuse laws are punishable by criminal and civil sanctions, including fines and civil monetary penalties, the possibility of exclusion from federal healthcare programs (including Medicare and Medicaid) and corporate integrity agreements, which impose, among other things, rigorous operational and monitoring requirements on companies.

Given the significant penalties and fines that can be imposed on companies and individuals if convicted, allegations of violations often result in settlements even if the company or individual being investigated admits no wrongdoing. Settlements often include significant civil sanctions, including fines and civil monetary penalties, and corporate integrity agreements. If the government were to allege or convict us or our executive officers of violating these laws, our business could be harmed. In addition, private individuals have the ability to bring similar actions under the False Claims Act. Our activities could be subject to challenge for the reasons discussed above and due to the broad scope of these laws and the increasing attention being given to them by law enforcement authorities. Further, an increasing number of state laws require manufacturers to make reports to states on pricing and marketing information. Many of these laws contain ambiguities as to what is required to comply with the laws. Given the lack of clarity in laws and their implementation, our reporting actions could be subject to the penalty provisions of the pertinent state authorities.

Similar rigid restrictions are imposed on the promotion and marketing of medicinal products in the European Union and other countries. Laws (including those governing promotion, marketing and anti-kickback provisions), industry regulations and professional codes of conduct often are strictly enforced. Even in those countries where we are not directly responsible for the promotion and marketing of our products, inappropriate activity by our international distribution partners can have adverse implications for us.

We may not be able to comply with requirements of foreign jurisdictions in conducting trials outside of the United States.

To date, we have not conducted any clinical trials outside of the United States. Our ability to successfully initiate, enroll and complete a clinical trial in any foreign country, should we attempt to do so, is subject to numerous risks unique to conducting business in foreign countries, including:

- difficulty in establishing or managing relationships with contract research organizations, or CROs, and physicians;
- different standards for the conduct of clinical trials;
- our inability to locate qualified local consultants, physicians and partners;
- the potential burden of complying with a variety of foreign laws, medical standards and regulatory requirements, including the regulation of pharmaceutical and biotechnology products and treatment; and

- the acceptability of data obtained from trials conducted outside the United States to the FDA in support of a BLA.

Risks Related to Commercialization of Our Product

If we are unable to establish effective marketing and sales capabilities or enter into agreements with third parties to market and sell our product candidates, if they are approved, we may be unable to generate product revenues.

We currently do not have a commercial infrastructure for the marketing, sale and distribution of biological products. If approved, in order to commercialize our products, we must build our marketing, sales and distribution capabilities or make arrangements with third parties to perform these services. We may not be successful in doing so. If PRT-201 is approved by the FDA, we plan to build a specialty hospital sales force in the United States of approximately 75-100 representatives, supported by reimbursement specialists and a medical affairs team. We may seek to further penetrate the U.S. market in the future by expanding our sales force or through collaborations with other pharmaceutical or biotechnology companies or third party manufacturing and sales organizations. If approved for marketing outside the United States, we may commercialize outside the United States with our own specialty hospital sales force and/or with a commercial partner.

As a company we have no prior experience in the marketing, sale and distribution of biological products, and there are significant risks involved in the building and managing of a commercial infrastructure. The establishment and development of our own sales force and related compliance plans to market any products we may develop will be expensive and time consuming and could delay any product launch, and we may not be able to successfully develop this capability. We, or our future collaborators, will have to compete with other companies to recruit, hire, train, manage and retain marketing and sales personnel. In the event we are unable to develop a marketing and sales infrastructure, we may not be able to commercialize PRT-201 or any additional product candidates, which would limit our ability to generate product revenues. Our ability to generate product revenues would be impaired by:

- our inability to recruit, train, manage and retain adequate numbers of effective sales and marketing personnel;
- the inability of sales personnel to obtain access to vascular surgeons or persuade adequate numbers of vascular surgeons to use PRT-201 or any additional product candidates;
- our inability to effectively oversee a geographically dispersed sales and marketing team; and
- unforeseen costs and expenses associated with creating an independent sales and marketing organization.

Although our current plan is to hire most of our sales and marketing personnel only if PRT-201 is approved by the FDA, we will incur expenses prior to product launch in recruiting this sales force and developing a marketing and sales infrastructure. If the commercial launch of PRT-201 is delayed as a result of FDA requirements or other reasons, we would incur these expenses prior to being able to realize any revenue from sales of PRT-201. Even if we are able to effectively hire a sales force and develop a marketing and sales infrastructure, our sales force and marketing teams may not be successful in commercializing PRT-201 or any additional product candidates.

In the event we are unable to hire a sales force or collaborate with a third-party marketing and sales organization to commercialize any approved product candidates outside the United States, our ability to generate product revenues may be limited. To the extent we rely on third parties to commercialize any products for which we obtain regulatory approval, we may receive less revenues than if we commercialized these products ourselves. In addition, we would have less control over the sales efforts of any other third parties involved in our commercialization efforts.

Even if PRT-201 or any additional product candidates receive regulatory approval, they may fail to achieve the broad degree of physician adoption and use necessary for commercial success.

The commercial success of PRT-201 and any product candidates that we may develop will depend upon the degree of market acceptance by physicians, patients, healthcare payors and others in the medical community. Even if the FDA approves PRT-201 or one or more of our future product candidates, physicians and patients may not accept and use them. Acceptance and use of any of our products will depend upon a number of factors including:

- perceptions by members of the healthcare community, including physicians, about the safety and effectiveness of our products;
- cost-effectiveness of our products relative to any competing products;
- availability of coverage and reimbursement for our products from government or other healthcare payors; and
- effectiveness of marketing and distribution efforts by us and our licensees and distributors, if any.

Because we expect sales of PRT-201, if approved, to generate substantially all of our product revenues for the foreseeable future, the failure of PRT-201 to gain market acceptance would harm our business and would require us to seek additional financing.

PRT-201 or any additional product candidates, if approved, may face significant competition and our failure to effectively compete may prevent us from achieving significant market penetration and expansion.

The biotechnology and pharmaceutical industries are characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary products. We face potential competition from many different sources, including major pharmaceutical, specialty pharmaceutical and biotechnology companies, medical device companies, academic institutions, governmental agencies and public and private research institutions. While we believe that PRT-201's features, safety and efficacy, will differentiate it from any competitive products that may become available in the future, we expect to face potential competition from many different sources, including larger and better-funded pharmaceutical, specialty pharmaceutical and biotechnology companies and medical device companies, as well as from academic institutions and governmental agencies and public and private research institutions that may develop potentially competitive products or technologies.

Some of our competitors have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved products than we do. Smaller or early stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies.

The key competitive factors affecting the success of PRT-201, if approved, are likely to be its efficacy, safety, convenience, price, and the availability of reimbursement from government and other third party payors. Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, more convenient or less expensive than any products that we may develop. Our competitors may also obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours.

We are not aware of any therapeutic products approved in the United States or Europe for the prevention of vascular access failure. We are aware of other therapies in development with companies including Vascular Therapies and Celladon. PRT-201 could face competition from companies developing vascular access technologies, including BioConnect Systems, Caymus Medical, Phraxis, CreatiVasc, and TVA Medical. Other potential competition includes new synthetic grafts, including those that may be developed by companies that currently compete in the graft market, such as W.L. Gore, C.R. Bard and Maquet, as well as tissue engineered grafts, including those in development by Cytograft and Humacyte.

Finally, PRT-201's commercial success could be affected by the development of technologies to improve the outcomes of interventions to restore patency, including stents, stent grafts and drug eluting balloons.

PRT-201 or any additional product candidates for which we intend to seek approval as biologic products may face competition sooner than anticipated.

With the enactment of the Biologics Price Competition and Innovation Act of 2009, or BPCIA, as part of the Affordable Care Act, an abbreviated pathway for the approval of biosimilar and interchangeable biological products was created. The abbreviated regulatory pathway establishes legal authority for the FDA to review and approve biosimilar biologics, including the possible designation of a biosimilar as "interchangeable" based on its similarity to an existing brand product. Under the BPCIA, an application for a biosimilar product cannot be approved by the FDA until 12 years after the original branded product was approved under a BLA. The law is complex and is still being interpreted and implemented by the FDA. As a result, its ultimate impact, implementation, and meaning are subject to uncertainty. While it is uncertain when such processes intended to implement BPCIA may be fully adopted by the FDA, any such processes could have a material adverse effect on the future commercial prospects for our biological products.

We believe that PRT-201 or any additional product candidates approved as a biological product under a BLA should qualify for the 12-year period of exclusivity. However, there is a risk that the FDA will not consider PRT-201 or any additional product candidates to be reference products for competing products, potentially creating the opportunity for generic competition sooner than anticipated. Additionally, this period of regulatory exclusivity does not apply to companies pursuing regulatory approval via their own traditional BLA, rather than via the abbreviated pathway. Moreover, the extent to which a biosimilar, once approved, will be substituted for any one of our reference products in a way that is similar to traditional generic substitution for non-biological products is not yet clear, and will depend on a number of marketplace and regulatory factors that are still developing.

If the government or third-party payors fail to provide coverage and adequate coverage and payment rates for PRT-201 or any additional product candidates or if surgeons or hospitals choose not to use PRT-201, our revenue and prospects for profitability will be limited.

In both domestic and foreign markets, sales of our future products will depend in part upon the availability of coverage and reimbursement from third-party payors. The majority of incident and prevalent hemodialysis patients have Medicare coverage and other third-party payors include other government health programs such as Medicaid, managed care providers, private health insurers and other organizations. Coverage decisions may depend upon clinical and economic standards that disfavor new drug products when more established or lower cost therapeutic alternatives are already available or subsequently become available. Assuming coverage is approved, the resulting reimbursement payment rates might not be adequate. Accordingly, PRT-201 or any of our other product candidates, if approved, will face competition from other therapies and drugs for limited financial resources. We may need to conduct post-marketing studies in order to demonstrate the cost-effectiveness of any future products to the satisfaction of outpatient clinics, hospitals, other target customers and their third-party payors. Such studies might require us to commit a significant amount of management time and financial and other resources. Our future products might not ultimately be considered cost-effective. Adequate third-party coverage and reimbursement might not be available to enable us to maintain price levels sufficient to realize an appropriate return on investment in product development.

Third party payors, whether foreign or domestic, or governmental or commercial, are developing increasingly sophisticated methods of controlling healthcare costs. In addition, in the United States, no uniform policy of coverage and reimbursement for drug products exists among third-party payors. Therefore, coverage and reimbursement for drug products can differ significantly from payor to payor. Further, we believe that future coverage and reimbursement will likely be subject to increased restrictions both in the United States and in international markets. Third party coverage and reimbursement for our products or product candidates for which we receive regulatory approval may not be available or adequate in either the United States or international markets, which could have a negative effect on our business, results of operations, financial condition and prospects.

Risks Related to Dependence on Third Parties

We and our contract manufacturers are subject to significant regulation with respect to manufacturing our product candidates. The manufacturing facilities on which we rely may not continue to meet regulatory requirements and have limited capacity.

We currently have a relationship with only one supplier, Lonza AG, for the manufacturing of active pharmaceutical ingredient, or API, for PRT-201 for clinical testing purposes, and intend to continue to utilize Lonza as our sole or primary supplier in the future. We have used two companies, Jubilant HollisterStier and DSM Pharmaceuticals, to vial and make our PRT-201 finished product. We also expect to rely upon third parties to produce materials required for the commercial production of PRT-201 or any additional product candidates if we succeed in obtaining the necessary regulatory approvals.

All entities involved in the preparation of drugs or biologics for clinical trials or commercial sale, including our existing contract manufacturers, are subject to extensive regulation. Ingredients of a finished therapeutic biologic product approved for commercial sale or used in late-stage clinical trials must be manufactured in accordance with cGMP and equivalent foreign standards. These regulations govern manufacturing processes and procedures (including record keeping) and the implementation and operation of quality systems to control and assure the quality of investigational products and products approved for sale. Poor control of production processes can lead to the introduction of adventitious agents or other contaminants, or to inadvertent changes in the properties or stability of product candidate that may not be detectable in final product testing. We or our contract manufacturers must supply all necessary documentation in support of a BLA on a timely basis and must adhere to the FDA's good laboratory practices, or GLPs, and cGMP regulations enforced by the FDA through its facilities inspection program. Any failure by our third-party manufacturers to comply with cGMP or failure to scale-up manufacturing processes, including any failure to deliver sufficient quantities of product candidates in a timely manner for the process validation required in connection with a BLA filing, could lead to a delay in, or failure to obtain, regulatory approval of PRT-201 or any additional product candidates. For example, on November 27, 2013, our third-party supplier of finished biological product, Jubilant HollisterStier, received a Warning Letter from the FDA alleging that the company was not complying with cGMPs. We received a letter from the FDA on February 13, 2014, stating that the Warning Letter does not impact the batch of finished product we intend to use for our Phase 3 clinical trials. However, this third party or other third parties could encounter similar difficulties that could impede our clinical trials or commercialization. Our facilities and quality systems and the facilities and quality systems of some or all of our third-party contractors must also pass a pre-approval inspection for compliance with the applicable regulations as a condition of regulatory approval of PRT-201 or any additional product candidates. In addition, the regulatory authorities may, at any time, audit or inspect a manufacturing facility involved with the preparation of our product candidate or the associated quality systems for compliance with the regulations applicable to the activities being conducted. If these facilities and quality systems do not pass a pre-approval plant inspection from the FDA or a comparable foreign authority, approval of our product candidate by the FDA or the equivalent approvals in other jurisdictions will not be granted until the regulatory authority is satisfied that the facility complies with applicable regulations.

Regulatory authorities also may, at any time following approval of a product for sale, audit our manufacturing facilities or those of our third-party contractors. If any such inspection or audit identifies a failure to comply with applicable regulations or if a violation of our product specifications or applicable regulations occurs independent of such an inspection or audit, we or the relevant regulatory authority may require remedial measures that may be costly and/or time-consuming for us or a third party to implement and that may include the temporary or permanent suspension of a clinical trial or commercial sales or the temporary or permanent closure of a facility. Any such remedial measures imposed upon us or third parties with whom we contract could materially harm our business.

If we or any of our third-party manufacturers fail to maintain regulatory compliance, the FDA can impose regulatory sanctions including, among other things, refusal to approve a pending application for a new drug or biologic product or revocation of a pre-existing approval. If any such event occurs, our business, financial condition and results of operations may be materially harmed.

We rely on third parties to conduct some or all aspects of our product manufacturing, protocol development, research, and preclinical and clinical testing, and these third parties may not perform satisfactorily.

We do not currently, and do not expect in the future, to independently conduct all aspects of our product manufacturing, protocol development, research and monitoring and management of our clinical programs. PRT-201 API is produced by our contract manufacturer, Lonza. PRT-201 finished product is produced by our contract fill/finish provider, Jubilant HollisterStier. Release testing and stability for API and finished product is performed by PPD, Inc. We currently rely, and expect to continue to rely, on third parties with respect to these items. While we will have agreements governing their activities, we will have limited influence over their actual day-to-day performance. Nevertheless, we will be responsible for ensuring that the manufacturing is conducted in accordance with regulatory requirements such as cGMPs. Our reliance on the third parties does not relieve us of our regulatory responsibilities.

Any of these third parties may terminate their engagements with us under the terms of our agreements upon notice to us. If we need to enter into alternative arrangements, our product candidate development activities may be delayed. Our reliance on these third parties for research and development activities reduces our day-to-day control over these activities but does not relieve us of our responsibility to ensure compliance with all required legal, regulatory and scientific standards and any applicable trial protocols. For example, for PRT-201 or any additional product candidates that we develop and commercialize on our own, we will remain responsible for ensuring that each of our clinical trials is conducted in accordance with its protocol and analyzed in accordance with its statistical analysis plan for the clinical trial.

If these third parties do not successfully carry out their contractual duties, meet expected deadlines or conduct our studies in accordance with regulatory requirements or our protocols, we may be delayed in completing, or unable to complete, the clinical trials required to support future approval of PRT-201 or any additional product candidates.

We rely on our manufacturers to purchase from third-party suppliers the materials necessary to produce our product candidate, PRT-201, for our clinical trials. There are a small number of suppliers for certain raw materials that we use to manufacture PRT-201. These suppliers may not sell these raw materials to our manufacturers at the times we need them or on commercially reasonable terms. We do not have any control over the process or timing of the acquisition of these raw materials by our manufacturers. Moreover, we currently do not have any agreements for the commercial production of these raw materials. Although the API and the finished product for each of our Phase 3 trials has already been manufactured and is held in storage, we will need supply of finished product as part of the process validation and for any stability or other tests in connection with a BLA application and also to conduct additional clinical trials, for example for additional PRT-201 indications. Any significant delay in the supply of the ingredients thereof due to the need to replace a third-party manufacturer could considerably delay completion of our

clinical trials, product testing and potential regulatory approval of PRT-201 or any additional product candidate as we believe that replacing Lonza as the manufacturer of our API would take one to two years. If our manufacturers or we are unable to purchase these raw materials after regulatory approval has been obtained for our product candidate, our ability to commercially launch and/or generate revenues from the sale of any approved product would be impaired. Reliance on third-party manufacturers entails exposure to risks to which we would not be subject if we manufactured the product candidate ourselves, including:

- failure to negotiate manufacturing agreements with third parties under commercially reasonable terms;
- reduced day-to-day control over the manufacturing process for our product candidates as a result of using third-party manufacturers for all aspects of manufacturing activities;
- reduced control over the protection of our trade secrets and know-how from misappropriation or inadvertent disclosure;
- termination or nonrenewal of manufacturing agreements with third parties in a manner or at a time that may be costly or damaging to us or result in delays in the development or commercialization of our product candidates; and
- disruptions to the operations of our third-party manufacturers or suppliers caused by conditions unrelated to our business or operations, including the bankruptcy of the manufacturer or supplier.

Any of these events could lead to delays in the development of PRT-201 or any additional product candidates, including delays in our clinical trials, or failure to obtain regulatory approval for our product candidates, or it could impact our ability to successfully commercialize PRT-201 or any additional product candidates. Some of these events could be the basis for FDA or other regulatory action, including injunction, recall, seizure or total or partial suspension of production. Any of these events could have a material adverse effect on our business.

We rely on third parties to conduct, supervise and monitor our clinical trials. If these third parties do not successfully carry out their contractual duties or meet expected deadlines, we may not be able to obtain regulatory approval for, or commercialize, PRT-201 or any additional product candidates and our business could be substantially harmed.

We rely on CROs and clinical trial sites to ensure our clinical trials are conducted properly and on time. While we will have agreements governing their activities, we will have limited influence over their actual day-to-day performance. Nevertheless, we will be responsible for ensuring that each of our clinical trials is conducted in accordance with the applicable protocol, and legal, regulatory and scientific standards and recognize that our reliance on the CROs does not relieve us of our regulatory responsibilities.

We and our CROs are required to comply with the FDA's good clinical practices, or GCPs, for conducting, recording and reporting the results of clinical trials to assure that the data and reported results are credible and accurate and that the rights, integrity and confidentiality of clinical trial participants are protected. The FDA and comparable foreign regulatory authorities enforce these GCPs through periodic inspections of trial sponsors, principal investigators and clinical trial sites. If we or our CROs fail to comply with applicable GCPs, the clinical data generated in our future clinical trials may be deemed unreliable and the FDA, the EMA, or other foreign regulatory authorities may require us to perform additional clinical trials before approving any marketing applications. Upon inspection, the FDA may determine that our clinical trials did not comply with GCPs. In addition, our future clinical trials will require a sufficient number of test subjects to evaluate the safety and effectiveness of PRT-201 or any additional product candidates. Accordingly, if our CROs fail to comply with these regulations or fail to recruit a sufficient number of patients, we may be required to repeat such clinical trials, which would delay the regulatory approval process.

Our CROs are not our employees, and we are therefore unable to monitor on a day-to-day basis whether or not they devote sufficient time and resources to our clinical and nonclinical programs. These CROs may also have relationships with other commercial entities, including our competitors, for whom

they may also be conducting clinical trials or other product development activities that could harm our competitive position. If our CROs do not successfully carry out their contractual duties or obligations, fail to meet expected deadlines, or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols or regulatory requirements, or for any other reasons, our clinical trials may be extended, delayed or terminated, and we may not be able to obtain regulatory approval for, or successfully commercialize, PRT-201 or any additional product candidates. If any such event were to occur, our financial results and the commercial prospects for PRT-201 or any additional product candidates would be harmed, our costs could increase, and our ability to generate revenues could be delayed.

If any of our relationships with these third-party CROs terminates, we may not be able to enter into arrangements with alternative CROs or to do so on commercially reasonable terms. Further, switching or adding additional CROs involves additional costs and requires management time and focus. In addition, a transition period may be required when a new CRO commences work. As a result, delays may occur, which could materially impact our ability to meet our desired clinical development timelines. Though we carefully manage our relationships with our CROs, there can be no assurance that we will not encounter challenges or delays in the future or that these delays or challenges will not have a material adverse impact on our business, financial condition and prospects.

We also rely on other third parties to store and distribute our products for the clinical trials that we conduct. Any performance failure on the part of our distributors could delay clinical development or marketing approval of PRT-201 or any additional product candidates or commercialization of our product, if approved, producing additional losses and depriving us of potential product revenue.

We may seek to form partnerships in the future with respect to PRT-201 or any additional product candidates, and we may not realize the benefits of such partnerships.

We may form partnerships, create joint ventures or collaborations or enter into licensing arrangements with third parties for the development and commercialization of PRT-201 or any additional product candidates. We face significant competition in seeking appropriate strategic partners and the negotiation process is time-consuming and complex. Any delays in entering into new strategic partnership agreements related to our product candidates could delay the development and commercialization of our product candidates and reduce their competitiveness even if they reach the market. Moreover, we may not be successful in our efforts to establish a strategic partnership or other collaborative arrangement for any additional product candidates because the potential partner may consider that our research and development pipeline is insufficiently developed to justify a collaborative effort, or that PRT-201 or any additional product candidates and programs do not have the requisite potential to demonstrate safety and efficacy in the target population. Even if we are successful in establishing such a strategic partnership or collaboration, we cannot be certain that, following such a strategic transaction or license, we will be able to progress the development and commercialization of the applicable product candidates as envisioned, or that we will achieve the revenues that would justify such transaction.

Risks Related to Our Intellectual Property

If our efforts to protect our intellectual property related to PRT-201 or any additional product candidates are not adequate, we may not be able to compete effectively in our market.

We rely upon a combination of patents, patent applications, know-how and confidentiality agreements to protect the intellectual property related to our only product candidate, PRT-201, and will use a similar strategy to protect any additional product candidates. The patent position of biotechnology companies is generally uncertain because it involves complex legal and factual considerations. The standards applied by the United States Patent and Trademark Office, or USPTO, and foreign patent offices in granting patents are not always applied uniformly or predictably. For example, there is no uniform worldwide policy

regarding patentable subject matter or the scope of claims allowable in biotechnology patents. The patent applications that we own may fail to result in issued patents with claims that cover PRT-201 or any additional product candidates in the United States or in other countries. There is no assurance that all potentially relevant prior art relating to our patents and patent applications has been found, and prior art that is not before the patent examiners, as well as prior art that is before the patent examiners, could be used by a third party to invalidate a patent or could be relied on to prevent a patent from issuing from a pending patent application. Even if patents do successfully issue and even if these patents cover PRT-201 or any additional product candidates, third parties may challenge their validity, enforceability or scope, which may result in our patents being narrowed or invalidated. Furthermore, even if they are unchallenged, our patents and patent applications may not adequately provide exclusivity for PRT-201 or any additional product candidates, prevent others from designing around our patents with similar products that are outside the scope of our patents, or prevent others from operating in jurisdictions in which we did not pursue patent protection. Any of these outcomes could impair our ability to prevent competition from third parties, which may have an adverse impact on our business.

If patent applications we hold with respect to PRT-201 or any additional product candidates fail to issue, if their breadth or strength of protection is threatened, or if they fail to provide meaningful exclusivity for PRT-201 or any additional product candidates, it could dissuade companies from collaborating with us. We own 20 issued patents and own 25 pending patent applications, most of which cover aspects of PRT-201 or its use. We cannot offer any assurances about which, if any, of the pending patent applications will issue as patents, the breadth of any such patents or any of our currently issued patents, or whether any issued patents will be challenged by third parties or will be found invalid and unenforceable if challenged. Any successful challenge to these patent applications, or patents that may issue from them, or to currently issued patents owned by us, could deprive us of rights necessary for the successful commercialization of PRT-201 or any other product candidate that we may develop. Since patent applications in the United States and most other countries are confidential for a period of time after filing, and some remain so until issued, we cannot be certain that we were the first to file a patent application relating to any particular aspect of a product candidate. Furthermore, if third parties have filed such patent applications, an interference proceeding in the United States can be initiated by these third parties, or by the USPTO itself, to determine who was the first to invent any of the subject matter covered by the patent claims of our patents and patent applications.

In the United States, for patent applications filed prior to March 16, 2013, assuming the other requirements for patentability are met, the first to invent is entitled to the patent, while outside the United States, the first to file a patent application is entitled to the patent. Our currently pending patent applications are examined under the system in place before March 16, 2013. Third parties are allowed to submit prior art prior to the issuance of a patent by the USPTO, and may become involved in reexamination, *inter partes* review or interference proceedings challenging our patent rights. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate, our patent rights, which could adversely affect our competitive position with respect to third parties.

In addition, patents have a limited lifespan. In most countries, the statutory term of a patent is 20 years from the earliest domestic priority date claimed. In the United States, for applications filed after June 7, 1995, the statutory term of a patent is 20 years from earliest non-provisional priority date claimed. Various extensions of patent protection may be available in particular countries; however, in all circumstances, the life of a patent, and the protection it affords, has a limited term. If we encounter delays in obtaining regulatory approvals, the period of time during which we could market a product under patent protection could be reduced. We expect to seek extensions of patent protection where these are available in any countries where we are prosecuting patents. Such possible extensions include those permitted under the Drug Price Competition and Patent Term Restoration Act of 1984 in the United States, which permits up to five years' extension of patent protection. The scope of protection available during an extension of a patent claiming a product is limited to the approved product itself for approved uses, and the scope of

protection available during an extension of a patent claiming a method of using a product is limited to the uses claimed in the patent and approved for the product. The actual length of the extension will depend on the amount of patent term lost while the product was in clinical trials and while the BLA was under review by the FDA. However, the applicable authorities, including the FDA and the USPTO in the United States, and any equivalent regulatory authority in other countries, may not agree with our assessment of whether such extensions are available, and may refuse to grant extensions to our patents, or may grant more limited extensions than we request. If this occurs, our competitors may be able to take advantage of our investment in development and clinical trials by referencing our clinical and preclinical data, and then may be able to launch their product earlier than might otherwise be the case.

Any loss of, or failure to obtain, patent protection could have a material adverse impact on our business. We may be unable to prevent competitors from entering the market with a product that is similar to or the same as our products.

Confidentiality agreements with employees and third parties may not prevent unauthorized disclosure of proprietary information.

We seek to protect our proprietary technology and processes, in part, by entering into confidentiality agreements with our employees, consultants, scientific advisors and contractors. We also seek to preserve the integrity and confidentiality of our data and know-how by maintaining physical security of our premises and physical and electronic security of our information technology systems. Nonetheless, despite these precautions, agreements or security measures may be breached, and we may not have adequate remedies for any breach. In addition, our know-how may otherwise become known or be independently discovered by competitors. To the extent that our consultants, contractors or collaborators use intellectual property owned by others in their work for us, disputes may arise as to the rights in related or resulting know-how and inventions.

Enforcing a claim that a third party illegally obtained and is using any of our know-how is expensive and time consuming, and the outcome is unpredictable. In addition, courts outside the United States sometimes are less willing than United States courts to protect know-how. Misappropriation or unauthorized disclosure of our know-how could impair our competitive position and may have a material adverse effect on our business.

We may become involved in lawsuits to protect or enforce our intellectual property, which could be expensive, time consuming and unsuccessful, and which may lead to a finding that our patents are invalid and/or unenforceable.

Competitors may infringe our patents or misappropriate or otherwise violate our intellectual property rights. To counter infringement or unauthorized use, litigation may be necessary to enforce or defend our intellectual property rights, to protect our know-how and/or to determine the validity and scope of our own intellectual property rights. Intellectual property litigation can be expensive and time consuming. Many of our current and potential competitors have the ability to dedicate substantially greater resources to litigate intellectual property rights than we can. Accordingly, despite our efforts, we may not be able to prevent third parties from infringing or misappropriating our intellectual property. Litigation could result in substantial costs and diversion of management resources, which could harm our business and financial results. In addition, in an infringement proceeding, a court may decide that our patents are invalid or unenforceable, and may refuse to stop the other party from using the technology at issue, including on the grounds that our patents are invalid or unenforceable or do not cover the technology in question. An adverse result in any litigation proceeding could put one or more of our patents at risk of being invalidated, held unenforceable or interpreted narrowly. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation.

Third-party claims of intellectual property infringement or misappropriation may prevent or delay our development and commercialization efforts.

Our commercial success depends in part on our ability to develop, manufacture, market and sell PRT-201 or any additional product candidates, and to use proprietary technologies without infringing the patents and proprietary rights of third parties. There is a substantial amount of litigation and adversarial proceedings, both within and outside the United States, involving patent and other intellectual property rights in the biotechnology and pharmaceutical industries, including patent infringement lawsuits, interferences, oppositions, reexamination, and *inter partes* review proceedings before the USPTO and corresponding foreign patent offices. Third parties own patent rights both within and outside the U.S. in the fields in which we are developing and may develop PRT-201 or any additional product candidates. As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that PRT-201 or any additional product candidates may be subject to claims of infringement of the patent rights of third parties.

Third parties may assert that we are employing their proprietary technology without authorization. There may be third-party patents or patent applications with claims that may cover PRT-201 or any additional product candidates and/or the use, manufacture, sale and/or offer for sale of PRT-201 or any additional product candidates. We are aware of European Patent No. EP 1 012 307 B1, or the '307 patent, which claims, among other things, autocatalytically cleavable zymogenic precursor of a serine protease wherein a naturally occurring non-autocatalytic cleavage site is replaced in the zymogenic precursor by an autocatalytic cleavage site. The '307 patent expires on August 12, 2018. We currently estimate that the soonest that we will market PRT-201 is after this date.

In some cases, we may have failed to identify relevant third-party patents or patent applications. For example, applications filed before November 29, 2000, and certain applications filed after that date that will not be filed outside the United States remain confidential until patents issue. Except for the preceding exceptions, patent applications in the United States and elsewhere are generally published but, only after a waiting period of approximately 18 months after the earliest filing. Therefore, patent applications covering PRT-201 or future product candidates could have been filed by others without our knowledge. Additionally, pending patent applications which have been published can, subject to certain limitations, be later amended in a manner that could cover PRT-201 or any additional product candidates and/or the use, manufacture, sale and/or offer for sale of PRT-201 or any additional product candidates.

If any valid and enforceable third-party patents were held by a court of competent jurisdiction to cover PRT-201 or any additional product candidates and/or their use, manufacture, sale, and/or offer for sale, the holders of any of these patents may be able to block our ability to develop and commercialize the applicable product candidate until the patent expired or unless we obtain a license. Licenses may not be available on acceptable terms, if at all. Even if we were able to obtain a license, the rights may be nonexclusive, which could result in our competitors gaining access to the same intellectual property. Ultimately, we could be prevented from commercializing a product, or be forced to cease some aspect of our business operations, if, as a result of actual or threatened patent infringement claims, we are unable to enter into licenses on acceptable terms.

Some of our early research of recombinant expression of PRT-201, but not the corresponding development work, utilized some technology under license from a third party. The third party may contend that we use the licensed technology for our commercial recombinant expression of PRT-201. Litigation may be necessary to defend against such a claim. Even if we are successful in defending against such a claim, litigation could result in substantial costs and be a distraction to management. If we are not successful in defending against such a claim, in addition to paying monetary damages, we may have to reconfigure the PRT-201 expression system, which would materially adversely affect our commercial development efforts.

Parties making claims against us may obtain injunctive or other equitable relief, which could effectively block our ability to commercialize PRT-201 or any additional product candidates. We may face a claim of misappropriation if a third party believes that we inappropriately obtained and used trade secrets of that third party. If we are found to have misappropriated a third party's trade secrets, we may be prevented from further using such trade secrets, limiting our ability to develop PRT-201 or any additional product candidates, and we may be required to pay damages.

Defending against claims of patent infringement or misappropriation of trade secrets could be costly and time consuming, regardless of the outcome. Thus, even if we were to ultimately prevail, or to settle at an early stage, any litigation could burden us with substantial unanticipated costs. In addition, litigation or threatened litigation could result in significant demands on the time and attention of our management team, distracting them from the pursuit of other company business. In the event of a successful claim of infringement against us, we may have to pay substantial damages, including treble damages and attorneys' fees for willful infringement, pay royalties, redesign our infringing products or obtain one or more licenses from third parties, which may be impossible or require substantial time and monetary expenditure.

During the course of any patent or other intellectual property litigation, there could be public announcements of the results of hearings, rulings on motions, and other interim proceedings in the litigation. If securities analysts or investors regard these announcements as negative, the perceived value of our products, programs, or intellectual property could be diminished. Accordingly, the market price of our common stock may decline.

If we are unable to adequately protect our proprietary technology, or obtain and maintain issued patents which are sufficient to protect our current product candidate, PRT-201, or any additional product candidates, others could compete against us more directly, which would have a material adverse impact on our business, results of operations, financial condition and prospects.

We strive to protect and enhance the proprietary technologies that we believe are important to our business, including seeking patents intended to cover our products and compositions, their methods of use and any other inventions that are important to the development of our business. We also rely on know-how to protect aspects of our business that are not amenable to, or that we do not consider appropriate for, patent protection.

Our success will depend significantly on our ability to obtain and maintain patent and other proprietary protection for commercially important technology, inventions and know-how related to our business, defend and enforce our current patents and any future patents that may issue, preserve the confidentiality of our know-how and operate without infringing the valid and enforceable patents and proprietary rights of third parties. We also rely on know-how and in-licensing opportunities to develop, strengthen and maintain the proprietary position of PRT-201 or any additional product candidates.

We cannot provide any assurances that any of our pending patent applications will mature into issued patents and, if they do, that such patents or our currently issued patents will include claims with a scope sufficient to protect PRT-201 or any additional product candidates or otherwise provide any competitive advantage. For example, one of our patents that may provide coverage for PRT-201 only covers particular formulations. As a result, this patent would not prevent third-party competitors from creating, making and marketing alternative formulations that fall outside the scope of our patent claims. There can be no assurance that any such alternative formulations will not be equally effective.

Moreover, other parties have developed technologies that may be related or competitive to our approach, and may have filed or may file patent applications and may have received or may receive patents that may overlap or conflict with our patent applications, either by claiming the same methods or formulations or by claiming subject matter that could dominate our patent position. Such third party patent positions may limit or even eliminate our ability to obtain patent protection for certain inventions.

The patent positions of biotechnology and pharmaceutical companies, including our patent position, involve complex legal and factual questions, and, therefore, the issuance, scope, validity and enforceability of any patent claims that we may obtain cannot be predicted with certainty. Patents, if issued, may be challenged, deemed unenforceable, invalidated, or circumvented. United States patents and patent applications may also be subject to interference proceedings, *ex parte* reexamination, or *inter partes* review proceedings, and challenges in district court. Patents may be subjected to opposition, revocation proceedings, or comparable proceedings lodged in various foreign, both national and regional, patent offices. These proceedings could result in either loss of the patent or denial of the patent application or loss or reduction in the scope of one or more of the claims of the patent or patent application. In addition, such proceedings may be costly. Thus, any patents that we may own or exclusively license may not provide any protection against competitors. Furthermore, an adverse decision in an interference proceeding can result in a third party receiving the patent right sought by us, which in turn could affect our ability to develop, market or otherwise commercialize PRT-201 or any additional product candidates.

Furthermore, though a patent is presumed valid and enforceable, its issuance is not conclusive as to its validity or its enforceability and it may not provide us with adequate proprietary protection or competitive advantages against competitors with similar products. Even if a patent issues and is held to be valid and enforceable, competitors may be able to design around our patents, such as using pre-existing or newly developed technology. Other parties may develop and obtain patent protection for more effective technologies, designs or methods. We may not be able to prevent the unauthorized disclosure or use of our technical knowledge or know-how by consultants, vendors, former employees and current employees. The laws of some foreign countries do not protect our proprietary rights to the same extent as the laws of the United States, and we may encounter significant problems in protecting our proprietary rights in these countries. If these developments were to occur, they could have a material adverse effect on our sales.

In addition, proceedings to enforce or defend our patents, if and when issued, could put our patents at risk of being invalidated, held unenforceable, or interpreted narrowly. Such proceedings could also provoke third parties to assert claims against us, including that some or all of the claims in one or more of our patents are invalid or otherwise unenforceable. If any of our patents, if and when issued, covering PRT-201, or any additional product candidates, are invalidated or found unenforceable, our financial position and results of operations would be materially and adversely impacted. In addition, if a court found that valid, enforceable patents held by third parties covered PRT-201, or any additional product candidates, our financial position and results of operations would also be materially and adversely impacted.

The degree of future protection for our proprietary rights is uncertain, and we cannot ensure that:

- any of our patents or pending patent applications, if issued, will include claims having a scope sufficient to protect PRT-201 or any additional product candidates;
- any of our pending patent applications will issue as patents at all;
- we will be able to successfully commercialize product candidates, if approved, before our relevant patents expire;
- we were the first to make the inventions covered by each of our patents and pending patent applications;
- we were the first to file patent applications for these inventions;
- others will not develop similar or alternative technologies that do not infringe our patents;
- others will not use pre-existing technology to effectively compete against us;
- any of our patents will be found ultimately to be valid and enforceable;
- any patents issued to us will provide a basis for an exclusive market for our commercially viable products, will provide us with any competitive advantages or will not be challenged by third parties;
- we will develop additional proprietary technologies or product candidates that are separately patentable; or
- that our commercial activities or products will not infringe the patents or proprietary rights of others.

We rely upon unpatented know-how to maintain our competitive position, which we seek to protect, in part, by confidentiality agreements with our employees and our collaborators and consultants. It is possible that technology relevant to our business will be independently developed by a person that is not a party to such an agreement. Furthermore, if the employees and consultants who are parties to these agreements breach or violate the terms of these agreements, we may not have adequate remedies for any such breach or violation, and our confidential know-how could become known to others through such breaches or violations. Further, our know-how could otherwise become known or be independently discovered by our competitors. Further, the term of confidentiality requirements for current and terminated agreements with some of our consultants, contract manufacturing or research organizations and other third parties is finite.

We may be subject to claims challenging the inventorship or ownership of our patents and other intellectual property.

We enter into confidentiality and intellectual property assignment agreements with our employees, consultants, outside scientific collaborators, sponsored researchers and other advisors. These agreements generally provide that inventions conceived by the party in the course of rendering services to us will be our exclusive property. However, these agreements may not be honored and may not effectively assign intellectual property rights to us. For example, even if we have a consulting agreement in place with an academic advisor pursuant to which such academic advisor is required to assign any inventions developed in connection with providing services to us, such academic advisor may not have the right to assign such inventions to us, as it may conflict with his or her obligations to assign all such intellectual property to his or her employing institution.

Litigation may be necessary to defend against these and other claims challenging inventorship or ownership of inventions. If we are unsuccessful in defending against any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, valuable intellectual property. Such an outcome could have a material adverse effect on our business. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees.

Obtaining and maintaining our patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for non-compliance with these requirements.

The USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other provisions during the patent process. There are situations in which noncompliance can result in abandonment or lapse of a patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, competitors might be able to enter the market earlier than would otherwise have been the case.

Issued patents covering PRT-201 or covering any additional product candidates could be found invalid or unenforceable if challenged in court.

If we initiated legal proceedings against a third party to enforce a patent, if and when issued, covering PRT-201 or any additional product candidate, the defendant could counterclaim that the patent covering our product candidate is invalid and/or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity and/or unenforceability are commonplace. Grounds for a validity challenge include alleged failures to meet any of several statutory requirements, including lack of novelty, obviousness or non-enablement. Grounds for unenforceability assertions include allegations that someone connected with prosecution of the patent withheld relevant information from the USPTO, or made a misleading statement, during prosecution. Third parties may also raise similar claims before administrative bodies in the United States or abroad, even outside the context of litigation. Such mechanisms include reexamination and *inter partes* review in the United States and equivalent proceedings in foreign jurisdictions, *e.g.*, opposition proceedings. Such proceedings could result in revocation or amendment of

our patents in such a way that they no longer cover, for example, PRT-201 or competitive products. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to validity, for example, we cannot be certain that there is no invalidating prior art, including prior art of which we and the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity and/or unenforceability, we would lose at least part, and perhaps all, of the patent protection on the applicable product candidate. Such a loss of patent protection would have a material adverse impact on our business.

We will not seek to protect our intellectual property rights in all jurisdictions throughout the world and we may not be able to adequately enforce our intellectual property rights even in the jurisdictions where we seek protection.

Filing, prosecuting and defending patents on product candidates in all countries and jurisdictions throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States could be less extensive than those in the United States, assuming that rights are obtained in the United States. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the United States. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions.

Competitors may use our technologies in jurisdictions where we do not pursue and obtain patent protection to develop their own products and further, may export otherwise infringing products to territories where we have patent protection, but enforcement is not as strong as that in the United States. These products may compete with our products and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing. Even if we pursue and obtain issued patents in particular jurisdictions, our patent claims or other intellectual property rights may not be effective or sufficient to prevent third parties from so competing.

The laws of some foreign countries do not protect intellectual property rights to the same extent as the laws of the United States. Many companies have encountered significant problems in protecting and defending intellectual property rights in certain foreign jurisdictions. The legal systems of some countries, particularly developing countries, do not favor the enforcement of patents and other intellectual property protection, especially those relating to biotechnology. This could make it difficult for us to stop the infringement of our patents, if obtained, or the misappropriation of our other intellectual property rights. For example, many foreign countries have compulsory licensing laws under which a patent owner must grant licenses to third parties. In addition, many countries limit the enforceability of patents against third parties, including government agencies or government contractors. In these countries, patents may provide limited or no benefit. Patent protection must ultimately be sought on a country-by-country basis, which is an expensive and time-consuming process with uncertain outcomes. Accordingly, we may choose not to seek patent protection in certain countries, and we will not have the benefit of patent protection in such countries.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents and other intellectual property protection, particularly those relating to biopharmaceuticals, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our proprietary rights generally. Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly, could put our patent applications at risk of not issuing and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts

to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

Some of our intellectual property may have been discovered through government funded programs and thus may be subject to federal regulations such as government "march-in" rights, certain reporting requirements, and a preference for United States industry. Compliance with such regulations may limit our exclusive rights, subject us to expenditure of resources with respect to reporting requirements, and limit our ability to contract with non-United States manufacturers.

Some of our intellectual property rights may have been generated through the use of United States government funding and therefore are subject to certain federal regulations. For example, our patents relating to some therapeutic uses of PRT-201 and associated systems and kits that include a catheter, which we refer to as the "therapy family," arose from research funded by the United States government. As a result, the United States government has certain rights to this intellectual property pursuant to the Bayh-Dole Act of 1980, or Bayh-Dole Act. These United States government rights in certain inventions developed under a government-funded program include a non-exclusive, non-transferable, irrevocable worldwide license to use inventions for any governmental purpose. In addition, the United States government has the right to require us to grant exclusive, partially exclusive, or non-exclusive licenses to any of these inventions to a third party if it determines that: (i) adequate steps have not been taken to commercialize the invention; (ii) government action is necessary to meet public health or safety needs; or (iii) government action is necessary to meet requirements for public use under federal regulations, also referred to as "march-in rights." The United States government also has the right to take title to these inventions if we, or the applicable licensor, fail to disclose the invention to the government and fail to file an application to register the intellectual property within specified time limits. In addition, the United States government may acquire title to these inventions in any country in which a patent application is not filed within specified time limits. Intellectual property generated under a government funded program is also subject to certain reporting requirements, compliance with which may require us or the applicable licensor to expend substantial resources. In addition, the United States government requires that any products embodying the subject invention or produced through the use of the subject invention be manufactured substantially in the United States. The manufacturing preference requirement can be waived if the owner of the intellectual property can show that reasonable but unsuccessful efforts have been made to grant licenses on similar terms to potential licensees that would be likely to manufacture substantially in the United States or that under the circumstances domestic manufacture is not commercially feasible. This preference for United States manufacturers may limit our ability to contract with non-United States product manufacturers for products covered by such intellectual property.

We currently do not plan to apply for additional United States government funding, but if we do, and we discover compounds or drug or biological candidates as a result of such funding, intellectual property rights to such discoveries may be subject to the applicable provisions of the Bayh-Dole Act.

If we do not obtain additional protection under the Hatch-Waxman Amendments and similar foreign legislation by extending the patent protection for PRT-201, our business may be materially harmed.

Depending upon the timing, duration and specifics of the first FDA marketing approval of PRT-201 and, if applicable, any additional product candidates, a United States patent that we own or license may be eligible for limited patent term restoration under the Drug Price Competition and Patent Term Restoration Act of 1984, referred to as the Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit extension of patent protection for up to five years as compensation for patent term lost during product development and the FDA regulatory review process. During this period of extension, the scope of protection is limited to the approved product for approved uses (for patents claiming a product) and any use claimed by the patent and approved for the product (for patents claiming a method of using a product).

Although we plan on seeking patent term restoration for our products, it may not be granted if, for example, we fail to apply within applicable deadlines, fail to apply prior to expiration of relevant patents or otherwise fail to satisfy applicable requirements. Moreover, the applicable time period or the scope of patent protection afforded could be less than we request. If we are unable to obtain patent term restoration or the term of any such patent restoration is less than we request, our competitors may be able to enter the market and compete against us sooner than we anticipate, and our ability to generate revenues could be materially adversely affected.

Changes in United States patent law could diminish the value of patents in general, thereby impairing our ability to protect our products.

As is the case with other biotechnology companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biotechnology industry involve both technological and legal complexity, and is therefore costly, time-consuming and inherently uncertain. In addition, the United States has recently enacted and is currently implementing wide-ranging patent reform legislation: the Leahy-Smith America Invents Act. The America Invents Act includes a number of significant changes to United States patent law. These include provisions that affect the way patent applications will be prosecuted, provides expanded opportunities for post-grant administrative review of patents before the USPTO, and may also affect patent litigation. It is not yet clear what, if any, impact the America Invents Act will have on the operation of our business. However, the America Invents Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of any patents that may issue from our patent applications, all of which could have a material adverse effect on our business and financial condition.

In addition, recent United States Supreme Court rulings have narrowed the scope of patent protection available in certain circumstances and weakened the rights of patent owners in certain situations. The full impact of these decisions is not yet known. For example, on March 20, 2012 in *Mayo Collaborative Services v. Prometheus Laboratories, Inc.*, the Court held that several claims drawn to measuring drug metabolite levels from patient samples and correlating them to drug doses were not patent-eligible subject matter. The decision appears to impact diagnostics patents that merely apply a law of nature via a series of routine steps and it has created uncertainty around the ability to obtain patent protection for certain inventions. Additionally, on June 13, 2013 in *Association for Molecular Pathology v. Myriad Genetics, Inc.*, the Court held that claims to isolated genomic DNA are not patent-eligible, but claims to complementary DNA molecules are patent-eligible because they are not a natural product. The effect of the decision on patents for other isolated natural products is uncertain. However, on March 4, 2014, the USPTO issued a memorandum to patent examiners providing guidance for examining claims that recite laws of nature, natural phenomena or natural products under the *Myriad* and *Prometheus* decisions. This guidance did not limit the application of *Myriad* to DNA but, rather, applied the decision to other natural products.

In addition to increasing uncertainty with regard to our ability to obtain future patents, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on these and other decisions by the United States Congress, the federal courts and the USPTO, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our current or future patents.

We may be subject to damages resulting from claims that we or our employees have wrongfully used or disclosed alleged trade secrets of their former employers.

Our employees have been previously employed at other biotechnology or pharmaceutical companies, including our competitors or potential competitors, or at universities or academic medical centers. We also engage advisors and consultants who are concurrently employed at universities or who perform services for other entities. Although we are not aware of any claims currently pending against us, we may be subject to

claims that we or our employees, advisors or consultants have inadvertently or otherwise used or disclosed intellectual property, including trade secrets or other proprietary information, of a former employer or other third party. We may in the future also be subject to claims that an employee, advisor or consultant performed work for us that conflicts with that person's obligations to a third party, such as an employer, and thus, that the third party has an ownership interest in the intellectual property arising out of work performed for us. Litigation may be necessary to defend against these claims. Even if we are successful in defending against these claims, litigation could result in substantial costs and be a distraction to management. If we are unsuccessful in defending against such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. A loss of key personnel or their work product could hamper or prevent our ability to commercialize PRT-201 or any additional product candidates, which would materially adversely affect our commercial development efforts.

Numerous factors may limit any potential competitive advantage provided by our intellectual property rights.

The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations, and may not adequately protect our business, provide a barrier to entry against our competitors or potential competitors, or permit us to maintain our competitive advantage. Moreover, if a third party has intellectual property rights that cover the practice of our technology, we may not be able to exercise or extract value from our intellectual property rights fully or at all. The following examples are illustrative:

- we might not have been the first to make the inventions covered by a patent or pending patent application that we own;
- we might not have been the first to file patent applications covering an invention;
- others may independently develop similar or alternative technologies without infringing our intellectual property rights;
- third parties may compete with us in jurisdictions where we do not pursue and obtain patent protection;
- pending patent applications that we own may not lead to issued patents;
- patents that we own may not provide us with any competitive advantages, or may be held invalid or unenforceable;
- third parties may assert an ownership interest in our intellectual property;
- we may not develop or in-license additional proprietary technologies that are patentable; and
- the patents or proprietary rights of others may have an adverse effect on our business.

Should any of these events occur, they could significantly harm our business and results of operations.

Risks Related to Our Business and Industry

If we fail to attract and keep senior management and key scientific personnel, we may be unable to successfully develop our products, conduct our clinical trials and commercialize our product candidates.

Our future growth and success depend on our ability to recruit, retain, manage and motivate our employees. We are highly dependent on our senior management team, in particular, Timothy Noyes, our President and Chief Executive Officer, Steven Burke, our Senior Vice President and Chief Medical Officer, George Eldridge, our Senior Vice President, Chief Financial Officer, Treasurer and Secretary and Daniel Gottlieb, our Vice President, Marketing and Business Development, as well as the other principal members of our management and scientific teams. Although we have formal employment agreements with our executive officers, these agreements do not prevent them from terminating their employment with us at any time. The loss of the services of any member of our senior management or scientific team or the inability to hire or retain experienced management personnel could adversely affect our ability to execute our business plan and harm our operating results.

Because of the specialized scientific and managerial nature of our business, we rely heavily on our ability to attract and retain qualified scientific, technical and managerial personnel. We do not currently carry "key person" insurance on the lives of members of executive management. The competition for qualified personnel in the pharmaceutical field is intense. Due to this intense competition, we may be unable to continue to attract and retain qualified personnel necessary for the development of our business or to recruit suitable replacement personnel. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy including, F. Nicholas Franano, our scientific founder. Our consultants and advisors may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us.

We will need to significantly increase the size of our organization, and we may experience difficulties in managing growth.

We are currently a small company with 11 full-time employees and one part-time employee as of June 30, 2014. In order to commercialize our potential products, we will need to increase our operations and expand our use of our third-party contractors. We plan to continue to build our compliance, financial and operating infrastructure to ensure the maintenance of a well-managed company including hiring additional staff within our regulatory and clinical groups after Phase 3 is complete. We intend to recruit an in-house commercial organization in the United States focused on promoting PRT-201, if it is approved. We currently do not have a sales and marketing capability and therefore intend to recruit a specialty hospital sales force of approximately 75-100 representatives in anticipation of PRT-201's approval. We estimate it will take three to six months to recruit this specialty hospital sales force. We will need to expand our employment base when we are in the full commercial stages of our current potential product's life cycle.

Future growth will impose significant added responsibilities on members of management, including the need to identify, recruit, maintain and integrate additional employees. In addition, to meet our obligations as a public company, we will need to increase our general and administrative capabilities. Our management, personnel and systems currently in place may not be adequate to support this future growth. Our future financial performance and our ability to commercialize our potential products and to compete effectively will depend, in part, on our ability to manage any future growth effectively. To that end, we must be able to:

- manage our clinical trials and the regulatory process effectively;
- manage the manufacturing of product candidates and potential products for clinical and commercial use;
- integrate current and additional management, administrative, financial and sales and marketing personnel;
- develop a marketing and sales infrastructure;
- hire new personnel necessary to effectively commercialize PRT-201 and any additional product candidates;
- develop our administrative, accounting and management information systems and controls; and
- hire and train additional qualified personnel.

Product candidates that we may acquire or develop in the future may be intended for patient populations that are large. In order to continue development and marketing of these product candidates, if approved, we would need to significantly expand our operations. Our staff, financial resources, systems, procedures or controls may be inadequate to support our operations and our management may be unable to manage successfully future market opportunities or our relationships with customers and other third parties.

Our disclosure controls and procedures may not prevent or detect all errors or acts of fraud.

Upon completion of this offering, we will become subject to the periodic reporting requirements of the Securities Exchange Act of 1934, as amended, or the Exchange Act. Our disclosure controls and procedures are designed to reasonably assure that information required to be disclosed by us in reports we file or submit under the Exchange Act is accumulated and communicated to management, and recorded, processed, summarized and reported within the time periods specified in the rules and forms of the Securities and Exchange Commission, or SEC. We believe that any disclosure controls and procedures or internal controls and procedures, no matter how well conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met.

These inherent limitations include the realities that judgments in decision-making can be faulty, and that breakdowns can occur because of simple error or mistake. Additionally, controls can be circumvented by the individual acts of some persons, by collusion of two or more people or by an unauthorized override of the controls. Accordingly, because of the inherent limitations in our control system, misstatements due to error or fraud may occur and not be detected.

If product liability lawsuits are successfully brought against us, our insurance may be inadequate and we may incur substantial liability.

We face an inherent risk of product liability claims as a result of the clinical testing of PRT-201 or any additional product candidates. We will face an even greater risk if we commercially sell PRT-201 or any additional product candidate that we develop. We maintain primary product liability insurance and excess product liability insurance that cover our clinical trials, and we plan to maintain insurance against product liability lawsuits for commercial sale of our potential products. Historically, the potential liability associated with product liability lawsuits for pharmaceutical products has been unpredictable. Although we believe that our current insurance is a reasonable estimate of our potential liability and represents a commercially reasonable balancing of the level of coverage as compared to the cost of the insurance, we may be subject to claims in connection with our clinical trials and, in the future, commercial use of our potential products, for which our insurance coverage may not be adequate, and the cost of any product liability litigation or other proceeding, even if resolved in our favor, could be substantial.

For example, we may be sued if any product we develop allegedly causes injury or is found to be otherwise unsuitable during clinical testing, manufacturing, marketing or sale. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product, negligence, strict liability or a breach of warranties. Large judgments have been awarded in class action lawsuits based on drugs or biologics that had unanticipated adverse effects. Claims could also be asserted under state consumer protection acts. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit commercialization of PRT-201 or any additional product candidates. Regardless of the merits or eventual outcome, liability claims may result in:

- reduced resources of our management to pursue our business strategy;
- decreased demand for our product candidates or products that we may develop;
- injury to our reputation and significant negative media attention;
- withdrawal of clinical trial participants;
- termination of clinical trial sites or entire trial programs;
- initiation of investigations by regulators;
- product recalls, withdrawals or labeling, marketing or promotional restrictions;
- significant costs to defend resulting litigation;
- diversion of management and scientific resources from our business operations;
- substantial monetary awards to trial participants or patients;
- loss of revenue; and
- the inability to commercialize any products that we may develop.

We currently have a $5 million product liability insurance coverage in connection with our clinical trials and we will need to increase our insurance coverage if and when we begin selling PRT-201 or any additional product candidates if and when they receive marketing approval. However, the product liability insurance we will need to obtain in connection with the commercial sales of PRT-201 or any additional product candidates if and when they receive regulatory approval may be unavailable in meaningful amounts or at a reasonable cost. In addition, insurance coverage is becoming increasingly expensive. If we are unable to obtain or maintain sufficient insurance coverage at an acceptable cost or to otherwise protect against potential product liability claims, it could prevent or inhibit the development and commercial production and sale of PRT-201 or any additional product candidates if and when they obtain regulatory approval, which could materially adversely affect our business, financial condition, results of operations, cash flows and prospects.

Additionally, we do not carry insurance for all categories of risk that our business may encounter. Some of the policies we currently maintain include general liability, employment practices liability, property, auto, workers' compensation, products liability and directors' and officers' insurance. We do not know, however, if we will be able to maintain insurance with adequate levels of coverage. Any significant uninsured liability may require us to pay substantial amounts, which would materially adversely affect our financial position, cash flows and results of operations.

If we engage in acquisitions in the future, we will incur a variety of costs and we may never realize the anticipated benefits of such acquisitions.

We may attempt to acquire businesses, technologies, services, products or product candidates in the future that we believe are a strategic fit with our business. We have no present agreement regarding any material acquisitions. If we do undertake any acquisitions, however, the process of integrating an acquired business, technology, service, products or product candidates into our business may result in unforeseen operating difficulties and expenditures, including diversion of resources and management's attention from our core business. In addition, we may fail to retain key executives and employees of the companies we acquire, which may reduce the value of the acquisition or give rise to additional integration costs. Future acquisitions could result in additional issuances of equity securities that would dilute the ownership of existing stockholders. Future acquisitions could also result in the incurrence of debt, actual or contingent liabilities or the amortization of expenses related to other intangible assets, any of which could adversely affect our operating results. In addition, we may fail to realize the anticipated benefits of any acquisition.

We currently have our active pharmaceutical ingredient, or API, produced for us by a contract manufacturer exclusively in one manufacturing facility and if this or any future facility, any facility we use for storage of the finished product or our equipment were damaged or destroyed, our ability to continue to operate our business would be materially harmed.

Our executive offices are located at 200 Waltham, Massachusetts, and our API is manufactured at Lonza's facility located at Visp, Switzerland. We expect that Lonza plans to utilize this facility in the future to support commercial production if our product candidate is approved. We have manufactured all our finished product for the planned Phase 3 clinical trials of PRT-201 and currently store the finished product in only one location. Extended delays in our Phase 3 clinical trials causing us to need to manufacture new clinical supply would cause a significant disruption in our operations and cause us to incur unexpected costs to manufacture new finished product. We are vulnerable to natural disasters, such as severe storms and other events that could disrupt our operations. We do not carry insurance for natural disasters and we may not carry sufficient business interruption insurance to compensate us for losses that may occur. If the current manufacturing facility or any future facility, stored product or equipment were damaged or destroyed, or if we experience a significant disruption in our operations for any reason, our ability to continue to operate our business would be materially harmed.

If supply is interrupted, there could be a significant disruption in our clinical development and commercial supply. If the supply is interrupted after approval of the BLA, an alternative manufacturer would need to be qualified through a BLA supplement which could result in further delay. The regulatory agencies may also require additional studies if a new manufacturer is relied upon for commercial production. Switching manufacturers may involve substantial costs and would likely result in a delay in our desired clinical and commercial timelines.

These factors could cause the delay of clinical trials, regulatory submissions, required approvals or commercialization of PRT-201 or any additional product candidates, cause us to incur higher costs and prevent us from commercializing our products successfully. Furthermore, if our suppliers fail to meet contractual requirements, and we are unable to secure one or more replacement suppliers capable of production at a substantially equivalent cost, our clinical trials may be delayed or we could lose potential revenue.

Our business and operations would suffer in the event of system failures.

Despite the implementation of security measures, our internal computer systems, and those of our CROs and other third parties on which we rely, are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. If issues were to arise and cause interruptions in our operations, it could result in a material disruption of our drug and biologic development programs. For example, the loss of clinical trial data from completed or ongoing or planned clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach were to result in a loss of or damage to our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability and the further development of PRT-201 or any additional product candidates could be delayed.

Our employees may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements and insider trading, which could significantly harm our business.

We are exposed to the risk of employee fraud or other misconduct. Misconduct by employees could include intentional failures to comply with the regulations of the FDA and non-United States regulators, provide accurate information to the FDA and non-United States regulators, comply with healthcare fraud and abuse laws and regulations in the United States and abroad, and report financial information or data accurately or disclose unauthorized activities to us. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Employee misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. We intend to adopt a code of conduct prior to completion of this offering, but it is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations. If any actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of significant fines or other sanctions.

Recent federal legislation may increase the difficulty and cost for us to commercialize PRT-201 affect the prices we may obtain, and impair our ability to profitably sell PRT-201, if approved.

In the United States and some foreign jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay

marketing approval for PRT-201, restrict or regulate post-approval activities and affect our ability to profitably sell PRT-201, if approved. Legislative and regulatory proposals have been made to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical products. We do not know whether additional legislative changes will be enacted, or whether the FDA regulations, targets or interpretations will be changed, or what the impact of such changes on the marketing approvals of PRT-201, if any, may be. In addition, increased scrutiny by the U.S. Congress of the FDA's approval process may significantly delay or prevent marketing approval, as well as subject us to more stringent product labeling and post-marketing testing and other requirements.

In the United States, the pharmaceutical industry has been significantly affected by legislative initiatives. For example, the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, or the MMA, changed the way Medicare covers and pays for pharmaceutical products. The legislation expanded Medicare coverage for drug purchases by the elderly and introduced a new reimbursement methodology based on average sales prices for drugs. Cost reduction initiatives and other provisions of this legislation could decrease the coverage of, or the reimbursement rate that we receive for, PRT-201, if approved, and could seriously harm our business. While the MMA applies only to reimbursement of drugs under the Medicare program, private payors often follow Medicare coverage policy and payment limitations in setting their own reimbursement rates, and any reduction in reimbursement that results from the MMA may result in a similar reduction in payments from non-governmental payors.

In March 2010, President Obama signed the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act of 2010 or, collectively, the Affordable Care Act, which substantially changes the way healthcare will be financed by both governmental and private insurers, and significantly impacts the pharmaceutical industry. Among the provisions of the Affordable Care Act of importance to our business, including, without limitation, our ability to commercialize, and the prices we may obtain for, PRT-201, if approved for sale, are the following:

- an annual, nondeductible fee on any entity that manufactures or imports specified branded prescription drugs and biologic agents, apportioned among these entities according to their market share in certain government healthcare programs;
- increases in the statutory minimum rebates a manufacturer must pay as a condition to having a drug available for coverage under the Medicaid program;
- expansion of healthcare fraud and abuse laws, including the federal False Claims Act and the federal Anti-Kickback Statute, and the addition of new government investigative powers and enhanced penalties for non-compliance;
- extension of a manufacturer's Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations;
- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to additional individuals and by adding new eligibility categories for certain individuals with income at or below 133% of the federal poverty level beginning in 2014, thereby potentially increasing a manufacturer's Medicaid rebate liability;
- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program;
- new requirements under the federal Open Payments program and its implementing regulations;
- a new requirement to annually report drug samples that manufacturers and distributors provide to physicians; and
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research.

In addition, other legislative changes have been proposed and adopted since the Affordable Care Act was enacted. These changes include aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, which went into effect in April 2013. In January 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, which, among other things, reduced Medicare payments to several

types of providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. The full impact on our business of the Affordable Care Act and other new laws is uncertain but may result in additional reductions in Medicare and other healthcare funding. Nor is it clear whether other legislative changes will be adopted, if any, or how such changes would affect the demand for PRT-201, if approved.

Governments outside the United States tend to impose strict price controls, which may adversely affect our revenues, if any.

In international markets, reimbursement and health care payment systems vary significantly by country, and many countries have instituted price ceilings on specific products and therapies. In some countries, particularly the countries of the European Union, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product. To obtain coverage and reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost-effectiveness of our product candidate to other available therapies. There can be no assurance that our products will be considered cost-effective by third-party payors, that an adequate level of reimbursement will be available or that the third-party payors' reimbursement policies will not adversely affect our ability to sell our products profitably. If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be harmed, possibly materially.

Risks Related to Our Common Stock and This Offering

We are an "emerging growth company" and as a result of the reduced disclosure and governance requirements applicable to emerging growth companies, our common stock may be less attractive to investors.

We are an "emerging growth company" as defined in the JOBS Act, and we intend to take advantage of certain exemptions from various reporting requirements that are applicable to other public companies that are not emerging growth companies, including: not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act, reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements, and exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved.

We may take advantage of these reporting exemptions until we are no longer an emerging growth company. We will remain an emerging growth company until the earlier of (1) the last day of the fiscal year (a) following the fifth anniversary of the completion of this offering, (b) in which we have total annual gross revenue of at least $1 billion, or (c) in which we are deemed to be a large accelerated filer, which means the market value of our common stock that is held by non-affiliates exceeds $700 million as of June 30th of such fiscal year, and (2) the date on which we have issued more than $1 billion in non-convertible debt during the prior three-year period.

We have taken advantage of reduced reporting burdens in this prospectus. In particular, in this prospectus, we have provided only two years of audited financial statements and have not included all of the executive compensation related information that would be required if we were not an emerging growth company. We cannot predict whether investors will find our common stock less attractive if we rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile. In addition, the JOBS Act provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards. This allows an emerging growth company to delay the adoption of these accounting standards until they would otherwise apply to private companies. We have irrevocably elected not to avail ourselves of this exemption and, therefore, we will be subject to the

same new or revised accounting standards as other public companies that are not emerging growth companies.

Even after we no longer qualify as an emerging growth company, we may still qualify as a "smaller reporting company" which would allow us to take advantage of many of the same exemptions from disclosure requirements, including not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act and reduced disclosure obligations regarding executive compensation in this prospectus and our periodic reports and proxy statements. We cannot predict if investors will find our common stock less attractive because we will rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile.

There has been no public market for our common stock prior to this offering, and you may not be able to resell our shares at or above the price you paid, or at all.

Prior to this offering, there has been no public market for our common stock. We intend to apply to list our common stock on The NASDAQ Global Market, or NASDAQ, but an active trading market for our common stock may never develop or be sustained following this offering. If an active trading market for our common stock does not develop after this offering, the market price and liquidity of our common stock will be materially and adversely affected. You may not be able to sell your shares quickly or at the market price if trading in our common shares is not active. The offering price for our common stock will be determined by negotiations between us and the underwriters and may bear no relationship to the market price for our common stock after this offering. An active trading market for our common stock may not develop and the market price of our common stock may decline below the offering price. Further, an inactive market may also impair our ability to raise capital by selling shares of our common stock and may impair our ability to enter into strategic partnerships or acquire companies or products by using our shares of common stock as consideration.

The market price for our common stock may be volatile, which could contribute to the loss of your investment.

Fluctuations in the price of our common stock could contribute to the loss of all or part of your investment. Prior to this offering, there has not been a public market for our common stock. Accordingly, the initial public offering price for the shares of our common stock may not be indicative of the price that will prevail in the trading market, if any, that develops following this offering. If an active market for our common stock develops and continues, the trading price of our common stock following this offering is likely to be highly volatile and could be subject to wide fluctuations in response to various factors, some of which are beyond our control. Any of the factors listed below could have a material adverse effect on your investment in our common stock and our common stock may trade at prices significantly below the initial public offering price. In such circumstances the trading price of our common stock may not recover and may experience a further decline.

Factors affecting the trading price of our common stock may include:

- our failure to develop and commercialize PRT-201 or any additional product candidates;
- actual or anticipated fluctuations in our quarterly financial results or the quarterly financial results of companies perceived to be similar to us;
- changes in the market's expectations about our operating results;
- adverse results or delays in preclinical studies or clinical trials;
- our decision to initiate a clinical trial, not to initiate a clinical trial or to terminate an existing clinical trial;
- adverse regulatory decisions, including failure to receive regulatory approval for PRT-201 or any additional product candidates;
- success of competitive products;

- adverse developments concerning our collaborations and our manufacturers;
- inability to obtain adequate product supply for any product candidate for clinical trials or commercial sale or inability to do so at acceptable prices;
- the termination of a collaboration or the inability to establish additional collaborations;
- unanticipated serious safety concerns related to the use of any of PRT-201 or any additional product candidates;
- our ability to effectively manage our growth;
- the size and growth, if any, of the targeted market;
- our operating results failing to meet the expectation of securities analysts or investors in a particular period or failure of securities analysts to publish reports about us or our business;
- changes in financial estimates and recommendations by securities analysts concerning our company, our market opportunity, or the biotechnology and pharmaceutical industries in general;
- operating and stock price performance of other companies that investors deem comparable to us;
- overall performance of the equity markets;
- announcements by us or our competitors of acquisitions, new product candidates or programs, significant contracts, commercial relationships or capital commitments;
- our ability to successfully market PRT-201 or any additional product candidates;
- changes in laws and regulations affecting our business, including but not limited to clinical trial requirements for approvals;
- disputes or other developments relating to proprietary rights, including patents, litigation matters and our ability to obtain patent protection for PRT-201 or any additional product candidates;
- commencement of, or involvement in, litigation involving our company, our general industry, or both;
- changes in our capital structure, such as future issuances of securities or the incurrence of additional debt;
- the volume of shares of our common stock available for public sale;
- additions or departures of key scientific or management personnel;
- any major change in our board or management;
- changes in accounting practices;
- ineffectiveness of our internal control over financial reporting;
- sales of substantial amounts of common stock by our directors, executive officers or significant stockholders or the perception that such sales could occur; and
- general economic and political conditions such as recessions, interest rates, fuel prices, international currency fluctuations and acts of war or terrorism.

Broad market and industry factors may materially harm the market price of our common stock irrespective of our operating performance. The stock market in general, and NASDAQ and the market for biotechnology companies in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of the particular companies affected. The trading prices and valuations of these stocks, and of ours, may not be predictable. A loss of investor confidence in the market for technology or software stocks or the stocks of other companies which investors perceive to be similar to us, the opportunities in the digital simulation market or the stock market in general, could depress our stock price regardless of our business, prospects, financial conditions or results of operations.

Raising additional funds through debt or equity financing could be dilutive and may cause the market price of our common stock to decline.

Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of equity offerings and debt financings, and potentially through license and development agreements with strategic partnerships with third parties. To the extent that additional capital is raised through the sale of equity or convertible debt securities, the issuance of those securities

could result in substantial dilution for our current stockholders and the terms may include liquidation or other preferences that adversely affect the rights of our current stockholders. Furthermore, the issuance of additional securities, whether equity or debt, by us, or the possibility of such issuance, may cause the market price of our common stock to decline and existing stockholders may not agree with our financing plans or the terms of such financings. Moreover, the incurrence of debt financing could result in a substantial portion of our operating cash flow being dedicated to the payment of principal and interest on such indebtedness and could impose restrictions on our operations, such as limitations on our ability to incur additional debt, limitations on our ability to acquire, sell or license intellectual property rights and other operating restrictions that could adversely impact our ability to conduct our business. Additional funding may not be available to us on acceptable terms, or at all.

If securities analysts do not publish research or reports about our business or if they downgrade our stock, the price of our common stock could decline.

The trading market for our common stock will rely in part on the research and reports that industry or financial analysts publish about us, our business, our markets and our competitors. We do not control these analysts. If securities analysts do not cover our common stock after the closing of this offering, the lack of research coverage may adversely affect the market price of our common stock. Furthermore, if one or more of the analysts who do cover us downgrade our stock or if those analysts issue other unfavorable commentary about us or our business, our stock price would likely decline. If one or more of these analysts cease coverage of us or fails to regularly publish reports on us, we could lose visibility in the market and interest in our stock could decrease, which in turn could cause our stock price or trading volume to decline and may also impair our ability to expand our business with existing customers and attract new customers.

The concentration of our capital stock ownership with insiders upon the closing of this offering will likely limit your ability to influence corporate matters.

We anticipate that our executive officers, employees, directors, current 5% or greater stockholders, and their respective affiliates will together beneficially own or control, in aggregate, approximately % of the shares of our outstanding common stock, after giving effect to the conversion of all outstanding preferred stock and assuming no exercise of outstanding options or warrants following the closing of this offering (assuming no exercise of the underwriters' option to purchase additional shares). As a result, these executive officers, directors and principal stockholders, acting together, will have substantial influence over most matters that require approval by our stockholders, including the election of directors, any merger, consolidation or sale of all or substantially all or of our assets or any other significant corporate transaction. Corporate action might be taken even if other stockholders, including those who purchase shares in this offering, oppose such action. These stockholders may delay or prevent a change of control or otherwise discourage a potential acquirer from attempting to obtain control of our company, even if such change of control would benefit our other stockholders. This concentration of stock ownership may adversely affect investors' perception of our corporate governance or delay, prevent or cause a change in control of our company, any of which could adversely affect the market price of our common stock.

Sales of a substantial number of shares of our common stock by our existing stockholders in the public market may cause our stock price to decline.

Sales of our common stock in the public market after this offering, or the perception that these sales may occur, could cause the market price of our common stock to decline. Based on our shares of common stock outstanding as of June 30, 2014, upon the closing of this offering, we will have shares of common stock outstanding, assuming no exercise of the underwriters' over-allotment option. Of these, only the shares of our common stock sold in this offering, plus any shares sold upon exercise of the underwriters' over-allotment option, will be freely transferable without restriction or additional registration under the Securities Act of 1933, as amended, or the Securities Act. The remaining shares outstanding after this offering will be available for sale, upon the expiration of the 180-day lock-up period

beginning from the date of this prospectus, if applicable, subject to volume and other restrictions as applicable under Rule 144 under the Securities Act. Any or all of these shares may be released prior to expiration of the lock-up period at the discretion of the lead underwriter for this offering. After the lock-up agreements expire, up to an additional shares of common stock will be eligible for sale in the public market, of which shares are held by directors, executive officers and other affiliates and will be subject to volume limitations under Rule 144 under the Securities Act, assuming an initial public offering price of $ per share (the midpoint of the price range set forth on the cover page of this prospectus). In addition, shares of common stock that are either subject to outstanding options or reserved for future issuance under our employee benefit plans will become eligible for sale in the public market to the extent permitted by the provisions of various vesting schedules, the lock-up agreements and Rule 144 and Rule 701 under the Securities Act. To the extent these shares are sold, or if it is perceived that they will be sold, into the market, the market price of our common stock could decline. For a further description of the dilution that you will experience immediately after this offering, see the section entitled "Share Eligible for Future Sale."

Future sales and issuances of our common stock or rights to purchase common stock, including pursuant to our equity incentive plans, could result in additional dilution of the percentage ownership of our stockholders and could cause our stock price to fall.

We expect that significant additional capital will be needed in the future to continue our planned operations, including conducting clinical trials, commercialization efforts, expanded research and development activities and costs associated with operating a public company. To raise capital, we may sell common stock, convertible securities or other equity securities in one or more transactions at prices and in a manner we determine from time to time. If we sell common stock, convertible securities or other equity securities in more than one transaction, investors may be materially diluted by subsequent sales. Such sales may also result in material dilution to our existing stockholders, and new investors could gain rights, preferences and privileges senior to the holders of our common stock, including shares of common stock sold in this offering.

You will experience immediate and substantial dilution in the net tangible book value of the shares you purchase in this offering.

If you purchase shares of our common stock in this offering, you will experience immediate and substantial dilution, as the initial public offering price of our common stock will be substantially greater than the net tangible book value per share of our common stock. Based on an initial offering price of $ per share, which is the midpoint of the range on the cover page of this prospectus, if you purchase our common stock in this offering, you will suffer immediate and substantial dilution of approximately $ per share. Further, investors purchasing common stock in this offering will contribute approximately % of the total amount invested by stockholders since our inception, but will own only approximately % of the shares of common stock outstanding after giving effect to this offering. If the underwriters exercise their over-allotment option, or if outstanding options and warrants to purchase our common stock are exercised, you will experience additional dilution. For a further description of the dilution that you will experience immediately after this offering, see the section entitled "Dilution."

We have broad discretion in the use of net proceeds from this offering and may not use them effectively.

We currently intend to use the net proceeds from this offering to fund the continued development of PRT-201 and for working capital and other general corporate purposes, including funding the costs of operating a public company. We may also use the proceeds to acquire and develop other products, including other drugs and biologics. For a further description of our use of proceeds from this offering, see the section entitled "Use of Proceeds." Any remaining amounts will be used for general corporate purposes, general and administrative expenses, capital expenditures, working capital and prosecution and maintenance of our intellectual property. Although we currently intend to use the net proceeds from this

offering in such a manner, we will have broad discretion in the application of the net proceeds. Our failure to apply these funds effectively could affect our ability to continue to develop and commercialize our product candidate.

We will incur significant increased costs as a result of operating as a public company, and our management will be required to devote substantial time to new compliance initiatives.

As a newly public company, we will incur significant legal, accounting and other expenses that we did not incur as a private company. In addition, the Sarbanes-Oxley Act, and rules of the SEC and those of NASDAQ have imposed various requirements on public companies including requiring establishment and maintenance of effective disclosure and financial controls. Our management and other personnel will need to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations have increased and will continue to increase our legal and financial compliance costs and will make some activities more time-consuming and costly.

The Sarbanes-Oxley Act requires, among other things, that we maintain effective internal control over financial reporting and disclosure controls and procedures. In particular, we must perform system and process evaluation and testing of our internal control over financial reporting to allow management to report on the effectiveness of our internal control over financial reporting, as required by Section 404 of the Sarbanes-Oxley Act. In addition, we will be required to have our independent registered public accounting firm attest to the effectiveness of our internal control over financial reporting the later of our second annual report on Form 10-K or the first annual report on Form 10-K following the date on which we are no longer an emerging growth company. Our compliance with Section 404 of the Sarbanes-Oxley Act will require that we incur substantial accounting expense and expend significant management efforts. We currently do not have an internal audit group, and we will need to hire additional accounting and financial staff with appropriate public company experience and technical accounting knowledge. If we are not able to comply with the requirements of Section 404 in a timely manner, or if we or our independent registered public accounting firm identify deficiencies in our internal control over financial reporting that are deemed to be material weaknesses, the market price of our stock could decline and we could be subject to sanctions or investigations by NASDAQ, the SEC or other regulatory authorities, which would require additional financial and management resources.

Our ability to successfully implement our business plan and comply with Section 404 requires us to be able to prepare timely and accurate financial statements. We expect that we will need to continue to improve existing, and implement new operational and financial systems, procedures and controls to manage our business effectively. Any delay in the implementation of, or disruption in the transition to, new or enhanced systems, procedures or controls, may cause our operations to suffer and we may be unable to conclude that our internal control over financial reporting is effective and to obtain an unqualified report on internal controls from our auditors as required under Section 404 of the Sarbanes-Oxley Act. This, in turn, could have an adverse impact on trading prices for our common stock, and could adversely affect our ability to access the capital markets.

We do not expect to pay any cash dividends for the foreseeable future.

You should not rely on an investment in our common stock to provide dividend income. We do not anticipate that we will pay any cash dividends to holders of our common stock in the foreseeable future. Instead, we plan to retain any earnings to maintain and expand our operations. Accordingly, investors must rely on sales of their common stock after price appreciation, which may never occur, as the only way to realize any return on their investment. As a result, investors seeking cash dividends should not purchase our common stock.

Our ability to use our net operating loss carryovers and certain other tax attributes may be limited.

As described above under "—Risks Related to Our Financial Condition and Need for Additional Capital", we have incurred net losses since our inception and anticipate that we will continue to incur significant losses for the foreseeable future. Under the Internal Revenue Code of 1986, as amended, or the Code, a corporation is generally allowed a deduction for net operating losses, or NOLs, carried over from a prior taxable year. Under that provision, we can carry forward our NOLs to offset our future taxable income, if any, until such NOLs are used or expire. The same is true of other unused tax attributes, such as tax credits. The amounts of our unused carryovers of NOLs and tax credits as of December 31, 2013, and a description of the valuation allowance we have recorded with respect to those items, are set forth below under "Management's Discussion and Analysis of Financial Condition and Results of Operations."

If a corporation undergoes an "ownership change," generally defined as a greater than 50% change (by value) in its equity ownership over a three-year period, Sections 382 and 383 of the Code limit the corporation's ability to use carryovers of its pre-change NOLs, credits and certain other tax attributes to reduce its tax liability for periods after the ownership change. Our issuance of common stock pursuant to this offering may result in a limitation under Sections 382 and 383, either separately or in combination with certain prior or subsequent shifts in the ownership of our common stock. As a result, our ability to use carryovers of our pre-change NOLs and credits to reduce our future U.S. federal income tax liability may be subject to limitations. This could result in increased U.S. federal income tax liability for us if we generate taxable income in a future period. Limitations on the use of NOLs and other tax attributes could also increase our state tax liability. The use of our tax attributes will also be limited to the extent that we do not generate positive taxable income in future tax periods.

We could be subject to securities class action litigation.

In the past, securities class action litigation has often been brought against a company following a decline in the market price of its securities. This risk is especially relevant for us because biotechnology companies have experienced significant stock price volatility in recent years. If we face such litigation, it could result in substantial costs and a diversion of management's attention and resources, which could harm our business.

Provisions in our restated certificate of incorporation, our amended and restated bylaws and Delaware law may have anti-takeover effects that could discourage an acquisition of us by others, even if an acquisition would be beneficial to our stockholders, and may prevent attempts by our stockholders to replace or remove our current management.

Our restated certificate of incorporation, amended and restated bylaws and Delaware law contain provisions that may have the effect of delaying or preventing a change in control of us or changes in our management. Our restated certificate of incorporation and bylaws include provisions that:

- authorize "blank check" preferred stock, which could be issued by our board of directors without stockholder approval and may contain voting, liquidation, dividend and other rights superior to our common stock;
- create a classified board of directors whose members serve staggered three-year terms;
- specify that special meetings of our stockholders can be called only by our board of directors;
- prohibit stockholder action by written consent;
- establish an advance notice procedure for stockholder approvals to be brought before an annual meeting of our stockholders, including proposed nominations of persons for election to our board of directors;
- provide that our directors may be removed only for cause;
- provide that vacancies on our board of directors may be filled only by a majority of directors then in office, even though less than a quorum;
- specify that no stockholder is permitted to cumulate votes at any election of directors;

- expressly authorize our board of directors to modify, alter or repeal our amended and restated bylaws; and
- require supermajority votes of the holders of our common stock to amend specified provisions of our restated certificate of incorporation and amended and restated bylaws.

These provisions, alone or together, could delay or prevent hostile takeovers and changes in control or changes in our management.

In addition, because we are incorporated in the state of Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which limits the ability of stockholders owning in excess of 15% of our outstanding voting stock to merge or combine with us.

Any provision of our restated certificate of incorporation or amended and restated bylaws or Delaware law that has the effect of delaying or deterring a change in control could limit the opportunity for our stockholders to receive a premium for their shares of our common stock, and could also affect the price that some investors are willing to pay for our common stock.

Our restated certificate of incorporation designates the Court of Chancery of the State of Delaware and federal court within the State of Delaware as the exclusive forum for certain types of actions and proceedings that may be initiated by our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers or employees.

Our restated certificate of incorporation provides that, subject to limited exceptions, the Court of Chancery of the State of Delaware and federal court within the State of Delaware will be exclusive forums for (1) any derivative action or proceeding brought on our behalf, (2) any action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers or other employees to us or our stockholders, (3) any action asserting a claim against us arising pursuant to any provision of the Delaware General Corporation Law, our restated certificate of incorporation or our amended and restated bylaws, or (4) any other action asserting a claim against us that is governed by the internal affairs doctrine. Any person or entity purchasing or otherwise acquiring any interest in shares of our capital stock shall be deemed to have notice of and to have consented to the provisions of our restated certificate of incorporation described above. This choice of forum provision may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers or other employees, which may discourage such lawsuits against us and our directors, officers and employees. Alternatively, if a court were to find these provisions of our restated certificate of incorporation inapplicable to, or unenforceable in respect of, one or more of the specified types of actions or proceedings, we may incur additional costs associated with resolving such matters in other jurisdictions, which could adversely affect our business and financial condition.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus contains forward-looking statements, which reflect our current views with respect to, among other things, our operations and financial performance. You can identify these forward-looking statements by the use of words such as "outlook," "believes," "expects," "potential," "continues," "may," "will," "should," "seeks," "approximately," "predicts," "intends," "plans," "estimates," "anticipates" or the negative version of these words or other comparable words. These forward-looking statements are subject to various risks and uncertainties. Accordingly, there are or will be important factors that could cause actual outcomes or results to differ materially from those indicated in these statements. We believe these factors include but are not limited to those described under "Risk Factors" and include, among other things:

- the timing of results of our ongoing and planned clinical trials for PRT-201;
- our estimates regarding the amount of funds we require to complete our two planned Phase 3 clinical trials for PRT-201;
- our estimate of when we will require additional funding;
- our plans to commercialize PRT-201;
- the timing of, and our ability to, obtain and maintain regulatory approvals for our product candidates;
- the rate and degree of market acceptance and clinical utility of any approved product candidate;
- the potential benefits of strategic partnership agreements and our ability to enter into selective strategic partnership arrangements;
- our ability to quickly and efficiently identify and develop product candidates;
- our commercialization, marketing and manufacturing capabilities and strategy;
- our intellectual property position; and
- our estimates regarding expenses, future revenues, capital requirements, the sufficiency of our current and expected cash resources and our need for additional financing.

These factors should not be construed as exhaustive and should be read in conjunction with the other cautionary statements that are included in this prospectus. We undertake no obligation to publicly update or review any forward-looking statement, whether as a result of new information, future developments or otherwise.

USE OF PROCEEDS

We estimate that our net proceeds from this offering will be approximately $ million, assuming an initial public offering price of $ per share, which is the midpoint of the price range set forth on the cover page of this prospectus, after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. If the underwriters exercise their option to purchase additional shares in full, we estimate that our net proceeds from this offering will be approximately $ million.

Each $1.00 increase or decrease in the assumed initial public offering price of $ per share, which is the midpoint of the price range set forth on the cover page of this prospectus, would result in an approximately $ million increase or decrease in our net proceeds from this offering, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same, and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us. Each increase or decrease of one million shares in the number of shares to be offered by us would increase or decrease our net proceeds from this offering by approximately $ million, assuming that the public offering price is $ per share, the midpoint of the price range set forth on the cover page of this prospectus and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us.

We expect to use the net proceeds of this offering as follows:

- approximately $ million to accelerate the commencement of the second of our Phase 3 trials for PRT-201 in its lead indication;
- approximately $ million to accelerate our chemistry and manufacturing controls, or CMC, activities;
- approximately $ million to fund additional research and development activities, including preliminary clinical work for additional indications; and
- the remainder for working capital and general corporate purposes and the costs associated with being a public company.

Our expected use of net proceeds from this offering represents our intentions based upon our present plans and business conditions, which could change in the future as our plans and business conditions evolve. The amount and timing of our actual expenditures will depend upon numerous factors, including the results of our ongoing clinical trials and clinical trials that we may commence, feedback from regulatory agencies, the timing of approval of any of our product candidates, the results of any commercialization efforts and other factors. As a result, our management will have broad discretion over the use of the net proceeds from this offering.

Pending the use of the proceeds from this offering, we intend to invest the net proceeds in short-term, interest-bearing, investment-grade securities, certificates of deposit or government securities.

DIVIDEND POLICY

We have never declared or paid any cash dividends on our common stock. We currently intend to retain all of our future earnings, if any, to finance the growth and development of our business. We do not intend to pay cash dividends to holders of our common stock in the foreseeable future.

CAPITALIZATION

The following table sets forth our cash and capitalization as of June 30, 2014 on:

- an actual basis;
- a pro forma basis to give effect to the automatic conversion of all outstanding shares of our preferred stock into an aggregate of 134,918,694 shares of common stock upon the closing of this offering and the filing of our amended and restated certificate of incorporation upon the closing of this offering; and
- a pro forma as adjusted basis to give further effect to the sale of shares of our common stock offered in this offering, assuming an initial public offering price of $ per share, the midpoint of the price range set forth on the cover page of this prospectus, after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us.

You should read this table together with the information contained in this prospectus, including "Management's Discussion and Analysis of Financial Condition and Results of Operations" and the historical financial statements and related notes included elsewhere in this prospectus.

	As of June 30, 2014		
	Actual	Pro Forma	Pro Forma as Adjusted
	(unaudited)		
	(in thousands, except share and per share data)		
Cash and cash equivalents	$ 25,416	$ 25,416	
Convertible Preferred Stock:			
Series A redeemable convertible preferred stock, par value $0.001 per share; 22,638,465 shares authorized, issued and outstanding, actual; no shares authorized, issued or outstanding, pro forma and pro forma as adjusted	35,015	—	
Series A-1 redeemable convertible preferred stock, par value $0.001 per share; 10,909,091 shares authorized, issued and outstanding, actual; no shares authorized, issued or outstanding, pro forma and pro forma as adjusted	17,790	—	
Series B redeemable convertible preferred stock, par value $0.001 per share; 20,754,461 shares authorized, issued and outstanding, actual; no shares authorized, issued or outstanding, pro forma and pro forma as adjusted	28,573	—	
Series C redeemable convertible preferred stock, par value $0.001 per share; 17,550,758 shares authorized, 13,202,932 shares issued and outstanding, actual; no shares authorized, issued or outstanding, pro forma and pro forma as adjusted	17,982	—	
Series D redeemable preferred stock, par value $0.01 per share including associated investors' rights liability of $6,580; 86,789,527 shares authorized, 52,813,827 shares issued and outstanding, actual; no shares authorized issued or outstanding, pro forma and pro forma as adjusted	31,124		
Total convertible preferred stock	130,193	—	—
Stockholders' deficit:			
Preferred stock, par value $0.001 per share; no shares authorized, issued and outstanding, actual, shares authorized, no shares issued and outstanding pro forma and pro forma as adjusted	—	—	—
Common stock, par value $0.001 per share; 205,926,290 shares authorized, 3,833,606 shares issued and outstanding, actual; 205,926,290 shares authorized, 138,752,300 shares issued and outstanding, pro forma and shares authorized, shares issued and outstanding, pro forma as adjusted	4	139	
Additional paid-in capital	—	123,769	
Accumulated deficit	(109,271)	(102,691)	
Accumulated other comprehensive income	(23)	(23)	
Total stockholders' (deficit) equity	(109,290)	21,194	
Total capitalization	$ 21,194	$ 21,194	

Each $1.00 increase or decrease in the assumed initial public offering price of $ per share, the mid-point of the price range set forth on the cover page of this prospectus, would increase or decrease each of cash and cash equivalents, additional paid-in capital, total stockholders' deficit and total capitalization on a pro forma as adjusted basis by approximately $ million, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. Each increase or decrease of 1,000,000 shares in the number of shares offered by us would increase or decrease each of cash and cash equivalents, additional paid-in capital, total stockholders' deficit and total capitalization on a pro forma as adjusted basis by approximately $ million, assuming no change in the assumed initial public offering price of $ per share and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us.

The table above does not include the following potentially dilutive shares of common stock outstanding at June 30, 2014:

- 17,982,120 shares of our common stock issuable upon the exercise of stock options outstanding at a weighted-average exercise price of $0.22 per share;
- 10,471,282 shares of our common stock issuable upon the exercise of outstanding warrants at a weighted average exercise price of $0.29 per share that we expect to be exercised in full prior to the closing of this offering;
- 18,361 shares of common stock reserved for issuance pursuant to future equity awards under our 2006 Equity Incentive Plan; and
- shares of common stock reserved for future issuance under our 2014 Equity Incentive Plan, which will become effective immediately prior to the closing of this offering (including shares reserved for issuance under our 2006 Equity Incentive Plan, which will be added to the shares reserved for issuance under the 2014 Equity Incentive Plan upon its effectiveness).

Series D Convertible Preferred Stock

Initial issuance of Series D convertible preferred stock. On May 13, 2014, we entered into a Series D Convertible Preferred Stock Purchase Agreement, or the Series D Purchase Agreement, pursuant to which (i) we sold and issued a total of 10,344,201 shares of Series D convertible preferred stock upon the conversion of approximately $4.5 million of principal and accrued interest outstanding under convertible promissory notes at a conversion price of $0.4414 per share, and (ii) we sold and issued 42,469,626 shares of Series D convertible preferred stock to new and existing investors for aggregate gross proceeds of $25.0 million at a price per share of $0.588656.

Additional issuances of Series D convertible preferred stock. The Series D Purchase Agreement also contemplates our sale in two additional subsequent closings, which we refer to as the second tranche and third tranche closings, of up to an additional 33,975,700 shares of our Series D convertible preferred stock. Our right to cause the second and third tranche closings to occur will terminate at the closing of this offering.

Individual Purchase Rights after the closing of this offering. Following the closing of this offering, the investors that are parties to the Series D Purchase Agreement will have individual purchase rights under the Series D Purchase Agreement to purchase from us, at any time and from time to time until May 13, 2024, an aggregate of shares of our common stock, assuming an initial public offering price of $ per share, the midpoint of the price range set forth on the cover page of this prospectus, and assuming also that such individual purchase rights are not terminated, in whole or in part, as described below in this paragraph. The purchase price per share for common stock purchased pursuant to such individual purchase rights will be the lower of (i) 0.588656, the Series D conversion price immediately prior to this offering and (ii) the initial public offering price. If we or our underwriters offer to the investors that

are parties to the Series D Purchase Agreement the opportunity to purchase shares of common stock in this offering, which offer to purchase will be made only if so determined by us or our underwriters at the sole discretion of us or our underwriters, then the individual purchase rights under the Series D Purchase Agreement of such investors shall terminate at the closing of this offering to the extent of the number of shares of our common stock that such investors are offered the opportunity to purchase in this offering, regardless of whether such investors actually purchase any of such shares so offered in this offering. For example, if the individual purchase rights under the Series D Purchase Agreement of the investors that are parties to the Series D Purchase Agreement are exercisable to purchase from us an aggregate of shares of our common stock, and if we or our underwriters offer to such investors the opportunity to purchase an aggregate of shares of our common stock in this offering, then the individual purchase rights under the Series D Purchase Agreement of such investors shall terminate at the closing of this offering, regardless of whether such investors actually purchase any of the shares of our common stock that such investors are offered the opportunity to purchase in this offering. On the other hand, if, for example, the individual purchase rights under the Series D Purchase Agreement of the investors that are parties to the Series D Purchase Agreement are exercisable to purchase from us an aggregate of shares of our common stock, and if we or our underwriters offer to such investors the opportunity to purchase an aggregate of only shares of our common stock in this offering, then, regardless of whether such investors actually purchase any of such shares so offered in this offering, the individual purchase rights under the Series D Purchase Agreement of such investors shall terminate at the closing of this offering with respect to an aggregate of shares of our common stock and shall remain exercisable, at any time and from time to time until May 13, 2024, with respect to an aggregate of shares of our common stock.

Anti-dilution protection for Series D convertible preferred stock. At the closing of this offering, our Series D convertible preferred stock will automatically convert into a number of shares of our common stock equal to (i) shares plus (ii) an incremental amount of shares. This incremental amount of shares will be applicable only if we or our underwriters offer to the holders of shares of our Series D convertible preferred stock the opportunity to purchase shares in this offering, such holders purchase shares in this offering and the initial public offering price per share is greater than $, the purchase price per share of our Series D convertible preferred stock. This incremental amount of shares will be determined by multiplying (x) the number of shares of common stock purchased in this offering by the holders of our Series D convertible preferred stock up to a maximum number of shares of our common stock equal to shares, which number of shares is equal to the number of shares of our Series D convertible preferred stock that such holders would have been entitled to purchase under the Series D Purchase Agreement at the second and third tranche closings if the second and third tranche closings had been consummated prior to the closing of this offering, by (y) the remainder obtained by subtracting the number one from the quotient obtained by dividing the initial public offering price per share by $, the purchase price per share of our Series D convertible preferred stock.

Upon the closing of this offering, assuming an initial public offering price of $ per share, the midpoint of the price range set forth on the cover page of this prospectus, and assuming that none of the holders of our Series D convertible preferred stock purchase shares of our common stock in this offering, then the shares of our Series D convertible preferred stock outstanding as of , 2014 automatically will convert into shares of our common stock.

Upon the closing of this offering, assuming an initial public offering price of $ per share, the midpoint of the price range set forth on the cover page of this prospectus, and assuming that the holders of our Series D convertible preferred stock purchase in this offering an aggregate of at least shares of our common stock, which number of shares is equal to the number of shares of our Series D convertible preferred stock that such holders would have been entitled to purchase under the Series D Purchase Agreement at the second and third tranche closings if the second and third tranche closings had been consummated prior to the closing of this offering, then the shares of our Series D convertible preferred stock outstanding as of , 2014 automatically will convert into shares of our

common stock. Each $1.00 decrease in the assumed initial public offering price (until the assumed initial public offering price is equal to $) would decrease by an additional shares the number of shares of our common stock that would be issued upon the conversion of our Series D convertible preferred stock at the closing of this offering. In the event of a decrease in the assumed initial public offering price to a price that is equal to or less than $, the shares of our Series D convertible preferred stock outstanding as of , 2014 automatically will convert into shares of our common stock upon the closing of this offering. Each $1.00 increase in the assumed initial public offering price above $ would increase by an additional shares the number of shares of our common stock that would be issued upon the conversion of our Series D convertible preferred stock at the closing of this offering. In the event that the assumed initial public offering price is greater than $, each decrease of shares in the number of shares purchased in this offering by holders of our Series D convertible preferred stock would decrease by an additional shares the number of shares of our common stock that would be issued upon the conversion of our Series D convertible preferred stock at the closing of this offering.

The following number of shares of common stock would be outstanding upon the conversion of our Series D convertible preferred stock, assuming the initial public offering prices for our common stock shown below:

	Assumed Initial Public Offering Price				
	$ .00	$ .00	$ .00	$ .00	$ .00
Shares Outstanding					

DILUTION

If you invest in our common stock in this offering, your ownership interest will be diluted immediately to the extent of the difference between the public offering price per share of our common stock and the pro forma net tangible book value per share of our common stock after this offering.

Our historical net tangible book deficit as of June 30, 2014 was $(109.3) million or $(28.51) per share of common stock, based on 3,833,606 shares of common stock outstanding as of June 30, 2014. Historical net tangible book value per share is determined by dividing our total tangible assets less total liabilities and redeemable preferred stock by the actual number of shares of common stock outstanding.

Our pro forma net tangible book gain as of June 30, 2014 was $21.2 million, or $0.15 per share of common stock, based on 138,752,300 shares of common stock outstanding after giving effect to the automatic conversion of all of our outstanding series A, A-1, B, C and D convertible preferred stock into 134,918,694 shares of common stock upon the listing of our common stock on the NASDAQ Global Market. These shares include an additional 14,599,918 shares of common stock issuable upon conversion of all of our outstanding series A, A-1, B and C convertible preferred stock, which additional shares are issuable as a result of conversion price adjustments in the anti-dilution provisions of our series A, A-1, B and C convertible preferred stock, as a result of the issue price of our series D convertible preferred stock and which is described in the section of this prospectus entitled "Capitalization—Series D Preferred Stock Financing."

Pro forma net tangible book value per share is determined by dividing our total tangible assets less total liabilities and redeemable preferred stock by the pro forma number of shares of common stock outstanding at June 30, 2014 before giving effect to our sale of shares of common stock in this offering.

After giving further effect to our issuance and sale of shares of our common stock in this offering at an assumed initial public offering price of $ per share, which is the midpoint of the price range set forth on the cover page of this prospectus, after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us, our pro forma net tangible book value as of June 30, 2014 would have been $ million, or $ per share. This represents an immediate increase in pro forma net tangible book value per share of $ to existing stockholders and immediate dilution of $ in pro forma net tangible book value per share to new investors purchasing common stock in this offering.

Dilution per share to new investors is determined by subtracting pro forma net tangible book value per share after this offering from the initial public offering price per share paid by new investors. The following table illustrates this dilution on a per share of common stock basis assuming the underwriters do not exercise their option to purchase additional shares of common stock:

Assumed initial public offering price per share		$
Historical net tangible book value per share as of June 30, 2014	$ (28.51)	
Pro forma increase per share as of June 30, 2014 attributable to conversion of convertible preferred stock	$ 28.66	
Pro forma net tangible book value per share as of June 30, 2014 before giving effect to this offering	$ 0.15	
Increase per share attributable to this offering		
Pro forma net tangible book value per share, as adjusted to give effect to this offering		
Dilution in pro forma net tangible book value per share to new investors in this offering		$

Each $1.00 increase or decrease in the assumed initial public offering price of $ per share, which is the midpoint of the price range listed on the cover page of this prospectus, would increase or decrease our pro forma net tangible book value by approximately $ million, our pro forma net tangible book value per share by approximately $ and dilution per share to new investors by approximately $, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. We may also increase or decrease the number of shares we are offering. An increase of one million in the number of shares offered by us would increase the pro forma as adjusted net tangible book value by approximately $ million, or $ per share, and would decrease the dilution per share to new investors in this offering by $ per share, assuming that the assumed initial public offering price remains the same, and after deducting the estimated underwriting discounts and commissions and estimated offering expenses. Similarly, a decrease of one million shares in the number of shares offered by us would decrease the pro forma as adjusted net tangible book value by approximately $ million, or $ per share, and would increase the dilution per share to new investors in this offering by $ per share, assuming that the assumed initial public offering price remains the same, and after deducting the estimated underwriting discounts and commissions and estimated offering expenses. The pro forma as adjusted information discussed above is illustrative only and will adjust based on the actual initial price to the public and other terms of this offering determined at pricing.

If the underwriters exercise their option to purchase additional shares in full or if any additional shares are issued in connection with outstanding options, you will experience further dilution. If the underwriters exercise their over-allotment option in full, the following will occur:

- the percentage of shares of our common stock held by existing stockholders will decrease to approximately % of the total number of shares of our common stock outstanding after this offering; and
- the number of shares of our common stock held by new investors will increase to, or approximately % of the total number of shares of our common stock outstanding after this offering.

The following table summarizes, on the same pro forma basis as adjusted as of June 30, 2014, the total number of shares of common stock purchased from us, the total cash consideration paid to us and the average price per share of common stock paid by our existing owners and by new investors purchasing shares of common stock in this offering:

	Shares Purchased		Total Consideration		Average Price Per Share
	Number	Percent	Amount	Percent	
Existing stockholders		%	$	%	$
Investors participating in this offering					
Total		100.0%	$	100.0%	

Each $1.00 increase or decrease in the assumed public offering price of $ per share, which is the midpoint of the price range listed on the cover page of this prospectus, would increase or decrease the total consideration paid by new investors by $ million and increase or decrease the percentage of total consideration paid by new investors by approximately %, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same.

The foregoing tables and calculations are based upon 138,752,300 shares of common stock outstanding as of June 30, 2014, including 134,918,694 shares of common stock after giving effect to the conversion of our outstanding series A, A-1, B, C and D convertible preferred stock, and excludes:

- 17,982,120 shares of our common stock issuable upon the exercise of stock options outstanding as of June 30, 2014 at a weighted-average exercise price of $0.22 per share;
- 10,471,282 shares of our common stock issuable upon the exercise of outstanding warrants at a weighted average exercise price of $0.29 per share;
- 18,361 shares of common stock reserved for issuance pursuant to future equity awards under our 2006 Equity Incentive Plan; and
- shares of common stock reserved for future issuance under our 2014 Equity Incentive Plan, which will become effective immediately prior to the closing of this offering (including shares of common stock reserved for issuances under our 2006 Equity Incentive Plan, which will be added to the shares reserved under the 2014 Equity Incentive Plan upon its effectiveness).

Furthermore, we may choose to raise additional capital through the sale of equity or convertible debt securities due to market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans. New investors will experience further dilution if any of our outstanding options or warrants are exercised, new options are issued and exercised under our equity incentive plans or we issue additional shares of common stock, other equity securities or convertible debt securities for lower consideration per share than in this offering in the future.

SELECTED FINANCIAL DATA

The selected statements of operations data for the years ended December 31, 2012 and 2013 and the balance sheet data at December 31, 2012 and 2013 have been derived from our audited financial statements included elsewhere in this prospectus. The selected statement of operations data for the six months ended June 30, 2013 and 2014 and the selected balance sheet data as of June 30, 2014 were derived from our unaudited financial statements appearing elsewhere in this prospectus. These unaudited financial statements have been prepared on a basis consistent with our audited financial statements and, in our opinion, contain all adjustments, consisting only of normal and recurring adjustments, necessary for a fair presentation of such financial data. Our historical results for any prior period are not necessarily indicative of results to be expected in any future period, and our interim period results are not necessarily indicative of results to be expected for a full year or any other interim period.

The information set forth below should be read in conjunction with the "Management's Discussion and Analysis of Financial Condition and Results of Operations" section of this prospectus and with our financial statements and notes thereto included elsewhere in this prospectus. The selected financial data in this section are not intended to replace the financial statements and are qualified in their entirety by the financial statements and related notes included elsewhere in this prospectus.

	Proteon Therapeutics, Inc.			
	Years Ended December 31,		Six Months Ended June 30,	
	2012	2013	2013	2014
			(Unaudited)	
	(in thousands except share and per share data)			
Operating expenses:				
Research and development	$ 5,907	$ 3,994	$ 2,003	$ 2,785
General and administrative	2,089	3,128	1,417	1,656
Acquired in-process research and development	—	—	—	—
Total operating expenses	7,996	7,122	3,420	4,441
Loss from operations	(7,996)	(7,122)	(3,420)	(4,441)
Other income (expense):				
Investment income	20	4	3	3
Interest expense	—	(861)	—	(857)
Other income (expense)	6	67	5	(99)
Total other income (expense)	26	(790)	8	(953)
Net loss	$ (7,970)	$ (7,912)	$ (3,412)	$ (5,394)
Unrealized loss on available-for-sale investments	(5)	(1)	—	(23)
Comprehensive loss	$ (7,975)	$ (7,913)	$ (3,412)	$ (5,417)
Reconciliation of net loss to net loss attributable to common stockholders				
Net loss	$ (7,970)	$ (7,912)	$ (3,412)	$ (5,394)
Accretion of redeemable convertible preferred stock to redemption value	(6,133)	(6,119)	(3,039)	(3,409)
Extinguishment of Series B redeemable convertible preferred stock	—	—	—	—
Net loss attributable to common stockholders	$ (14,103)	$ (14,031)	$ (6,451)	$ (8,803)
Net loss per share attributable to common stockholders—basic and diluted	$ (3.85)	$ (3.76)	$ (1.76)	$ (2.31)
Weighted-average number of common shares used in net loss per share attributable to common stockholders—basic and diluted	3,659,790	3,732,436	3,659,790	3,812,904
Pro forma net loss per share attributable to common stockholders—basic and diluted (unaudited)		$ (0.10)		$ (0.04)
Pro forma weighted-average number of common shares used in net loss per share attributable to common stockholders—basic and diluted (unaudited)		72,457,068		107,333,127

	As of December 31, 2012	As of December 31, 2013	As of June 30, 2014 (unaudited)
		(in thousands)	
Balance Sheet Data:			
Cash and cash equivalents	$ 2,409	$ 2,793	$ 8,646
Working capital	6,499	(4,438)	19,915
Total assets	7,782	5,659	27,142
Preferred stock	90,286	96,405	123,904
Common stock and additional paid-in capital	4	4	4
Total stockholders' deficit	(86,656)	(100,514)	(109,290)

(1) See Note 2 within the notes to our financial statements appearing elsewhere in this prospectus for a description of the method used to calculate basic and diluted net loss per common share and pro forma basic and diluted net loss per common share.

(2) Pro forma to reflect the conversion of our preferred stock into shares of common stock upon the closing of this offering.

MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

You should read the following discussion and analysis of our financial condition and results of operations together with "Summary financial data," "Selected financial data" and our financial statements and related notes appearing elsewhere in this prospectus. Some of the information contained in this discussion and analysis or set forth elsewhere in this prospectus, including information with respect to our plans and strategy for our business and related financing, includes forward-looking statements that involve risks and uncertainties. As a result of many factors, including those factors set forth in the "Risk Factors" section of this prospectus, our actual results could differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis.

Overview

We are a late-stage biopharmaceutical company focused on the development of novel, first-in-class pharmaceuticals to address the needs of patients with renal and vascular disease. Our product candidate, PRT-201, is a recombinant human elastase that we are developing to reduce vascular access failure in patients with chronic kidney disease undergoing or preparing for hemodialysis, a lifesaving treatment that cannot be conducted without a functioning vascular access. We believe the data from our completed Phase 2 trial of PRT-201 in patients undergoing creation of an arteriovenous fistula, or AVF, support that a one-time, local application of PRT-201 during AVF surgical placement reduces AVF failure, thereby improving patient outcomes and reducing the burden on patients and the healthcare system. We are not aware of any approved preventative treatments to reduce the failure rate of AVFs. We initiated the first of two Phase 3 trials for PRT-201 in radiocephalic AVFs, our initial indication, in the third quarter of 2014 and initiate the second Phase 3 trial in the first half of 2015.

We commenced business operations in June 2001. Our operations to date have been limited to organizing and staffing our company, business planning, raising capital, undertaking preclinical studies and clinical trials of PRT-201, protecting our intellectual property and providing general and administrative support for these operations. To date, we have not generated any product revenue and have primarily financed our operations through the private placement of our equity securities, business development activities, convertible note financings, and government grants. As of June 30, 2014, we had received an aggregate of $111.9 million of net proceeds comprised of $94.0 million from the issuance of equity securities, $7.7 million from the issuance of convertible notes, $10.0 million from business development activities and $0.2 million from government grants.

As of June 30, 2014, we had an accumulated deficit of $109.3 million. Our net losses were $8.0 million and $7.9 million for the years ended December 31, 2012 and 2013, respectively, and $3.4 million and $5.4 million, for the six months ended June 30, 2013 and 2014, respectively. We expect to incur significant expenses and increasing operating losses for the foreseeable future. We expect our research and development expenses to increase as we continue the clinical trials of, and seek regulatory approval for, PRT-201. If we obtain regulatory approval for PRT-201, we expect to incur significant commercialization expenses related to product sales, marketing, manufacturing and distribution. Furthermore, following the closing of this offering, we expect that our general and administrative costs will increase as we grow and operate as a public company. As a result, we will need to generate significant revenue if we are to achieve profitability, and we may never be able to do so.

We believe that our available funds subsequent to this offering will be sufficient to fund our operations through , allowing us to obtain results from our first Phase 3 clinical trial of PRT-201 in radiocephalic AVFs and to accelerate the commencement of our second Phase 3 trial and the chemistry and manufacturing controls, or CMC, activities.

We do not expect to generate revenue from product sales unless and until we successfully complete development and obtain regulatory approval for PRT-201, which we expect will take a number of years and

is subject to significant uncertainty. We have no manufacturing facilities and all of our manufacturing activities are contracted out to third parties. Additionally, we currently use third-party clinical research organizations, or CROs, to carry out our clinical development activities and we do not yet have a sales organization. If we obtain regulatory approval for PRT-201, we expect to incur significant commercialization expenses related to product sales, marketing, manufacturing, and distribution. Accordingly, we may seek to fund our operations through public or private equity or debt financings or other sources, including strategic collaborations. We may, however, be unable to raise additional funds or enter into such other arrangements when needed on favorable terms or at all. Our failure to raise capital or enter into such other arrangements as and when needed would have a negative impact on our financial condition and our ability to develop PRT-201 or any additional product candidates, if developed.

Financial Overview

Grant Revenue

To date, our revenue has been derived solely from government grants. We did not receive any government grants during the reported periods and have no plans to receive additional government grants in the future.

Research and Development Expenses

Research and development expenses consist primarily of costs incurred for the development of PRT-201, which include:

- employee-related expenses, including salaries, benefits, travel and stock-based compensation expense;
- expenses incurred under agreements with CROs and investigative sites that will conduct our clinical trials;
- the cost of acquiring, developing, and manufacturing clinical trial materials;
- costs associated with regulatory operations; and
- facilities, depreciation, and other expenses, which include direct and allocated expenses for rent and maintenance of facilities, insurance, and other supplies.

We expense research and development costs to operations as incurred. We recognize costs for certain development activities, such as clinical trials, based on an evaluation of the progress to completion of specific tasks using data such as patient enrollment, clinical site activations or information provided to us by our vendors.

We cannot determine with certainty the duration and completion costs of the current or future clinical trials or if, when, or to what extent we will generate revenues from the commercialization and sale of PRT-201. We may never succeed in achieving regulatory approval for PRT-201. The duration, costs, and timing of clinical trials and development of PRT-201 will depend on a variety of factors, which include:

- the scope, rate of progress, and expense of our ongoing as well as any additional clinical trials and other research and development activities;
- uncertainties in clinical trial enrollment rate;
- future clinical trial results;
- significant and changing government regulation; and
- the timing and receipt of any regulatory approvals.

A change in any of these factors could mean a significant change in the costs and timing associated with the development of PRT-201. For example, if the FDA, or another regulatory authority were to require us to conduct clinical trials beyond those that we currently anticipate will be required for the completion of clinical development or if we experience significant delays in enrollment in any of our

clinical trials, we could be required to expend significant additional financial resources and time on the completion of clinical development.

We expect our research and development expenses to increase for the foreseeable future as we continue the development of PRT-201. Our current planned development activities include the following:

- we commenced our first Phase 3 clinical trial of PRT-201 for patients undergoing creation of a radiocephalic AVF in the third quarter of 2014. Prior to completing enrollment in the first Phase 3 trial, we intend to initiate our second Phase 3 trial. If the results from the first Phase 3 trial are sufficiently compelling, we intend to meet with the FDA to discuss the possibility of submitting a BLA, supported by the single Phase 3 trial and may decide to submit a BLA to the FDA prior to completing the second Phase 3 trial;
- we may, based on additional data including the data from our Phase 3 clinical trials and if sufficient funds become available, choose to conduct a clinical trial of PRT-201 in Europe;
- we may, based on additional data including the data from our Phase 3 clinical trials and if sufficient funds become available, study the effects of a 30 microgram dose of PRT-201 versus placebo on brachiocephalic AVFs and in patients undergoing placement of an arteriovenous graft, or AVG; and
- we expect to continue to manufacture clinical trial materials in support of our clinical trials.

Our direct research and development expenses consist principally of external costs, such as fees paid to CROs, investigators, consultants and central laboratories in connection with our clinical trials, and costs related to acquiring and manufacturing clinical trial materials as well as of salaries and related costs for personnel, including stock-based compensation and travel expenses.

General and Administrative Expenses

General and administrative expenses consist principally of salaries and related costs for personnel, including stock-based compensation and travel expenses, in executive and other administrative functions. Other general and administrative expenses also include professional fees for legal, patent review, consulting and accounting services as well as facility related costs. We anticipate increased expenses related to audit, legal, regulatory, and tax-related services associated with maintaining compliance with our NASDAQ listing and Securities and Exchange Commission requirements, director and officer insurance premiums, and investor relations costs associated with being a public company.

Additionally, if and when we believe a regulatory approval of our first product candidate appears likely, we anticipate that we will increase our salary and personnel costs and other expenses as a result of our preparation for commercial operations.

Interest Expense, Net

Interest expense, net, consists of interest incurred on debt instruments, amortized deferred financing costs and amortized debt discount, as offset by any interest income earned on our cash, cash equivalents and marketable securities. The debt discount primarily consists of the fair value of the bifurcated features embedded in the convertible notes issued in September 2013. As of June 30, 2014, the debt discount had been fully amortized to interest expense.

Other Income (Expense)

Other income consists of the gain realized by the sale of fixed assets as well as changes in fair market value of the derivative liability associated with the convertible notes.

Accretion of Preferred Stock

Subsequent to the May 2014 Series D convertible preferred stock financing, our shares of preferred stock are redeemable beginning in 2019 at their original issuance price plus any declared or accrued but

unpaid dividends upon written election of the preferred stockholders in accordance with the terms of our certificate of incorporation. Accretion of preferred stock reflects the accretion of issuance costs and cumulative dividends on our preferred stock based on their respective redemption values.

Critical Accounting Policies and Significant Judgments and Estimates

Our management's discussion and analysis of our financial position and results of operations is based on our financial statements, which have been prepared in accordance with U.S. generally accepted accounting principles, or GAAP. The preparation of financial statements in conformity with GAAP requires us to make estimates and assumptions that affect the amounts reported in the financial statements and accompanying notes. On an ongoing basis, we evaluate estimates, which include estimates related to clinical trial accruals, stock-based compensation expense, embedded derivatives, and reported amounts of revenues and expenses during the reported period. We base our estimates on historical experience and other market-specific or other relevant assumptions that we believe to be reasonable under the circumstances. Actual results may differ materially from those estimates or assumptions.

While our significant accounting policies are described in more detail in the notes to our financial statements appearing elsewhere in this prospectus, we believe the following accounting policies to be most critical to the judgments and estimates used in the preparation of our financial statements.

Accrued Research and Development Expenses

As part of the process of preparing our financial statements, we are required to estimate our accrued expenses. This process involves reviewing open contracts and purchase orders, communicating with our personnel to identify services that have been performed for us and estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of the actual cost. The majority of our service providers invoice us monthly in arrears for services performed or when contractual milestones are met. We make estimates of our accrued expenses as of each balance sheet date in our financial statements based on facts and circumstances known to us at that time. We periodically confirm the accuracy of our estimates with the service providers and make adjustments if necessary. Examples of estimated accrued research and development expenses include fees paid to CROs in connection with clinical trials and vendors related to manufacturing, development and distribution of clinical supplies.

We base our expenses related to clinical trials on our estimates of the services received and efforts expended pursuant to contracts with multiple CROs that conduct and manage clinical trials on our behalf. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows. There may be instances in which payments made to our vendors will exceed the level of services provided and result in a prepayment of the clinical expense. Payments under some of these contracts depend on factors such as the successful enrollment of subjects and the completion of clinical trial milestones. In accruing service fees, we estimate the time period over which services will be performed, enrollment of subjects, number of sites activated and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from our estimate, we adjust the accrual or prepaid accordingly. Although we do not expect our estimates to be materially different from amounts actually incurred, if our estimates of the status and timing of services performed differs from the actual status and timing of services performed we may report amounts that are too high or too low in any particular period. To date, there have been no material differences from our estimates to the amount actually incurred.

Derivative Instruments

We occasionally issue financial instruments in which a derivative instrument is "embedded." Upon issuing the financial instrument, we assesses whether the economic characteristics of the embedded derivative are clearly and closely related to the economic characteristics of the remaining component of the financial instrument (*i.e.*, the host contract) and whether a separate, non-embedded instrument with the same terms as the embedded instrument would meet the definition of a derivative instrument as defined in ASC 815 *Derivatives and Hedging*. When it is determined that (1) the embedded derivative possesses economic characteristics that are not clearly and closely related to the economic characteristics of the host contract and (2) a separate, stand-alone instrument with the same terms would qualify as a derivative instrument, the embedded derivative is separated from the host contract and carried at fair value with changes in fair value recorded in current period earnings.

Convertible Notes

On September 4, 2013, we issued, at par value, convertible promissory notes with an aggregate principal amount of approximately $4.3 million. The notes were due March 31, 2014, upon written notice from holders of a majority of the then-outstanding aggregate principal amount, and accrued interest at an annual rate of 8%. We determined that the debt contained certain features requiring evaluation for separate accounting from the fixed interest rate host instrument including (i) holder's optional conversion upon maturity; (ii) mandatory conversion upon a reverse acquisition; (iii) automatic conversion upon a qualified financing; (iv) holder's optional conversion upon a non-qualified financing; (v) issuer's optional redemption; (vi) redemption upon a change in control; (vii) put upon a breach; and (viii) a put upon an event of default. In certain cases these features require us to either convert the notes or accelerate their repayment at a significant premium to the principal and accrued interest then outstanding.

The embedded features requiring separate accounting were combined and valued upon issuance using a single income valuation approach. As of September 4, 2013 and December 31, 2013, we ascribed a probability to the automatic conversion upon a qualified financing of 85% and 100%, respectively. As of September 4, 2013 and December 31, 2013, we ascribed a probability to the redemption feature upon a change in control of 15% and 0%, respectively. From December 31, 2013 to the conversion of the convertible notes into Series D convertible preferred stock on May 13, 2014, as described below, the estimates of these probabilities did not change. For all other features included in the combined embedded derivative, we estimated a 0% probability of occurrence at all times.

We recorded approximately $1.4 million as the fair value of the combined embedded derivative liability on September 4, 2013, with a corresponding amount recorded as debt discount. The debt discount has been amortized to interest expense over the life of the notes using the effective interest method. As of December 31, 2013 and June 30, 2014, the fair value of the combined embedded derivative liability was $1.4 million and $0, respectively. Changes in the estimated fair value of the embedded features were recorded in earnings in the period in which they occurred.

In connection with the issuance of our Series D convertible preferred stock on May 13, 2014, the notes in the aggregate amount of approximately $4.6 million in principal plus accrued interest were converted into 10,344,201 shares of Series D convertible preferred stock. As the debt discount had been fully amortized prior to conversion, there was no gain or loss recognized upon conversion of the notes.

Stock-Based Compensation

From our inception in June 2001, until December 31, 2005, we applied the guidance in Accounting Principles Bulletin, or APB 25. Under APB 25, there is no stock-based compensation expense recognized for awards granted with an exercise price equal to the fair value of the underlying stock on the date of grant.

Since January 1, 2006, we have applied the fair value recognition provisions of Financial Accounting Standards Board, or FASB, Accounting Standards Codification or ASC, Topic 718, *Compensation—Stock Compensation*, or ASC 718, to account for stock-based compensation for employees. ASC 718 applies to any awards granted, modified, repurchased, or canceled after December 31, 2005, and requires the measurement and recognition of costs for all stock-based awards made to employees and directors, including stock options, stock appreciation rights, stock units, and discounted employee stock purchases. We recognize compensation costs related to employees based on the estimated fair value of the awards on the date of grant and over the requisite service periods, using the straight-line method. The options vest periodically over various schedules and all options expire no later than ten years after the date of grant.

We have applied the fair value recognition provisions of ASC 718 and FASB ASC 505, *Equity*, to account for stock-based compensation for non-employees. Stock-based compensation related to non-employee awards is re-measured at each reporting period until the awards are vested and is estimated using an expected term equal to the remaining contractual term of the award. Compensation expense is recognized for the fair value of the consideration received, or the equity instruments issued, whichever is more reliably measurable. We recorded compensation expense for non-employee awards with graded vesting using the accelerated expense attribution method.

We estimate the fair value of our stock-based awards to employees and non-employees using the Black-Scholes option pricing model, which requires the input of highly subjective assumptions, including: (1) the expected volatility of our stock, (2) the expected term of the award, (3) the risk-free interest rate and (4) expected dividends. Due to the lack of a public market for the trading of our common stock and a lack of company specific historical and implied volatility data, we have based our estimate of expected volatility on the historical volatility of a group of comparable companies that are publicly traded. For these analyses, we selected representative companies from the life sciences industry with characteristics similar to ours, including enterprise value, risk profiles, position within the industry and historical share price information, sufficient to meet the expected life of the stock-based awards. We compute the historical volatility data using the daily closing prices for the selected companies' shares during the equivalent period of the calculated expected term of our stock-based awards. We will continue to apply this process until a sufficient amount of historical information regarding the volatility of our own stock price becomes available. We use a dividend yield of zero based on the fact that we have never declared cash dividends and have no current intention of paying cash dividends over the expected term of the option. As we do not have sufficient historical stock option activity data to provide a reasonable basis upon which to estimate the expected term of stock options granted to employees, we have estimated the expected life of our employee stock options using the "simplified" method, whereby the expected life equals the average of the vesting term and the original contractual term of the option. For non-employee options, we have determined the expected life based on the respective contractual life. The risk-free interest rates for periods within the expected life of the option are based on the U.S. Treasury yield curve in effect during the period the options were granted and with maturity dates equivalent to the expected term of the option.

The following table presents the grant dates of shares subject to awards from January 1, 2012 through June 30, 2014 along with the corresponding exercise price for each option grant and our current estimate of the fair value per share of our common stock on each grant date, which we utilize to calculate stock-based compensation expense:

Date of Grant	Number of Underlying Options Granted	Exercise Price per Share	Current Estimate of Common Stock Fair Value per Share on Grant Date
3/25/2013	50,000	$ 1.40	$ 1.40
6/24/2014	8,375,000	$ 0.31	$ 0.31

Determination of the Fair Value of Common Stock on Grant Dates

Following the consummation of this offering, the fair value of our common stock will be determined based on the quoted market price of our common stock. We have historically granted stock options at exercise prices not less than the fair value of our common stock. Our board of directors determined the fair value of our common stock considering, in part, the work of an independent third-party valuation specialist. The board determined the estimated per share fair value of our common stock at various dates considering contemporaneous valuations performed in accordance with the guidance outlined in the American Institute of Certified Public Accountants Practice Aid, *Valuation of Privately-Held Company Equity Securities Issued as Compensation*, also known as the "Practice Aid".

In conducting the valuations, the independent third-party valuation specialist considered all objective and subjective factors that it believed to be relevant for each valuation conducted in accordance with the Practice Aid, including our best estimate of our business condition, prospects and operating performance at each valuation date. Other significant factors included:

- the prices of our preferred stock sold to outside investors in arm's length transactions, and the rights, preferences and privileges of our preferred stock as compared to those of our common stock, including the liquidation preferences of our preferred stock;
- the provisions of an option agreement to acquire Proteon that has since terminated;
- our results of operations, financial position and the status of research and development efforts;
- the composition of, and changes to, our management team and board of directors;
- the lack of liquidity of our common stock;
- our stage of development and business strategy and the material risks related to our business and industry;
- the valuation of publicly traded companies in the life sciences sector, as well as recently completed mergers and acquisitions of guideline companies;
- any external market conditions affecting the life sciences industry sector; and
- the likelihood of achieving a liquidity event for the holders of our common stock and stock options, such as an initial public offering, or IPO, or a sale of our company, given prevailing market conditions, and the state of the IPO market for similarly situated privately held life sciences companies.

The dates of our contemporaneous and retrospective valuations have not always coincided with the dates of our stock option grants. In determining the exercise prices of the stock options set forth in the table above, our board of directors considered, among other things, the most recent contemporaneous and retrospective valuation of our common stock and their assessment of additional objective and subjective factors that were relevant as of the grant dates. The additional factors considered when determining whether any changes in the fair value of our common stock had occurred between the most recent contemporaneous valuation and the grant dates included our stage of research and development, our operating and financial performance and current business conditions.

The estimates of fair value of our common stock are highly complex and subjective. There are significant judgments and estimates inherent in the determination of the fair value of our common stock. These judgments and estimates include assumptions regarding our future operating performance, the time to completing an IPO or other liquidity event, the related valuations associated with these events, and the determinations of the appropriate valuation methods at each valuation date. If we had made different assumptions, our stock-based compensation expense, net loss and net loss per share applicable to common stockholders could have been materially different.

Common Stock Valuation Methodologies

The valuations we obtained were prepared in accordance with the guidelines in the Practice Aid, which prescribes several valuation approaches for setting the value of an enterprise, such as the cost,

market and income approaches, and various methodologies for allocating the value of an enterprise to its common stock. We generally used the market approach, in particular the guideline public company and guideline transaction methodologies, based on inputs from comparable public companies' equity valuations and comparable acquisition transactions, to estimate the enterprise value of our company.

Methods Used to Allocate Our Enterprise Value to Classes of Securities

In accordance with the Practice Aid, we considered the various methods for allocating the enterprise value across our classes and series of capital stock to determine the fair value of our common stock at each valuation date. The methods and scenarios considered consisted of the following:

- *Probability-Weighted Expected Return Method, or PWERM.* The PWERM is a scenario-based analysis that estimates the value per share based on the probability-weighted present value of expected future investment returns, considering each of the possible outcomes available to us, as well as the economic and control rights of each share class. Our PWERM analyses assume a range of exit scenarios, including an IPO, and allocate the value in each scenario according to our capital structure, probability-weighting each exit and discounting the value to a present value equivalent using a risk-adjusted discount rate.
- *Option Pricing Method, or OPM.* Under the option pricing method, shares are valued by creating a series of call options with exercise prices based on the liquidation preferences and conversion terms of each equity class. The values of the preferred and common stock are inferred by analyzing these options. Our OPM analysis evaluates a scenario where we remain private and is modeled over a weighted average term to exit using a recent financing round as the basis for fair market value determination.
- *Hybrid Method.* The hybrid method employs the concepts of the PWERM and OPM merged into a single framework.

The foregoing valuation methodologies are not the only methodologies available and they will not be used to value our common stock once this offering is complete. We cannot make assurances as to any particular valuation for our common stock. Accordingly, investors are cautioned not to place undue reliance on the foregoing valuation methodologies as an indicator of future stock prices.

Results of Operations

Comparison of the Six Months Ended June 30, 2013 and June 30, 2014

	Six Months Ended June 30,		Period-to-Period Change
	2013	2014	
	(in thousands)		
Operating expenses:			
Research and development	$ 2,003	$ 2,785	$ 782
General and administrative	1,417	1,656	239
Total operating expenses	3,420	4,441	1,021
Loss from operations	(3,420)	(4,441)	(1,021)
Other income (expense):			
Interest expense, net	3	(854)	(857)
Other income (expense)	5	(99)	(104)
Total other income (expense)	8	(953)	(961)
Net loss	$ (3,412)	$ (5,394)	$ (1,982)

Research and Development Expenses. The following table identifies research and development expenses on both an external and internal basis for the six months ended June 30, 2013 and 2014:

	Six Months Ended June 30,		Period-to-Period Change
	2013	2014	
	(in thousands)		
External research and development expenses	$ 922	$ 1,706	$ 784
Internal research and development expenses	1,081	1,709	$ (2)
Total research and development expenses	$ 2,003	$ 2,785	$ 782

During the six months ended June 30, 2014, our total research and development expenses increased by $0.8 million compared to the six months ended June 30, 2013 due to $0.5 million in increased external manufacturing, process development and quality assurance expenses related to preparation for our upcoming radiocephalic AVF Phase 3 clinical trial and $0.3 million in increased external clinical expenses related to preparation for the radiocephalic AVF Phase 3 clinical trial. Our internal research and development expenses were unchanged in the six months ended June 30, 2014 as compared to the six months ended June 30, 2013.

General and Administrative Expenses. During the six months ended June 30, 2014, our total general and administrative expenses were $0.2 million higher as compared to the six months ended June 30, 2013. Changes from the prior period were primarily due to additional overhead and personnel costs in the six months ended June 30, 2014 of $0.2 million to support our on-going corporate activities

Other Expense. During the six months ended June 30, 2014, other expenses increased by $0.1 million as compared to the six months ended June 30, 2013 primarily related to the change in fair market value of the derivative liability associated with the convertible promissory notes.

Interest Expense, Net. During the six months ended June 30, 2014, interest expense, net increased by $0.9 million as compared to the six months ended June 30, 2013 due to the interest expense on our convertible promissory notes.

Comparison of the Years Ended December 31, 2012 and December 31, 2013

	Years Ended December 31,		Period-to-Period Change
	2012	2013	
	(in thousands)		
Operating expenses:			
Research and development	$ 5,907	$ 3,994	$ (1,913)
General and administrative	2,089	3,128	1,039
Total operating expenses	7,996	7,122	(874)
Loss from operations	(7,996)	(7,122)	874
Other income (expense):			
Interest expense, net	20	(857)	(877)
Other income	6	67	61
Total other income (expense)	26	(790)	(816)
Net loss	$ (7,970)	$ (7,912)	$ 58

Research and Development Expenses. The following table identifies research and development expenses on both an external and internal basis for the years ended December 31, 2012 and 2013:

	Years Ended December 31,		Period-to-Period Change
	2012	2013	
	(in thousands)		
External research and development expenses	$ 3,514	$ 1,962	$ (1,552)
Internal research and development expenses	2,393	2,032	(361)
Total research and development expenses	$ 5,907	$ 3,994	$ (1,913)

During the year ended December 31, 2013, our total research and development expenses decreased by $1.9 million compared to the prior year, primarily due to the completion of our AVF Phase 2 trial and our AVG Phase 1/2 trial. Our external research and development expenses decreased by $1.5 million primarily due to a reduction in expenses related to our clinical trials and our manufacturing and process development. Our internal research and development expenses decreased by $0.4 million primarily due to a reduction in our research and development employees and contractors.

General and Administrative Expenses. During the year ended December 31, 2013, our total general and administrative expenses increased by $1.0 million compared to the prior year. This increase was primarily due to additional overhead and personnel costs in 2013 of $0.5 million to support our ongoing corporate activities and $0.5 million related to higher legal expenses.

Other Income (Expense). During the year ended December 31, 2013, our other income increased by $0.1 million due to a gain from the sale of fixed assets.

Interest Expense, Net. During the year ended December 31, 2013, our interest expense, net increased by $0.8 million due to the interest expense on our convertible promissory notes.

Liquidity and Capital Resources

Overview

Since our inception and through June 30, 2014, we had received $111.9 million in net proceeds million comprised of $94.0 million from the issuance of equity securities, $7.7 million from the issuance of convertible notes, $10.0 million from business development activities and $0.2 million from government grants. At June 30, 2014, our cash and cash equivalents and available-for-sale investments totaled $25.4 million.

Convertible Note Financings

In April 2013, we entered into a convertible note purchase agreement with some of our existing preferred stockholders whereby we had the option, but not the obligation, to issue convertible promissory notes in the aggregate principal amount of approximately $4.3 million, subject to meeting at least one of two pre-determined conditions. In September 2013, upon satisfying one of the conditions, we issued the notes, which accrue interest at 8% annum and mature on or after March 31, 2014 upon written notice from a majority of the outstanding note holders.

As further described above and within our financial statements appearing elsewhere in this prospectus, in connection with the issuance of the convertible notes, we recorded $1.4 million as a discount on the convertible notes related to the estimated fair value of the combined embedded derivative liability and certain issuance costs. The discount was amortized to interest expense over the life of the convertible notes. Changes in the estimated fair value of the combined embedded derivative liability were recorded in earnings in the periods in which they occurred.

On May 13, 2014, upon the closing of our Series D convertible preferred stock financing described below, the convertible notes, in the aggregate amount of approximately $4.5 million principal and accrued interest automatically converted into 10,344,201 shares of our Series D convertible preferred stock at a conversion price per share of $0.4414.

Series D Financing

On May 13, 2014, we received net proceeds of approximately $24.7 million from the issuance of Series D convertible preferred stock to new and existing investors at a price per share of $0.588656. In aggregate, we issued 52,813,827 shares of Series D preferred stock including 10,344,201 shares for the conversion of $4.6 million of convertible notes and accrued interest at a conversion price of $0.4414 per share. As provided by the Series D stock purchase agreement, the investors in the Series D convertible preferred stock have the potential opportunity to invest an additional $20.0 million in Series D convertible preferred stock at $0.588656 per share. The investors' rights to purchase additional shares of Series D preferred stock will terminate with this offering.

Operating Capital Requirements

We expect to incur increasing operating losses for at least the next several years as we conduct our Phase 3 clinical trials for PRT-201 in radiocephalic AVFs, thereafter seeking marketing approval for PRT-201 in radiocephalic AVFs assuming successful trial outcomes, and pursue development of PRT-201 for additional indications, including in brachiocephalic AVFs and AVGs. We may not be able to complete the development and initiate commercialization of PRT-201 if, among other things, our clinical trials are not successful, the Food and Drug Administration does not approve PRT-201 when we expect, or at all.

We believe that the net proceeds of this offering, together with our existing cash and cash equivalents, will be sufficient to fund our operations through . Based on our planned use of the net proceeds of this offering and our existing cash resources, we believe that our available funds subsequent to this offering will be sufficient to enable us to obtain results from our first Phase 3 clinical trial of PRT-201 in radiocephalic AVFs and to accelerate the commencement of our second Phase 3 trial and the chemistry and manufacturing controls, or CMC, activities.

Unless or until we can generate a sufficient amount of revenue from our product sales we expect to fund our operations through a combination of equity offerings debt financings or other sources including potential collaborations. Additional capital may not be available on favorable terms, if at all. If we are unable to raise additional capital in sufficient amounts or on terms acceptable to us, we may have to significantly delay, scale back or discontinue the development or commercialization of one or more of our protein therapeutic candidates. If we raise additional funds through the issuance of debt or equity securities, it could result in dilution to our existing stockholders and increased fixed payment obligations, and these securities may have rights senior to those of our common stock. If we incur indebtedness, we could become subject to covenants that would restrict our operations and potentially impair our competitiveness, such as limitations on our ability to incur additional debt, limitations on our ability to acquire, sell or license intellectual property rights and other operating restrictions that could adversely impact our ability to conduct our business. We may not be able to enter into collaboration arrangements for PRT-201 in targeted geographies. Any of these events could significantly harm our business, financial condition and prospects.

Our forecast of the period of time through which our financial resources will be adequate to support our operations is a forward-looking statement and involves risks and uncertainties, and actual results could vary as a result of a number of factors. We have based this estimate on assumptions that may prove to be wrong, and we could exhaust our available capital resources sooner than we currently expect. Our future funding requirements, both near and long-term, will depend on many factors, including:

- the timing and costs of our planned Phase 3 clinical trials of PRT-201 in radiocephalic AVFs;

- the timing and costs of developing PRT-201 for additional indications;
- the outcome, timing and costs of seeking regulatory approvals;
- the costs of commercialization activities for PRT-201 in radiocephalic AVFs and other indications if we receive marketing approval, including the costs and timing of establishing product sales, marketing, distribution and manufacturing capabilities;
- subject to receipt of marketing approval, revenue received from commercial sales of PRT-201;
- the terms and timing of any future collaborations, licensing, consulting or other arrangements that we may establish;
- the amount and timing of any payments we may be required to make, or that we may receive, in connection with the licensing, filing, prosecution, defense and enforcement of any patents or other intellectual property rights, including royalty payments that we are obligated to pay to Johns Hopkins University pursuant to our assignment agreement related to PRT-201;
- the costs of preparing, filing and prosecuting patent applications, maintaining and protecting our intellectual property rights and defending against intellectual property related claims; and
- the extent to which we in-license or acquire other products and technologies.

Cash Flows

The following table summarizes our sources and uses of cash:

	Years Ended December 31,		Six Months Ended June 30,	
	2012	2013	2013	2014
	(in thousands)			
Net cash used in operating activities	$ (8,234)	$ (6,657)	$ (3,386)	$ (4,234)
Net cash provided by investing activities	7,382	2,727	4,294	(14,476)
Net cash (used in) provided by financing activities	(9)	4,314	—	24,563
Net (decrease) increase in cash and cash equivalents	$ (861)	$ 384	$ 908	$ 5,853

Comparison of the Six Months Ended June 30, 2013 and 2014

Net cash used in operating activities was $3.4 million during the six months ended June 30, 2013 compared to $4.2 million during the six months ended June 30, 2014. The increase of $0.8 million in cash used in operating activities in the first six months of 2014 was primarily driven by an increase in our operating expenses of $1.0 million, offset by a decrease in working capital balances and an increase in non-cash operating expenses of $0.2 million as compared to the first six months of 2013.

Net cash provided by investing activities was $4.3 million during the six months ended June 30, 2013 compared to a use of cash of $14.5 million during the six months ended June 30, 2014. The increase in cash used in investing activities of $18.8 million in the first six months of 2014 was driven by an increase in the purchases of available for sale investments of $15.3 million combined with a decrease in maturities of short term investments of $3.5 million compared to the first six months of 2013.

There was no net cash provided by financing activities during the six months ended June 30, 2013 compared to $24.6 million during the first six months of 2014. This increase was a result of the Series D Preferred Stock issuance in May 2014.

Comparison of the Years Ended December 31, 2012 and 2013

Net cash used in operating activities was $8.2 million for the year ended December 31, 2012 compared to $6.7 million for the year ended December 31, 2013. The decrease of $1.6 million in cash used in operating activities was primarily driven by a $0.9 million decrease in our operating expenses and the

$0.7 million increase in the non-cash adjustment for the accretion of the debt discount and the debt issuance cost provided by convertible notes payable.

Net cash provided by investing activities was $7.4 million for the year ended December 31, 2012 compared to net cash provided of $2.7 million for the year ended December 31, 2013. The decrease of $4.7 million in cash provided by investing activities was driven by a decrease in net proceeds from maturities of available for sale short term investments of $9.5 million offset by a decrease in purchases of available for sale short term investments of $4.8 million compared to the prior year.

Net cash provided by financing activities during the year ended December 31, 2012 was immaterial. Net cash provided by financing activities during the year ended December 31, 2013 of approximately $4.3 million was attributable to our September 2013 convertible promissory note financing.

Off-Balance Sheet Arrangements

We did not have during the periods presented, and we do not currently have, any off-balance sheet arrangements, as defined under the applicable regulations of the Securities Exchange Commission, or SEC.

Net Operating Loss Carryforwards

As of December 31, 2013, we had federal and state net operating loss carryforwards of approximately $69.9 million and $45.4 million, respectively, to offset future federal and state taxable income, which will expire at various times between 2014 and 2033. We also had federal and state research and development tax credit carryforwards of approximately $2.0 million and $1.1 million, respectively, to offset future income taxes, which will expire at various times between 2022 and 2033. Lastly, as of December 31, 2013, we had federal Orphan Drug tax credit carryforwards of approximately $7.2 million, to offset future income taxes, which will expire at various times between 2029 and 2033. Net operating loss and tax credit carryforwards are subject to review and possible adjustment by the Internal Revenue Service and state tax authorities and may become subject to an annual limitation in the event of certain cumulative changes in the ownership interest of significant stockholders over a three-year period in excess of 50%, as defined under Sections 382 and 383 of the United States Internal Revenue Code of 1986, as amended, as well as similar state provisions. This could limit the amount of tax attributes that can be utilized annually to offset future taxable income or tax liabilities. The amount of the annual limitation is determined based on the value of our company immediately prior to the ownership change. Subsequent ownership changes may further affect the limitation in future years. On December 31, 2013, we recorded a 100% valuation allowance against our net operating loss and tax credit carryforwards, as we believe it is more likely than not that the tax benefits will not be fully realized. In the future, if we determine that a portion or all of the tax benefits associated with our tax carryforwards will be realized, net income would increase in the period of such determination.

Contractual Obligations

The following table summarizes our outstanding contractual obligations as of payment due date by period at December 31, 2013:

	Total	Less than 1 Year	1 to 3 Years	3 to 5 Years	More than 5 Years
			(in thousands)		
Convertible promissory notes(1)	$ 4,452	$ 4,452	$ —	$ —	$ —
Operating leases(2)	188	188	—	—	—
Total obligations	$ 4,640	$ 4,640	$ —	$ —	$ —

(1) The convertible promissory notes represent the aggregate $4.3 million principal amount of convertible notes issued in September of 2013 plus accrued interest totaling $0.1 million. The convertible notes were converted into Series D preferred stock in May 2014.

(2) In July 2009 we entered into a multi-year non-cancelable lease for our offices in Waltham, Massachusetts. In October 2011, we amended the lease extending its expiration to December 2014. In August 2014 we amended the lease extending its expiration to June 2018 with one optional one-year extension period. The minimum lease payments above do not include common area maintenance charges or real estate taxes.

The contractual obligations table does not include any potential future royalty payments we may be required to make under our license assignment with Johns Hopkins University, due to the uncertainty of the occurrence of the events requiring payment under that agreement.

We enter into contracts in the normal course of business with CROs and clinical sites for the conduct of clinical trials, professional consultants for expert advice and other vendors for clinical supply manufacturing or other services. These contracts are not included in the table above as they provide for termination on notice, and therefore are cancelable contracts and do not include any minimum purchase commitments.

Qualitative and Quantitative Disclosures about Market Risk

The market risk inherent in our financial instruments and in our financial position represents the potential loss arising from adverse changes in interest rates. As of June 30, 2014, we had cash equivalents of $8.6 million consisting primarily of investments in U.S. Treasuries and certificates of deposit. Our primary exposure to market risk is interest rate sensitivity, which is affected by changes in the general level of U.S. interest rates, particularly because our investments are in short-term marketable securities. Our marketable securities are subject to interest rate risk and could fall in value if market interest rates increase. Due to the short-term duration of our investment portfolio and the low risk profile of our investments, an immediate 10% change in interest rates would not have a material effect on the fair market value of our investment portfolio. We have the ability to hold our marketable securities until maturity, and therefore we would not expect our operating results or cash flows to be affected to any significant degree by the effect of a change in market interest rates on our investments.

We contract with CROs and contract manufacturers internationally. Transactions with these providers are predominantly settled in U.S. dollars and, therefore, we believe that we have only minimal exposure to foreign currency exchange risks. We do not hedge against foreign currency risks.

The JOBS Act

In April 2012, the Jumpstart Our Business Startups Act of 2012, or the JOBS Act, was enacted. Section 107 of the JOBS Act provides that an "emerging growth company," or EGC, can take advantage of the extended transition period provided in Section 7(a)(2)(B) of the Securities Act of 1933, as amended, or the Securities Act, for complying with new or revised accounting standards. As a result, an EGC can delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have irrevocably elected not to avail ourselves of this extended transition period and, as a result, we will adopt new or revised accounting standards on the relevant dates on which adoption of such standards is required for other public companies.

BUSINESS

Overview

We are a late-stage biopharmaceutical company focused on the development of novel, first-in-class pharmaceuticals to address the needs of patients with renal and vascular disease. Our product candidate, PRT-201, is a recombinant human elastase that we are developing to reduce vascular access failure in patients with chronic kidney disease undergoing or planning for hemodialysis, a lifesaving treatment that cannot be conducted without a functioning vascular access. We believe the data from our completed Phase 2 trial of PRT-201 in patients undergoing creation of an arteriovenous fistula, or AVF, support that a one-time, local application of PRT-201 during AVF surgical placement reduces AVF failure, thereby improving patient outcomes and reducing the burden on patients and the healthcare system. We are not aware of any approved preventative treatments to reduce the failure rate of AVFs. We expect to initiate the first of two Phase 3 trials for PRT-201 in radiocephalic AVFs, our initial indication, in the third quarter of 2014 and initiate the second Phase 3 trial in the first half of 2015.

The need to improve vascular access outcomes is well established in the hemodialysis community. A 2014 publication estimated the total cost of managing hemodialysis vascular access dysfunction in the United States to be approximately $2.9 billion annually. AVFs are the gold standard of vascular access for hemodialysis, given they are associated with fewer complications and reduced rates of hospitalization than other forms of vascular access. We estimate there are approximately 130,000 AVFs created in the United States annually, a procedure in which a surgeon transects a vein and sutures it to the side of a nearby artery, typically in the arm. However AVFs have a greater than 50% failure rate in their first year after placement, resulting in frequent surgical or interventional procedures and a high rate of abandonment, leading to increased morbidity, mortality and costs of care. Function can usually be restored via additional procedures, either an intervention such as angioplasty, which is dilation of a blood vessel with a balloon, or a surgical revision. However, these procedures are costly, invasive, painful, associated with a number of complications and often need to be repeated. AVF patients in the United States on average require greater than 1.5 procedures per year, each of which typically costs Medicare between $5,000 and $13,000.

We demonstrated that PRT-201 generates fragments of elastin, a protein present in blood vessels, and we believe the fragments of elastin inhibit formation of neointimal hyperplasia, which is the growth of tissue inside vessels that narrows AVFs and reduces blood flow. During the AVF placement surgery, the surgeon administers drops of PRT-201 onto the surface of the artery and vein of the AVF for 10 minutes followed by a saline irrigation. We believe that a one-time, local application of PRT-201 to the external surface of the vessels during AVF surgical placement can modify the injury response, or scarring, resulting from surgery and thereby reduce the severity of neointimal hyperplasia and AVF failure following surgery.

We have completed a multicenter, randomized double-blind, placebo-controlled Phase 2 trial of PRT-201 in 151 patients undergoing surgical creation of AVFs in the wrist, known as radiocephalic AVF, or upper arm, known as brachiocephalic AVF. The primary efficacy endpoint was primary unassisted patency, defined as the time from surgical creation of the AVF to occurrence of a thrombosis or an intervention such as angioplasty, to restore or maintain patency, or functionality. Both the 10 microgram and 30 microgram doses of PRT-201 showed a trend toward efficacy on the primary endpoint, although neither dose met the primary endpoint with statistical significance. For all AVFs, median patency, the time at which 50% of patients in a group lost primary unassisted patency, was 224 days in the placebo group and greater than 365 days in each of the PRT-201 treatment groups, indicating that PRT-201 prolonged primary unassisted patency. In the trial, patients treated with PRT-201 reported adverse events comparable to placebo. These events were consistent with the medical events experienced by chronic kidney disease patients undergoing AVF placement surgery.

An analysis of the primary endpoint data revealed an uneven distribution in patency loss events in patients with a brachiocephalic AVF due to central stenosis in the shoulder and chest, remote from the site of an AVF. Central stenoses commonly exist prior to AVF placement and are unmasked following placement of brachiocephalic AVFs, which have higher blood flow than radiocephalic AVFs. These

stenoses are unrelated to treatment with PRT-201. To correct for this uneven distribution, we conducted a non-prespecified analysis of the primary endpoint that excluded patency loss events due to central stenoses. This analysis demonstrated a significant reduction in the risk of primary unassisted patency loss in the 30 microgram PRT-201 dose group (p=0.04) compared to placebo.

The benefit of PRT-201 on primary unassisted patency was most pronounced in the subset of patients undergoing placement of a radiocephalic AVF. The subset analysis of this endpoint for radiocephalic AVF patients receiving the 30 microgram dose, which was not prespecified, showed a significant increase in median primary unassisted patency of >365 days as compared to 125 days in the placebo group. In addition, we observed beneficial drug effects on additional efficacy endpoints, including unassisted maturation, defined as increased vessel diameter and blood flow without the need for an intervention such as angioplasty; rate of procedures to restore or maintain AVF patency; secondary patency, defined as abandonment of the AVF and the need for creation of a new vascular access; use for hemodialysis and hemodynamically significant stenosis, or narrowing of blood vessels.

In April 2013, we held an end of Phase 2 meeting with the United States Food and Drug Administration, or FDA, during which we confirmed elements of our Phase 3 development plan, including the primary endpoint. We plan to perform two 300-patient Phase 3 trials of PRT-201 using a 30 microgram dose, which will enroll patients undergoing a surgical procedure to create a radiocephalic AVF. We began enrolling patients in our first Phase 3 clinical trial in the third quarter of 2014, and anticipate that results will be available in 2017. We expect to initiate our second Phase 3 clinical trial in the first half of 2015. In May 2014, following the results from our Phase 2 trial and to fund our first Phase 3 trial, we closed on the $25.0 million first tranche of a $45.0 million total financing. The financing was led by Abingworth, Deerfield and Pharmstandard and included investments from our existing venture investors. While the FDA offered no assurances that it will not require us to conduct any additional clinical studies, we believe we will not need to conduct any additional clinical studies after our Phase 3 trials. Further, if the results of the first Phase 3 trial are sufficiently compelling, we intend to meet with the FDA to discuss the possibility of submitting a Biologics License Application, or BLA, supported by the single Phase 3 trial and may decide to submit a BLA to the FDA prior to completing the second Phase 3 trial. PRT-201 has received fast track designation which is designed to facilitate the development and expedite the review of drugs to treat serious conditions and fill an unmet medical need, from the FDA and orphan drug designation in the United States and European Union, for hemodialysis vascular access indications.

We believe that if our Phase 3 clinical program is successful PRT-201 will potentially become the standard of care for patients with chronic kidney disease who are undergoing surgical placement of a radiocephalic AVF. We retain worldwide commercial rights to PRT-201. If approved by regulatory authorities, we intend to commercialize this product in the United States ourselves with a specialty hospital sales force, focused primarily on vascular surgeons, and intend to seek one or more collaborators to commercialize the product in additional markets. Our patents include claims covering formulations, methods of manufacturing and use of elastases, providing protection in the United States through mid 2029 and European Union through 2028, with potential extension through 2032 in the United States and the European Union.

Our Strengths

We believe our company and PRT-201 possess the following attributes that increase the likelihood that we will be successful in developing and commercializing PRT-201:

- *Entering Phase 3 trials for radiocephalic AVF placement.* We plan to conduct our Phase 3 clinical trials in radiocephalic AVF placement using a 30 microgram dose of PRT-201, the population and dose in which, in a non prespecified analysis, we observed an improvement in primary unassisted patency with PRT-201 in our Phase 2 trial.
- *Phase 3 endpoints same as our Phase 2 trial.* The primary endpoint in our Phase 3 trial, primary unassisted patency, will be the same as we used in our Phase 2 trial. In addition, our secondary

endpoint (secondary patency) and tertiary endpoints (unassisted maturation, use for hemodialysis and average procedure rates) in our Phase 3 trial were all endpoints in our Phase 2 trial. In April 2013, we held an end of Phase 2 meeting with the FDA during which we confirmed elements of our Phase 3 development plan, including the primary endpoint.

- *Safety profile supports approval.* Based on results from our clinical trials and preclinical studies, we believe PRT-201, which is administered once and only acts locally, has demonstrated a safety profile that will support approval if our planned Phase 3 clinical program is successful. Because PRT-201 is administered in a one-time, local application and is inactivated by antiproteases, substances that inhibit the activity of a protease, in the blood, there is no systemic activity. In clinical trials assessing safety, there were no material increases in adverse events in the PRT-201 treatment groups as compared to placebo and no material findings related to physical examinations or clinical laboratory testing including chemistry, hematology and coagulation panels or antibodies to PRT-201. At our end of Phase 2 meeting with the FDA, we confirmed that we do not need to conduct any additional preclinical studies to support a BLA filing.
- *Unmet medical need.* While AVFs are considered the most desirable form of vascular access by the medical community, they are also associated with high failure rates, a serious complication for hemodialysis patients that results in substantially higher healthcare costs. A 2014 publication estimated the total cost of managing hemodialysis vascular access dysfunction in the United States to be approximately $2.9 billion annually. We are not aware of any approved preventative treatments to reduce AVF failure rate. PRT-201 has received fast track designation from the FDA, which is designed to facilitate the development and expedite the review of drugs to treat serious conditions and fill an unmet medical need. We believe PRT-201 reduces vascular access failure in patients with chronic kidney disease, or CKD, undergoing hemodialysis and, if approved, could become the standard of care by reducing the cycle of interventions, improving patient outcomes and reducing the overall burden on patients and the healthcare system
- *Substantial and readily-addressable market opportunity.* If PRT-201 is approved, we intend to commercialize this product in the United States and potentially certain European countries ourselves with a specialty hospital sales force, focused primarily on vascular surgeons, and intend to seek one or more collaborators to commercialize the product in additional markets. We estimate a sales force of approximately 75-100 representatives will enable us to call on the approximately 1,300 hospitals that account for more than 90% of the AVF surgical placements performed in the United States annually. We believe PRT-201 will be supported by key stakeholders, including referring nephrologists, patient advocacy groups, large dialysis organizations and payors. We believe PRT-201 will be reimbursed adequately as costs related to AVF surgical placement, which is typically performed in the hospital outpatient setting, are not included in the ESRD bundle, the single bundled payment from Medicare for a number of the costs of hemodialysis treatments, medications, labs and supplies for patients with end stage renal disease.
- *Experienced team.* Our executive management team has extensive experience in the renal and vascular disease fields through their substantial involvement in companies such as Abbott, GelTex, Genzyme, Glaxo, and Merck. Our Chief Executive Officer and Chief Medical Officer were senior executives at GelTex, a biopharmaceutical company, where they played leading roles in the development and commercialization of Renagel, a treatment for hemodialysis patients that led to Genzyme's acquisition of GelTex for more than $1 billion.

Our Strategy

Our strategy is to develop and commercialize PRT-201 for patients suffering from renal and vascular diseases, beginning with patients with CKD undergoing surgical creation of a radiocephalic AVF. Key elements of our strategy include our plans to:

- *Complete clinical development of PRT-201 and seek regulatory approval in the United States in its lead indication.* We plan to commence our first Phase 3 clinical trial of PRT-201 for patients with CKD

undergoing creation of a radiocephalic AVF in the third quarter of 2014. Prior to completing enrollment in the first Phase 3 trial, we will initiate our second Phase 3 trial in the first half of 2015. If the results of the first Phase 3 trial are sufficiently compelling, we intend to meet with the FDA to discuss the possibility of submitting a BLA supported by the single Phase 3 trial and may decide to submit a BLA to the FDA prior to completing the second Phase 3 trial.

- *Commercialize PRT-201 directly in the United States.* If PRT-201 is approved by the FDA, we intend to commercialize it ourselves in the United States with a specialty hospital sales force focused primarily on vascular surgeons. There are approximately 2,800 vascular surgeons in the United States. In 2011, according to the U.S. Renal Data System 2013 Annual Data Report, there were approximately 395,000 hemodialysis patients in the United States at the end of the year. Based on various third-party sources, we estimate that approximately 130,000 AVFs are placed annually. We believe a specialty hospital sales force of approximately 75-100 representatives will enable us to call on the approximately 1,300 hospitals that account for more than 90% of the AVF surgical placements performed in the United States annually. We believe that PRT-201's potential benefits to patients undergoing surgical creation of an AVF will result in its broad adoption.
- *Undertake clinical development of PRT-201 in Europe and establish partnerships for commercialization of PRT-201 in all or parts of Europe.* We are currently evaluating our existing clinical program to support filing in Europe. We may, based on additional data including the data from our Phase 3 clinical trials in the United States and if sufficient funds become available, choose to conduct a clinical trial of PRT-201 in Europe. We estimate that there are approximately 316,000 hemodialysis patients in Europe. Prior to enrolling our first patient in Europe, we plan to formally seek guidance from the European Medicines Agency, or EMA, regarding its requirements for regulatory approval. We expect results from this trial to be available two to three years after the first patient is enrolled. If this European trial successfully meets its primary endpoint and depending on the guidance obtained from the EMA, we would expect to submit a Marketing Authorization Application, or MAA. If PRT-201 is approved by the EMA, we intend to commercialize it in some European countries with our own specialty hospital sales force and/or with a commercial partner in the other European countries. Like in the United States, we intend to target both vascular surgeons who create AVFs as well as key referring nephrologists.
- *Pursue additional indications for PRT-201.* We believe that our Phase 2 clinical data support further development of PRT-201 in brachiocephalic AVF placement. We may, based on additional data including the data from our Phase 3 clinical trials and if sufficient funds become available, study the effects of a 30 microgram dose of PRT-201 versus placebo on brachiocephalic AVFs. If this trial successfully meets its primary endpoint, we would expect to submit a supplemental BLA, or sBLA, to the FDA and a supplemental MAA, or sMAA, to the EMA. Further, if sufficient funds become available and after reviewing the results from our Phase 3 clinical trials, we may commence a clinical trial of PRT-201 in patients undergoing placement of an arteriovenous graft, or AVG. We believe PRT-201's potential to reduce neointimal hyperplasia could offer a significant medical benefit in these patients.
- *Establish partnerships for development and commercialization of PRT-201 in Japan and other Asian countries.* We estimate that there are approximately 295,000 patients on hemodialysis in Japan and more than 750,000 throughout all of Asia. Approximately 90% of Japanese hemodialysis patients receive AVFs. We may enter into collaborations for the development and commercialization of PRT-201 in Asia.
- *In-license or acquire additional product opportunities.* We plan to search for additional product opportunities that could be sold and marketed by the specialty hospital sales force required to successfully launch PRT-201 in the United States if it is approved for marketing.

Background on Hemodialysis

Healthy kidneys serve many functions, including removing waste and excess water, helping to control blood pressure and keeping electrolytes, such as sodium and potassium, in balance. Patients with CKD,

have lost most or all kidney function, most commonly due to diabetes or hypertension. Kidney disease is progressive and once a patient has reached end-stage CKD, the kidneys are no longer able to remove waste and fluids from the body. At this point, some form of renal replacement therapy is required, such as hemodialysis, in which blood is processed by a hemodialysis machine, peritoneal dialysis, a process using a cavity in the abdomen called the peritoneum as a membrane across which fluids are exchanged from the blood, or kidney transplant.

According to the U.S. Renal Data System 2013 Annual Data Report, in 2011 there were approximately 395,000 hemodialysis patients in the United States, and an incremental 104,000 patients initiated hemodialysis in the United States. As reported by Fresenius Medical, a major provider of hemodialysis services and renal care products, there are approximately 316,000 hemodialysis patients in Europe, 295,000 hemodialysis patients in Japan and 2 million hemodialysis patients worldwide, with an annual worldwide growth rate of 6-7%.

Hemodialysis is the most common form of treatment for end-stage CKD. Hemodialysis is a chronic therapy performed by cannulating, or piercing, a vein with a large bore needle so that blood can be pumped through a hemodialysis machine, which removes waste and excess fluid normally excreted by the kidney. The cleansed blood is then returned to the same vein via a second needle. A hemodialysis session typically lasts three to four hours and is performed three times a week in an outpatient dialysis clinic.

To enable sufficient blood to pass through the hemodialysis machine to complete treatment within four hours, a vein must have blood flow of at least 500 milliliters per minute. The arm is the most convenient location for accessing the blood stream on a recurring basis, but blood flow in the arm is approximately 50 milliliters per minute. Therefore, most hemodialysis patients undergo a surgical procedure in which a surgeon establishes a direct connection between an artery and a vein to create a high flow circuit of sufficient diameter, most often in an arm. The direct artery-vein connection effectively bypasses the capillary circulation in the hand and leads to a process known as maturation, where the internal diameter, or lumen, of the vein and blood flow increase over a period of weeks, resulting in a lumen diameter greater than 4 millimeters and blood flow of 500-2,000 milliliters per minute in successful cases.

The gold standard for vascular access is an AVF, in which a surgeon transects a vein in the arm and sutures it to the side of a nearby artery. AVFs are preferred because they are less prone to patency loss than arteriovenous grafts, or AVGs; approximately 50% of AVFs and up to 75% of AVGs will lose primary patency and 20-30% of AVFs and 28-35% of AVGs will lose secondary patency in the first year after surgical placement. As compared to AVGs, AVFs require approximately 40% fewer interventional or surgical procedures and suffer from a rate of vascular access infection that is 54% lower. Patients dialyzing with an AVF have lower rates of thrombosis and hospitalization, longer survival, reduced mortality and lower cost of care. Beyond the substantial medical advantages of an AVF, available data from the U.S. Renal Data System show that patients who dialyze with an AVF cost Medicare approximately $15,000 less annually than patients who dialyze with an AVG and approximately $25,000 less annually than patients who dialyze with a catheter. According to published data, approximately 60% of hemodialysis patients in the United States dialyze with an AVF compared to 67-83% of patients in the major European countries and approximately 90% of patients in Japan.

Based on various third-party sources, we estimate there are approximately 130,000 AVFs created in the United States annually. There are a limited number of potential artery-vein combinations in the arm that can be used to create an AVF, principally the following:

- radiocephalic AVF at the wrist (radial artery sutured to cephalic vein), which we estimate is created in 40% of new AVF placements;
- brachiocephalic AVF at the elbow (brachial artery sutured to cephalic vein), which we estimate is created in 50% of new AVF placements; and
- brachiobasilic AVF in the upper arm (brachial artery sutured to basilic vein), which we estimate is created in 10% of new AVF placements.

The medical community endorses radiocephalic AVFs as the optimal form of vascular access and the recommended first choice for new hemodialysis patients. Creating the vascular access site at the wrist preserves the potential future use of other access further up in the arm, is simpler to create, and is less likely to create heart failure or steal syndrome, where the diversion of flow through the AVF reduces blood to the hand. Radiocephalic AVFs are also less likely to suffer from central stenoses in the shoulder and chest, remote from the site of the AVF. The Kidney Disease Outcome Quality Initiative Guidelines, or KDOQI Guidelines, authored by the National Kidney Foundation, or NKF, specifically recommend starting with a radiocephalic AVF if possible, stating that "starting [closer to the hand] and moving [further up the arm] provides for the possibility of preserving as many potential sites as possible for future access creation." If a radiocephalic AVF must be abandoned, a surgeon can create a new vascular access higher up the arm, most likely a brachiocephalic AVF. However, if a brachiocephalic AVF is placed first, the surgeon cannot later move down that same arm to create a radiocephalic AVF because the cephalic vein has already been transected for use in the brachiocephalic AVF.

Radiocephalic (wrist) AVFs suffer from high rates of patency loss and maturation failure, with up to 70% being subject to primary unassisted patency loss and up to 35% being abandoned within twelve months after their surgical placement. Patency loss in radiocephalic AVFs occurs due to stenosis formation at or near the AVF 75% - 95% of the time. Some patients never receive a radiocephalic AVF because the surgeon believes the risk of failure is too high for those patients. These patients will typically undergo placement of an AVF higher up on the arm and permanently lose at least one of their access sites. We believe that the number of radiocephalic AVFs created annually may rise significantly if PRT-201 improves outcomes and allows vascular surgeons to create radiocephalic AVFs in sites that they previously considered to pose an unacceptably high risk of failure.

The second choice for vascular access after AVF is an AVG in which a surgeon connects an artery and vein using a synthetic tube. Based on reported data, approximately 20% of hemodialysis patients in the United States dialyze with an AVG, compared to approximately 5-12% of patients in the major European countries and approximately 7% of patients in Japan.

The least desirable type of vascular access is a catheter, a plastic tube that is placed directly through the skin into a vein, typically via an incision in the neck enabling placement of the catheter into a large vein that leads directly to the heart. The catheter connects the patient's vasculature to the hemodialysis machine. Because the catheter penetrates the skin continuously, it is subject to a high risk of infection and increased mortality. One of the primary goals of hemodialysis care is to keep patients off catheters. However, patients most often initiate hemodialysis through a catheter until an AVG or AVF is ready to be used, and are dialyzed temporarily through a catheter when the AVF or AVG they have been using fails and a new one has to be created. Approximately 20% of hemodialysis patients in the United States dialyze with a catheter, compared to 10-28% of patients in the major European countries and 2% of patients in Japan, based on published data.

Established Medical Need

The need to improve vascular access outcomes is well established in the hemodialysis community. The health-related and economic cost of creating and maintaining vascular access for hemodialysis has led to a global effort to address the problem. Over the last ten years, the NKF has established guidelines in an effort to increase the use of AVFs while reducing the rate of complications, mostly through the identification and promulgation of best practices. The National Institutes of Health joined the effort in 2000 with the creation of a multi-center consortium of medical centers, the Dialysis Access Clinical Trials Consortium to coordinate the testing of new treatments designed to improve AVF and AVG outcomes. The intensity of these efforts increased markedly in 2004, when the Centers for Medicare and Medicaid Services, or CMS, reacting to health and economic data, announced the "Fistula First" initiative to increase the use of AVFs while reducing complications. According to Fistula First, AVFs should be considered for every patient needing hemodialysis because AVFs last longer than AVGs, require fewer surgical and endovascular interventions, are associated with lower rates of infection, hospitalization and

death, and are less costly. As a result of these efforts, AVF use has approximately doubled since 2004 to 60% of United States hemodialysis patients.

A major problem with AVFs and AVGs is patency loss, in which the access experiences either a significant or complete reduction in blood flow, precluding hemodialysis and placing the access at risk of abandonment. However, the increased use of AVFs has led to a concurrent increase in AVF patency loss as AVFs are placed in patients with higher risks of AVF failure, such as the elderly, diabetics or patients with smaller blood vessels. Additionally, physicians have become more aggressive in monitoring and intervening earlier upon AVFs in an attempt to treat patency loss before it results in abandonment of that access site. These factors have resulted in an approximate doubling in the rate of AVF interventions in less than a decade.

We are not aware of any approved preventative measures to reduce the rate of vascular access patency loss, and the clinical implications of patency loss are severe. An episode of patency loss must be addressed urgently to restore blood flow, enable the patient to resume hemodialysis and avoid access abandonment. Treatment of patency loss typically involves an outpatient procedure, either an endovascular intervention, such as balloon angioplasty, stenting or thrombectomy, or a surgical revision.

Procedures to address patency loss are invasive, painful, and associated with a number of complications, and there are a number of problems associated with them:

- *The procedures are not always successful in restoring patency.* Procedures to address AVF patency loss are unsuccessful up to 27% of the time. When these procedures are unsuccessful or the physician determines that a procedure to restore patency is futile, the access site must be abandoned, resulting in the urgent need for catheter placement to enable hemodialysis. Recent data indicate that hemodialysis patients who switch from a permanent vascular access to a catheter have a mortality rate that is double those who remain on a permanent access. Access abandonment also results in surgical placement of a new AVF or AVG, reducing the number of future access sites available to the patient.
- *The procedures often fail to provide a durable benefit, resulting in a cycle of interventions for the patient.* Recent data indicate that 50% of AVFs that undergo angioplasty to treat patency loss experience another episode of patency loss within 12 months, resulting in the need for additional procedures to restore patency. AVF patients in the United States on average require greater than 1.5 procedures per year, each of which typically costs Medicare between $5,000 and $13,000. A United States hospital recently published data indicating that maintaining a radiocephalic AVF can cost on average more than $17,000 in the first year after surgical placement. A 2014 publication estimated the total cost of managing vascular access dysfunction in the United States to be approximately $2.9 billion annually.

AVFs and AVGs are also prone to secondary patency loss, in which the access must be abandoned. Patients on hemodialysis must dialyze with a catheter until a new permanent access can be surgically placed and becomes usable for hemodialysis, a process that typically requires a minimum of three months for AVFs. During this time, patients are at a heightened risk of serious infection, hospitalization and death. According to the U.S. Renal Data System, in 2011 hemodialysis patients averaged approximately 12 hospital days per year.

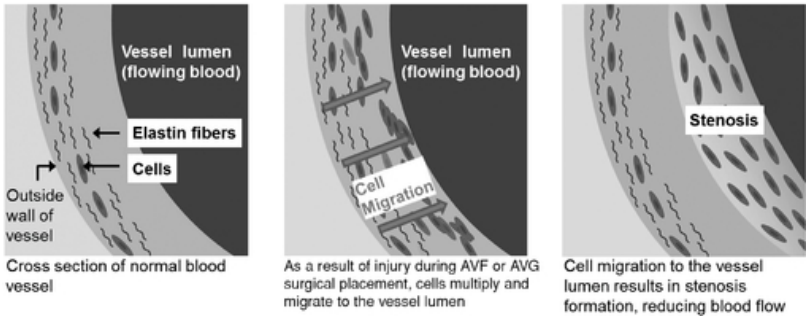
PRT-201

PRT-201 is a recombinant human elastase under development as a treatment to prevent AVF and AVG patency loss. We initiated the first of two Phase 3 trials for PRT-201 in radiocephalic AVF, our lead indication, in the third quarter of 2014 and expect to initiate the second Phase 3 trial in the first half of 2015.

Mechanism of Action

AVF patency loss occurs most commonly due to progressive scarring in the wall of the outflow vein near the lumen, resulting in stenosis of the lumen of the vein and obstruction of blood flow in the AVF. This form of vascular scarring is commonly known as neointimal hyperplasia. When surgeons create an AVF they handle and manipulate blood vessels resulting in mechanical vessel injury. Furthermore, after AVF creation the rapid flow of blood from the artery into the outflow vein results in unnatural physiologic changes and mechanical stresses in the vein wall. The response of the vein to this injury and stress results in activation and recruitment of scar forming cells, which multiply and migrate from the outside wall to the inside wall of the blood vessel and produce a thick layer of tissue, creating a narrowing in the vein lumen and a reduction in AVF blood flow. This blood vessel response to injury occurs during the first two to three weeks following vascular surgery and is shown in the following figure.

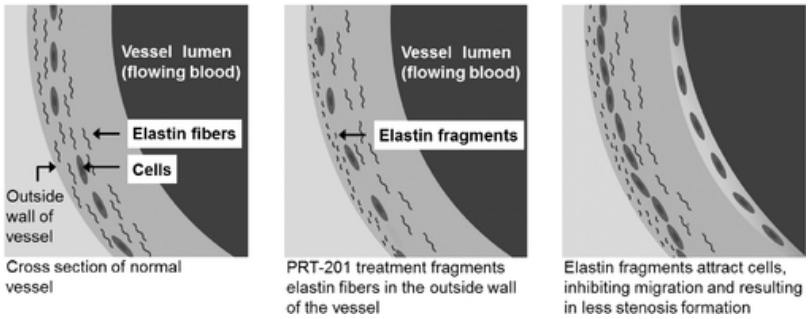
Vessel Injury During AVF and AVG Surgical Placement Results in Stenosis Formation



We demonstrated that PRT-201 fragments elastin, a protein present in blood vessel walls. The fragmentation of elastin in the outside wall of the blood vessel is thought to inhibit formation of neointimal hyperplasia thereby reducing the risk of patency loss. Elastase causes localized fragmentation of elastin protein fibers present in blood vessel walls. The elastin fragments generated by elastase are chemoattractants for scar forming cells, meaning that the fragments attract these scar forming cells, inhibiting their migration to the lumen. The cells recognize the elastin fragments via receptors present on the cell surface that bind to specific elastin fragment sub-types. The importance of elastin fragments in vascular biology, including the response to vascular injury has been established in the scientific literature over three decades. Published academic studies conducted in animals provide evidence that fragmentation of elastin in the outer wall of the blood vessels from administration of elastase after vascular injury resulted in a 38-42% reduction in neointimal hyperplasia at 28 days following the surgical procedure. Based on our preclinical *in vivo* and *ex vivo* studies in human vessels, applying PRT-201 to the external surface of the blood vessels generates localized elastin fragments in the outside wall of injured blood vessels. We have established this effect in the doses we plan to advance in our clinical trials. We believe that a one-time, local application of a 30 microgram dose of PRT-201 to the external surface of the vessels during AVF surgical placement can reduce the vascular scarring on the inside of the vessel wall resulting from surgery and thereby reduce the severity of neointimal hyperplasia and the risk of AVF failure. During the AVF placement surgery, the surgeon administers drops of PRT-201 onto the surface of the artery and vein at the

AVF for 10 minutes followed by a saline irrigation. We believe the elastin fragments that are generated by PRT-201 attract scar forming cells to the outside wall of the injured vessel, reducing their movement to the inside wall of the vessel, thereby inhibiting lumen stenosis. This mechanism is portrayed in the following figure:

PRT-201 Treatment Inhibits Stenosis Formation



This injury response and the role of elastase-generated fragments are operative in other cardiovascular surgeries, such as bypass, and interventional procedures, such as angioplasty.

Clinical Development of PRT-201

Our Phase 2 AVF Clinical Trial

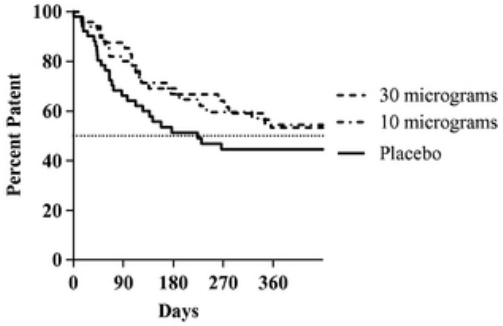
We completed a multicenter, randomized, double-blind, placebo-controlled Phase 2 trial of PRT-201 in AVF that treated 151 patients with CKD undergoing creation of a radiocephalic AVF (n=67) or brachiocephalic AVF (n=84). Patients were treated with PRT-201 at doses of 10 or 30 micrograms or placebo at the time of AVF placement and were followed for up to 12 months.

Primary endpoint

The primary efficacy endpoint was primary unassisted patency over 12 months. Primary unassisted patency was defined as the time from access creation until the first occurrence of either AVF thrombosis or a procedure, such as balloon angioplasty, to restore or maintain patency.

Both doses of PRT-201 showed a trend toward efficacy, although neither dose met the primary endpoint with statistical significance. Median patency, the time at which 50% of patients in a group lost primary unassisted patency, was 224 days in the placebo group and greater than 365 days in each of the PRT-201 treatment groups indicating patency in the PRT-201 treatment groups was prolonged by PRT-201. Treatment with PRT-201 at 10 and 30 microgram doses was associated with a reduction of 31% and 33%, respectively, in the risk of primary unassisted patency loss. After adjusting for differences in baseline characteristics associated with the risk of primary unassisted patency loss, treatment with PRT-201 at 10 and 30 microgram doses was associated with a reduction of 24% and 41%, respectively, in the risk of primary unassisted patency loss. The following Kaplan-Meier curves and table display primary unassisted patency for all AVFs.

Primary Unassisted Patency—All AVFs



Note: Prespecified analysis.

The table below shows the primary unassisted patency data in the placebo and PRT-201 treatment groups.

Reduction in Risk of Primary Unassisted Patency Loss vs. Placebo—All AVFs

	PRT-201 10 microgram dose	PRT-201 30 microgram dose
Number of Patients	N=51	N=49
Unadjusted Risk vs. Placebo	-31% (p=0.19)	-33% (p=0.17)
Adjusted Risk(1) vs. Placebo	-24% (p=0.35)	-41% (p=0.10)

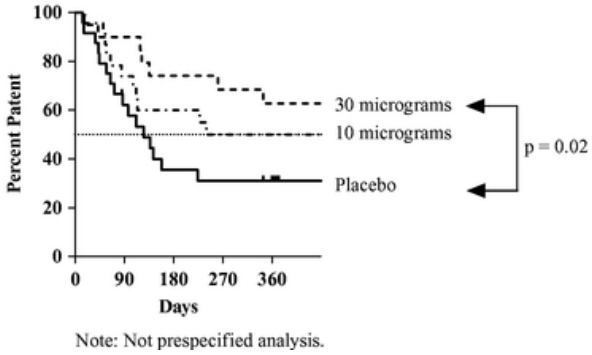
Note: Prespecified analysis.

(1) Adjusted for differences in baseline characteristics associated with the risk of primary unassisted patency loss between treatment groups using a prespecified Cox regression analysis.

Patients completing 12 months of follow-up in the initial trial were followed in a registry to obtain additional data related to the efficacy endpoints. In this follow-up, the PRT-201 benefit on primary unassisted patency persisted out to 900 days.

Radiocephalic AVFs. The benefit of PRT-201 on primary unassisted patency was most pronounced in the subset of patients undergoing placement of a radiocephalic AVF than in the subset of patients undergoing placement of a brachiocephalic AVF or all patients undergoing placement of an AVF. The subset analysis of this endpoint was not prespecified. The following Kaplan-Meier curves and table summarize the reduction in risk of primary unassisted patency loss in the subset of patients with radiocephalic AVFs. Treatment with PRT-201 at doses of 10 and 30 micrograms was associated with a reduction of 41% and 63%, respectively, in the risk of primary unassisted patency loss. Median patency was 125 days in the placebo group and 377 days in the 30 microgram group (in some cases the 12 month follow up occurred after day 365 due to patient schedules), indicating a significant improvement in primary unassisted patency.

Primary Unassisted Patency—Radiocephalic AVFs



Note: Not prespecified analysis.

Reduction in Risk of Primary Unassisted Patency Loss vs. Placebo—Radiocephalic AVFs

	PRT-201 10 micrograms	PRT-201 30 micrograms
Number of Patients	N=23	N=20
Unadjusted Risk vs. Placebo	-41% (p=0.18)	-63% (p=0.02)
Adjusted Risk(1) vs. Placebo	-40% (p=0.20)	-61% (p=0.04)

Note: Not prespecified analysis.

(1) Adjusted for differences in baseline characteristics associated with the risk of primary unassisted patency loss between treatment groups using a prespecified Cox regression analysis.

Brachiocephalic AVFs. The benefit of PRT-201 on primary unassisted patency was less pronounced in the subset of patients undergoing placement of a brachiocephalic AVF. This was in part due to an uneven distribution between brachiocephalic AVF groups in the number of patency loss events occurring in the central veins and cephalic arch, also known as central stenosis, which are remote from the site of the AVF. Patency loss in brachiocephalic AVFs occurs due to central stenosis 50% of the time. Central stenoses commonly exist prior to surgery due to the venous anatomy or scarring from a prior hemodialysis catheter, but are typically unmasked following placement of the higher blood flow brachiocephalic AVFs. Since PRT-201 is active locally at the site where it is applied on the AVF, and because we have demonstrated that PRT-201 is not active remotely, we believe that central stenoses are unrelated to PRT-201. Therefore, to correct for this uneven distribution, we conducted a non-prespecified analysis of the primary endpoint in brachiocephalic AVFs which excluded patency loss events due to central stenoses. The following table summarizes the risk of primary unassisted patency loss in brachiocephalic AVFs including and then excluding patency loss events related to central stenoses.

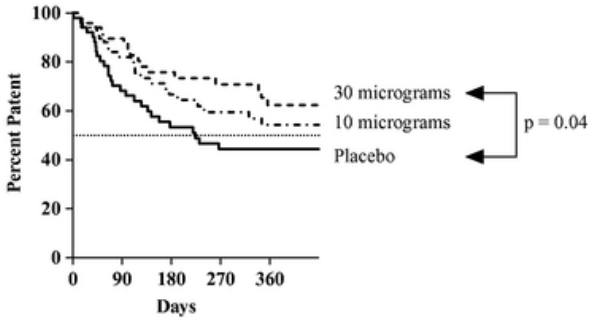
Reduction in Risk of Primary Unassisted Patency Loss vs. Placebo—Brachiocephalic AVFs

	PRT-201 10 micrograms	PRT-201 30 micrograms
Number of Patients	N=28	N=29
Unadjusted Risk vs. Placebo	-14% (p=0.72)	+10% (p=0.82)
Unadjusted Risk vs. Placebo Excluding Central Stenoses	-12% (p=0.76)	-26% (p=0.46)

Note: Not prespecified analysis.

We also conducted a non-prespecified analysis across all patients of the primary endpoint correcting for this uneven distribution in central stenoses. The following Kaplan-Meier curves for primary unassisted patency for all AVFs (excluding central stenoses) and table demonstrate a significant reduction in the risk of primary unassisted patency loss for the 30 microgram dose (p=0.04, for the 30 microgram dose) versus placebo. Treatment with PRT-201 at doses of 10 and 30 micrograms was associated with a reduction of 31% and 48%, respectively, in the risk of primary unassisted patency loss. After adjusting for differences in baseline characteristics associated with the risk of primary unassisted patency loss, treatment with PRT-201 at doses of 10 and 30 micrograms was associated with a reduction of 25% and 52%, respectively, in the risk of primary unassisted patency loss.

Primary Unassisted Patency—All AVFs
(Excluding Central Stenoses)



Note: Not prespecified analysis.

Reduction in Risk of Primary Unassisted Patency Loss vs. Placebo—All AVFs
(Excluding Central Stenoses)

	PRT-201 10 micrograms	PRT-201 30 micrograms
Number of Patients	N=51	N=49
Unadjusted Risk vs. Placebo	-31% (p=0.20)	-48% (p=0.04)
Adjusted Risk vs. Placebo(1)	-25% (p=0.33)	-52% (p=0.02)

Note: Not prespecified analysis.

(1) Adjusted for differences in baseline characteristics associated with the risk of primary unassisted patency loss between treatment groups using a prespecified Cox regression analysis.

In a larger trial of brachiocephalic AVFs, we expect that the occurrence of patency loss due to central stenosis would be evenly distributed between treatment groups. In the Phase 3 clinical trials we have planned, we expect that patency loss due to central stenosis would be rare since we intend to enroll radiocephalic AVF patients exclusively and radiocephalic AVFs rarely suffer from patency loss due to central stenosis because of lower blood flow. In our Phase 2 trial, no radiocephalic AVF in any group lost primary patency due to central stenosis.

Secondary and other endpoints

PRT-201 showed results consistent with a beneficial drug effect on multiple secondary efficacy endpoints. The prespecified efficacy endpoints were unassisted maturation, secondary patency, use for hemodialysis and hemodynamically significant lumen stenosis. In addition, we performed a prespecified efficacy analysis of average rate of procedures to restore or maintain AVF patency, a component of our primary endpoint. As with the primary efficacy analyses, we performed a number of prespecified and exploratory analyses of the data from this Phase 2 trial.

- *Unassisted maturation*. Maturation is necessary for use of an AVF for hemodialysis. Unassisted maturation was defined as achieving maturation at three months without an intervention. Maturation was assessed using ultrasound measuring blood flow and lumen vein diameter. All ultrasounds were reviewed by a central reader masked to treatment assignment and AVF outcome. Two well-accepted criteria for measuring maturation were used, as shown in the footnotes in the table below. The 30 microgram dose, which we intend to study in our Phase 3 trials, showed statistically significant improvement in maturation at Month 3, with more benefit seen in patients receiving radiocephalic AVFs (figure below) than in patients receiving brachiocephalic AVFs. In the subset of patients with brachiocephalic AVFs, there was a trend toward improvement in unassisted maturation at both the 10 and 30 microgram doses.

Unassisted Maturation at Three Months—% of Patients (p-Value vs. Placebo)

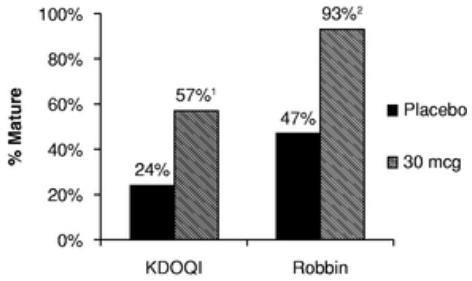
	Placebo	PRT-201 10 micrograms	PRT-201 30 micrograms
All AVFs			
Number of Patients	N=39	N=39	N=37
Percentage Mature NKF-KDOQI(1)	46%	64% (p=0.11)	70% (p=0.03)
Percentage Mature Robbin(2)	67%	87% (p=0.03)	92% (p<0.01)
Radiocephalic AVFs			
Number of Patients	N=17	N=19	N=14
Percentage Mature NKF-KDOQI(1)	24%	37% (p=0.48)	57% (p=0.08)
Percentage Mature Robbin(2)	47%	74% (p=0.17)	93% (p<0.01)
Brachiocephalic AVFs			
Number of Patients	N=22	N=20	N=23
Percentage Mature NKF-KDOQI(1)	64%	90% (p=0.07)	78% (p=0.34)
Percentage Mature Robbin(2)	82%	100% (p=0.11)	91% (p=0.41)

Note: Prespecified analysis.

(1) National Kidney Foundation Kidney Disease Outcomes Quality Initiative (NKF-KDOQI) maturation is defined as average vein lumen diameter ³6 millimeters and an outflow vein blood flow rate ³600 milliliters/minute.

(2) Robbin maturation is defined as average vein lumen diameter ³4 millimeters and an outflow vein blood flow rate ³500 milliliters/minute.

Unassisted Maturation—Radiocephalic AVFs



Note: Prespecified analysis.

(1) p-value=0.08 vs. placebo

(2) p-value<0.01 vs. placebo

- *The average rate of procedures to restore or maintain patency per patient year at risk.* Patients undergoing a procedure often require repeated procedures over time because procedures such as balloon angioplasty can restore blood flow acutely but also damage the blood vessel. These data can be expressed as a procedure rate calculated as the number of days in which procedure to restore or maintain patency was performed per patient divided by the patient's time on the trial. Procedures included thrombectomy, angioplasty, stent deployment and surgical revision. There was a 56% reduction in the rate of procedures in the 30 microgram group versus the placebo group. In the radiocephalic subset there was a 69% reduction in the average rate of procedures in the 30 microgram group versus the placebo group. In the brachiocephalic subset there was a 43% reduction in the average rate of procedure in the 30 microgram group versus the placebo group. Excluding procedures to treat central stenosis, in the brachiocephalic subset there was an 86% reduction in the average rate of procedures in the 30 microgram group versus the placebo group.

Average Procedure Rate to Restore/Maintain Patency (p-Value vs. Placebo)

	Placebo	PRT-201 10 micrograms	PRT-201 30 micrograms
All AVFs (Prespecified)			
Number of Patients	N=51	N=50	N=48
Procedures per Year	0.9	0.8 (p=0.53)	0.4 (p=0.07)
All AVFs Excluding Central Stenoses (Non-prespecified)			
Number of Patients	N=51	N=50	N=48
Procedures per Year	0.8	0.7 (p=0.44)	0.2 (p<0.01)
Radiocephalic AVFs (Non-prespecified)			
Number of Patients	N=24	N=23	N=20
Procedures per Year	1.0	0.8 (p=0.63)	0.3 (p=0.06)
Brachiocephalic AVFs (Non-prespecified)			
Number of Patients	N=27	N=27	N=28
Procedures per Year	0.7	0.7 (p=0.72)	0.4 (p=0.50)
Brachiocephalic AVFs Excluding Central Stenoses (Non-prespecified)			
Number of Patients	N=27	N=27	N=28
Procedures per Year	0.7	0.7 (p=0.54)	0.1 (p=0.07)

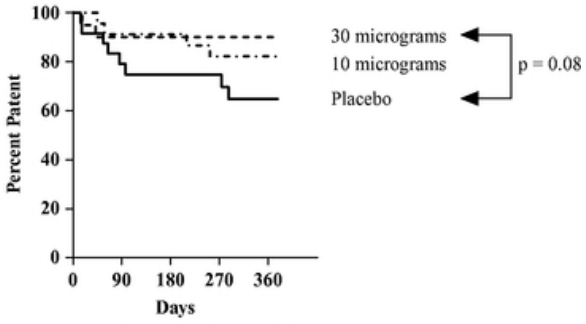
Patients completing 12 months of follow-up in the initial trial were followed in a registry to obtain additional data related to the efficacy endpoints. In this follow up, the PRT-201 benefit on procedure rates persisted out to 900 days as set out in the following table.

Average Procedure Rate to Restore/Maintain Patency Including Registry Data (p-Value vs. Placebo)

	Placebo	PRT-201 10 micrograms	PRT-201 30 micrograms
All AVFs (Prespecified analysis)			
Number of Patients	N=51	N=50	N=48
Procedures per Year	0.8	0.8 (p=0.61)	0.3 (p=0.03)
Radiocephalic AVFs (Non-prespecified analysis)			
Number of Patients	N=24	N=23	N=20
Procedures per Year	1.0	0.8 (p=0.47)	0.2 (p=0.03)
Brachiocephalic AVFs (Non-prespecified analysis)			
Number of Patients	N=27	N=27	N=28
Procedures per Year	0.7	0.8 (p=1.00)	0.4 (p=0.40)

- *Secondary patency.* Secondary patency loss was defined as abandonment of the AVF, which typically occurs following loss of primary unassisted patency due to thrombosis or failure of a procedure to restore patency and leads to additional surgery to create a new vascular access. We observed no significant differences in the risk of secondary patency loss in the overall AVF population or the subset of patients receiving brachiocephalic AVFs. However, as seen in the Kaplan-Meier curves and table below, a trend toward prolonged secondary patency was seen in patients receiving radiocephalic AVFs. In this non-prespecified subset analysis, treatment with PRT-201 at doses of 10 and 30 micrograms was associated with reductions of 55% and 73%, respectively, in the risk of secondary patency loss.

Secondary Patency—Radiocephalic AVFs



Note: Not prespecified analysis.

	PRT-201 10 microgram dose	PRT-201 30 microgram dose
Number of Patients	N=23	N=20
Unadjusted Risk vs. Placebo	-55% (p=0.19)	-73% (p=0.08)

Note: Not prespecified analysis.

Patients completing 12 months of follow-up in the initial trial were followed in a registry to obtain additional data related to the efficacy endpoints. In this follow-up, the PRT-201 benefit on secondary patency in radiocephalic AVFs persisted out to 900 days.

- *Use for hemodialysis*. Use was defined as use of the AVF for hemodialysis at any time without a previous intervention. Although the results were not statistically significant, there was a trend to more patients using the AVF for hemodialysis in the 30 microgram group (69%) compared with the placebo group (53%).
- *Hemodynamically significant lumen stenosis*. Hemodynamically significant lumen stenosis, or narrowing of blood vessels, impairs AVF maturation and contributes to AVF patency loss. Hemodynamically significant stenosis was defined as a 50% or greater stenosis and a significant elevation in peak blood flow velocity across the stenosis detected by ultrasound. Ultrasounds were performed using a standard protocol and reviewed by a central reader masked to treatment assignment and AVF outcome. Although the results were not statistically significant, there was a trend to fewer patients with a hemodynamically significant stenosis in the patients receiving 10 micrograms (30%) and 30 micrograms (39%) of PRT-201 compared with the placebo group (51%) at 6 weeks. Detecting hemodynamically significant stenosis is technically challenging and often confounded by the performance of procedures, such as angioplasty to treat stenosis prior to the ultrasound examination.

Safety and tolerability

PRT-201 is administered topically at the vascular access and only acts locally. We have not observed systemic activity or toxicity in our preclinical animal studies, even following intravenous administration at very high multiples of the Phase 2 clinical trial doses. Safety evaluations in Phase 2 included ascertainment of adverse events, physical examinations, ultrasounds of the AVFs and nearby vessels, vital signs and laboratory studies. No significant safety signals were identified. In the trial, patients treated with PRT-201 reported adverse events, the most common of which are summarized in the following table, comparable to placebo. These events were consistent with the medical events experienced by CKD patients undergoing AVF placement surgery. The most common adverse events were AVF incision pain, venous stenosis, AVF thrombosis, steal syndrome and hypoesthesia. Serious adverse events, or SAEs, reported by the investigator as possibly drug-related occurred in two 10 microgram PRT-201 patients (both AVF thrombosis), and two 30 microgram patients (one chest pain and one swelling at the surgical incision). There were no SAEs reported by the investigator as possibly drug-related in the placebo group. There was one SAE reported by the investigator to be drug-related in the 10 microgram PRT-201 group (AVF maturation failure), and there were none in the other treatment groups.

Number and Proportion (%) of Patients with Common Adverse Events(1)

N (%)	Placebo N=51	PRT-201 10 micrograms N=51	PRT-201 30 micrograms N=49
Any adverse event	42 (82)	39 (77)	43 (88)
AVF thrombosis	13 (26)	8 (16)	7 (14)
Venous stenosis	10 (20)	7 (14)	8 (16)
Steal syndrome	7 (14)	2 (4)	6 (12)
Hypoesthesia	7 (14)	6 (12)	6 (12)
AVF incisional pain	5 (10)	9 (18)	9 (18)
AVF site complication	5 (10)	4 (8)	4 (8)
Nausea	5 (10)	1 (2)	2 (4)
Peripheral edema	5 (10)	0 (0)	2 (4)
Arterial stenosis	4 (8)	5 (10)	0 (0)
Paresthesia	1 (2)	1 (2)	5 (10)
Pain in extremity(2)	0 (0)	1 (2)	5 (10)

Note: None of the differences between groups were statistically significant.

(1) Adverse events occurring in at least 10% of placebo or either PRT-201 treatment groups.

(2) All but one unrelated to limb used in AVF surgery.

Phase 1/2 AVF Clinical Trial

We submitted an investigational new drug application, IND, for PRT-201 as a treatment for patients undergoing AVF placement on April 30, 2008. Our initial clinical trial of PRT-201 was a Phase 1/2, randomized, double-blind, placebo-controlled, dose-escalation safety and exploratory efficacy trial in 66 patients undergoing creation of a radiocephalic or brachiocephalic AVF. Patients were treated with PRT-201 at nine dose levels ranging from 3.3 micrograms to 9 milligrams or placebo at the time of AVF placement and were followed for up to one year. This trial did not meet its primary endpoint, an endpoint we did not pursue in our Phase 2 trial. However, consistent with our mechanism of action that involves partial fragmentation of elastin doses of PRT-201 at 3.3, 10 and 33 micrograms were associated with a trend toward prolonged primary unassisted patency (secondary endpoint p=0.66 in the All Treated population and p=0.15 in the All Treated Minus 3 population), fewer procedures to restore or maintain patency (collected as supportive data) and less hemodynamically significant AVF lumen stenosis (collected as supportive data) compared with placebo treated patients or patients treated with higher PRT-201 doses. Higher doses showed results similar to placebo and no dose met the primary efficacy endpoint with statistical significance. No dose-related increases in adverse events were observed in the trial. Based on the results of this trial, we selected 10 microgram and 30 microgram doses for further study in the Phase 2 trial.

Our Phase 3 Program

We plan to conduct two randomized, double-blind Phase 3 trials, with staggered start dates, comparing a 30 microgram dose of PRT-201 to placebo. We plan to initiate our first Phase 3 pivotal trial for PRT-201 in patients with CKD undergoing placement of a radiocephalic AVF in the third quarter of 2014. The trials will enroll patients undergoing a surgical procedure to create a radiocephalic AVF. Each Phase 3 trial will enroll approximately 300 patients, for a total of approximately 600 patients, who will be randomized such that twice as many will receive PRT-201 as compared to placebo.

In April 2013, we held an end of Phase 2 meeting with the FDA, during which we confirmed the following key elements of our Phase 3 development plan: (i) the primary efficacy endpoint in our Phase 3 trials, primary unassisted patency, which is the same as our primary endpoint in our Phase 2 trial and suitable for approval of PRT-201 in the United States; (ii) the secondary efficacy endpoint in our Phase 3 trials, secondary patency, which was a secondary endpoint in our Phase 2 trial, could be acceptable for inclusion in the approved product labeling in the United States if we hit statistical significance on both the primary endpoint and the secondary endpoint, and possibly even if we do not hit statistical significance on the secondary endpoint; (iii) the total number of patients expected to be treated through our Phase 3 trial will provide a sufficient safety database to support a BLA filing; (iv) we do not need to conduct additional preclinical studies prior to conducting its Phase 3 clinical trials or to support a BLA filing; and (v) we have Phase 3-ready drug substance and drug product.

We began enrolling patients in our first Phase 3 trial in the third quarter of 2014. Each patient will be followed for 12 months. We expect that results will be available in 2017.

Our Phase 3 trials will be conducted at sites in the United States with the second trial potentially including Canadian sites. In addition to collecting data on the primary and secondary endpoints, the Phase 3 clinical trials will collect information related to the tertiary endpoints of maturation, use for hemodialysis and the rate of procedures to restore or maintain patency. Patients who consent will be enrolled in a patient registry to obtain long-term follow-up efficacy information.

We have designed each Phase 3 trial to have over 95% power *i.e.* there is more than a 95% probability that the study will detect observed clinical effects of PRT-201 if the observed effects are true. For the first Phase 3 trial, 300 patients will be randomly allocated by site in a 2:1 ratio to either PRT-201, at 30 micrograms, or to placebo. With the 300 patient sample size (200 PRT-201 and 100 placebo), the study is powered to approximately 96% power to detect an increase in median primary unassisted patency from 5 months to 10 months and 97% power to detect an increase in the proportion of patients with secondary

patency at 12 months from 65% to 85%. A 10% drop out rate has been assumed in all of the calculations. The study will follow each patient for a maximum of 12 months. If the results of the first Phase 3 trial are sufficiently compelling, we intend to meet with the FDA to discuss the possibility of submitting a BLA, supported by the single Phase 3 trial and may decide to submit a BLA to the FDA prior to completing the second Phase 3 trial.

Preclinical Development

We have conducted an extensive preclinical program to evaluate the safety and tolerability of single doses of PRT-201 administered locally in animal models of AVF and AVG placement, by percutaneous and endovascular injection in animal models of peripheral artery disease, or PAD, as well as intravenously. We have conducted preclinical studies in multiple species at doses up to 50 milligrams of PRT-201, which is over 1500 times higher than the dose we intend to study in our planned Phase 3 clinical trials. We observed no systemic activity or toxicity for PRT-201 in any of our preclinical studies. We observed no toxicity in any of the doses that we subsequently studied or plan to study in humans. Only local toxicity was observed at surgical sites at high doses (10 and 50 milligrams, which is over 300-1500 times higher than the dose we intend to study in our planned Phase 3 clinical trials). These changes were reversible, with normal wound healing observed at 14 days except at the highest (50 milligrams) dose, in which there were some mild persistent changes in the jugular vein and subcutaneous tissue. Normal wound healing was observed in all the AVF studies in rabbits at doses up to 10 milligrams and in all the AVG studies in dogs and pigs at doses up to 20 milligrams (the highest doses tested).

In our preclinical studies, we observed dose-dependent activity of PRT-201 on elastin removal as studies have established correlates with a reduction in neointimal hyperplasia.

Other Programs, Indications and Trials

Other AVF Trials

European clinical program

We are currently evaluating our clinical program to support filing in Europe. We may, based on additional data including the data from our Phase 3 clinical trials in the United States and if sufficient funds become available, choose to conduct a clinical trial of PRT-201 in Europe. Prior to initiating a European clinical trial, we plan to formally seek guidance from the European Medicines Agency, or EMA, regarding their requirements for regulatory approval.

Brachiocephalic AVF

We believe that our Phase 2 clinical data supports further development of PRT-201 in brachiocephalic AVF placement. We may, based on additional data including the data from our Phase 3 clinical trials and if sufficient funds become available, study the effects of a 30 microgram dose of PRT-201 versus placebo on brachiocephalic AVFs. Prior to initiation of this trial, we expect to seek guidance from the FDA regarding trial design.

Arteriovenous Grafts

An arteriovenous graft, or AVG, is a surgical procedure in which a surgeon places a synthetic tube to connect a vein and an artery. We submitted an IND for PRT-201 as a treatment for patients undergoing AVG placement on April 30, 2008. We conducted a Phase 1/2 randomized, double-blind, placebo-controlled, dose-escalation trial in 89 patients undergoing placement of an AVG. Patients were treated with placebo or eight different doses of PRT-201 ranging from 10 micrograms to 9 milligrams at the time of AVG placement and were followed for up to one year. Those patients who had not lost secondary patency were subsequently enrolled in a registry to obtain additional follow-up information on the AVG.

The primary outcome measure was safety. Adverse events were consistent with the medical conditions experienced by patients with CKD undergoing AVG surgery and showed no significant differences between groups. Some of the data showed indications of efficacy, especially in secondary patency, which is an approvable endpoint for hemodialysis access, for the groups treated with PRT-201 at doses of 10 micrograms and 30 micrograms.

After reviewing the results from our first Phase 3 clinical trial and if sufficient funds become available, we may commence a clinical trial of PRT-201 in patients undergoing placement of an AVG.

Peripheral Artery Disease

In addition to vascular access indications, we are investigating PRT-201 as a treatment for patients with symptomatic peripheral artery disease, or PAD. Patients with lower extremity PAD suffer from stenosis formation in the arteries providing blood to the legs. These patients typically present with exercise-induced leg pain, a condition known as intermittent claudication. Patients with claudication are unable to adequately maintain their activities of daily living because they quickly experience pain that can be resolved only through rest. Severe cases result in critical limb ischemia, or lack of oxygen, and the possibility of amputation. PAD is a global problem affecting a large number of people throughout the industrialized world. Approximately 8 million Americans suffer from PAD.

Patients with early stage PAD typically undergo lifestyle management such as smoking cessation, weight reduction and/or diabetes management, and treatment with oral medications. Approximately 350,000 patients in the United States do not respond to lifestyle management and have worsening symptoms, resulting in the need for endovascular procedures, typically balloon angioplasty with or without stenting. While these procedures work acutely to restore blood flow, they suffer from poor long-term durability, resulting in the need for repeat procedures.

We believe that PRT-201 may improve the outcomes associated with angioplasty procedures, resulting in prolonged intervention-free patency while eliminating the need for permanent implant of a stent. We submitted an IND for PRT-201 as a treatment for PAD patients on April 9, 2012. Our initial PAD clinical trial is an ongoing Phase 1, open-label, dose-escalation safety/technical feasibility trial in 16 patients undergoing balloon angioplasty of an occluded or partially occluded superficial femoral or popliteal artery in the leg. Following successful angioplasty, patients are treated with PRT-201 via an FDA-cleared drug delivery catheter that allows PRT-201 to be administered locally in the outer layer of the artery, which is called the adventitia. Patients are being followed for up to 12 months. We expect data from this trial to be available in the second half of 2015.

Manufacturing and Supply

We depend on third-party contract manufacturers for the production of PRT-201. Our active pharmaceutical ingredient, or API, is produced at our contract manufacturer, Lonza AG, which is required to comply with the FDA's Current Good Manufacturing Practice (cGMP) regulations. PRT-201 finished product is produced at our contract fill/finisher provider, Jubilant HollisterStier, which is required to comply with cGMP regulations. We used API manufactured at Lonza to create finished product that was used in our Phase 2 AVF clinical trial and will be used for our Phase 3 clinical trials. We also plan to manufacture API at Lonza for our commercial launch and future trials. Release and stability testing for API and finished product are performed at PPD, Inc. The tests indicate stability of at least four years for our API and at least six months for our finished product.

In preparation for commercial launch, we modified our finished product for our Phase 3 trials in order to facilitate ease of administration and fill and finish at 30 microgram doses. The modified finished product is reconstituted with sterile water to create a dosing solution containing 30 micrograms of PRT-201. We demonstrated that the modified finished product had the same elastase activity as the previous finished product using synthetic and natural elastin substrates and documented the same elastin removal from

blood vessels following ex vivo treatments. The modified finished product formulation was similar to the previous finished product formulation in maintaining the health and viability of live cells in culture. These data suggest the modified finished product will have the same efficacy and safety as the previous finished product in clinical trials.

At our end of Phase 2 meeting, the FDA confirmed that our API and modified finished product are acceptable for Phase 3 clinical trials. We have already manufactured finished product for the AVF Phase 3 clinical trials.

In anticipation of a potential BLA filing, we plan to manufacture a minimum of three batches of API and of finished product as part of process validation and to test these batches for stability with a goal of establishing a commercial shelf-life of at least two years for finished product and a longer expiry for API.

Sales and Marketing

Our commercialization strategy is to develop PRT-201 into a leading therapy worldwide for the treatment of AVFs and in other renal and vascular diseases.

We have not yet established a sales and marketing organization. Our Chief Executive Officer has significant commercial experience in the industry, including commercial launch experience in the renal market. We intend to recruit an in-house specialty hospital sales force in the United States focused on promoting PRT-201. We plan to target our marketing and sales efforts to vascular surgeons who create AVFs. There are approximately 2,800 vascular surgeons in the United States. We believe a specialty hospital sales force of approximately 75-100 representatives, supported by reimbursement specialists and a medical affairs team, will enable us to call on the approximately 1,300 hospitals that account for more than 90% of the AVF placements performed in the United States annually.

We believe that the market for PRT-201 in the five largest countries in the European Union represents the bulk of the potential European market and that a launch using a direct sales force may be achievable in these markets. If PRT-201 is approved by the EMA, we may commercialize it in some European countries with our own specialty hospital sales force and/or with a commercial partner in the other European countries. We hope to enter into collaborations for the development and commercialization of PRT-201 in Japan and other Asian countries.

We believe PRT-201 will be reimbursed appropriately as costs related to AVF surgical placement, which is typically performed in the hospital outpatient setting, are not included in the ESRD bundle.

Intellectual Property

We strive to protect and enhance the proprietary technology, inventions and improvements that are commercially important to our business, including seeking, maintaining and defending patent rights. We also rely on know-how that may be important to the development of our business. We additionally expect to rely on regulatory protection afforded through data exclusivity, market exclusivity and patent term extensions where available.

Our commercial success may depend in part on our ability to obtain and maintain patent and other proprietary protection for commercially important technology, inventions and know-how related to our business; to defend and enforce our patents and to operate without infringing the valid enforceable patents and proprietary rights of third parties.

Our ability to prevent third parties from making, using, selling, offering to sell or importing competing products to ours, including a competitor to PRT-201, depends on the scope of our patents. We have several patents and patent applications relating to the PRT-201 formulation and its therapeutic uses, and possess substantial know-how relating to the development and commercialization of PRT-201. We cannot be sure that any of our pending patent applications or future patent filings will lead to the issuance of new patents, nor can we be sure that any of our existing patents or any patents that may be granted to us in the future will be adequate to protect our market.

We plan on pursuing in-licensing opportunities to develop, strengthen and maintain our proprietary position in our field. We expect to use trademark protection for our products as they are marketed.

Patents

We own 20 issued patents and 25 pending patent applications. The patents and applications primarily fall into two families, a first relating to the PRT-201 formulation and its manufacture and use, as well as other formulations of elastases (the "formulation family"), and the second relating to certain therapeutic uses of PRT-201, and associated systems and kits that include a catheter and are suitable for a subset of those therapeutic uses (the "therapy family"). The formulation family includes one issued United States patent, one issued European patent, additional patents issued in Israel, Mexico, and New Zealand, and patent applications pending in several major jurisdictions worldwide, including Japan, China, South Korea, Brazil, Mexico, Russia, India, Europe and the United States. The expected expiration date for any patents that have issued or may issue from the formulation family is December 4, 2028, exclusive of possible patent term extension available for one patent covering PRT-201 under the Hatch-Waxman Amendments or comparable provisions in other jurisdictions, except in the United States where we were awarded a patent term adjustment of 199 days due to USPTO delays, taking the expiration date to June 20, 2029. The therapy family includes seven issued United States patents and two issued European patents, and applications pending in the United States, Europe, Canada and Japan. The expected expiration date for any patents that have issued or may issue from the therapy family patents is September 24, 2020, except in the United States where several patents were awarded a patent term adjustment and the expected expiration date of two therapy family patents related to systems and kits including elastase and a catheter is June 30, 2021, exclusive of possible patent term extension.

Patent Term

The base term of a U.S. patent is 20 years from the filing date of the earliest-filed non-provisional patent application from which the patent claims priority. The term of a U.S. patent can be lengthened by patent term adjustment, which compensates the owner of the patent for administrative delays at the USPTO. In some cases, the term of a U.S. patent is shortened by terminal disclaimer that reduces its term to that of an earlier-expiring patent.

The term of a U.S. patent may be eligible for patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, referred to as the Hatch-Waxman Act or Hatch-Waxman Amendment, to account for at least some of the time a product is under development and regulatory review after the patent is granted. With regard to a product for which FDA approval is the first permitted marketing of the active ingredient, the Hatch-Waxman Act allows for extension of protection of one U.S. patent that includes at least one claim covering the composition of matter of an FDA-approved product, an FDA-approved method of treatment using the product, and/or a method of manufacturing the FDA-approved product. The extended protection cannot exceed the shorter of five years beyond the non-extended expiration of the patent or 14 years from the date of the FDA approval of the product. Some foreign jurisdictions, including Europe have analogous patent extension provisions, which allow for extension of the protection of a patent that covers a drug approved by the applicable foreign regulatory agency. In the future, if and when PRT-201 receives FDA approval, we expect to apply for patent extension to extend the protection of one of our patents covering PRT-201 or its use.

Assignment of Rights and License Agreement

As successor to Proteon Therapeutics, LLC by merger, we acquired all of the assets of the LLC, including all of the intellectual property rights in a patent family entitled "Local, Transcatheter Delivery of Proteases to Reopen Obstructed Biological Conduits" (the "JHU patent family"). This patent family was originally developed by our founder, Dr. F. Nicholas Franano, at The Johns Hopkins University, or Johns Hopkins, and includes United States patent Nos. 7,063,838; 7,153,505; 7,361,335; 7,632,494; 7,883,699;

8,524,226; 8,562,983; and 8,568,716. Johns Hopkins assigned all of the intellectual property rights to Dr. Franano who in turn assigned the rights to the LLC. Under the terms of the assignment of rights and license agreement with Johns Hopkins, Dr. Franano reimbursed certain costs of Johns Hopkins and agreed to pay the future costs and expenses of patent prosecution and maintenance, as well as any costs related to infringement. In addition, under the agreement, Dr. Franano granted to Johns Hopkins rights to practice under the intellectual property rights for non-profit purposes. The rights granted to us are further subject to any rights the United States Government may have in inventions that are the subject matter of the acquired patents under the Bayh Dole Act due to its sponsorship of research that led to certain of such inventions. The agreement does not specify a term and does not include any termination provisions. Dr. Franano agreed that upon commercialization of the assigned invention, he would remit to Johns Hopkins 2.5% of any revenues or fees received from certain net sales of any product covered by the JHU patent family. We assumed, and are the successor to, all of Dr. Franano's payment and other obligations to Johns Hopkins. Seven U.S. patents in the JHU patent family, and their foreign counterparts, described above as the therapy family, relate to certain therapeutic uses of PRT-201, and the associated systems and kits that include a catheter and are suitable for a subset of those therapeutic uses.

Competition

The biotechnology and pharmaceutical industries are characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary products. We face potential competition from many different sources, including major pharmaceutical, specialty pharmaceutical and biotechnology companies, academic institutions and governmental agencies and public and private research institutions.

Some of our potential competitors have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved products than we do. Smaller or early stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies.

The key competitive factors that will differentiate PRT-201, if approved, are likely to be its efficacy, safety, convenience, price, and the availability of reimbursement from government and other third party payors. Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, more convenient or less expensive than products that we may develop. Our competitors may also obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours.

We are not aware of any therapeutic products approved in the United States or Europe for the prevention of AVF or AVG patency loss. We are aware of other therapies in development for AVF or AVG failure with companies including Vascular Therapies and Celladon. PRT-201 could face competition from companies developing vascular access technologies. Other potential competition includes new synthetic grafts, including those that may be developed by companies that currently compete in the graft market, such as W.L. Gore, C.R. Bard and Maquet, as well as tissue engineered grafts, including those in development by Cytograft and Humacyte, including BioConnect Systems, Caymus Medical, Phraxis, CreatiVasc and TVA Medical. Finally, PRT-201's commercial success could be affected by the development of technologies to improve the outcomes of interventions to restore patency, including stents, stent grafts and drug eluting balloons.

Government Regulation and Approval

United States—FDA process

In the United States, pharmaceutical products are subject to extensive regulation by the FDA. The FDCA, and other federal and state statutes and regulations, govern, among other things, the research, development, testing, manufacture, storage, recordkeeping, approval, labeling, promotion and marketing,

distribution, post-approval monitoring and reporting, sampling, and import and export of pharmaceutical products. Biological products used for the prevention, treatment, or cure of a disease or condition of a human being are subject to regulation under the Federal Food, Drug, and Cosmetic Act, the FDCA, except the section of the FDCA which governs the approval of new drug applications, or NDAs. Biological products, such as PRT-201, are approved for marketing under provisions of the Public Health Service Act, or PHSA, via a Biologics License Application, or BLA. However, the application process and requirements for approval of BLAs are very similar to those for NDAs, and biologics are associated with similar approval risks as drugs. Failure to comply with applicable United States requirements may subject a company to a variety of administrative or judicial sanctions, such as FDA refusal to approve pending NDAs or BLAs, warning or untitled letters, clinical holds, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, civil penalties, and criminal prosecution.

Approval process

FDA approval is required before any new unapproved product or a product with certain changes to a previously approved product may be marketed in the United States. FDA approval is required before any new unapproved drug or dosage form, including a new use of previously approved drug, can be marketed in the United States. The steps required to be completed before a drug may be marketed in the United States include:

- preclinical laboratory tests, animal studies, and formulation studies, all performed in accordance with the FDA's Good Laboratory Practice, or GLP, regulations;
- submission to the FDA of an IND application for human clinical testing, which must become effective before human clinical trials may begin and must be updated annually;
- adequate and well-controlled human clinical trials to establish the safety and efficacy of the drug for each indication to FDA's satisfaction;
- submission to the FDA of a BLA;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the drug is produced to assess compliance with current good manufacturing practices or, cGMP, regulations; and
- FDA review and approval of the BLA.

Satisfaction of FDA pre-market approval requirements typically takes many years and the actual time required may vary substantially based upon the type, complexity, and novelty of the product or disease.

Preclinical tests include laboratory evaluation of product chemistry, formulation, and toxicity, as well as animal trials to assess the characteristics and potential safety and efficacy of the product. The conduct of the preclinical tests must comply with federal regulations and requirements, including GLP. The results of preclinical testing are submitted to the FDA as part of an IND along with other information, including information about product chemistry, manufacturing and controls, and a proposed clinical trial protocol. Long term preclinical tests, such as animal tests of reproductive toxicity and carcinogenicity, may continue after the IND is submitted.

A 30-day waiting period after the submission of each IND is required prior to the commencement of clinical testing in humans. If the FDA has neither commented on nor questioned the IND within this 30-day period, the clinical trial proposed in the IND may begin. However, the FDA may within the 30-day time period raise concerns or questions relating to one or more proposed clinical trials and place the clinical trial on a clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. Accordingly, submission of an IND may or may not result in the FDA allowing clinical trials to commence. A separate submission to an existing IND must also be made for each successive clinical trial conducted during product development.

Clinical trials involve the administration of the investigational new drug or biologic to healthy volunteers or patients under the supervision of a qualified investigator. Clinical trials must be conducted:

(i) in compliance with federal regulations; (ii) in compliance with good clinical practice, or GCP, an international standard meant to protect the rights and health of patients and to define the roles of clinical trial sponsors, administrators, and monitors; as well as (iii) under protocols detailing the objectives of the trial, the parameters to be used in monitoring safety, and the effectiveness criteria to be evaluated. Each protocol involving testing on United States patients and subsequent protocol amendments must be submitted to the FDA as part of the IND.

The FDA may order the temporary, or permanent, discontinuation of a clinical trial at any time, or impose other sanctions, if it believes that the clinical trial either is not being conducted in accordance with FDA requirements or presents an unacceptable risk to the clinical trial patients. The trial protocol and informed consent information for patients in clinical trials must also be submitted to an institutional review board, or IRB, for approval. An IRB may also require the clinical trial at the site to be halted, either temporarily or permanently, for failure to comply with the IRB's requirements, or may impose other conditions.

Clinical trials to support NDAs or BLAs for marketing approval are typically conducted in three sequential phases, but the phases may overlap. In Phase 1, the initial introduction of the drug or biologic into a limited population of healthy human subjects or patients, the product is tested to assess metabolism, pharmacokinetics, pharmacological actions, side effects associated with increasing doses, and, if possible, early evidence on effectiveness. Phase 2 usually involves trials in a limited patient population to evaluate preliminarily the effectiveness of the drug or biologic for a particular indication, dosage tolerance, and optimum dosage, and to identify common adverse effects and safety risks. If a compound demonstrates evidence of effectiveness and an acceptable safety profile in Phase 2 evaluations, Phase 3 trials are undertaken in a larger number of patients, typically at geographically dispersed clinical trial sites, to provide substantial evidence of clinical efficacy, to further test for safety in an expanded and diverse patient population, to permit the FDA to evaluate the overall benefit-risk relationship of the drug or biologic and to provide adequate information for the labeling of the product. In most cases, the FDA requires two adequate and well-controlled Phase 3 clinical trials to demonstrate the efficacy of the drug or biologic. A single Phase 3 trial with other confirmatory evidence may be sufficient in rare instances where the trial is a large multicenter trial demonstrating internal consistency and a statistically very persuasive finding of a clinically meaningful effect on mortality, irreversible morbidity or prevention of a disease with a potentially serious outcome and confirmation of the result in a second trial would be practically or ethically impossible.

After completion of the required clinical testing, an NDA or BLA is prepared and submitted to the FDA. FDA approval of the NDA or BLA is required before marketing of the product may begin in the United States. The NDA or BLA must include, among other things, the results of all preclinical, clinical, and other testing and a compilation of data relating to the product's pharmacology, chemistry, manufacture, and controls. The cost of preparing and submitting an NDA or BLA is substantial. The submission of most NDAs and BLAs is additionally subject to a substantial application user fee, currently exceeding $2,169,000, and the manufacturer and/or sponsor under an approved new drug application are also subject to annual product and establishment user fees, currently exceeding $104,000 per product and $554,000 per establishment. These fees are typically increased annually.

The FDA has 60 days from its receipt of an NDA or BLA to determine whether the application will be accepted for filing based on the agency's threshold determination that it is sufficiently complete to permit substantive review. Once the submission is accepted for filing, the FDA begins an in-depth review. The FDA has agreed to certain performance goals in the review of NDAs and BLAs. Under the Prescription Drug User Fee Act, the FDA has a goal of responding to standard review NDAs within ten months after the 60-day filing review period, but this timeframe is often extended. Most applications for standard review drug or biologic products are reviewed within ten to 12 months; most applications for priority review drugs or biologics are reviewed in six to eight months. Priority review can be applied to drugs that the FDA determines offer major advances in treatment, or provide a treatment where no adequate therapy exists.

For biologics, priority review is further limited only for products intended to treat a serious or life-threatening disease relative to the currently approved products. The review process for both standard and priority review may be extended by the FDA for three additional months to consider certain late-submitted information, or information intended to clarify information already provided in the submission.

The FDA may also refer applications for novel drug or biologic products, or drug or biologic products that present difficult questions of safety or efficacy, to an advisory committee—typically a panel that includes clinicians and other experts—for review, evaluation, and a recommendation as to whether the application should be approved. The FDA is not bound by the recommendation of an advisory committee, but it generally follows such recommendations. Before approving an NDA or BLA, the FDA will typically inspect one or more clinical sites to assure compliance with GCP. Additionally, the FDA will inspect the facility or the facilities at which the drug is manufactured. FDA will not approve the product unless compliance with cGMP is satisfactory and the NDA or BLA contains data that provide evidence that the drug or biologic is safe and effective in the indication studied.

After the FDA evaluates the NDA or BLA and the manufacturing facilities, it issues either an approval letter or a complete response letter. A complete response letter indicates that the review cycle of the application is complete and the application is not ready for approval. A complete response letter generally outlines the deficiencies in the submission and may require substantial additional clinical data and/or other significant, expensive, and time-consuming requirements related to clinical trials, preclinical studies and/or manufacturing. The FDA has committed to reviewing resubmissions of the NDA or BLA addressing such deficiencies in two or six months depending on the type of information included. Even if such data are submitted, however, the FDA may ultimately decide that the NDA or BLA does not satisfy the criteria for approval.

An approval letter authorizes commercial marketing of the drug or biologic with specific prescribing information for specific indications. As a condition of NDA or BLA approval, the FDA may require a risk evaluation and mitigation strategy, or REMS, to help ensure that the benefits of the drug or biologic outweigh the potential risks. REMS can include medication guides, communication plans for healthcare professionals, and elements to assure safe use, or ETASU. ETASU can include, but are not limited to, special training or certification for prescribing or dispensing, dispensing only under certain circumstances, special monitoring, and the use of patient registries. The requirement for REMS can materially affect the potential market and profitability of the product. Moreover, product approval may also be conditioned on substantial post-approval testing and surveillance to monitor the product's safety or efficacy. Once granted, product approvals may be withdrawn if compliance with regulatory standards is not maintained or problems are identified following initial marketing.

Changes to some of the conditions established in an approved application, including changes in indications, labeling, or manufacturing processes or facilities, require submission and FDA approval of a new NDA or BLA or NDA or BLA supplement before the change can be implemented. An NDA or BLA supplement for a new indication typically requires clinical data similar to that in the original application, and the FDA uses the same procedures and actions in reviewing NDA or BLA supplements as it does in reviewing NDAs or BLAs. As with new NDAs, the review process is often significantly extended by the FDA requests for additional information or clarification.

U.S. Patent Term Restoration

Depending upon the timing, duration and specifics of the FDA approval of PRT-201 and any future product candidates, some of our U.S. patents may be eligible for limited patent term extension. The Hatch-Waxman Amendments permit a patent restoration term, often referred to as patent term extension, of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. However, patent term restoration cannot extend the remaining term of a patent beyond a

total of 14 years from the product's approval date. The patent term restoration period is generally one-half the time between the effective date of an IND and the submission date of an NDA or BLA plus the time between the submission date of an NDA or BLA and the approval of that application. Only one patent applicable to an approved drug or biologic is eligible for the extension and the application for the extension must be submitted prior to the expiration of the patent. The USPTO, in consultation with the FDA, reviews and approves or denies the application for any patent term extension or restoration. In the future, we intend to apply for extension of patent term for one of our patents covering PRT-201 to add patent life beyond its current expected expiration date.

Post-approval requirements

Once an NDA or BLA is approved, a product will be subject to certain post-approval requirements. For instance, the FDA closely regulates the post-approval marketing and promotion of drugs and biologics, including standards and regulations for direct-to-consumer advertising, off-label promotion, industry-sponsored scientific and educational activities and promotional activities involving the internet. Drugs and biologics may be marketed only for the approved indications and in accordance with the provisions of the approved labeling. Failure to comply with these requirements can result in adverse publicity, warning letters, corrective advertising, and potential civil and criminal penalties.

Adverse event reporting and submission of periodic reports is required following FDA approval of an NDA or BLA. The FDA also may require post-marketing testing, known as Phase 4 testing, REMS, and surveillance to monitor the effects of an approved product, or the FDA may place conditions on an approval that could restrict the distribution or use of the product. In addition, quality control, drug manufacture, packaging, and labeling procedures must continue to conform to cGMPs after approval. Drug and biologic manufacturers and certain of their subcontractors are required to register their establishments with the FDA and certain state agencies. Registration with the FDA subjects entities to periodic unannounced inspections by the FDA, during which the agency inspects manufacturing facilities to assess compliance with cGMPs. Accordingly, manufacturers must continue to expend time, money, and effort in the areas of production and quality-control to maintain compliance with cGMPs. Regulatory authorities may withdraw product approvals or request product recalls if a company fails to comply with regulatory standards, if it encounters problems following initial marketing, or if previously unrecognized problems are subsequently discovered.

Orphan drug designation

Under the Orphan Drug Act, the FDA may grant orphan drug designation to drugs or biologics intended to treat a rare disease or condition—generally a disease or condition that affects fewer than 200,000 individuals in the United States. Orphan drug designation must be requested before submitting an NDA or BLA. After the FDA grants orphan drug designation, the generic identity of the drug or biologic and its potential orphan use are disclosed publicly by the FDA. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process. The first NDA or BLA applicant to receive FDA approval for a particular active ingredient to treat a particular disease with FDA orphan drug designation is entitled to a seven-year exclusive marketing period in the United States for that product, for that indication. During the seven-year exclusivity period, the FDA may not approve any other applications to market the same drug or biologic for the same disease, except in limited circumstances, such as a showing of clinical superiority to the product with orphan drug exclusivity. Orphan drug exclusivity does not prevent the FDA from approving a different drug or biologic for the same disease or condition, or the same drug or biologic for a different disease or condition. Among the other benefits of orphan drug designation are tax credits for certain research and a waiver of the NDA or BLA application user fee.

Fast track designation and accelerated approval

The FDA is required to facilitate the development, and expedite the review, of drugs or biologics that are intended for the treatment of a serious or life-threatening disease or condition for which there is no effective treatment and which demonstrate the potential to address unmet medical needs for the condition. Under the fast track program, the sponsor of a new drug or biologic candidate may request that the FDA designate the candidate for a specific indication as a fast track drug or biologic concurrent with, or after, the filing of the IND for the candidate. The FDA must determine if the drug or biologic candidate qualifies for fast track designation within 60 days of receipt of the sponsor's request. Unique to a fast track product, the FDA may initiate review of sections of a fast track product's NDA or BLA before the application is complete. This rolling review is available if the applicant provides, and the FDA approves, a schedule for the submission of the remaining information and the applicant pays applicable user fees. However, the FDA's time period goal for reviewing an application does not begin until the last section of the NDA or BLA is submitted. Additionally, the fast track designation may be withdrawn by the FDA if the FDA believes that the designation is no longer supported by data emerging in the clinical trial process.

Any product submitted to the FDA for marketing, including under a fast track program, may be eligible for other types of FDA programs intended to expedite development and review, such as accelerated approval. Drug or biological products studied for their safety and effectiveness in treating serious or life-threatening illnesses and that provide meaningful therapeutic benefit over existing treatments may receive accelerated approval, which means the FDA may approve the product based upon a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments.

In clinical trials, a surrogate endpoint is a measurement of laboratory or clinical signs of a disease or condition that substitutes for a direct measurement of how a patient feels, functions, or survives. Surrogate endpoints can often be measured more easily or more rapidly than clinical endpoints. A drug or biologic candidate approved on this basis is subject to rigorous post-marketing compliance requirements, including the completion of Phase 4 or post-approval clinical trials to confirm the effect on the clinical endpoint. Failure to conduct required post-approval studies, or confirm a clinical benefit during post-marketing studies, will allow the FDA to withdraw the drug or biologic from the market on an expedited basis. All promotional materials for drug candidates approved under accelerated regulations are subject to prior review by the FDA.

Pediatric information

Under the Pediatric Research Equity Act, or PREA, NDAs or BLAs or supplements to NDAs or BLAs must contain data to assess the safety and effectiveness of the drug for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the drug is safe and effective. The FDA may grant full or partial waivers, or deferrals, for submission of data. Unless otherwise required by regulation, PREA does not apply to any drug for an indication for which orphan designation has been granted.

Additional controls for biologics

To help reduce the increased risk of the introduction of adventitious agents, the PHSA emphasizes the importance of manufacturing controls for products whose attributes cannot be precisely defined. The PHSA also provides authority to the FDA to immediately suspend licenses in situations where there exists a danger to public health, to prepare or procure products in the event of shortages and critical public health needs, and to authorize the creation and enforcement of regulations to prevent the introduction or spread of communicable diseases in the United States and between states.

After a BLA is approved, the product may also be subject to official lot release as a condition of approval. As part of the manufacturing process, the manufacturer is required to perform certain tests on each lot of the product before it is released for distribution. If the product is subject to official release by the FDA, the manufacturer submits samples of each lot of product to the FDA together with a release protocol showing a summary of the history of manufacture of the lot and the results of all of the manufacturer's tests performed on the lot. The FDA may also perform certain confirmatory tests on lots of some products, such as viral vaccines, before releasing the lots for distribution by the manufacturer. In addition, the FDA conducts laboratory research related to the regulatory standards on the safety, purity, potency, and effectiveness of biological products. As with drugs, after approval of biologics, manufacturers must address any safety issues that arise, are subject to recalls or a halt in manufacturing, and are subject to periodic inspection after approval.

Biosmilars

The Biologics Price Competition and Innovation Act of 2009, or BPCIA, creates an abbreviated approval pathway for biological products shown to be highly similar to or interchangeable with an FDA-licensed reference biological product. Biosimilarity sufficient to reference a prior FDA-approved product requires that there be no differences in conditions of use, route of administration, dosage form, and strength, and no clinically meaningful differences between the biological product and the reference product in terms of safety, purity, and potency. Biosimilarity must be shown through analytical studies, animal studies, and at least one clinical trial, absent a waiver by the Secretary. A biosimilar product may be deemed interchangeable with a prior approved product if it meets the higher hurdle of demonstrating that it can be expected to produce the same clinical results as the reference product and, for products administered multiple times, the biologic and the reference biologic may be switched after one has been previously administered without increasing safety risks or risks of diminished efficacy relative to exclusive use of the reference biologic. No biosimilar or interchangeable products have been approved under the BPCIA to date. Complexities associated with the larger, and often more complex, structures of biological products, as well as the process by which such products are manufactured, pose significant hurdles to implementation which are still being evaluated by the FDA.

A reference biologic is granted twelve years of exclusivity from the time of first licensure of the reference product, and no application for a biosimilar can be submitted for four years from the date of licensure of the reference product. The first biologic product submitted under the abbreviated approval pathway that is determined to be interchangeable with the reference product has exclusivity against a finding of interchangeability for other biologics for the same condition of use for the lesser of (i) one year after first commercial marketing of the first interchangeable biosimilar, (ii) eighteen months after the first interchangeable biosimilar is approved if there is no patent challenge, (iii) eighteen months after resolution of a lawsuit over the patents of the reference biologic in favor of the first interchangeable biosimilar applicant, or (iv) 42 months after the first interchangeable biosimilar's application has been approved if a patent lawsuit is ongoing within the 42-month period.

Disclosure of clinical trial information

Sponsors of clinical trials of FDA-regulated products, including drugs, are required to register and disclose certain clinical trial information. Information related to the product, patient population, phase of investigation, trial sites and investigators, and other aspects of the clinical trial is then made public as part of the registration. Sponsors are also obligated to discuss the results of their clinical trials after completion. Disclosure of the results of these trials can be delayed until the new product or new indication being studied has been approved. Competitors may use this publicly available information to gain knowledge regarding the progress of development programs.

European Union—EMA process

In the European Union, medicinal products are authorized following a similar demanding process as that required in the United States and applications are based on the ICH Common Technical Document. Prior to submitting a European Marketing Authorization Application, or MAA, it is necessary to gain approval of a detailed Pediatric Investigation Plan, or PIP, with the European Medicines Agency's Pediatric Committee, or PDCO. After gaining PIP approval, medicines can be authorized in the European Union by using either the centralized authorization procedure or national authorization procedures.

Centralized procedure

Under the centralized procedure, after the EMA issues an opinion, the European Commission issues a single marketing authorization valid across the European Union, as well as Iceland, Liechtenstein and Norway. The centralized procedure is compulsory for human medicines that are: derived from biotechnology processes, such as genetic engineering; contain a new active substance indicated for the treatment of certain diseases, such as HIV/AIDS, cancer, diabetes, neurodegenerative disorders or autoimmune diseases and other immune dysfunctions; and officially designated orphan medicines. For medicines that do not fall within these categories, an applicant has the option of submitting an application for a centralized marketing authorization to the EMA, as long as the medicine concerned is a significant therapeutic, scientific or technical innovation, or if its authorization would be in the interest of public health.

National authorization procedures

There are also two other possible routes to authorize medicinal products in several countries, which are available for products that fall outside the scope of the centralized procedure:

- *Decentralized procedure*. Using the decentralized procedure, an applicant may apply for simultaneous authorization in more than one European Union country of a medicinal product that has not yet been authorized in any European Union country and that does not fall within the mandatory scope of the centralized procedure.
- *Mutual recognition procedure.* In the mutual recognition procedure, a medicine is first authorized in one European Union Member State, in accordance with the national procedures of that country. Thereafter, further marketing authorizations can be sought from other European Union countries in a procedure whereby the countries concerned agree to recognize the validity of the original, national marketing authorization.

While we believe that our development program, proposed Phase 3 trial design, and overall non-clinical and clinical data package could support future regulatory approval of PRT-201 in the European Union, we have not submitted such information to the European Union for their review.

Good manufacturing practices

Like the FDA, the EMA, the competent authorities of the European Union Member States and other regulatory agencies regulate and inspect equipment, facilities and processes used in the manufacturing of pharmaceutical and biologic products prior to approving a product. If, after receiving clearance from regulatory agencies, a company makes a material change in manufacturing equipment, location, or process, additional regulatory review and approval may be required. Once we or our partners commercialize products, we will be required to comply with cGMP, and product-specific regulations enforced by, the European Commission, the EMA and the competent authorities of European Union Member States following product approval. Also like the FDA, the EMA, the competent authorities of the European Union Member States and other regulatory agencies also conduct regular, periodic visits to re-inspect equipment, facilities, and processes following the initial approval of a product. If, as a result of these inspections, it is determined that our or our partners' equipment, facilities, or processes do not comply

with applicable regulations and conditions of product approval, regulatory agencies may seek civil, criminal or administrative sanctions and/or remedies against us, including the suspension of our manufacturing operations or the withdrawal of our product from the market.

Data and market exclusivity

Similar to the United States, there is a process for authorization of generic versions of innovator drug products in the European Union. Abridged applications for the authorization of generic versions of drugs authorized by EMA can be submitted to the EMA through a centralized procedure referencing the innovator's data and demonstrating bioequivalence to the reference product, among other things.

New medicinal products in the European Union can receive eight years of data exclusivity coupled with two years of market exclusivity, and a potential one year extension, if the marketing authorizations holder obtains an authorization for one or more new therapeutic indications that demonstrates "significant clinical benefit" in comparison with existing therapies; this system is usually referred to as "8+2+1". We expect to be eligible for at least ten years of market exclusivity following any approval of PRT-201.

Abridged applications cannot rely on an innovator's data until after expiry of the eight year date exclusivity term; applications for a generic product can be filed but the product cannot be marketed until the end of the market exclusivity term.

Other international markets—drug approval process

In some international markets (*e.g.*, China or Japan), although data generated in United States or European Union trials may be submitted in support of a marketing authorization application, additional clinical trials conducted in the host territory, or studying people of the ethnicity of the host territory, may be required prior to the filing or approval of marketing applications within the country.

Pricing and reimbursement

In the United States and internationally, sales of products that we market in the future, and our ability to generate revenues on such sales, are dependent, in significant part, on the availability and level of reimbursement from third-party payors such as state and federal governments, managed care providers and private insurance plans. Substantial uncertainty exists as to the reimbursement status of newly approved healthcare products by third-party payors. In the United States no uniform policy of coverage and reimbursement for drug products exists. Accordingly, decisions regarding the extent of coverage and amount of reimbursement to be provided for any of our products will be made on a payor by payor basis. As a result, the coverage determination process is often a time-consuming and costly process that will require us to provide scientific and clinical support for the use of our product candidates to each payor separately, with no assurance that coverage and adequate reimbursement will be obtained.

Private insurers, such as health maintenance organizations and managed care providers, have implemented cost-cutting and reimbursement initiatives and likely will continue to do so in the future. These include establishing formularies that govern the drugs and biologics that will be offered and also the out-of-pocket obligations of member patients for such products. In addition, particularly in the United States and increasingly in other countries, we may be required to provide discounts and pay rebates to state and federal governments and agencies in connection with purchases of our products that are reimbursed by such entities. It is possible that future legislation in the United States and other jurisdictions could be enacted which could potentially impact the reimbursement rates for the products we are developing and may develop in the future and also could further impact the levels of discounts and rebates paid to federal and state government entities. Any legislation that impacts these areas could impact, in a significant way, our ability to generate revenues from sales of products that, if successfully developed, we bring to market.

There is no legislation at the European Union level governing the pricing and reimbursement of medicinal products in the European Union. As a result, the competent authorities of each of the 27 European Union Member States have adopted individual strategies regulating the pricing and reimbursement of medicinal products in their territory. These strategies often vary widely in nature, scope and application. However, a major element that they have in common is an increased move towards reduction in the reimbursement price of medicinal products, a reduction in the number and type of products selected for reimbursement and an increased preference for generic products over innovative products. These efforts have mostly been executed through these countries' existing price control methodologies. The government of the UK announced the phase-out of its established Pharmaceutical Pricing Reimbursement Scheme approach in January 2014 and the adoption of a new value-based pricing approach. Under this approach, in a complete departure from established methodologies, reimbursement levels of each drug will be explicitly based on an assessment of value, looking at the benefits for the patient, unmet need, therapeutic innovation, and benefit to society as a whole. It is increasingly common in many European Union Member States for Marketing Authorization Holders to be required to demonstrate the pharmaco-economic superiority of their products as compared to products already subject to pricing and reimbursement in specific countries. In order for drugs to be evaluated positively under such criteria, pharmaceutical companies may need to re-examine, and consider altering, a number of traditional functions relating to the selection, study, and management of drugs, whether currently marketed, under development, or being evaluated as candidates for research and/or development.

Sales and marketing

Sales, promotion and other activities following product approval are subject to regulation by numerous regulatory authorities in addition to the FDA, including, in the United States, the Centers for Medicare & Medicaid Services, other divisions of the Department of Health and Human Services, the U.S. Department of Justice, and similar foreign, state, and local government authorities.

As described above, the FDA regulates all advertising and promotion activities for products under its jurisdiction both prior to and after approval. A company can make only those claims relating to safety and efficacy that are approved by the FDA in labeling. Physicians may prescribe legally available drugs for uses that are not described in the drug's labeling and that differ from those tested by us and approved by the FDA. Such off-label uses are common across medical specialties, and often reflect a physician's belief that the off-label use is the best treatment for the patients. The FDA does not regulate the behavior of physicians in their choice of treatments, but FDA regulations do impose stringent restrictions on manufacturers' communications regarding off-label uses. Failure to comply with applicable FDA requirements may subject a company to adverse publicity, enforcement action by the FDA, corrective advertising, consent decrees and the full range of civil and criminal penalties available to the FDA.

In the United States sales, marketing and scientific/educational programs must also comply with various federal and state laws pertaining to healthcare "fraud and abuse," including anti-kickback laws and false claims laws. Anti-kickback laws make it illegal for a prescription drug manufacturer to solicit, offer, receive, or pay any remuneration in exchange for, or to induce, the referral of business, including the purchase or prescription of a particular drug. Due to the breadth of the statutory provisions and the absence of guidance in the form of regulations and very few court decisions addressing industry practices, it is possible that our practices might be challenged under anti-kickback or similar laws. Moreover, recent healthcare reform legislation has strengthened these laws. For example, the recently enacted Patient Protection and Affordable Care Act, or PPACA, among other things, amends the intent requirement of the federal anti-kickback and criminal healthcare fraud statutes to clarify that a person or entity does not need to have actual knowledge of this statute or specific intent to violate it. In addition, PPACA clarifies that the government may assert that a claim that includes items or services resulting from a violation of the federal anti-kickback statute constitutes a false or fraudulent claim for purposes of the false claims statutes to clarify that. False claims laws prohibit anyone from knowingly and willingly presenting, or causing to be

presented for payment, to third-party payors (including Medicare and Medicaid) claims for reimbursed drugs or services that are false or fraudulent, claims for items or services not provided as claimed, or claims for medically unnecessary items or services. Our activities relating to the sale and marketing of our products may be subject to scrutiny under these laws. Violations of fraud and abuse laws may be punishable by criminal and civil sanctions, including fines and civil monetary penalties, the possibility of exclusion from federal healthcare programs (including Medicare and Medicaid) and corporate integrity agreements, which impose, among other things, rigorous operational and monitoring requirements on companies. Similar sanctions and penalties also can be imposed upon executive officers and employees, including criminal sanctions against executive officers under the so-called "responsible corporate officer" doctrine, even in situations where the executive officer did not intend to violate the law and was unaware of any wrongdoing.

Given the significant penalties and fines that can be imposed on companies and individuals if convicted, allegations of such violations often result in settlements even if the company or individual being investigated admits no wrongdoing. Settlements often include significant civil sanctions, including fines and civil monetary penalties, and corporate integrity agreements. If the government were to allege or convict us or our executive officers of violating these laws, our business could be harmed. In addition, private individuals have the ability to bring similar actions. Our activities could be subject to challenge for the reasons discussed above and due to the broad scope of these laws and the increasing attention being given to them by law enforcement authorities. Further, there are an increasing number of state laws that require manufacturers to make reports to states on pricing and marketing information. Many of these laws contain ambiguities as to what is required to comply with the laws. Given the lack of clarity in laws and their implementation, our reporting actions could be subject to the penalty provisions of the pertinent state authorities.

Similar rigid restrictions are imposed on the promotion and marketing of medicinal products in the European Union and other countries. Laws (including those governing promotion, marketing and anti-kickback provisions), industry regulations and professional codes of conduct often are strictly enforced. Even in those countries where we are not directly responsible for the promotion and marketing of our products, inappropriate activity by our international distribution partners can have adverse implications for us.

Other laws and regulatory processes

We will become subject to a variety of financial disclosure and securities trading regulations as a public company in the United States, including laws relating to the oversight activities of the SEC and, following the listing of our capital stock on the NASDAQ Global Market, we will be subject to the regulations of the NASDAQ Global Market. In addition, the Financial Accounting Standards Board, or FASB, the SEC and other bodies that have jurisdiction over the form and content of our accounts, our financial statements and other public disclosure are constantly discussing and interpreting proposals and existing pronouncements designed to ensure that companies best display relevant and transparent information relating to their respective businesses.

Our international operations are subject to compliance with the Foreign Corrupt Practices Act, or the FCPA, which prohibits corporations and individuals from paying, offering to pay, or authorizing the payment of anything of value to any foreign government official, government staff member, political party, or political candidate in an attempt to obtain or retain business or to otherwise influence a person working in an official capacity. We also may be implicated under the FCPA for activities by our partners, collaborators, CROs, vendors or other agents.

Our present and future business has been and will continue to be subject to various other laws and regulations. Various laws, regulations and recommendations relating to safe working conditions, laboratory practices, the experimental use of animals, and the purchase, storage, movement, import and export and

use and disposal of hazardous or potentially hazardous substances used in connection with our research work are or may be applicable to our activities. Certain agreements entered into by us involving exclusive license rights or acquisitions may be subject to national or supranational antitrust regulatory control, the effect of which cannot be predicted. The extent of government regulation, which might result from future legislation or administrative action, cannot accurately be predicted.

Legal Proceedings

We are not currently a party to any material legal proceedings.

Facilities

Our primary facility is located in Waltham, Massachusetts, where we occupy approximately 4,943 square feet of office space. Our lease expires in June 2018. We also have facility located in Kansas City, Kansas, where we occupy approximately 250 square feet of office space. Our lease in Kansas City expires in December 2014. We are currently reviewing options with respect to our primary facility in Waltham, Massachusetts upon expiration of our current lease, including re-letting our current facility or re-locating our primary facility to another location in the greater Boston, Massachusetts metropolitan area. We believe that suitable space will be available on commercially reasonable terms.

Employees

As of July 31, 2014, we had 11 full-time employees and one part-time employee, including seven in research and development and five in general and administrative functions. None of our employees is subject to a collective bargaining agreement or represented by a labor or trade union. We believe that our relations with our employees are good.

MANAGEMENT

Executive Officers and Directors

The following table sets forth the names, ages and positions of the directors and executive officers of Proteon as of July 31, 2014:

Name	Age	Position(s)
Timothy P. Noyes	52	President, Chief Executive Officer and Director
Steven K. Burke, M.D.	54	Senior Vice President and Chief Medical Officer
George A. Eldridge	51	Senior Vice President, Chief Financial Officer, Treasurer and Secretary
Daniel P. Gottlieb	44	Vice President, Marketing and Business Development
Non-Employee Directors		
Hubert Birner, Ph.D.(1)(2)(3)	48	Director
Todd Foley(2)(3)	42	Director
F. Nicholas Franano, M.D.	47	Director
John G. Freund, M.D.	60	Director
Tim Haines(1)(3)	56	Director
Dmitry Kobyzev, Ph.D.(2)(3)	29	Director
Brendan M. O'Leary, Ph.D.(1)(2)	42	Director
Gregory D. Phelps(1)	65	Chairman of the Board of Directors

(1) Member of the Compensation Committee.

(2) Member of the Audit Committee.

(3) Member of the Nominating and Corporate Governance Committee.

Executive Officers

Timothy P. Noyes joined Proteon in April 2006 as our President and Chief Executive Officer and has also been a member of our board of directors since joining Proteon. From 2002 to 2006, Mr. Noyes served as Chief Operating Officer of Trine Pharmaceuticals, Inc. Before joining Trine, Mr. Noyes held several management positions with GelTex Pharmaceuticals from 1996 to 2001, prior to its acquisition by Genzyme Corporation. After the acquisition, from 2001 to 2002, he held the positions of President, Renal Division and President, GelTex Pharmaceuticals. Prior to GelTex, he worked for several years at Merck & Co. across multiple roles in its hypertension and heart failure group and managed care division, and on its Vasotec and Prilosec products. Mr. Noyes received an A.B. from Harvard College and an M.B.A. from Harvard Business School. We believe Mr. Noyes is qualified to serve as a member of our board of directors because of his role with us and his extensive operational knowledge of, and executive level management experience in, the biopharmaceutical industry.

Steven K. Burke, M.D., joined Proteon in August 2006 as our Senior Vice President and Chief Medical Officer. Prior to joining Proteon, Dr. Burke held various roles at Genzyme Corporation from 2000 to 2006, where he served most recently as Senior Vice President of Medical and Regulatory Affairs and Vice President of Clinical Research. From 1994 to 2000, Dr. Burke held roles at GelTex Pharmaceuticals, including Vice President of Clinical Research and Medical Director, and before that he held positions at Glaxo. Dr. Burke received an A.B. from Harvard College and an M.D. from Cornell University Medical College. He completed a medical residency and fellowship at Brigham and Women's Hospital and is certified by the American Board of Internal Medicine.

George A. Eldridge joined Proteon in September 2013 as our Senior Vice President and Chief Financial Officer. Prior to joining Proteon, from 2009 to 2013, Mr. Eldridge served as a consultant to companies in the biotechnology industry, acting as a chief financial officer and providing advisory services. From 2006 to 2009, Mr. Eldridge was Chief Financial Officer of Targanta Therapeutics Corporation until its acquisition in 2009 by The Medicines Company. Before working at Targanta, Mr. Eldridge served as Chief Financial Officer of Therion Biologics from 2002 to 2006. In the fourth quarter of 2006, Therion filed a petition under the federal bankruptcy laws, which was rejected. Prior to Therion Mr. Eldridge served as Chief Financial Officer of Curis, Inc. (previously Ontogeny, Inc.) and Boston Life Sciences, Inc. Prior to working in the biotechnology field, Mr. Eldridge was an investment banker at Kidder Peabody & Co, Inc.. He holds a B.A. from Dartmouth College and an M.B.A. from the University of Chicago, Booth School of Business.

Daniel P. Gottlieb joined Proteon in September 2007 and has served as our Vice President, Marketing and Business Development since March 2013, prior to which he was the Senior Director of Marketing and Business Development from June 2010 until March 2013 and Director of Marketing and Business Development from 2007 until 2010. Prior to joining Proteon, Mr. Gottlieb served as Strategic Marketing Manager of Endovascular Products at Abbott Vascular from 2006 to 2007. Prior to that, Mr. Gottlieb spent seven years, from 1999 to 2006, at Guidant Corporation in a variety of roles, including marketing and market research, strategic planning, and business development and corporate venture investing as part of Guidant's Compass Group. Mr. Gottlieb holds a B.A. from the University of Pennsylvania and an M.B.A. from the Tuck School of Business at Dartmouth College.

Non-Employee Directors

Hubert Birner, Ph.D., has served as a member of our board of directors since 2007. Dr. Birner is the managing partner of TVM Capital, a venture capital firm, which he joined in 2000. Before joining TVM Capital, Dr. Birner served as Head of Business Development Europe and Director of Marketing for Germany at Zeneca from 1998 to 2000. Dr. Birner joined Zeneca from McKinsey & Company's European Health Care and Pharmaceutical practice where he worked from 1995 to 1998. From 1992 to 1994, Dr. Birner was also an Assistant Professor for biochemistry at the Ludwig-Maximilian-University in Munich. Dr. Birner currently serves as Chairman of the Board of Argos Therapeutics Inc. and Spepharm Holding BV and he previously served as a member of the board of directors of Horizon Pharma, Evotec AG, and BioXell SPA. Dr. Birner received an M.B.A. from Harvard Business School and a Ph.D. in biochemistry from Ludwig-Maximilian-University Munich, where he graduated summa cum laude. We believe Dr. Birner is qualified to serve as a member of our board of directors because of his business and professional experience.

Todd Foley has served as a member of our board of directors since May 2012. Mr. Foley is a managing director with MPM Capital, a venture capital firm, which he joined in 1999. Prior to joining MPM, Mr. Foley worked in business development at Genentech in 1998 and in management consulting with Arthur D. Little from 1994 to 1997. Mr. Foley currently serves as a member of the board of directors of Chiasma, Inc., Iconic Therapeutics, Inc., OSS Inc., Selexys Pharmaceuticals Corporation, Valeritas Inc. and Rhythm Pharmaceuticals Inc. and he previously served as a member of the board of directors of Aires Pharmaceuticals, Inc., Celladon Corporation, and Zalicus Inc. Mr. Foley received a B.S. in chemistry from the Massachusetts Institute of Technology and an M.B.A. from Harvard Business School. We believe Mr. Foley is qualified to serve as a member of our board of directors because of his business and professional experience

F. Nicholas Franano, M.D., has served as a member of our board of directors since March 2006. Dr. Franano is currently President and Chief Executive Officer of Flow Forward Medical, Inc., and Metactive Medical, Inc., two companies developing cardiovascular medical devices that may compete with our products, where he has served since January 2014. Prior to this, Dr. Franano was founder, President and Chief Executive Officer of Novita Therapeutics, a medical device incubator company, from 2009 to 2013. Dr. Franano founded Proteon, and served as our Chief Executive Officer from 2001 to 2006, and,

after that, as our Chief Scientific Officer from 2006 to 2009. Dr. Franano received an M.D. and an M.A. in biomedical research from Washington University, St. Louis, and a B.S. in cell biology from the University of Kansas. He completed a residency in diagnostic radiology and a fellowship in interventional radiology at the Johns Hopkins Hospital. Prior to founding Proteon, Dr. Franano maintained a clinical practice in interventional radiology from 2000 through 2005. We believe Dr. Franano is qualified to serve as a member of our board of directors because of his business and professional experience.

John G. Freund, M.D., became a member of our board of directors in February 2014. Dr. Freund co-founded Skyline Ventures, a venture capital firm, in September 1997, where he has served as a partner since its founding. Prior to joining Skyline, Dr. Freund served as managing director in the private equity group of Chancellor Capital Management from 1995 to 1997. In 1995, he co-founded Intuitive Surgical, Inc. and served on its board of directors until 2000. From 1988 to 1994, Dr. Freund served in various positions at Acuson Corporation, now part of Siemens, most recently as Executive Vice President. Prior to joining Acuson, Dr. Freund was a general partner of Morgan Stanley Venture Partners from 1987 to 1988. From 1982 to 1988, Dr. Freund worked at Morgan Stanley & Co., where he co-founded the Healthcare Group in the Corporate Finance Department. Dr. Freund currently serves as a member of the board of directors of the following public companies: XenoPort, Inc., Tetraphase Pharmaceuticals, Inc. and Concert Pharmaceuticals, Inc. He was on the board of MAKO Surgical Corp. from 2008 until its acquisition in 2013. Dr. Freund also serves as a member of the board of directors of the following private companies: Advion, Inc., Collegium Pharmaceuticals, Inc., DiscoveRx Corporation, SI Bone, Inc. and Sutro Biopharma, Inc. He is a director of three mutual funds managed by Capital Research and Management. He is a member of the Advisory Board for the Harvard Business School Healthcare Initiative and is a member of the Therapeutics Advisory Council of Harvard Medical School. He received an A.B. in history from Harvard College, an M.D. from Harvard Medical School and an M.B.A. from Harvard Business School, where he was a Baker Scholar and won the Loeb Fellowship in Finance. We believe Dr. Freund is qualified to serve as a member of our board of directors because of his business and professional experience.

Tim Haines became a member of our board of directors in May 2014. Mr. Haines joined Abingworth in 2005 and is currently a partner. From 2000 to 2005, he was Chief Executive of Astex Therapeutics, an Abingworth portfolio company. From 1993 to 2000, Mr. Haines was Chief Executive of two divisions of the publicly-listed medical technology company, Datascope Corp. Prior to Datascope, he held a number of other senior management positions in the US and Europe, including CEO of Thackray Inc and General Manager Baxter UK. Current and past board positions include Astex Pharmaceuticals, Chroma, Fovea, Pixium Vision, PowderMed, Kspine, Stanmore Implants, Lombard Medical, Sientra, and XCounter. Mr. Haines received a B.Sc. from Exeter University and an M.B.A. from INSEAD. We believe Mr. Haines is qualified to serve as a member of our board of directors because of his business and professional experience.

Dmitry Kobyzev, Ph.D., became a member of our board of directors in May 2014. Dr. Kobyzev joined Inbio Ventures, a venture capital management company representing Pharmstandard International S.A., in 2014 and is an Investment Manager. From 2009 to 2014, he served as an Investment Manager of one of the top Russian life science venture capital teams at OJSC RUSNANO. From 2007 to 2009, Dr. Kobyzev advised international private equity and Russian corporate clients within the transactions practice at PricewaterhouseCoopers Russia. Dr. Kobyzev received a Ph.D. degree in economics from Moscow State University. We believe Dr. Kobyzev is qualified to serve as a member of our board of directors because of his business and professional experience.

Brendan M. O'Leary, Ph.D., has been a member of our board of directors since March 2006. Dr. O'Leary joined Prism VentureWorks, a venture capital firm, in 2003 and is currently a general partner. Dr. O'Leary began his professional career with numerous operating roles at IGEN International, a medical diagnostics company (acquired by Roche), where he served from 1999 to 2003, and Meso Scale Discovery, a high-throughput drug discovery start-up, where he served from 1999 to 2003. Dr. O'Leary previously

served on the board of directors of Trius Therapeutics. Dr. O'Leary received a Ph.D. in organic chemistry from the Massachusetts Institute of Technology and a B.A. in chemistry and economics from Middlebury College, and was a Kauffman Fellow. We believe Dr. O'Leary is qualified to serve as a member of our board of directors because of his business and professional experience.

Gregory D. Phelps has been a member of our board of directors since February 2008 and has served as Chairman of the Board since July 2009. Mr. Phelps is an independent advisor to biotechnology and pharmaceutical companies. He was a founder and Partner of Red Sky Partners LLC, an advisory firm providing corporate development, product strategy and leadership support to life sciences companies, from February 2009 to February 2014. Prior to that, Mr. Phelps served as Chairman and Chief Executive Officer of RenaMed Biologics, Inc. from 2004 to 2007. Prior to that, he served as Chief Executive Officer of Ardais Corporation from 2002 to 2003, as Vice Chairman and member of the executive committee of Dyax Corporation from 1998 to 2002, as Executive Vice President and Senior Vice President of Genzyme Corporation from 1991 to 1997. Mr. Phelps has previously served as a member of the board of directors of the following companies: EPIX Pharmaceuticals Inc. from 2004 to 2009, Ostex International Inc. from 1995 to 2001, Atlantic Biopharmaceuticals (now Merrimack Pharmaceuticals Inc.) from 1998 to 2000, Neozyme II Corporation from 1992 to 1996, and Genzyme Transgenics Corporation (now rEVO Biologics Inc.) from 1993 to 1995. Mr. Phelps received a B.S. in electrical engineering from Bradley University and an M.B.A. from Harvard Business School. We believe Mr. Phelps is qualified to serve as a member of our board of directors because of his business and professional experience.

Composition of the Board of Directors after this Offering

Our board of directors currently consists of nine members. Our board of directors has determined that each of our Board members except Mr. Noyes is independent for NASDAQ purposes. The members of our board of directors were elected in compliance with the provisions of the voting agreement among us and our major stockholders. The voting agreement will terminated upon the closing of this offering, and at present we do not have any contractual obligations regarding the election of our directors. See "Certain Relationships and Related Party Transactions." Our directors hold office until their successors have been elected and qualified or until their earlier death, resignation or removal. There are no family relationships among any of our directors or executive officers.

Board Committees

Our board of directors has three standing committees: an audit committee, a compensation committee and a nominating and governance committee. The initial composition and responsibilities of each committee are described below.

Audit Committee

Our audit committee is composed of Todd Foley, Hubert Birner, Dmitry Kobyzev and Brendan O'Leary, with serving as chairman of the committee. Our board of directors has determined that each of satisfies the NASDAQ Stock Market independence standards and the independence standards of Rule 10A-3(b)(1) of the Securities Exchange Act. Our board of directors has determined that is an "audit committee financial expert" under applicable rules and regulations of the SEC and the NASDAQ Stock Market.

Our audit committee will provide oversight of our accounting and financial reporting process, the audit of our financial statements and our internal control function. Among other things, our audit committee will be responsible for the following:

- appointing, approving the compensation of, and assessing the qualifications, performance and independence of our independent registered public accounting firm;

- pre-approving audit and permissible non-audit services, and the terms of such services, to be provided by our independent registered public accounting firm;
- reviewing the internal audit plan with the independent registered public accounting firm and members of management responsible for preparing our financial statements;
- reviewing and discussing with management and the independent registered public accounting firm our annual and quarterly financial statements and related disclosures as well as critical accounting policies and practices used by us;
- reviewing the adequacy of our internal control over financial reporting;
- establishing policies and procedures for the receipt and retention of accounting-related complaints and concerns;
- recommending, based upon the audit committee's review and discussions with management and the independent registered public accounting firm, whether our audited financial statements shall be included in our Annual Report on Form 10-K;
- monitoring our compliance with legal and regulatory requirements as they relate to our financial statements and accounting matters;
- preparing the audit committee report required by the rules of the SEC to be included in our annual proxy statement;
- viewing all related party transactions for potential conflict of interest situations and approving all such transactions; and
- reviewing and discussing with management and our independent registered public accounting firm our earnings releases and scripts.

Compensation Committee

The members of our compensation committee are Hubert Birner, Tim Haines, Brendan O'Leary and Gregory Phelps, with Brendan O'Leary serving as chairman of the committee. Our board of directors has determined that each of satisfies the NASDAQ Stock Market independence standards. Among other things, our compensation committee will be responsible for the following:

- annually reviewing and approving corporate goals and objectives relevant to the compensation of our Chief Executive Officer;
- evaluating the performance of our Chief Executive Officer in light of such corporate goals and objectives and determining and approving the compensation of our Chief Executive Officer;
- reviewing and approving the compensation of our other executive officers;
- appointing, compensating and overseeing the work of any compensation consultant, legal counsel or other advisor retained by the compensation committee;
- conducting the independence assessment outlined in NASDAQ rules with respect to any compensation consultant, legal counsel or other advisor retained by the compensation committee;
- annually reviewing and reassessing the adequacy of the committee charter in its compliance with the listing requirements of NASDAQ;
- reviewing and establishing our overall management compensation, philosophy and policy;
- overseeing and administering our equity compensation and other compensatory plans;
- reviewing and approving our equity and incentive policies and procedures for the grant of equity-based awards and approving the grant of such equity-based awards;
- reviewing and making recommendations to the board of directors with respect to director compensation; and
- reviewing and discussing with management the compensation discussion and analysis to be included in our annual proxy statement or Annual Report on Form 10-K.

Governance and Nominating Committee

Our governance and nominating committee is composed of Hubert Birner, Dmitry Kobyzev, Todd Foley and Tim Haines with Hubert Birner serving as chair of the committee. Our board of directors has determined that each of satisfies the NASDAQ Stock Market independence standards.

Our governance and nominating committee will be responsible for, among other things, making recommendations regarding corporate governance, the composition of our board of directors, identification, evaluation and nomination of director candidates and the structure and composition of committees of our board of directors. In addition, our governance and nominating committee will:

- oversee our corporate governance guidelines;
- approve our committee charters;
- oversee compliance with our code of business conduct and ethics;
- contribute to succession planning;
- review actual and potential conflicts of interest of our directors and officers other than related party transactions reviewed by the related-party matters committee; and
- oversee the board self-evaluation process.

Compensation Committee Interlocks and Insider Participation

None of the members of our compensation committee is or has at any time during the past year been one of our officers or employees. None of our executive officers currently serves, or in the past year has served, as a member of the board of directors or compensation committee of any entity that has one or more executive officers serving on our board of directors or compensation committee.

Code of Business Conduct and Ethics

We plan to adopt a code of business conduct and ethics that will apply to all of our employees, including our officers and directors, and those employees responsible for financial reporting. The code of business conduct and ethics will be available on our website. We expect that, to the extent required by law, any amendments to the code, or any waivers of its requirements, will be disclosed on our website.

EXECUTIVE AND DIRECTOR COMPENSATION

Summary Compensation Table

The following table presents compensation awarded in 2013 to our principal executive officer and our two other most highly compensated persons serving as executive officers as of December 31, 2013 or paid to or accrued for those executive officers for services rendered during 2013. We refer to these executive officers as our "named executive officers."

Name & Principal Position	Year	Salary ($)	Bonus ($) (1)	Option Awards ($)(2)	All Other Compensation ($)(3)	Total ($)
Timothy P. Noyes *President and Chief Executive Officer*	2013	393,710	73,830	—	4,595	472,135
Steven K. Burke, M.D. *Senior Vice President and Chief Medical Officer*	2013	359,870	80,980	—	5,624	446,474
Daniel Gottlieb *Vice President, Marketing and Business Development*	2013	203,772	38,630	10,364	1,867	254,633

(1) Amounts represent cash bonuses earned in 2013, and paid during 2014, based on achievement of performance goals and other factors deemed relevant by our board of directors. Our 2013 company objectives related primarily to development and strategic achievements.

(2) The amounts reported in the Option Awards column granted to our named executive officers represent the retrospective fair value of the stock options as of the grant date as computed in accordance with Accounting Standards Codification, or ASC, Topic 718, not including any estimates of forfeitures. The assumptions used in calculating the grant date fair value of the stock options reported in the option awards column are set forth in Note 11 to our financial statements included elsewhere in this prospectus. Note that the amounts reported in this column reflect the accounting cost for these stock options, and do not correspond to the actual economic value that may be received by the named executive officers from the options.

(3) This column reflects term life and disability insurance premiums paid by us on behalf of the named executive officers. All of these benefits are provided to the named executive officers on the same terms as provided to all of our regular full-time employees.

Executive Compensation

Overview

Our executive compensation program is based on a pay-for-performance philosophy. We designed our executive compensation program to achieve the following primary objectives: provide compensation and benefit levels that will attract, retain, motivate and reward a highly talented executive team within the context of responsible cost management; establish a direct link between our individual/team performance and results and our executives' compensation; and align the interests and objectives of our executives with those of our stockholders by linking executive equity awards to stockholder value creation. Compensation for our executive officers is composed primarily of the following three main components: base salary; annual cash incentive bonuses and long-term equity incentives.

Base Salary

Base salaries are determined on a case-by-case basis for each named executive officer, including consideration of each officer's experience, expertise and performance, as well as market compensation levels for similar positions.

Name	2013 Base Salary ($)	2014 Base Salary ($)
Timothy P. Noyes	393,710	401,590
Steven Burke	359,870	367,070
Daniel P. Gottlieb	206,000	210,120

The 2013 base salary for Mr. Gottlieb became effective in connection with a promotion effective March 1, 2013. The 2013 base salary for Mr. Noyes and Dr. Burke became effective January 1, 2013. The 2014 base salary for each named executive officer became effective January 1, 2014.

Annual Cash Incentive Bonuses

Annual cash incentive bonuses are contingent upon our achievement of certain operational and financial objectives, which for 2013 consisted primarily of research and development goals. Each named executive officer's target bonus amount is expressed as a percentage of the officer's base salary and is intended to be commensurate with the officer's position and responsibilities. Target bonuses for each officer were 25% of base salary for the year ended December 31, 2013.

Long-term Equity Incentives

We believe equity awards in the form of options to purchase shares of our common stock provide an incentive for our named executive officers to focus on driving growth in our stock price and long-term value creation and help us to attract and retain key talent. In addition, the granting of options helps ensure that the interests of our officers are aligned with those of our stockholders as the options only have value if the value of our common stock increases after the date the option is granted.

Our officers are entitled to certain benefits if the officer's employment terminates in certain circumstances or if a change of control occurs. We also may provide our officers with relocation, housing or other benefits in certain circumstances. However, we do not provide any of our officers with a tax gross-up payment on any severance or change-of-control benefits (although we may provide tax reimbursement payments on relocation and other benefits). Our board of directors reviews (and, after this offering, our compensation committee will review) our officers' overall compensation packages on an annual basis or more frequently as it deems appropriate. From time to time, we may retain independent compensation consultants as we consider appropriate to help identify appropriate peer group companies and to obtain and evaluate current executive compensation data. We did not retain compensation consultants in designing our executive compensation programs for 2013. However, the compensation committee has retained independent compensation consultants for 2014 and beyond.

Employment Agreements

Below are written descriptions of our agreements with each of our named executive officers. In addition to the specifics described below, our named executive officers' employment agreements also provide for grants of stock options as described in more detail in the "Outstanding Equity Awards at Fiscal Year End" table below and the footnotes that follow the table.

Timothy P. Noyes

In April 2006, we entered into an employment agreement with Mr. Noyes to serve as our President and Chief Executive Officer. We amended the employment agreement in April 2009. Mr. Noyes's

employment with us is "at-will," and the agreement does not include a specified term. The agreement provides that Mr. Noyes receives an annual base salary, initially established at $320,000 in 2009, and that he is eligible for an annual incentive bonus, with his target bonus being 25% of his base salary. The board of directors determines his actual bonus amount based on its assessment of Proteon's and his individual performance during the year. The agreement also provides for Mr. Noyes to participate in our benefit programs made available to our employees generally.

Under Mr. Noyes's agreement, if his employment is terminated by us without cause or by reason of constructive termination (as such terms are defined in the agreement), he will be entitled to receive cash severance equal to 12 months of his base salary; reimbursement of his COBRA premiums for up to twelve months; and 50% of any unvested stock options or unvested restricted shares (excluding certain grants) shall vest in full, accelerated to 100% if the termination occurs 30 days prior to or 180 days after a corporate transaction (as defined in the agreement). If a termination of Mr. Noyes's employment without cause (as defined in the agreement) occurs at such time as our business is being discontinued because rendered impracticable by substantial financial losses, lack of funding, dissolution or any reason beyond our control his cash severance would be equal to five months of his base salary and would be paid to him in a lump sum. Mr. Noyes's right to receive these severance benefits is subject to his providing a release of claims in favor of Proteon.

The agreement includes a noncompetition covenant during Mr. Noyes's employment under the agreement and for 12 months thereafter. The agreement provides that we shall indemnify Mr. Noyes against all losses, damages, expenses and claims against him by reason of act or omission in connection with the performance of his duties to the fullest extent permitted by the law.

Steven K. Burke, M.D.

In July 2006, we entered into an employment agreement with Dr. Burke to serve as our Senior Vice President and Chief Medical Officer. We amended the employment agreement in April 2009. Dr. Burke's employment with us is "at-will," and the agreement does not include a specified term. The agreement provides that Dr. Burke receives an annual base salary, initially established at $292,000 in 2009, and that he is eligible for an annual incentive bonus, with his target bonus being 25% of his base salary. The board of directors determines his actual bonus amount based on its assessment of Proteon's and his individual performance during the year. The agreement also provides for Dr. Burke to participate in our benefit programs made available to our employees generally.

Under Dr. Burke's agreement, if his employment is terminated by us without cause or by reason of constructive termination (as these terms are defined in the agreement), he will be entitled to receive cash severance equal to 12 months of his base salary; reimbursement of his COBRA premiums for up to twelve months; and 50% of any unvested stock options or unvested restricted shares (excluding certain grants) shall vest in full, accelerated to 100% if the termination occurs 30 days prior to or 180 days after a corporate transaction (as defined in the agreement). If a termination of Dr. Burke's employment without cause (as defined in the agreement) occurs at such time as our business is being discontinued because rendered impracticable by substantial financial losses, lack of funding, dissolution or any reason beyond our control his cash severance would be equal to four months of his base salary and would be paid to him in a lump sum. Dr. Burke's right to receive these severance benefits is subject to his providing a release of claims in favor of Proteon.

The agreement includes a noncompetition covenant during Dr. Burke's employment under the agreement and for 12 months thereafter. The agreement provides that we shall indemnify Dr. Burke against all losses, damages, expenses and claims against him by reason of act or omission in connection with the performance of his duties to the fullest extent permitted by the law.

Daniel P. Gottlieb

In July 2007 we entered into an employment agreement with Mr. Gottlieb to serve as our Director of Business Development. Mr. Gottlieb's employment with us is "at-will," and the agreement does not include a specified term. The agreement provides that Mr. Gottlieb receives an annual base salary, initially established at $160,000 in 2007, and that he is eligible for an annual incentive bonus, with his initial target bonus being 20% of his base salary. The board of directors will determine his actual bonus amount based on its assessment of Proteon's and his individual performance during the year. The agreement also provides for Mr. Gottlieb to participate in our benefit programs made available to our employees generally.

Under a separate severance agreement, if Mr. Gottlieb's employment is terminated by us without cause or by reason of constructive termination (as such terms are defined in the agreement), he will be entitled to receive cash severance equal to six months of his base salary; reimbursement of his COBRA premiums for up to six months; and 100% of any unvested stock options or unvested restricted shares shall vest in full if the termination occurs 30 days prior to or 365 days after a corporate transaction (as defined in the agreement).

Outstanding Equity Awards at Fiscal Year End

The following table sets forth information regarding outstanding equity awards held by our named executive officers as of December 31, 2013.

Name	Notes	Number of Securities Underlying Unexercised Options Exercisable(1)	Number of Securities Underlying Unexercised Options Unexercisable	Option Exercise Price ($)(2)	Option Expiration Date
Timothy P. Noyes	(3)	1,329,000	—	$ 0.12	8/1/2016
	(3)	500,000	—	$ 0.15	9/10/2017
	(3)	886,017	—	$ 0.20	6/18/2019
	(3)	55,221	—	$ 0.20	12/15/2019
	(4)	1,355,117	—	$ 0.08	10/26/2021
Steven K. Burke, M.D.	(3)	482,632	—	$ 0.12	8/1/2016
	(3)	195,000	—	$ 0.15	9/10/2017
	(3)	236,443	—	$ 0.20	6/18/2019
	(4)	919,416	—	$ 0.08	10/26/2021
Daniel P. Gottlieb	(3)	84,374	—	$ 0.15	9/10/2017
	(3)	29,442	—	$ 0.20	6/18/2019
	(4)	60,000	—	$ 0.08	10/26/2021
	(5)	10,000	—	$ 1.40	3/25/2023

(1) All of the outstanding option awards were granted under and subject to the terms of our 2006 Equity Incentive plan, described below under "—Equity Benefit and Stock Plans." Except as otherwise indicated, as of December 31, 2013, each option award is immediately exercisable but is subject to repurchase by us until vested. All vesting is subject to the officer's continuous service with us through the vesting dates and the potential vesting acceleration described above under "—Employment Agreements."

(2) All of the option awards were granted with a per share exercise price equal to the fair market value of one share of our common stock on the date of grant, as determined in good faith by our board of directors

(3) These grants are fully vested.

(4) The unvested shares under this option are scheduled to vest in approximately equal quarterly installments through October 1, 2015.

(5) The unvested shares under this option are scheduled to vest in approximately equal quarterly installments through January 1, 2017.

Employee Benefit and Stock Plans

2006 Equity Incentive Plan

We adopted our 2006 Equity Incentive Plan, or 2006 Plan, in March 2006, and stockholders approved the plan in March 2006. We amended the 2006 Plan in 2007. Under the 2006 Plan, we are generally authorized to grant options to purchase shares of our common stock to our employees, directors and consultants. Options under the 2006 Plan are either incentive stock options, within the meaning of Section 422 of the Internal Revenue Code, or nonqualified stock options. All options granted under the 2006 Plan expire no later than ten years from their date of grant.

No new awards will be granted under the 2006 Plan after the consummation of this initial public offering. Our board of directors, or a committee appointed by the board, administers the 2006 Plan. As is customary in incentive plans of this nature, the number of shares subject to outstanding awards under the 2006 Plan and the exercise prices of those awards are subject to adjustment in the event of changes in our capital structure, reorganizations and other extraordinary events. In the event that we are consolidated with, or acquired by, another entity in a merger, consolidation or sale of all or substantially all of our assets, the plan administrator will provide for the outstanding awards either to be assumed by our successor or to terminate on the transaction. If the awards terminate, the plan administrator has discretion to provide for the accelerated vesting of the awards prior to their termination.

Our board of directors may amend or terminate the 2006 Plan at any time, except that any such amendment or termination may not adversely affect the rights of a holder of an outstanding award without the holder's consent. The 2006 Plan requires that certain amendments, to the extent required by applicable law or any applicable listing agency or deemed necessary or advisable by the board of directors, be submitted to stockholders for their approval.

2014 Equity Incentive Plan

The following is a summary of the material terms of the 2014 Equity Incentive Plan, or 2014 Plan, which will be in effect upon the completion of this offering. It does not purport to be complete and is qualified by reference to the full text of the 2014 Equity Incentive Plan, which we will file as an exhibit to our registration statement of which this prospectus is a part.

The 2014 Plan provides for the grant of incentive stock option and nonstatutory stock options, stock appreciation rights, restricted stock and stock unit awards, performance units, stock grants and qualified performance-based awards, which we collectively refer to as "awards" in connection with the 2014 Plan. Directors, officers and other employees of Proteon and our subsidiaries, as well as others performing consulting or advisory services for us, are eligible for grants under the 2014 Plan. The purpose of the 2014 Plan is to provide incentives that will attract, retain and motivate highly competent officers, directors, employees and consultants to promote the success of our business.

Administration

Under its terms, the 2014 Plan is administered by the compensation committee of the board of directors. The board of directors itself may also exercise any of the powers and responsibilities under the

2014 Plan. Subject to the terms of the 2014 Plan, the plan administrator (the board or its compensation committee) will select the recipients of awards and determine, among other things, the:

- number of shares of common stock covered by the awards and the dates upon which such awards become exercisable or any restrictions lapse, as applicable;
- type of award and the exercise or purchase price and method of payment for each such award;
- vesting period for awards, risks of forfeiture and any potential acceleration of vesting or lapses in risks of forfeiture; and
- duration of awards.

All decisions, determinations and interpretations by the compensation committee with respect to the 2014 Plan and the terms and conditions of or operation of any award are final and binding on all participants, beneficiaries, heirs, assigns or other persons holding or claiming rights under the 2014 Plan or any award.

Available Shares

The aggregate number of shares of our common stock which may be issued or used for reference purposes under the 2014 Plan or with respect to which awards may be granted, subject to the automatic increase provisions described below, may not exceed shares, which may be either authorized and unissued shares of our common stock or shares of common stock held in or acquired for our treasury. In general, if awards under the 2014 Plan are for any reason cancelled, or expire or terminate unexercised, the number of shares covered by such awards will again be available for the grant of awards under the 2014 Plan. In addition, (i) shares used to pay the exercise price of a stock option and (ii) shares delivered to or withheld by us to pay the withholding taxes related to an award do not count as shares issued under the 2014 Plan.

The number of shares of common stock authorized under the 2014 Equity Incentive Plan also will be increased each January 1 starting in 2015 by an amount equal to the lesser of (i) % of our outstanding common stock on a fully diluted basis as of the end of our immediately preceding fiscal year, (ii) shares, and (iii) any lower amount determined by our board prior to each such January 1.

Eligibility for Participation

Members of our board of directors, as well as employees of, and consultants to, us or any of our subsidiaries and affiliates are eligible to receive awards under the 2014 Plan. The selection of participants is within the sole discretion of the compensation committee.

Incentive Stock Options

Incentive stock options are intended to qualify as incentive stock options under Section 422 of the Internal Revenue Code and will be granted pursuant to incentive stock option agreements. The plan administrator will determine the exercise price for an incentive stock option, which may not be less than 100% of the fair market value of the stock underlying the option determined on the date of grant. In addition, incentive options granted to employees who own, or are deemed to own, more than 10% of our voting stock, must have an exercise price not less than 110% of the fair market value of the stock underlying the option determined on the date of grant.

Nonstatutory Stock Options

Nonstatutory stock options are not intended to qualify as incentive stock options under Section 422 of the Internal Revenue Code and will be granted pursuant to nonstatutory stock option agreements. The plan administrator will determine the exercise price for a nonstatutory stock option, which may not be less than the fair market value of the stock underlying the option determined on the date of grant.

Stock Appreciation Rights

A stock appreciation right, or a SAR, entitles a participant to receive a payment equal in value to the difference between the fair market value of a share of stock on the date of exercise of the SAR over the grant price of the SAR. SARs may be granted in tandem with a stock option, such that the recipient has the opportunity to exercise either the stock option or the SAR, but not both. The base exercise price (above which any appreciation is measured) will not be less than 50% of the fair market value of the common stock on the date of grant of the SAR or, in the case of an SAR granted in tandem with a stock option, the exercise price of the related stock option. The administrator may pay that amount in cash, in shares of our common stock, or a combination. The terms, methods of exercise, methods of settlement, form of consideration payable in settlement, and any other terms and conditions of any SAR will be determined by the administrator at the time of the grant of award and will be reflected in the award agreement.

Restricted Stock and Stock Units

A restricted stock award or restricted stock unit award is the grant of shares of our common stock either currently (in the case of restricted stock) or at a future date (in the case of restricted stock units) at a price determined by the administrator (including zero), that is nontransferable and is subject to substantial risk of forfeiture until specific conditions or goals are met. Conditions are typically based on continuing employment. During the period of restriction, participants holding shares of restricted stock shall, except as otherwise provided in an individual award agreement, have full voting and dividend rights with respect to such shares. Participants holding restricted stock units may be entitled to receive payments equivalent to any dividends declared with respect to the common stock referenced in the grant of the restricted stock units, but only following the close of the applicable restriction period and then only if the underlying common stock has been earned. The restrictions will lapse in accordance with a schedule or other conditions determined by the administrator.

Performance Units

A performance unit award is a contingent right to receive predetermined shares of our common stock if certain performance goals are met. The value of performance units will depend on the degree to which the specified performance goals are achieved but are generally based on the value of our common stock. The administrator may, in its discretion, pay earned performance shares in cash, or stock, or a combination of both. Furthermore, based on the level of performance, the number of shares issued upon achievement of specified levels of performance could be up to % of the number of performance units.

Our compensation committee has discretion to select the length of any applicable restriction or performance period, the kind and/or level of the applicable performance goal, and whether the performance goal is to apply to us, one of our subsidiaries or any division or business unit, or to the recipient, provided that any performance goals be objective and otherwise meet the requirements of Section 162(m) of the Code. Generally, a recipient will be eligible to receive payment under a qualified performance-based award only if the applicable performance goal or goals are achieved within the applicable performance period, as determined by the compensation committee.

Stock Grants

A stock grant is an award of shares of common stock without restriction. Stock grants may only be made in limited circumstances, such as in lieu of other earned compensation. Stock grants are made without any forfeiture conditions.

Qualified Performance-Based Awards

Qualified performance-based awards include performance criteria intended to satisfy Section 162(m) of the Code. Section 162(m) of the Internal Revenue Code limits our federal income tax deduction for

compensation to certain specified senior executives to $1 million, but excludes from that limit "performance-based compensation." Any form of award permitted under the 2014 Plan, other than restricted stock, restricted stock units and stock grants, may be granted as a qualified performance-based award, but in each case will be subject to satisfaction of performance goals or (in the case of stock options) based on continued service. The performance criteria used to establish performance goals are limited to the following: (i) cash flow (before or after dividends); (ii) earnings per share (including, without limitation, earnings before interest, taxes, depreciation and amortization); (iii) stock price; (iv) return on equity; (v) stockholder return or total stockholder return; (vi) return on capital (including, without limitation, return on total capital or return on invested capital); (vii) return on investment; (viii) return on assets or net assets; (ix) market capitalization; (x) economic value added; (xi) debt leverage (debt to capital); (xii) revenue; (xiii) sales or net sales; (xiv) backlog; (xv) income, pre-tax income or net income; (xvi) operating income or pre-tax profit; (xvii) operating profit, net operating profit or economic profit; (xviii) gross margin, operating margin or profit margin; (xix) return on operating revenue or return on operating assets; (xx) cash from operations; (xxi) operating ratio; (xxii) operating revenue; (xxiii) market share improvement; (xxiv) general and administrative expenses and (xxv) customer service.

Transferability

Awards granted under the 2014 Plan are generally nontransferable (other than by will or the laws of descent and distribution), except that the compensation committee may provide for the transferability of nonstatutory stock options at the time of grant or thereafter to certain family members.

Adjustment for Corporate Actions

In the event of any change in the outstanding shares of common stock as a result of a reorganization, recapitalization, reclassification, stock dividend, stock split, reverse stock split or other similar distribution with respect to the shares of common stock, an appropriate and proportionate adjustment will be made in (i) the maximum numbers and kinds of shares subject to the 2014 Plan, (ii) the numbers and kinds of shares or other securities subject to then outstanding awards, (iii) the exercise price for each share or other unit of any other securities subject to then outstanding stock options or SARs (without change in the aggregate purchase price as to which such stock options or SARs remain exercisable), and (iv) the repurchase price of each share of restricted stock then subject to a risk of forfeiture in the form of a Company repurchase right. Any such adjustment in awards will be determined and made by the Compensation Committee in its sole discretion.

Transactions

In the event of a transaction, including (i) any merger or consolidation of Proteon, (ii) any sale or exchange of all of the common stock of Proteon, (iii) any sale, transfer or other disposition of all or substantially all of Proteon's assets, or (iv) any liquidation or dissolution of Proteon, the compensation committee may, with respect to all or any outstanding stock options and SARS, (1) provide that such awards will be assumed, or substantially equivalent rights shall be provided in substitution therefore, (2) provide that the recipient's unexercised awards will terminate immediately prior to the consummation of such transaction unless exercised within a specified period following written notice to the recipient, (3) provide that outstanding awards shall become exercisable in whole or in part prior to or upon the transaction, (4) provide for cash payments, net of applicable tax withholdings, to be made to the recipients, (5) provide that, in connection with a liquidation or dissolution of Proteon, awards shall convert into the right to receive liquidation proceeds net of the exercise price of the awards and any applicable tax withholdings, or (6) any combination of the foregoing. With respect to outstanding awards other than stock options or SARs, upon the occurrence of a transaction other than a liquidation or dissolution of the Company which is not part of another form of transaction, the repurchase and other rights of Proteon under each such award will transfer to Proteon's successor. Upon the occurrence of such a liquidation or dissolution of Proteon, all risks of forfeiture and performance goals applicable to such other awards will

automatically be deemed terminated or satisfied, unless specifically provided to the contrary in the award. Any determinations required to carry out any of the foregoing will be made by the compensation committee in its sole discretion.

Change of Control

Upon the occurrence of a change of control, all outstanding stock options and SARs will accelerate with respect to such percentage of the shares not then exercisable as is determined by the compensation committee, the risk of forfeiture applicable to all outstanding restricted stock and restricted stock units not based on achievement of performance goals will lapse with respect to such percentage of the restricted stock and restricted stock units still subject to such risk of forfeiture as is determined by the compensation committee, and such percentage of any outstanding awards of performance units will be deemed to have been satisfied as is determined by the compensation committee. In each case, a pro rata portion of each unvested award will be vested.

A change of control is defined as the occurrence of any of the following: (1) a transaction, as described above, unless securities possessing more than 50% of the total combined voting power of the resulting entity or ultimate parent entity are held by a person who held securities possessing more than 50% of the total combined voting power of Proteon immediately prior to the transaction; (2) any person or group of persons, excluding Proteon and certain other related entities, directly or indirectly acquires beneficial ownership of securities possessing more than 50% of the total combined voting power of Proteon, unless pursuant to a tender or exchange offer that Proteon's board of directors recommends stockholders accept; (3) over a period of no more than 24 consecutive months there is a change in the composition of Proteon's board such that a majority of the board members ceases to be composed of individuals who either (i) have been board members continuously since the beginning of that period, or (ii) have been elected or nominated for election as board members during such period by at least a majority of the remaining board members who have been board members continuously since the beginning of that period.

Amendment and Termination

Our board of directors may at any time amend any or all of the provisions of the 2014 Equity Incentive Plan, or suspend or terminate it entirely, retroactively or otherwise. Unless otherwise required by law or specifically provided in the 2014 Equity Incentive Plan, the rights of a participant under awards granted prior to any amendment, suspension or termination may not be adversely affected without the consent of the participant. The 2014 Equity Incentive Plan expires after ten years.

Allocation of Awards; Plan Benefits.

It is not presently possible to determine the dollar value of award payments that may be made or the number of options, shares of restricted stock, restricted stock units, or other awards that may be granted under the 2014 Equity Incentive Plan in the future, or the individuals who may be selected for such awards because awards under the 2014 Equity Incentive Plan are granted at the discretion of the compensation committee.

401(k) Plan

We maintain a defined contribution employee retirement plan, or 401(k) plan, for our employees. Our named executive officers are also eligible to participate in the 401(k) plan on the same basis as our other employees. The 401(k) plan is intended to qualify as a tax-qualified plan under Section 401(k) of the Code. The plan provides that each participant may contribute up to the statutory limit, which is $17,500 for calendar year 2014. Participants that are 50 years or older can also make "catch-up" contributions, which in calendar year 2014 may be up to an additional $5,500 above the statutory limit. We may also elect to provide for discretionary profit sharing contributions, but we did not provide any such contributions in 2013. In general, eligible compensation for purposes of the 401(k) plan includes an employee's earnings

reportable on IRS Form W-2 subject to certain adjustments and exclusions required under the Code. The 401(k) plan currently does not offer the ability to invest in our securities.

Disclosure of Commission Position on Indemnification for Securities Act Liabilities

Our amended and restated bylaws provide for the indemnification of officers, directors and third parties acting on our behalf if such persons act in good faith and in a manner reasonably believed to be in and not opposed to our best interest, and, with respect to any criminal action or proceeding, such indemnified party had no reason to believe his or her conduct was unlawful.

To the extent that indemnification for liabilities arising under the Securities Act may be permitted to directors, officers or persons controlling our company pursuant to the foregoing provisions, we have been informed that, in the opinion of the SEC, this indemnification is against public policy as expressed in the Securities Act and is therefore unenforceable. If a claim for indemnification against these liabilities (other than the payment by us of expenses incurred or paid by a director, officer or controlling person of our company in the successful defense of any action, suit or proceeding) is asserted by any of our directors, officers or controlling persons in connection with the securities being registered, we will, unless in the opinion of our counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether this indemnification by us is against public policy as expressed in the Securities Act and will be governed by the final adjudication of that issue.

Director Compensation

The following table sets forth a summary of the compensation we paid to our non-employee directors during 2013. Other than as set forth in the table below, we did not pay any compensation, make any equity awards or non-equity awards to, or pay any other compensation to any of the other non-employee members of our board of directors in 2013. Mr. Noyes received no compensation for his service as a director, and, consequently, is not included in this table.

Prior to this offering, we did not have a formal policy for compensating our non-employee directors. However, non-employee directors who are not affiliated with any of our major stockholders may receive stock options and other equity awards under our stock incentive plans from time to time as determined by our board of directors. We also reimburse non-employee directors for travel expenses incurred in connection with their duties as directors. We expect to adopt a new compensation program for our non-employee directors concurrent with the consummation of this offering. We are still considering the design of this program and have retained an independent compensation consultant to help us determine its terms.

Name	Fees Earned or Paid in Cash	Stock Options	All Other Compensation
Hubert Birner, Ph.D.	—	—	—
Todd Foley	—	—	—
F. Nicholas Franano, M.D.(1)	—	—	$ 43,000
John G. Freund, M.D.	—	—	—
Brendan M. O'Leary, Ph.D.	—	—	—
Gregory D. Phelps(2)	$ 20,000	—	—

(1) Amount represents consulting fees for services rendered by Dr. Franano.

(2) Amount represents annual director fee for Mr. Phelps. Amount was paid in equal quarterly installments.

CERTAIN RELATIONSHIPS AND RELATED PARTY TRANSACTIONS

Other than compensation arrangements, we describe below transactions and series of similar transactions, since January 1, 2011, to which we were a party or will be a party, in which:

- the amounts involved exceeded or will exceed $120,000; and
- any of the directors, executive officers or holders of more than 5% of the capital stock of Proteon, or any member of the immediate family of the foregoing persons, had or will have a direct or indirect material interest.

Compensation arrangements for our directors and named executive officers are described elsewhere in this prospectus.

Debt Financing

In April 2013, we entered into a convertible note purchase agreement with beneficial owners of more than 5% of our capital stock, pursuant to which, in September 2013, we issued secured convertible promissory notes. The notes carried interest at 8% per annum. In May 2014, these notes were converted and the aggregate amount of outstanding principal and unpaid accrued interest thereon was exchanged for shares of our Series D convertible preferred stock, as described below under "—Series D Preferred Stock Financing." The following table sets forth the aggregate principal amount of promissory notes that we issued to our directors, executive officers and 5% stockholders, and their affiliates or immediate family members:

Investor	Aggregate Principal Amount of Notes
Intersouth Partners VI, L.P.	$ 653,950
Prism Venture Partners and related funds	$ 937,000
Skyline Venture Partners Qualified Purchaser Fund IV, LP	$ 921,241
TVM Capital and related funds	$ 1,172,529

Preferred Stock Financing

Series C Preferred Stock Financing

In August 2011, we issued and sold to investors an aggregate of 13,202,932 shares of our Series C convertible preferred stock and warrants to purchase 10,471,282 shares of our common stock, at a purchase price of $1.15 per share, for aggregate consideration of approximately $15,183,371, which was paid for in cash. As of June 30, 2014, there are 10,471,282 shares of our common stock issuable upon exercise of outstanding warrants at a weighted average exercise price of $0.29 per share. The following table sets forth the aggregate amount of securities that we issued to our directors, executive officers and 5% stockholders, and their affiliates or immediate family members in this transaction:

Investor	Shares of Series C Preferred Stock Issued	Shares of Common Stock Underlying the Warrants	Purchase Price
TVM Capital and related funds	3,130,434	2,482,757	$ 3,599,999
Skyline Venture Partners Qualified Purchaser Fund IV, L.P.	2,436,437	1,932,346	$ 2,801,903
Prism Venture Partners and related funds	2,478,183	1,965,454	$ 2,849,910
Intersouth Partners VI, L.P.	1,729,523	1,371,690	$ 1,988,951
MPM Bio IV NVS Strategic Fund, LP	1,645,073	1,304,713	$ 1,891,834

Series D Preferred Stock Financing

On May 13, 2014, we issued and sold to investors an aggregate of 52,813,827 shares of our Series D convertible preferred stock, at a purchase price of $0.588656 per share, for aggregate consideration of $25,000,000. This included 10,344,201 shares of our Series D preferred stock that was paid for by converting of approximately $4.5 million of principal indebtedness and unpaid accrued interest thereon under the promissory notes described above under "—Debt Financing", at a conversion price of $0.4414 per share, which represented a 25% discount on the purchase price per share of our Series D convertible preferred stock issued and sold in the offering.

The following table sets forth the aggregate amount of securities that we issued to our directors, executive officers and 5% stockholders, and their affiliates or immediate family members in this transaction:

Investor	Shares of Series D Preferred Stock Issued	Purchase Price
Abingworth Bioventures VI, LP	16,044,081	$ 9,444,445
Pharmstandard International S.A.	8,493,925	$ 5,000,000
Deerfield and related funds	8,493,925	$ 5,000,000
TVM Capital and related funds	5,005,486	$ 2,534,850
Skyline Venture Partners Qualified Purchaser Fund IV, L.P.	3,932,747	$ 1,991,600
Prism Venture Partners and related funds	4,000,070	$ 2,025,698
Intersouth Partners VI, L.P.	2,319,806	$ 1,135,974
MPM Bio IV NVS Strategic Fund, LP	1,765,137	$ 1,039,058

Investors' Rights Agreement

In connection with our Series D convertible preferred stock financing, on May 13, 2014, we entered into the Fourth Amended and Restated Investors' Rights Agreement with the holders of all of our then-outstanding shares of preferred stock including certain of our executive officers and entities with which certain of our directors are affiliated. The agreement provides that these holders have the right to demand that we file a registration statement with respect to the common stock issued upon conversion of our preferred stock. These holders may also request that shares of common stock held by them be included in certain registration statements that we are otherwise filing. See "Description of Capital Stock—Registration Rights."

Right of First Refusal and Co-Sale Agreement

In connection with our Series D convertible preferred stock financing, on May 13, 2014, we entered into the Fourth Amended and Restated Right of First Refusal and Co-Sale Agreement with the holders of all of our then-outstanding shares of preferred stock including certain of our executive officers and entities with which certain of our directors are affiliated. Pursuant to the terms of this agreement, in the event of a proposed sale of shares of our common or preferred stock, the seller is required to first offer such shares to the company and to the other investors, subject to certain conditions and restrictions. This agreement will terminate upon the completion of this offering.

Voting Agreement

In connection with our Series D convertible preferred stock financing on May 13, 2014, we entered into the Fourth Amended and Restated Voting Agreement with the holders of all of our then outstanding shares of preferred stock including certain of our executive officers and entities with which certain of our directors are affiliated, with respect to the election of directors and certain other matters. All of our

current directors were elected pursuant to the terms of this agreement. This agreement will terminate upon the completion of this offering.

Related Party Transactions Policy

Prior to completion of the offering, we will adopt a related person transaction approval policy that will govern the review of related person transactions following the closing of this offering. Pursuant to this policy, if we want to enter into a transaction with a related person or an affiliate of a related person, our Chief Financial Officer will review the proposed transaction to determine, based on applicable NASDAQ and SEC rules, if such transaction requires pre-approval by the audit committee and/or board of directors. If pre-approval is required, the matters will be reviewed at the next regular or special audit committee and/or board of directors meeting. We may not enter into a related person transaction unless our Chief Financial Officer has either specifically confirmed in writing that no further reviews are necessary or that all requisite corporate reviews have been obtained.

Indemnification of Directors and Officers

Prior to the completion of this offering, we expect to enter into indemnification agreements with each of our directors and executive officers. These agreements will require us to indemnify these individuals and, in certain cases, affiliates of such individuals, to the fullest extent permissible under Delaware law against liabilities that may arise by reason of their service to us or at our direction, and to advance expenses incurred as a result of any proceeding against them as to which they could be indemnified.

PRINCIPAL STOCKHOLDERS

The following table sets forth information relating to the beneficial ownership of our common stock as of July 31, 2014, by: each person, or group of affiliated persons, known by us to beneficially own more than 5% of our outstanding shares of common stock; each of our directors; each of our named executive officers; and all of our directors and executive officers as a group.

The number of shares beneficially owned by each entity, person, director or executive officer is determined in accordance with the rules of the SEC, and the information is not necessarily indicative of beneficial ownership for any other purpose. Under such rules, beneficial ownership includes any shares over which the individual has sole or shared voting power or investment power as well as any shares that the individual has the right to acquire within 60 days of July 31, 2014 through the exercise of any stock option, warrants or other rights. Except as otherwise indicated, and subject to applicable community property laws, the persons named in the table have sole voting and investment power with respect to all shares of common stock held by that person.

The percentage of shares beneficially owned is computed on the basis of 138,752,300 shares of our common stock outstanding as of July 31, 2014, assuming for purposes of this table that all outstanding shares of our preferred stock have been converted to common stock and that the Series D convertible preferred stock converted on a one-for-one basis. For a description of the conversion, upon the completion of this offering, of shares of our Series D convertible preferred stock into shares of our common stock, see "Capitalization—Series D Convertible Preferred Stock." Shares of our common stock that a person has the right to acquire within 60 days of July 31, 2014 are deemed outstanding for purposes of computing the percentage ownership of the person holding such rights, but are not deemed outstanding for purposes of computing the percentage ownership of any other person, except with respect to the percentage ownership of all directors and executive officers as a group. Unless otherwise indicated below, the address for each beneficial owner listed is c/o Proteon Therapeutics, Inc., 200 West Street, Waltham, MA 02451.

	Prior to the Offering		After the Offering	
Beneficial Owner	**Number**	**Percent**	**Number**	**Percent**
5% Stockholders:				
TVM Capital and related funds(1)	25,950,984	18.4%		
Prism Venture Partners and related funds(2)	20,710,808	14.7		
Skyline Venture Partners Qualified Purchaser Fund IV, L.P.(3)	20,358,205	14.5		
Abingworth Bioventures VI, LP.(4)	16,044,081	11.6		
Intersouth Partners VI, L.P.(5)	13,992,824	10.0		
MPM Bio IV NVS Strategic Fund, L.P.(6)	13,126,423	9.4		
Deerfield and related funds(7)	8,493,925	6.1		
Pharmstandard International S.A.(8)	8,493,925	6.1		
Directors and Named Executive Officers:				
Timothy P. Noyes(9)	6,125,355	4.2		
Gregory D. Phelps(10)	502,635	*		
Hubert Birner, Ph.D.(1)	25,950,984	18.4		
Brendan M. O'Leary, Ph.D.(2)	20,710,808	14.7		
John G. Freund, M.D.(3)	20,358,205	14.5		
Timothy Haines(4)	16,044,081	11.6		
F. Nicholas Franano, M.D.(11)	4,923,744	3.5		
Todd Foley(6)	13,126,423	9.4		
Dmitry Kobyzev(8)	8,493,925	6.1		
Steven K. Burke(12)	3,133,491	2.2		
Daniel P. Gottlieb(13)	983,816	*		
All executive officers and directors as a group (12 persons)(14)	122,353,467	76.2%		

* *Indicates ownership of less than one percent.*

(1) Includes (a) 17,477,906 shares of common stock issuable upon conversion of convertible preferred stock and warrants to purchase 1,849,034 shares of common stock held by TVM Life Science Ventures VI GmbH & Co. KG and (b) 5,990,321 shares of common stock issuable upon conversion of convertible preferred stock and warrants to purchase 633,723 shares of common stock held by TVM Life Science Ventures VI L.P. Excludes 1,316,683 shares of common stock issuable upon conversion of convertible preferred stock and 451,276 shares of common stock issuable upon conversion of convertible preferred stock that TVM Life Science Ventures VI GmbH & Co. KG and TVM Life Science Ventures VI L.P., respectively, have the right to acquire, which right cannot be exercised during the period commencing on the date that the Company submits a registration statement on Form S-1 to the SEC and ending on the earlier of (x) the third business day following the withdrawal of such registration statement on Form S-1 in connection with any abandonment of the IPO and (y) the closing of the IPO. Alexandra Goll, Helmut Schühsler, Stefan Fischer, Axel Polack and Hubert Birner, our director, are members of the investment committee of TVM Life Science Ventures VI Management Limited Partnership, a special limited partner of TVM Life Science Ventures VI GMBH & Co. KG and TVM Life Science Ventures VI LP with voting and dispositive power over the share held by those entities. TVM Life Science Venture VI Management Limited Partnership and these individuals each disclaim beneficial ownership of such shares except to the extent of any pecuniary interest therein. The address for each of the individuals and entities listed above is c/o TVM Capital GmbH, Ottostrasse 4, 80333, Munich, Germany. Dr. Birner's address is c/o TVM Capital GmbH, Ottostrasse 4, 80333, Munich, Germany.

(2) Includes (a) 12,879,940 shares of common stock issuable upon conversion of convertible preferred stock and warrants to purchase 1,350,465 shares of common stock held by Prism Venture Partners V, L.P., and (b) 5,865,414 shares of common stock and warrants to purchase 614,989 shares of common stock held by Prism Venture Partners V-A, L.P. Excludes 970,780 shares of common stock issuable upon conversion of convertible preferred stock and 442,085 shares of common stock issuable upon conversion of convertible preferred stock that Prism Venture Partners V, L.P. and Prism Venture Partners V-A, L.P., respectively, have the right to acquire, which right cannot be exercised during the period commencing on the date that the Company submits a registration statement on Form S-1 to the SEC and ending in the earlier of (x) the third business day following the withdrawal of such registration statement on Form S-1 in connection with any abandonment of the IPO and (y) the closing of the IPO. Steven J. Benson, James A. Counihan, and Brendan M. O'Leary are the managing members of Prism Venture Partners V, LLC, the sole general partner of Prism Investment Partners V, L.P., which is the sole general partner of Prism Venture Partners V, L.P. and Prism Venture Partners V-A, L.P. Each of the managing members disclaims beneficial ownership of any such shares except to the extent of his proportionate pecuniary interest therein. The address for Dr. O'Leary and Prism Venture Partners is c/o Prism VentureWorks, 75 Second Avenue, Suite 210, Needham, MA 02494.

(3) Includes 18,425,859 shares of common stock issuable upon conversion of convertible preferred stock and warrants to purchase 1,932,346 shares of common stock. Excludes 1,389,064 shares of common stock issuable upon conversion of convertible preferred stock that the holder has the right to acquire, which right cannot be exercised during the period commencing on the date that the Company submits a registration statement on Form S-1 to the SEC and ending in the earlier of (a) the third business day following the withdrawal of such registration statement on Form S-1 in connection with any abandonment of the IPO and (b) the closing of the IPO. Skyline Venture Management IV, LLC ("SVM VI") is the sole general partner of Skyline Venture Partners Qualified Purchaser Fund IV, L.P. ("SVPQP IV"). Each of John G. Freund, our director, Yasunori Kaneko and Stephen Hoffman are managing directors of SVM IV and share voting and dispositive power over the shares held by the SVPQP IV; however, they disclaim beneficial ownership of the shares held by SVPQP IV, except to the extent of their pecuniary interests therein. The address for Dr. Freund and Skyline Venture Partners Qualified Purchaser Fund IV, L.P is 525 University Avenue, Suite 520, Palo Alto, CA 94301.

(4) Includes 16,044,081 shares of common stock issuable upon conversion of convertible preferred stock. Excludes 12,835,264 shares of common stock issuable upon conversion of convertible preferred stock that the holder has the right to acquire, which right cannot be exercised during the period commencing on the date that the Company submits a registration statement on Form S-1 to the SEC

and ending in the earlier of (a) the third business day following the withdrawal of such registration statement on Form S-1 in connection with any abandonment of the IPO and (b) the closing of the IPO. Abingworth Bioventures VI GP LP, a Scottish limited partnership, serves as the general partner of Abingworth Bioventures VI LP ("ABV VI"). Abingworth General Partner VI LLP, an English limited liability partnership, serves as the general partner of Abingworth Bioventures VI GP LP. ABV VI (acting by its general partner Abingworth Bioventures VI GP LP, acting by its general partner Abingworth General Partner VI LLP) has delegated to Abingworth LLP, an English limited liability partnership, all investment and dispositive power over the securities held by ABV VI. An investment committee of Abingworth LLP, comprised of Joseph Anderson, Michael F. Bigham, Stephen W. Bunting, Genghis Lloyd-Harris, and Timothy Haines, our director, approves investment and voting decisions by a majority vote, and no individual member has the sole control or voting power over the securities held by ABV VI. Each of Abingworth Bioventures VI GP LP, Abingworth General Partner VI LLP, Joseph Anderson, Michael F. Bigham, Stephen W. Bunting, Genghis Lloyd-Harris, and Timothy Haines disclaims beneficial ownership of the securities held by the ABV VI except to the extent of their proportionate pecuniary interest therein. The address of the principal place of business of each of the entities and individuals listed above is c/o Abingworth LLP, Princes House, 38 Jermyn Street, London, England SW1Y 6DN.

(5) Includes 12,621,134 shares of common stock issuable upon conversion of convertible preferred stock and warrants to purchase 1,371,690 shares of common stock. Excludes 608,529 shares of common stock issuable upon conversion of convertible preferred stock that the holder has the right to acquire, which right cannot be exercised during the period commencing on the date that the Company submits a registration statement on Form S-1 to the SEC and ending in the earlier of (a) the third business day following the withdrawal of such registration statement on Form S-1 in connection with any abandonment of the IPO and (b) the closing of the IPO. Dennis J. Dougherty and Mitchell Mumma are the managing partners of Intersouth Associates VI, LLC, the general partner of Intersouth Partners VI, L.P. Each of the managing partners disclaims beneficial ownership of any such shares except to the extent of his proportionate pecuniary interest therein. The address for Intersouth Partners VI, L.P. is 102 City Hall Plaza, Suite 200, Durham, NC 27701.

(6) Includes 11,821,710 shares of common stock issuable upon conversion of convertible preferred stock and warrants to purchase 1,304,713 shares of common stock. Excludes 1,412,109 shares of common stock issuable upon conversion of convertible preferred stock that the holder has the right to acquire, which right cannot be exercised during the period commencing on the date that the Company submits a registration statement on Form S-1 to the SEC and ending in the earlier of (a) the third business day following the withdrawal of such registration statement on Form S-1 in connection with any abandonment of the IPO and (b) the closing of the IPO. Todd Foley, our director, is a Member of MPM BioVentures IV LLC, which is the General Partner of MPM BioVentures IV GP LLC, which is the General Partner of MPM Bio IV NVS Strategic Fund, L.P. Mr. Foley shares the power to vote, hold and dispose of the shares held by MPM Bio IV NVS Strategic Fund, L.P. Mr. Foley disclaims beneficial ownership of any such shares except to the extent of his proportionate pecuniary interest therein. The address for Mr. Foley and MPM Bio IV NVS Strategic Fund, L.P. is 200 Clarendon Street, 54th Floor, Boston, MA 02116.

(7) Includes (a) 6,134,501 shares of common stock issuable upon conversion of convertible preferred stock held by Deerfield Private Design Fund III, L.P., (b) 1,311,840 shares of common stock issuable upon conversion of convertible preferred stock held by Deerfield Special Situations Fund, L.P., and (c) 1,047,584 shares of common stock issuable upon conversion of convertible preferred stock held by Deerfield Special Situations International Master Fund, L.P. Excludes 4,907,601 shares of common stock issuable upon conversion of convertible preferred stock, 1,049,472 shares of common stock issuable upon conversion of convertible preferred stock and 838,067 shares of common stock issuable upon conversion of convertible preferred stock that Deerfield Private Design Fund III, L.P., Deerfield Special Situations Fund, L.P. and Deerfield Special Situations International Master Fund, L.P., respectively, have the right to acquire, which right cannot be exercised during the period commencing on the date that the Company submits a registration statement on Form S-1 to the SEC and ending in the earlier of (x) the third business day following the withdrawal of such registration statement on Form S-1 in connection with any abandonment of the IPO and (y) the closing of the IPO. Deerfield

Mgmt, L.P. is the general partner of each of Deerfield Special Situations Fund, L.P. and Deerfield Special Situations International Master Fund, L.P. Deerfield Mgmt III, L.P. is the general partner of Deerfield Private Design Fund III, L.P. (together with Deerfield Special Situations Fund, L.P. and Deerfield Special Situations International Master Fund, L.P., the "Deerfield Funds"). Deerfield Management Company, L.P. is the investment manager of each of the Deerfield Funds. Mr. James E. Flynn is the sole member of the general partner of each of Deerfield Mgmt, L.P., Deerfield Mgmt III, L.P. and Deerfield Management Company, L.P. Deerfield Mgmt. L.P. may be deemed to beneficially own the shares held by Deerfield Special Situations Fund, L.P. and Deerfield Special Situations International Master Fund, L.P., Deerfield Mgmt III, L.P. may be deemed to beneficially own the shares held by Deerfield Private Design Fund III, L.P. Each of Deerfield Management Company, L.P. and Mr. Flynn may be deemed to beneficially own the shares held by the Deerfield Funds. The address of Deerfield Funds is 780 Third Avenue, 37th Floor, New York, NY 10017.

(8) Includes 8,493,925 shares of common stock issuable upon conversion of convertible preferred stock. Excludes 6,795,140 shares of common stock issuable upon conversion of convertible preferred stock that the holder has the right to acquire, which right cannot be exercised during the period commencing on the date that the Company submits a registration statement on Form S-1 to the SEC and ending in the earlier of (a) the third business day following the withdrawal of such registration statement on Form S-1 in connection with any abandonment of the IPO and (b) the closing of the IPO. Pharmstandard International S.A. is a wholly owned subsidiary of public joint stock company "Pharmstandard." As the parent entity Pharmstandard has voting and investment control over the shares of the Company held by Pharmstandard International S.A. Dmitry Kobyzev, our director, is the representative of Pharmstandard International S.A. Dr. Kobyzev disclaims beneficial ownership of any such shares except to the extent of his proportionate pecuniary interest therein. The address for Dr. Kobyzev and Pharmstandard International S.A. is 65, Boulevard Grande Duchesse Charlotte, L-1331 Luxembourg, Grand-Duchy of Luxembourg.

(9) Includes 6,125,355 shares of common stock which Mr. Noyes has the right to acquire upon the exercise of stock options that were exercisable as of July 31, 2014, or that will become exercisable within 60 days after that date.

(10) Includes 502,635 shares of common stock which Mr. Phelps has the right to acquire upon the exercise of stock options that were exercisable as of July 31, 2014, or that will become exercisable within 60 days after that date.

(11) Includes (a) 3,457,453 shares of common stock and 88,666 shares of common stock issuable upon conversion of convertible preferred stock held directly by Dr. Franano, (b) 6,567 shares of common stock issuable upon conversion of convertible preferred stock held by Mr. Franano and Lorie Beth Whitaker, and (c) 1,352,757 shares of common stock which Dr. Franano has the right to acquire upon the exercise of stock options that were exercisable as of July 31, 2014, or that will become exercisable within 60 days after that date.

(12) Includes 3,133,491 shares of common stock which Dr. Burke has the right to acquire upon the exercise of stock options that were exercisable as of July 31, 2014, or that will become exercisable within 60 days after that date.

(13) Includes 983,816 shares of common stock which Mr. Gottlieb has the right to acquire upon the exercise of stock options that were exercisable as of July 31, 2014, or that will become exercisable within 60 days after that date.

(14) Includes 14,098,054 shares of common stock which the directors and executive officers have the right to acquire upon the exercise of stock options that were exercisable as of July 31, 2014, or that will become exercisable within 60 days after that date.

DESCRIPTION OF CAPITAL STOCK

The following description of our capital stock and provisions of our amended and restated certificate of incorporation, amended and restated bylaws and investors' rights agreement are summaries and are qualified by reference to the amended and restated certificate of incorporation and amended and restated bylaws that will become effective upon the closing of this offering as well as to those provisions of the investors rights' agreement that will remain in effect following the closing. We have filed copies of these documents with the SEC as exhibits to our registration statement of which this prospectus forms a part. The description of our capital stock reflects changes to our capital structure that will occur upon the closing of this offering. Currently, there is no established public trading market for our common stock.

General

As of July 31, 2014, we had issued and outstanding:

- 3,833,606 shares of our common stock;
- 120,318,776 shares of our convertible preferred stock that will automatically convert into 134,918,694 shares of our common stock upon the closing of this offering;
- warrants to purchase a total of 10,471,282 shares of our common stock with a weighted-average exercise price of $0.29 per share that we expect to be exercised immediately prior to the closing of this offering; and
- options to purchase a total of 17,982,120 shares of our common stock with a weighted-average exercise price of $0.22 per share.

As of July 31, 2014, we had outstanding 149,223,582 shares of common stock held of record by 64 shareholders, assuming the conversion of 120,318,776 shares of preferred stock outstanding as of July 31, 2014 into shares of our common stock and assuming the exercise of warrants to purchase an aggregate of 10,471,282 shares outstanding as of July 31, 2014 into shares of our common stock.

Common Stock

Voting Rights. Each holder of our common stock is entitled to one vote for each share on all matters submitted to a vote of the stockholders, including the election of directors. Our stockholders do not have cumulative voting rights in the election of directors. Accordingly, the holders of a majority of the voting shares are able to elect all of the directors.

Dividends. Subject to preferences that may be applicable to any then outstanding preferred stock, holders of our common stock are entitled to receive dividends, if any, as may be declared from time to time by our board of directors out of legally available funds.

Liquidation. In the event of our liquidation, dissolution or winding up, holders of our common stock will be entitled to share ratably in the net assets legally available for distribution to stockholders after the payment of all of our debts and other liabilities and the satisfaction of any liquidation preference granted to the holders of any then outstanding shares of preferred stock.

Rights and Preferences. Holders of common stock have no preemptive, conversion or subscription rights and there are no redemption or sinking fund provisions applicable to the common stock. The rights, preferences and privileges of the holders of common stock are subject to, and may be adversely affected by, the rights of the holders of shares of any series of preferred stock that we may designate in the future.

Preferred Stock

Immediately prior to this offering, our certificate of incorporation provided for five series of preferred stock. As of July 31, 2014, we had outstanding an aggregate of 120,318,776 shares of preferred stock held of record by 60 stockholders.

Upon closing of this offering, all outstanding shares of preferred stock will be automatically converted into shares of our common stock. Under our amended and restated certificate of incorporation, our board of directors will have the authority, without further action by the stockholders, to issue up to shares of preferred stock in one or more series, to establish from time to time the number of shares to be included in each such series, to fix the rights, preferences and privileges of the shares of each wholly unissued series and any qualifications, limitations or restrictions thereon and to increase or decrease the number of shares of any such series, but not below the number of shares of such series then outstanding.

Our board of directors may authorize the issuance of preferred stock with voting or conversion rights that could adversely affect the voting power or other rights of the holders of the common stock. The issuance of preferred stock, while providing flexibility in connection with possible acquisitions and other corporate purposes, could, among other things, have the effect of delaying, deferring or preventing a change in our control that may otherwise benefit holders of our common stock and may adversely affect the market price of the common stock and the voting and other rights of the holders of common stock. We have no current plans to issue any shares of preferred stock.

Warrants

As of July 31, 2014, we had outstanding warrants to purchase an aggregate of 10,471,282 shares of common stock at a weighted average exercise price of $0.29, which we expect to be exercised in full immediately prior to the closing of the offering.

Registration Rights

After our initial public offering, certain holders of shares of our common stock, including those shares of our common stock that will be issued upon conversion of our preferred stock in connection with this offering, and those shares of our common stock that are issuable pursuant to our outstanding preferred stock warrants, or warrant shares, will be entitled to certain rights with respect to registration of such shares under the Securities Act. These shares are collectively referred to herein as registrable shares.

Under our Fourth Amended and Restated Investors' Rights Agreement, holders of registrable shares (other than warrant shares) can demand that we file a registration statement or request that their shares be included on a registration statement that we are otherwise filing, in either case, registering the resale of their shares of common stock. These registration rights are subject to conditions and limitations, including the right, in certain circumstances, of the underwriters of an offering to limit the number of shares included in such registration and our right, in certain circumstances, not to effect a requested registration on Form S-1 or Form S-3 within 90 days before or 180 days following our estimated date of filing of a registration statement pertaining to an underwritten public offering of securities for our account, including this offering.

These registration rights are contained in our investors' rights agreement, which is described under "Certain Relationships and Related Transactions—Investors' Rights Agreement" above and a copy of which will be filed as an exhibit to the registration statement of which this prospectus is a part.

Anti-Takeover Effects of Provisions of Delaware Law and Our Amended and Restated Certificate of Incorporation and Amended and Restated Bylaws

Our amended and restated certificate of incorporation and amended and restated bylaws will contain certain provisions that are intended to enhance the likelihood of continuity and stability in the composition of the board of directors and which may have the effect of delaying, deferring or preventing a future takeover or change in control of the company unless such takeover or change in control is approved by the board of directors. These provisions include:

Classified Board. Our amended and restated certificate of incorporation will provide that our board of directors will be divided into three classes of directors, with the classes as nearly equal in number as

possible. As a result, approximately one-third of our board of directors will be elected each year. The classification of directors will have the effect of making it more difficult for stockholders to change the composition of our board. Our amended and restated certificate of incorporation will also provide that, subject to any rights of holders of preferred stock to elect additional directors under specified circumstances, the number of directors will be fixed exclusively pursuant to a resolution adopted by our board of directors. Upon completion of this offering, we expect that our board of directors will have nine members.

Action by Written Consent; Special Meetings of Stockholders. Our certificate of incorporation will provide that stockholder action can be taken only at an annual or special meeting of stockholders and cannot be taken by written consent in lieu of a meeting. Our amended and restated certificate of incorporation and our amended and restated bylaws will also provide that, except as otherwise required by law, special meetings of the stockholders can be called only by or at the direction of the board of directors pursuant to a resolution adopted by a majority of the total number of directors. Except as described above, stockholders will not be permitted to call a special meeting or to require the board of directors to call a special meeting.

Removal of Directors. Our certificate of incorporation will provide that our directors may be removed only for cause by the affirmative vote of at least 75% of the voting power of our outstanding shares of capital stock, voting together as a single class. This requirement of a supermajority vote to remove directors could enable a minority of our stockholders to prevent a change in the composition of our board.

Advance Notice Procedures. Our amended and restated bylaws will establish an advance notice procedure for stockholder proposals to be brought before an annual meeting of our stockholders, including proposed nominations of persons for election to the board of directors. Stockholders at an annual meeting will only be able to consider proposals or nominations specified in the notice of meeting or brought before the meeting by or at the direction of the board of directors or by a stockholder who was a stockholder of record on the record date for the meeting, who is entitled to vote at the meeting and who has given our Secretary timely written notice, in proper form, of the stockholder's intention to bring that business before the meeting. Although the amended and restated bylaws will not give the board of directors the power to approve or disapprove stockholder nominations of candidates or proposals regarding other business to be conducted at a special or annual meeting, the amended and restated bylaws may have the effect of precluding the conduct of certain business at a meeting if the proper procedures are not followed or may discourage or deter a potential acquirer from conducting a solicitation of proxies to elect its own slate of directors or otherwise attempting to obtain control of the company.

Super Majority Approval Requirements. The Delaware General Corporation Law generally provides that the affirmative vote of a majority of the shares entitled to vote on any matter is required to amend a corporation's certificate of incorporation or amended and restated bylaws, unless either a corporation's certificate of incorporation or bylaws requires a greater percentage. Our amended and restated certificate of incorporation and amended and restated bylaws will provide that the affirmative vote of holders of at least 75% of the total votes eligible to be cast in the election of directors will be required to amend, alter, change or repeal the amended and restated bylaws. This requirement of a supermajority vote to approve amendments to our amended and restated bylaws could enable a minority of our stockholders to exercise veto power over any such amendments.

Authorized but Unissued Shares. Our authorized but unissued shares of common stock and preferred stock will be available for future issuance without stockholder approval. These additional shares may be utilized for a variety of corporate purposes, including future public offerings to raise additional capital, corporate acquisitions and employee benefit plans. The existence of authorized but unissued shares of common stock and preferred stock could render more difficult or discourage an attempt to obtain control of a majority of our common stock by means of a proxy contest, tender offer, merger or otherwise.

Exclusive Forum. Our amended and restated certificate of incorporation will provide that, subject to limited exceptions, the state or federal courts located in the State of Delaware will be the sole and

exclusive forum for (i) any derivative action or proceeding brought on our behalf, (ii) any action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers or other employees to us or our stockholders, (iii) any action asserting a claim against us arising pursuant to any provision of the Delaware General Corporation Law, our amended and restated certificate of incorporation or our amended and restated bylaws, or (iv) any other action asserting a claim against us that is governed by the internal affairs doctrine. Any person or entity purchasing or otherwise acquiring any interest in shares of our capital stock shall be deemed to have notice of and to have consented to the provisions of our amended and restated certificate of incorporation described above. Although we believe these provisions benefit us by providing increased consistency in the application of Delaware law for the specified types of actions and proceedings, the provisions may have the effect of discouraging lawsuits against our directors and officers. The enforceability of similar choice of forum provisions in other companies' certificates of incorporation has been challenged in legal proceedings, and it is possible that, in connection with one or more actions or proceedings described above, a court could find the choice of forum provisions contained in our certificate of incorporation to be inapplicable or unenforceable.

Section 203 of the Delaware General Corporation Law

Upon completion of this offering, we will be subject to the provisions of Section 203 of the Delaware General Corporation Law. In general, Section 203 prohibits a publicly-held Delaware corporation from engaging in a "business combination" with an "interested stockholder" for a three-year period following the time that this stockholder becomes an interested stockholder, unless the business combination is approved in a prescribed manner. A "business combination" includes, among other things, a merger, asset or stock sale or other transaction resulting in a financial benefit to the interested stockholder. An "interested stockholder" is a person who, together with affiliates and associates, owns, or did own within three years prior to the determination of interested stockholder status, 15% or more of the corporation's voting stock. Under Section 203, a business combination between a corporation and an interested stockholder is prohibited unless it satisfies one of the following conditions: before the stockholder became interested, the board of directors approved either the business combination or the transaction which resulted in the stockholder becoming an interested stockholder; upon consummation of the transaction which resulted in the stockholder becoming an interested stockholder, the interested stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction commenced, excluding for purposes of determining the voting stock outstanding, shares owned by persons who are directors and also officers, and employee stock plans, in some instances; or at or after the time the stockholder became interested, the business combination was approved by the board of directors of the corporation and authorized at an annual or special meeting of the stockholders by the affirmative vote of at least two-thirds of the outstanding voting stock which is not owned by the interested stockholder. A Delaware corporation may "opt out" of these provisions with an express provision in its original certificate of incorporation or an express provision in its certificate of incorporation or bylaws resulting from a stockholders' amendment approved by at least a majority of the outstanding voting shares. We have not opted out of these provisions. As a result, mergers or other takeover or change in control attempts of us may be discouraged or prevented.

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is .

Listing

We expect to apply for listing of our common stock on the NASDAQ Global Market under the symbol "PRTO."

SHARES ELIGIBLE FOR FUTURE SALE

Prior to this offering, there has been no public market for our common stock. Future sales of our common stock, including shares issued upon the exercise of outstanding options or warrants, in the public market after this offering, or the perception that those sales may occur, could cause the prevailing market price for our common stock to fall or impair our ability to raise equity capital in the future. As described below, only a limited number of shares of our common stock will be available for sale in the public market for a period of several months after completion of this offering due to contractual and legal restrictions on resale described below. Future sales of our common stock in the public market either before (to the extent permitted) or after restrictions lapse, or the perception that those sales may occur, could adversely affect the prevailing market price of our common stock at such time and our ability to raise equity capital at a time and price we deem appropriate.

Sale of Restricted Shares

As of July 31, 2014, based on the number of shares of our common stock then outstanding, upon the closing of this offering and assuming (1) the conversion of our outstanding preferred stock into common stock, (2) no exercise of the underwriters' option to purchase additional shares of common stock, and (3) no exercise of outstanding options or warrants, we would have had outstanding an aggregate of approximately 138,752,300 shares of common stock. Of these shares, all of the shares of common stock to be sold in this offering, and any shares sold upon exercise of the underwriters' option to purchase additional shares will be freely tradable in the public market without restriction or further registration under the Securities Act, unless the shares are held by any of our "affiliates" as such term is defined in Rule 144 of the Securities Act. All remaining shares of common stock held by existing stockholders immediately prior to the completion of this offering will be "restricted securities" as such term is defined in Rule 144. These restricted securities were issued and sold by us, or will be issued and sold by us, in private transactions and are eligible for public sale only if registered under the Securities Act or if they qualify for an exemption from registration under the Securities Act, including the exemptions provided by Rule 144 or Rule 701, which rules are summarized below.

As a result of the lock-up agreements referred to below and the provisions of Rule 144 and Rule 701 under the Securities Act, the shares of our common stock (excluding the shares sold in this offering) that will be available for sale in the public market are as follows:

Approximate Number of Shares	First Date Available for Sale into Public Market
	180 days after the date of this prospectus upon expiration of the lock up agreements referred to below, subject in some cases to applicable volume limitations under Rule 144.

Lock-up Agreements

In connection with this offering, we, our directors, our officers and stockholders beneficially owning approximately % of our shares of common stock outstanding as of June 30, 2014 (assuming conversion of all of our outstanding shares of preferred stock and warrants), have agreed with the underwriters not to dispose of or hedge any shares of our common stock or securities convertible into or exchangeable for shares of common stock during the period from the date of the lock-up agreement continuing through the date 180 days after the date of this prospectus, except with the prior written consent of and , the representatives of the underwriters. The representatives of the underwriters have advised us that they have no current intent or arrangement to release any of the shares subject to the lock-up agreements prior to the expiration of the lock-up period.

The lock-up agreements do not contain any pre-established conditions to the waiver by Stifel, Nicolaus & Company, Incorporated and JMP Securities LLC on behalf of the underwriters of any terms of the lock-up agreements. Any determination to release shares subject to the lock-up agreements would be based on a number of factors at the time of determination, including but not necessarily limited to the market price of the common stock, the liquidity of the trading market for the common stock, general market conditions, the number of shares proposed to be sold, contractual obligations to release certain shares subject to the lock-up agreements in the event any such shares are released, subject to certain specific limitations and thresholds, and the timing, purpose and terms of the proposed sale.

Following the lock-up periods set forth in the agreements described above, and assuming that the representatives of the underwriters do not release any parties from these agreements, all of the shares of our common stock that are restricted securities or are held by our affiliates as of the date of this prospectus will be eligible for sale in the public market in compliance with Rule 144 under the Securities Act.

In addition to the restrictions contained in the lock-up agreements described above, we have entered into agreements with certain of our security holders, including our amended and restated investors rights agreement and our standard forms of option agreements under our equity incentive plan, that contain market stand-off provisions imposing restrictions on the ability of such security holders to offer, sell or transfer our equity securities for a period of 180 days following the date of this prospectus.

Rule 144

In general, persons who have beneficially owned restricted shares of our common stock for at least six months, and any affiliate of the Company who owns either restricted shares of our common stock, are entitled to sell their securities without registration with the SEC under an exemption from registration provided by Rule 144 under the Securities Act.

Non-Affiliates

Any person who is not deemed to have been one of our affiliates at the time of, or at any time during the three months preceding, a sale may sell an unlimited number of restricted securities under Rule 144 if:

- the restricted securities have been held for at least six months, including the holding period of any prior owner other than one of our affiliates;
- we have been subject to the Exchange Act periodic reporting requirements for at least 90 days before the sale; and
- we are current in our Exchange Act reporting at the time of sale.

Any person who is not deemed to have been an affiliate of ours at the time of, or at any time during the three months preceding, a sale and has held the restricted securities for at least one year, including the holding period of any prior owner other than one of our affiliates, will be entitled to sell an unlimited number of restricted securities without regard to the length of time we have been subject to Exchange Act periodic reporting or whether we are current in our Exchange Act reporting.

Affiliates

Persons seeking to sell restricted securities who are our affiliates at the time of, or any time during the three months preceding, a sale would be subject to the restrictions described above. They are also subject to additional restrictions, by which such person would be required to comply with the manner of sale and notice provisions of Rule 144 and would be entitled to sell within any three-month period only that number of securities that does not exceed the greater of either of the following:

- 1% of the number of shares of our common stock then outstanding, which will equal approximately shares immediately after the completion of this offering based on the number of shares outstanding as of ; or

- the average weekly trading volume of our common stock on the NASDAQ Global Market during the four calendar weeks preceding the filing of a notice on Form 144 with respect to the sale.

Rule 701

In general, under Rule 701 a person who purchased shares of our common stock pursuant to a written compensatory plan or contract and who is not deemed to have been one of our affiliates during the immediately preceding 90 days may sell these shares in reliance upon Rule 144, but without being required to comply with the notice, manner of sale or public information requirements or volume limitation provisions of Rule 144. Rule 701 also permits affiliates to sell their Rule 701 shares under Rule 144 without complying with the holding period requirements of Rule 144. All holders of Rule 701 shares, however, are required to wait until 90 days after the date of this prospectus before selling such shares pursuant to Rule 701. Substantially all Rule 701 shares are subject to lock-up agreements as described below and in the section of this prospectus titled "Underwriting" and will become eligible for sale upon the expiration of the restrictions set forth in those agreements.

Registration Rights

Upon the completion of this offering, the holders of shares of our common stock issuable upon the conversion of our preferred stock, or their transferees, will be entitled to specified rights with respect to the registration of the offer and sale of their shares under the Securities Act. Registration of the offer and sale of these shares under the Securities Act would result in the shares becoming freely tradable without restriction under the Securities Act immediately upon the effectiveness of the registration. See the section of this prospectus titled "Description of Capital Stock—Registration Rights" for additional information.

Equity Incentive Plans

We intend to file with the SEC one or more registration statements on Form S-8 under the Securities Act covering the shares of common stock that we may issue upon exercise of outstanding options reserved for issuance under our 2006 Equity Incentive Plan and/or 2014 Equity Incentive Plan. This registration statement is expected to be filed and become effective as soon as practicable after the completion of this offering. Accordingly, shares registered under this registration statement will be available for sale in the open market following its effective date, subject to Rule 144 volume limitations and the lock-up agreements described above, if applicable.

MATERIAL UNITED STATES FEDERAL INCOME TAX CONSEQUENCES TO NON-U.S. HOLDERS OF OUR COMMON STOCK

The following is a summary of the material U.S. federal income tax consequences of the acquisition, ownership, and disposition of our common stock by a non-U.S. holder that purchases shares of our common stock for cash in this offering. For purposes of this summary, a "non-U.S. holder" means a beneficial owner of our common stock that is, for U.S. federal income tax purposes:

- an individual who is not a citizen or resident of the United States;
- a corporation (or an entity treated as a corporation for U.S. federal income tax purposes) that is created or organized under the laws of a jurisdiction other than the United States, any state thereof, or the District of Columbia;
- a foreign estate (i.e., an estate other than an estate the income of which is subject to U.S. federal income taxation regardless of its source); or
- a foreign trust (i.e., a trust other than a trust (i) with respect to which a court within the United States is able to exercise primary supervision over its administration and one or more U.S. persons (as defined in Section 386 of the Internal Revenue Code of 1986, as amended, the Code) have the authority to control all substantial decisions or (ii) that has in effect a valid election under the applicable Treasury regulations to be treated as a United States person).

In the case of a holder that is classified as a partnership for U.S. federal income tax purposes, the tax treatment of a person treated as a partner in that partnership for U.S. federal income tax purposes generally will depend upon the status of the partner and the activities of the partner and the partnership. Partnerships and other entities treated as partnerships for U.S. federal income tax purposes and persons holding our common stock through a partnership or such entity should consult with their own tax advisors.

This summary is based upon the provisions of the Code, the U.S. Treasury regulations promulgated thereunder, judicial decisions, and published rulings and administrative procedures of the Internal Revenue Service, or the IRS, all as in effect as of the date hereof. These authorities are subject to differing interpretations and to change, possibly with retroactive effect, which could result in U.S. federal income tax consequences different from those summarized below. No ruling has been or will be sought from the IRS with respect to the matters summarized below, and there can be no assurance that the IRS will not take a contrary position regarding the U.S. federal income tax consequences of the acquisition, ownership, or disposition of our common stock, or that any such contrary position would not be sustained by a court.

This summary is not a complete analysis of all of the potential U.S. federal income tax consequences relating to the acquisition, ownership, and disposition of our common stock by non-U.S. holders, nor does it address any U.S. federal estate or gift tax consequences, any tax consequences arising under any state, local, or foreign tax laws, any consequences under the unearned income Medicare contribution tax enacted by the Health Care and Education Reconciliation Act of 2010, or any consequences under other U.S. federal tax laws (including the alternative minimum tax). In addition, this discussion does not address tax consequences resulting from a non-U.S. holder's particular circumstances or to non-U.S. holders that may be subject to special tax rules, including, without limitation:

- partnerships, other pass-through entities, or beneficial owners of interests in those entities;
- foreign governments or entities they control;
- "controlled foreign corporations" and their shareholders;
- "passive foreign investment companies" and their shareholders;
- corporations that accumulate earnings to avoid U.S. federal income tax;
- U.S. expatriates or former long-term residents of the United States;
- banks, insurance companies or other financial institutions;
- persons subject to the alternative minimum tax;
- tax-exempt pension funds or other tax-exempt organizations;
- tax-qualified retirement plans;

- traders, brokers, or dealers in securities, commodities, or currencies;
- persons that own or have owned, or are deemed to own or have owned, more than 5% of our common stock (except to the extent specifically set forth below);
- persons who hold our common stock as a position in a hedging transaction, "straddle," "conversion transaction" or other risk reduction transaction;
- persons who do not hold our common stock as a capital asset within the meaning of Section 1221 of the Code (generally, for investment purposes);
- persons deemed to sell our common stock under the constructive sale provisions of the Code; or
- persons who hold or receive our common stock pursuant to the exercise of any employee stock option or otherwise as compensation.

Prospective investors should consult their tax advisors regarding the particular U.S. federal income tax consequences to them of acquiring, owning, and disposing of our common stock, as well as any tax consequences arising under any state, local, or foreign tax laws and any other U.S. federal tax laws.

Distributions on Common Stock

As described in the section entitled "Dividend Policy," we have never paid any dividends on our common stock and do not anticipate doing so in the foreseeable future. The disclosure in this section addresses the consequences should our board of directors, in the future, determine to make a distribution of cash or property with respect to our common stock (other than certain distributions of stock which may be made free of tax), or to effect a redemption that is treated for tax purposes as a distribution. Any such distribution will constitute a dividend for U.S. federal tax purposes to the extent paid from our current or accumulated earnings and profits, as determined under U.S. federal income tax principles. To the extent such a distribution exceeds both our current and our accumulated earnings and profits, such excess will be allocated ratably among the shares of common stock with respect to which the distribution is made, will constitute a return of capital, and will first be applied against and reduce the non-U.S. holder's adjusted tax basis in those shares of common stock, but not below zero. Distributions in excess of our current and accumulated earnings and profits and in excess of a non-U.S. holder's tax basis in that non-U.S. holder's shares of common stock then will be treated as gain from the sale of that common stock, subject to the tax treatment described below under "Gain on Disposition of Common Stock." A non-U.S. holder's adjusted tax basis in a share of common stock is generally the purchase price of the share, reduced by the amount of any distributions constituting a return of capital with respect to that share.

Any dividend paid to a non-U.S. holder of our common stock generally will be subject to U.S. federal withholding tax at a rate of 30% of the gross amount of the dividend, or such lower rate as may be specified by an applicable income tax treaty. If a non-U.S. holder is eligible for benefits under an income tax treaty and wishes to claim a reduced rate of withholding, the non-U.S. holder generally will be required to provide us or our paying agent with a properly completed IRS Form W-8BEN, Form W-8BEN-E, or other applicable form, certifying under penalties of perjury the non-U.S. holder's qualification for the reduced rate. This certification must be provided to us or our paying agent prior to the payment of the dividend and may be required to be updated periodically. Special certification requirements apply to non-U.S. holders that hold common stock through certain foreign intermediaries. Non-U.S. holders that do not timely provide the required certifications, but that qualify for a reduced treaty rate, may obtain a refund of any excess amounts withheld by timely filing an appropriate claim for refund with the IRS. If we are not able to determine whether or not a distribution will exceed current and accumulated earnings and profits at the time the distribution is made, we may withhold tax on the entire amount of any distribution at the same rate as we would withhold on a dividend. However, a non-U.S. holder may obtain a refund of amounts that we withhold to the extent attributable to the portion of the distribution in excess of our current and accumulated earnings and profits.

If a non-U.S. holder holds our common stock in connection with the conduct of a trade or business in the United States, and dividends paid on the common stock are effectively connected with the non-U.S.

holder's U.S. trade or business (and, if required by an applicable income tax treaty, are attributable to a permanent establishment or fixed base maintained by the non-U.S. holder in the United States, as defined under the applicable treaty), the non-U.S. holder will be exempt from U.S. federal withholding tax on the dividends. To claim the exemption, the non-U.S. holder must furnish a properly executed IRS Form W-8ECI (or other applicable form) prior to the payment of the dividends. Any dividends paid on our common stock that are effectively connected with a non-U.S. holder's U.S. trade or business (and satisfy any other applicable treaty requirements) generally will be subject to U.S. federal income tax on a net income basis at the regular graduated U.S. federal income tax rates generally applicable to U.S. persons or at such lower rate as may be specified by an applicable income tax treaty. A non-U.S. holder that is treated as a corporation for U.S. federal income tax purposes also may be subject to an additional branch profits tax equal to 30% (or such lower rate as is specified by an applicable income tax treaty) of a portion of its earnings and profits for the taxable year that are effectively connected with a U.S. trade or business, as adjusted for certain items.

Gain on Disposition of Common Stock

Subject to the discussions under "—Information Reporting and Backup Withholding" and "Foreign Account Tax Compliance Act," a non-U.S. holder generally will not be subject to U.S. federal income tax on any gain realized upon the sale, exchange, or other taxable disposition of our common stock unless:

- the gain is effectively connected with the non-U.S. holder's conduct of a U.S. trade or business (and, if required by an applicable income tax treaty, the gain is attributable to a permanent establishment or fixed base maintained by the non-U.S. holder in the United States), in which case the non-U.S. holder will be required to pay tax on the net gain derived from the sale, exchange, or other taxable disposition (net of certain deductions or credits) under regular graduated U.S. federal income tax rates generally applicable to U.S. persons or at such lower rate as may be specified by an applicable income tax treaty, and in the case of a non-U.S. holder that is treated as a corporation for U.S. federal income tax purposes, such non-U.S. holder may be subject to a branch profits tax at a 30% rate or such lower rate as may be specified by an applicable income tax treaty;
- the non-U.S. holder is an individual who is present in the United States for a period or periods aggregating 183 days or more during the taxable year in which the sale, exchange, or other taxable disposition occurs and certain other conditions are met, in which case the non-U.S. holder will be subject to U.S. federal income tax at a flat 30% rate (or such lower rate as is specified by an applicable income tax treaty) on the gain derived from the sale, exchange, or other taxable disposition, which gain may be offset by U.S. source capital losses (even though the non-U.S. holder is not considered a resident of the United States) provided that the non-U.S. holder has timely filed U.S. federal income tax returns reporting those losses; or
- our common stock is a U.S. real property interest by reason of our status as a U.S. real property holding corporation, or a USRPHC, for U.S. federal income tax purposes.

We believe we are not now and we do not anticipate becoming a USRPHC. However, because the determination of whether we are a USRPHC at any time depends on the proportion of our assets, by fair market value, that consists of U.S. real property interests, there can be no assurance are not now a USRPHC or we will not become one in the future. Even if we are or become a USRPHC, for so long as our common stock is "regularly traded," as defined by applicable Treasury Regulations, on an established securities market, sales of our common stock generally will not be subject to tax for non-U.S. holders that have held less than 5% of our common stock, actually or constructively, during the applicable statutory period.

Information Reporting and Backup Withholding

Generally, we must report annually to the IRS and to each non-U.S. holder the amount of dividends and other distributions paid to the non-U.S. holder and the amount of tax, if any withheld with respect to

those distributions. Pursuant to applicable income tax treaties or other agreements, the IRS may make these reports available to tax authorities in the non-U.S. holder's country of residence.

In addition, a non-U.S. holder may be subject to information reporting requirements and backup withholding with respect to dividends paid on, and the proceeds of disposition of, shares of our common stock, unless, generally, the non-U.S. holder certifies under penalties of perjury (usually on IRS Form W-8BEN or W-8BEN-E) that the non-U.S. holder is not a U.S. person or otherwise establishes an exemption. The current backup withholding rate is 28%. Additional rules relating to information reporting requirements and backup withholding with respect to payments of the proceeds from the disposition of shares of our common stock are as follows:

- If the proceeds are paid to or through the United States office of a broker, the proceeds generally will be subject to backup withholding and information reporting, unless the non-U.S. holder certifies under penalties of perjury (usually on IRS Form W-8BEN or W-8BEN-E) that the non-U.S. holder is not a U.S. person or otherwise establishes an exemption.
- If the proceeds are paid to or through a non-U.S. office of a broker that is not a U.S. person and is not a foreign person with certain specified U.S. connections, which we refer to below as a "U.S.-related person," information reporting and backup withholding generally will not apply.
- If the proceeds are paid to or through a non-U.S. office of a broker that is a U.S. person or a U.S.-related person, the proceeds generally will be subject to information reporting (but not to backup withholding), unless the non-U.S. holder certifies under penalties of perjury (usually on IRS Form W-8BEN or W-8BEN-E) that the non-U.S. holder is not a U.S. person.

Backup withholding is not a tax. Any amounts withheld from a non-U.S. holder under the backup withholding rules may be allowed as a refund or a credit against the non-U.S. holder's U.S. federal income tax liability, provided that the non-U.S. holder timely furnishes the required information to the IRS.

Foreign Account Tax Compliance Act

Legislation enacted in 2010 and related guidance, commonly referred to as "FATCA," will impose withholding taxes on certain types of payments made to "foreign financial institutions" and other non-U.S. entities after June 30, 2014 (or, as discussed below, after later dates) unless those institutions and entities meet additional certification, information reporting and other requirements. The legislation will generally impose a 30% withholding tax on dividends on, or gross proceeds from the sale or other disposition of, our common stock paid to a foreign financial institution unless the foreign financial institution enters into an agreement with the U.S. Treasury to, among other things, (i) undertake to identify accounts held by certain U.S. persons (including certain equity and debt holders of such institution) or by U.S.-owned foreign entities, (ii) annually report certain information about such accounts, and (iii) withhold 30% on payments to account holders whose actions prevent it from complying with these reporting and other requirements. In addition, subject to certain exceptions, the legislation will impose a 30% withholding tax on the same types of payments to a foreign entity that is not a foreign financial institution unless the entity certifies that it does not have any substantial U.S. owners (which generally include any U.S. persons who directly or indirectly own more than 10% of the entity) or furnishes identifying information regarding each such substantial U.S. owner. These withholding taxes will be imposed on dividends paid on our common stock after June 30, 2014 (or, in certain cases, after later dates), and on gross proceeds from sales or other dispositions of our common stock after December 31, 2016. Withholding under FATCA generally will not be reduced or limited by bilateral income tax treaties. However, a non-U.S. holder may be exempt from FATCA withholding under an applicable intergovernmental agreement between the United States and a foreign government relating to the implementation of FATCA, provided that the non-U.S. holder and the foreign government comply with the terms of the agreement.

UNDERWRITING

Subject to the terms and conditions set forth in an underwriting agreement, each of the underwriters named below has severally agreed to purchase from us the aggregate number of shares of common stock set forth opposite their respective names below:

Underwriters	Number of Shares
Stifel, Nicolaus & Company, Incorporated	
JMP Securities LLC	
Robert W. Baird & Co. Incorporated	
Oppenheimer & Co. Inc.	
Total	

The underwriting agreement provides that the obligations of the several underwriters are subject to various conditions, including approval of legal matters by counsel. The nature of the underwriters' obligations commits them to purchase and pay for all of the shares of common stock listed above if any are purchased. The underwriters reserve the right to withdraw, cancel or modify offers to the public and to reject orders in whole or in part.

Option to Purchase Additional Shares

We have granted the underwriters an option, exercisable for 30 days from the date of this prospectus, to purchase up to a total of additional shares of our common stock from us, at the initial public offering price, less the underwriting discounts and commissions payable by us, as set forth on the cover page of this prospectus. If the underwriters exercise this option in whole or in part, then each of the underwriters will be separately committed, subject to the conditions described in the underwriting agreement, to purchase the additional shares of our common stock in proportion to their respective commitments set forth in the table above. We will pay the expenses associated with the exercise of the option to purchase additional shares.

Determination of Offering Price

Prior to this offering, there has been no public market for our common stock. The initial public offering price will be determined through negotiations between us and Stifel, Nicolaus & Company, Incorporated and JMP Securities LLC, as the representatives of the several underwriters. In addition to prevailing market conditions, the factors to be considered in determining the initial public offering price will include:

- the information set forth in this prospectus and otherwise available to the representatives;
- our history and prospects, including our past and present financial performance and our prospects for future earnings;
- the history and prospects of companies in our industry;
- prior offerings of those companies;
- our capital structure;
- an assessment of our management and their experience;
- general conditions of the securities markets at the time of the offering; and
- other factors as we deem relevant.

We cannot assure you that an active or orderly trading market will develop for our common stock or that our common stock will trade in the public markets subsequent to this offering at or above the initial public offering price.

Commissions and Discounts

The underwriters propose to offer the shares of common stock directly to the public at the initial public offering price set forth on the cover page of this prospectus, and at this price less a concession not in excess of $ per share of common stock to other securities dealers. After this offering, the offering price, concessions, and other selling terms may be changed by the underwriters. Our common stock is offered subject to receipt and acceptance by the underwriters and to certain other conditions, including the right to reject orders in whole or in part.

The following table summarizes the compensation to be paid to the underwriters by us and the proceeds, before expenses, payable to us. Such amounts are shown assuming both no exercise and full exercise of the underwriters' option to purchase additional shares.

		Total	
	Per Share	No Exercise	Full Exercise
Public offering price	$	$	$
Underwriting discounts and commissions	$	$	$
Proceeds, before expenses, to us	$	$	$

Pursuant to the terms of the underwriting agreement, we have also agreed to reimburse the underwriters for certain expenses, including reasonable fees and expenses of counsel, relating to certain aspects of this offering that will not exceed $.

We estimate that the total expenses of the offering payable by us, including registration, filing and listing fees, printing fees and legal and accounting expenses, but excluding underwriting discounts and commissions, will be approximately $.

Indemnification of Underwriters

We will indemnify the underwriters against some civil liabilities, including liabilities under the Securities Act. If we are unable to provide this indemnification, we will contribute to payments the underwriters may be required to make in respect of those liabilities.

No Sale of Similar Securities

We and each of our directors and executive officers and holders of substantially all of our outstanding capital stock, options and warrants prior to this offering have agreed, subject to specified exceptions, that we and they will not, for a period of 180 days after the date of this prospectus, without the prior written consent of each of Stifel, Nicolaus & Company, Incorporated and JMP Securities LLC, directly or indirectly:

- offer, sell, contract to sell (including any short sale), pledge, hypothecate transfer, establish an open "put equivalent position" within the meaning of Rule 16a-1(h) under the Exchange Act, grant any option, right or warrant for the sale of, purchase any option or contract to sell, sell any option or contract to purchase;
- otherwise encumber, dispose of or transfer, or grant any rights with respect to, directly or indirectly, any shares of our common stock or securities convertible into or exchangeable or exercisable for any shares of our common stock, enter into a transaction which would have the same effect, or enter into any swap, hedge or other arrangement that transfers, in whole or in part, any of the economic consequences of ownership of our common stock, whether any such aforementioned transaction is to be settled by delivery of our common stock or such other securities, in cash or otherwise; or
- publicly disclose the intention to do any of the foregoing.

Stifel, Nicolaus & Company, Incorporated and JMP Securities LLC may, in their sole discretion and at any time or from time to time before the termination of the 180-day period, release all or any portion of

the securities subject to lock-up agreements. There are no existing agreements between the underwriters and any of our stockholders who will execute a lock-up agreement providing consent to the sale of shares prior to the expiration of the restricted period.

NASDAQ Market Listing

We have applied to list our common stock on the NASDAQ Global Market under the symbol "PRTO."

Short Sales, Stabilizing Transactions, and Penalty Bids

In order to facilitate this offering, persons participating in this offering may engage in transactions that stabilize, maintain, or otherwise affect the price of our common stock during and after this offering. Specifically, the underwriters may engage in the following activities in accordance with the rules of the SEC.

Short sales. Short sales involve the sales by the underwriters of a greater number of shares than they are required to purchase in the offering. Covered short sales are short sales made in an amount not greater than the underwriters' over-allotment option to purchase additional shares from us in this offering. The underwriters may close out any covered short position by either exercising their over-allotment option to purchase shares or purchasing shares in the open market. In determining the source of shares to close out the covered short position, the underwriters will consider, among other things, the price of shares available for purchase in the open market as compared to the price at which they may purchase shares through the over-allotment option. Naked short sales are any short sales in excess of such over-allotment option. The underwriters must close out any naked short position by purchasing shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of the common stock in the open market after pricing that could adversely affect investors who purchase in this offering.

Stabilizing transactions. The underwriters may make bids for or purchases of the shares for the purpose of pegging, fixing, or maintaining the price of the shares, so long as stabilizing bids do not exceed a specified maximum.

Penalty bids. If the underwriters purchase shares in the open market in a stabilizing transaction or syndicate covering transaction, they may reclaim a selling concession from the underwriters and selling group members who sold those shares as part of this offering. Stabilization and syndicate covering transactions may cause the price of the shares to be higher than it would be in the absence of these transactions. The imposition of a penalty bid might also have an effect on the price of the shares if it discourages resales of the shares.

The transactions above may occur on the NASDAQ Global Market or otherwise. Neither we nor the underwriters make any representation or prediction as to the effect that the transactions described above may have on the price of the shares. If these transactions are commenced, they may be discontinued without notice at any time.

Discretionary Sales

The underwriters have informed us that they do not expect to confirm sales of common stock offered by this prospectus to accounts over which they exercise discretionary authority without obtaining the specific approval of the account holder.

Electronic Distribution

A prospectus in electronic format may be made available on the internet sites or through other online services maintained by one or more of the underwriters participating in this offering, or by their affiliates. Other than the prospectus in electronic format, the information on any underwriter's web site and any information contained in any other web site maintained by an underwriter is not part of the prospectus or the registration statement of which this prospectus forms a part, has not been approved and/or endorsed by us or any underwriter in its capacity as underwriter and should not be relied upon by investors.

Relationships

The underwriters and their respective affiliates are full service financial institutions engaged in various activities, which may include securities trading, commercial and investment banking, financial advisory, investment management, principal investment, hedging, financing and brokerage activities. Certain of the underwriters and their affiliates may in the future from time to time provide, investment banking and other financing and banking services to us, for which they may receive, customary fees and reimbursement for their expenses. In the ordinary course of their various business activities, the underwriters and their respective affiliates may make or hold a broad array of investments and actively trade debt and equity securities (or related derivative securities) and financial instruments (including bank loans) for their own account and for the accounts of their customers and may at any time hold long and short positions in such securities and instruments. Such investment and securities activities may involve our securities and instruments.

Notice to Prospective Investors in the European Economic Area

In relation to each member state of the European Economic Area that has implemented the Prospectus Directive (each, a relevant member state), with effect from and including the date on which the Prospectus Directive is implemented in that relevant member state (the relevant implementation date), an offer of securities described in this prospectus may not be made to the public in that relevant member state other than:

- to any legal entity that is authorized or regulated to operate in the financial markets or, if not so authorized or regulated, whose corporate purpose is solely to invest in securities;
- to any legal entity that has two or more of (1) an average of at least 250 employees during the last financial year; (2) a total balance sheet of more than €43,000,000 and (3) an annual net turnover of more than €50,000,000, as shown in its last annual or consolidated accounts;
- to fewer than 100 natural or legal persons (other than qualified investors as defined in the Prospectus Directive) subject to obtaining the prior consent of the representatives; or
- in any other circumstances that do not require the publication of a prospectus pursuant to Article 3 of the Prospectus Directive,

provided that no such offer of securities shall require us or any underwriter to publish a prospectus pursuant to Article 3 of the Prospectus Directive. For purposes of this provision, the expression an "offer of securities to the public" in any relevant member state means the communication in any form and by any means of sufficient information on the terms of the offer and the securities to be offered so as to enable an investor to decide to purchase or subscribe the securities, as the expression may be varied in that member state by any measure implementing the Prospectus Directive in that member state, and the expression "Prospectus Directive" means Directive 2003/71/EC and includes any relevant implementing measure in each relevant member state.

We have not authorized and do not authorize the making of any offer of securities through any financial intermediary on their behalf, other than offers made by the underwriters with a view to the final placement of the securities as contemplated in this prospectus. Accordingly, no purchaser of the securities,

other than the underwriters, is authorized to make any further offer of the securities on behalf of us or the underwriters.

Notice to Prospective Investors in the United Kingdom

This prospectus is only being distributed to, and is only directed at, persons in the United Kingdom that are qualified investors within the meaning of Article 2(1)(e) of the Prospectus Directive (Qualified Investors) that are also (1) investment professionals falling within Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005 (the Order) or (2) high net worth entities, and other persons to whom it may lawfully be communicated, falling within Article 49(2)(a) to (d) of the Order (all such persons together being referred to as relevant persons). This prospectus and its contents are confidential and should not be distributed, published or reproduced (in whole or in part) or disclosed by recipients to any other persons in the United Kingdom. Any person in the United Kingdom that is not a relevant person should not act or rely on this document or any of its contents.

Notice to Prospective Investors in France

This prospectus has not been prepared in the context of a public offering of financial securities in France within the meaning of Article L.411-1 of the French Code Monétaire et Financier and Title I of Book II of the Reglement Général of the Autorité des marchés financiers, or the AMF, and therefore has not been and will not be filed with the AMF for prior approval or submitted for clearance to the AMF. Consequently, the shares of our common stock may not be, directly or indirectly, offered or sold to the public in France and offers and sales of the shares of our common stock may only be made in France to qualified investors (investisseurs qualifiés) acting for their own, as defined in and in accordance with Articles L.411-2 and D.411-1 to D.411-4, D.734-1, D.744-1, D.754-1 and D.764-1 of the French Code Monétaire et Financier. Neither this prospectus nor any other offering material may be released, issued or distributed to the public in France or used in connection with any offer for subscription on sale of the shares of our common stock to the public in France. The subsequent direct or indirect retransfer of the shares of our common stock to the public in France may only be made in compliance with Articles L.411-1, L.411-2, L.412-1 and L.621-8 through L.621-8-3 of the French Code Monétaire et Financier.

Notice to Prospective Investors in Germany

Each person who is in possession of this prospectus is aware of the fact that no German securities prospectus (wertpapierprospekt) within the meaning of the securities prospectus act (wertpapier-prospektgesetz, the "act") of the federal republic of Germany has been or will be published with respect to the shares of our common stock. In particular, each underwriter has represented that it has not engaged and has agreed that it will not engage in a public offering in the federal republic of Germany (ôffertliches angebot) within the meaning of the act with respect to any of the shares of our common stock otherwise than in accordance with the act and all other applicable legal and regulatory requirements.

Notice to Prospective Investors in Switzerland

The securities which are the subject of the offering contemplated by this prospectus may not be publicly offered in Switzerland and will not be listed on the SIX Swiss Exchange, or SIX, or on any other stock exchange or regulated trading facility in Switzerland. This prospectus has been prepared without regard to the disclosure standards for issuance prospectuses under art. 652a or art. 1156 of the Swiss Code of Obligations or the disclosure standards for listing prospectuses under art. 27 ff. of the SIX Listing Rules or the listing rules of any other stock exchange or regulated trading facility in Switzerland. None of this prospectus or any other offering or marketing material relating to the securities or the offering may be publicly distributed or otherwise made publicly available in Switzerland.

None of this prospectus or any other offering or marketing material relating to the offering, us or the securities have been or will be filed with or approved by any Swiss regulatory authority. In particular, this prospectus will not be filed with, and the offer of securities will not be supervised by, the Swiss Financial Market Supervisory Authority FINMA and the offer of securities has not been and will not be authorized under the Swiss Federal Act on Collective Investment Schemes, or CISA. The investor protection afforded to acquirers of interests in collective investment schemes under the CISA does not extend to acquirers of the securities.

Notice to Prospective Investors in the Netherlands

The offering of the shares of our common stock is not a public offering in The Netherlands. The shares of our common stock may not be offered or sold to individuals or legal entities in The Netherlands unless (1) a prospectus relating to the offer is available to the public, which has been approved by the Dutch Authority for the Financial Markets (Autoriteit Financiële Markten) or by the competent supervisory authority of another state that is a member of the European Union or party to the Agreement on the European Economic Area, as amended or (2) an exception or exemption applies to the offer pursuant to Article 5:3 of The Netherlands Financial Supervision Act (Wet op het financieel toezicht) or Article 53 paragraph 2 or 3 of the Exemption Regulation of the Financial Supervision Act, for instance due to the offer targeting exclusively "qualified investors" (gekwalificeerde beleggers) within the meaning of Article 1:1 of The Netherlands Financial Supervision Act.

Notice to Prospective Investors in Japan

The underwriters will not offer or sell any of the shares of our common stock directly or indirectly in Japan or to, or for the benefit of, any Japanese person or to others, for re-offering or re-sale directly or indirectly in Japan or to any Japanese person, except in each case pursuant to an exemption from the registration requirements of, and otherwise in compliance with, the Financial Instruments and Exchange Law of Japan and any other applicable laws and regulations of Japan. For purposes of this paragraph, "Japanese person" means any person resident in Japan, including any corporation or other entity organized under the laws of Japan.

Notice to Prospective Investors in Hong Kong

The underwriters and each of their affiliates have not (1) offered or sold, and will not offer or sell, in Hong Kong, by means of any document, any shares of our common stock other than (a) to "professional investors" within the meaning of the Securities and Futures Ordinance (Cap. 571) of Hong Kong and any rules made under that Ordinance or (b) in other circumstances which do not result in the document being a "prospectus" as defined in the Companies Ordinance (Cap. 32) of Hong Kong or which do not constitute an offer to the public within the meaning of that Ordinance; and (2) issued or had in its possession for the purposes of issue, and will not issue or have in its possession for the purposes of issue, whether in Hong Kong or elsewhere any advertisement, invitation or document relating to the shares of our common stock which is directed at, or the contents of which are likely to be accessed or read by, the public in Hong Kong (except if permitted to do so under the securities laws of Hong Kong) other than with respect to the shares of our common stock which are or are intended to be disposed of only to persons outside Hong Kong or only to "professional investors" within the meaning of the Securities and Futures Ordinance and any rules made under that Ordinance. The contents of this document have not been reviewed by any regulatory authority in Hong Kong. You are advised to exercise caution in relation to the offer. If you are in any doubt about any of the contents of this document, you should obtain independent professional advice.

Notice to Prospective Investors in Singapore

This document has not been registered as a prospectus with the Monetary Authority of Singapore. Accordingly, this document and any other document or material in connection with the offer or sale, or

invitation for subscription or purchase, of shares of our common stock may not be circulated or distributed, nor may shares of our common stock be offered or sold, or be made the subject of an invitation for subscription or purchase, whether directly or indirectly, to persons in Singapore other than (1) to an institutional investor under Section 274 of the Securities and Futures Act, Chapter 289 of Singapore, or the Securities and Futures Act, (2) to a relevant person, or any person pursuant to Section 275(1A), and in accordance with the conditions, specified in Section 275 of the Securities and Futures Act or (3) otherwise pursuant to, and in accordance with the conditions of, any other applicable provision of the Securities and Futures Act.

Where shares of our common stock are subscribed or purchased under Section 275 by a relevant person which is:

a) a corporation (which is not an accredited investor) the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor; or

b) a trust (where the trustee is not an accredited investor) whose sole purpose is to hold investments and each beneficiary is an accredited investor, shares, debentures and units of shares and debentures of that corporation or the beneficiaries' rights and interest in that trust shall not be transferable for six months after that corporation or that trust has acquired the shares of our common stock under Section 275 except:

1) to an institutional investor or to a relevant person, or to any person pursuant to an offer that is made on terms that such rights or interest are acquired at a consideration of not less than $200,000 (or its equivalent in a foreign currency) for each transaction, whether such amount is to be paid for in cash or by exchange of securities or other assets;

2) where no consideration is given for the transfer; or

3) by operation of law.

LEGAL MATTERS

The validity of the shares of common stock offered hereby will be passed upon for us by Bingham McCutchen LLP. Certain legal matters in connection with this offering will be passed upon for the underwriters by Ropes & Gray LLP.

EXPERTS

The financial statements of Proteon Therapeutics, Inc. at December 31, 2012 and 2013 and for the years then ended, appearing in this prospectus and registration statement, have been audited by Ernst & Young LLP, independent registered public accounting firm, as set forth in their report thereon appearing elsewhere herein, and are included in reliance upon such report given on the authority of such firm as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

We have filed with the SEC a registration statement on Form S-1 (including exhibits, schedules, and amendments) under the Securities Act with respect to the shares of common stock offered by this prospectus. This prospectus does not contain all the information set forth in the registration statement. For further information about us and the shares of common stock to be sold in this offering, you should refer to the registration statement. Statements contained in this prospectus relating to the contents of any contract, agreement or other document are not necessarily complete and are qualified in all respects by the complete text of the applicable contract, agreement or other document, a copy of which has been filed as an exhibit to the registration statement. Whenever this prospectus refers to any contract, agreement, or other document, you should refer to the exhibits that are a part of the registration statement for a copy of the contract, agreement, or document.

You may read and copy all or any portion of the registration statement or any other information we file at the SEC's public reference room at 100 F Street, N.E., Room 1580, Washington, D.C. 20549. You can request copies of these documents, upon payment of a duplicating fee, by writing to the SEC. Please call the SEC at 1-800-SEC-0330 for further information about the operation of the public reference rooms. Our SEC filings, including the registration statement, are also available to you on the SEC's Website (http://www.sec.gov).

Upon completion of this offering, we will become subject to the information and periodic reporting requirements of the Exchange Act. Under the Exchange Act, we will file annual, quarterly and current reports, as well as proxy statements and other information with the SEC. These periodic reports, proxy statements, and other information will be available for inspection and copying at the SEC's Public Reference Room and the website of the SEC referred to above.

Proteon Therapeutics, Inc.

Index to Financial Statements

Proteon Therapeutics, Inc.

Report of Independent Registered Public Accounting Firm

The Board of Directors and Shareholders of Proteon Therapeutics, Inc.

We have audited the accompanying balance sheets of Proteon Therapeutics, Inc. as of December 31, 2012 and 2013, and the related statements of operations and comprehensive loss, redeemable convertible preferred stock and stockholders' deficit, and cash flows for the years then ended. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits.

We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. We were not engaged to perform an audit of the Company's internal control over financial reporting. Our audits included consideration of internal control over financial reporting as a basis for designing audit procedures that are appropriate in the circumstances, but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion. An audit also includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements, assessing the accounting principles used and significant estimates made by management, and evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the financial statements referred to above present fairly, in all material respects, the financial position of Proteon Therapeutics, Inc. at December 31, 2012 and 2013, and the results of its operations and its cash flows for the years then ended, in conformity with U.S. generally accepted accounting principles.

/s/ Ernst & Young LLP

Boston, MA
June 25, 2014

Proteon Therapeutics, Inc.

Balance Sheets

(in thousands, except share and per share data)

	December 31,		June 30, 2014	
	2012	2013	Actual	Pro forma
			(unaudited)	
Assets				
Current assets:				
Cash and cash equivalents	$ 2,409	$ 2,793	$ 8,646	$ 8,646
Available-for-sale investments	5,062	2,359	16,770	16,770
Prepaid expenses	152	61	392	392
Other current assets	41	78	16	16
Short-term deposits	39	39	39	39
Total current assets	7,703	5,330	25,863	25,863
Property and equipment, net	79	62	85	85
Deferred tax asset		267	—	—
Other non-current assets	—	—	1,194	1,194
Total assets	$ 7,782	$ 5,659	$ 27,142	$ 27,142
Liabilities, redeemable convertible preferred stock and stockholders' equity (deficit)				
Current liabilities:				
Convertible notes, including accrued interest payable of $0 and $112 as of December 31, 2012 and 2013, $0 as of June 30, 2014, and $0 pro forma	$ —	$ 3,727	$ —	$ —
Derivative liability	—	1,443	—	—
Accounts payable	469	399	994	994
Accrued expenses	735	984	2,006	2,006
Deferred tax liability	—	267	—	—
Current portion of deferred revenue from sale of option to acquire company	—	2,948	2,948	2,948
Total current liabilities	1,204	9,768	5,948	5,948
Non-current liabilities:				
Deferred revenue from sale of option to acquire company	2,948	—	—	—
Investors' rights/obligations	—	—	6,580	—
Total liabilities	4,152	9,768	12,528	5,948
Commitments and contingencies (Note 8)	—	—	—	—
Redeemable convertible preferred stock:				
Series A redeemable convertible preferred stock, $0.001 par value, 22,638,465 shares authorized, issued, and outstanding at December 31, 2012, December 31, 2013, and June 30, 2014 (unaudited); no shares issued and outstanding pro forma (unaudited); aggregate liquidation preference of $22,638, $22,638 and $12,288 at December 31, 2012, 2013 and June 30, 2014 (unaudited) and none pro forma (unaudited)	32,633	34,230	35,015	—
Series A-1 redeemable convertible preferred stock, $0.001 par value, 10,909,091 shares authorized, issued, and outstanding at December 31, 2012, December 31, 2013 and June 30, 2014 (unaudited); and no shares issued and outstanding pro forma (unaudited); aggregate liquidation preference of $12,000, $12,000 and $6,514 at December 31, 2012, December 31, 2013, and June 30, 2014 (unaudited) and none pro forma (unaudited)	16,526	17,374	17,790	—
Series B redeemable convertible preferred stock, $0.001 par value, 20,754,461 shares authorized, issued, and outstanding at December 31, 2012, December 31, 2013, and June 30, 2014 (unaudited); no shares issued and outstanding pro forma (unaudited); aggregate liquidation preference of $23,867, $23,867 and $12,955 at December 31, 2012, December 31, 2013, and June 30, 2014 (unaudited) and none pro forma (unaudited)	24,926	27,401	28,573	—
Series C redeemable convertible preferred stock, $0.001 par value, 17,550,758 shares authorized, 13,202,932 issued, and outstanding at December 31, 2012, December 31, 2013, and June 30, 2014 (unaudited); no shares issued and outstanding pro forma (unaudited); aggregate liquidation preference of $15,183, $15,183 and $8,241 at December 31, 2012, December 31, 2013, and June 30, 2014 (unaudited) and none pro forma (unaudited)	16,201	17,400	17,982	—
Series D redeemable convertible preferred stock, $0.001 par value, 0, 0 and 86,789,527 shares authorized, 0, 0 and 52,813,827 issued, and outstanding at December 31, 2012, December 31, 2013, and June 30, 2014 (unaudited); no shares issued and outstanding pro forma (unaudited); aggregate liquidation preference of $0, $0 and $31,089 at December 31, 2012, December 31, 2013, and June 30, 2014 (unaudited) and none pro forma (unaudited)	—	—	24,544	—
Stockholders' equity (deficit):				
Common stock, $0.001 par value, 100,370,203, 100,370,203 and 205,926,290 shares authorized at December 31, 2012, December 31, 2013, June 30, 2014 (unaudited) and pro forma (unaudited); 3,659,790, 3,807,356 and 3,814,856 issued and outstanding at December 31, 2012, December 31, 2013, and June 30, 2014, respectively, and 138,733,550 shares issued and outstanding pro forma (unaudited)	4	4	4	139
Additional paid-in capital	—	—	—	123,769
Accumulated deficit	(86,661)	(100,518)	(109,271)	(102,691)
Accumulated other comprehensive income (loss)	1	—	(23)	(23)
Total stockholders' equity (deficit)	(86,656)	(100,514)	(109,290)	21,194
Total liabilities, redeemable convertible preferred stock and stockholders' equity (deficit)	$ 7,782	$ 5,659	$ 27,142	$ 27,142

See accompanying notes to financial statements.

Proteon Therapeutics, Inc.

Statements of Operations and Comprehensive Loss

(in thousands, except share and per share data)

	Year Ended December 31,		Six Months Ended June 30,	
	2012	2013	2013	2014
			(unaudited)	
Operating expenses:				
Research and development	$ 5,907	$ 3,994	$ 2,003	$ 2,785
General and administrative	2,089	3,128	1,417	1,656
Total operating expenses	7,996	7,122	3,420	4,441
Loss from operations	(7,996)	(7,122)	(3,420)	(4,441)
Other income (expense):				
Investment income	20	4	3	3
Interest expense	—	(861)	—	(857)
Other income (expense)	6	67	5	(99)
Total other income (expense)	26	(790)	8	(953)
Net loss	$ (7,970)	$ (7,912)	$ (3,412)	$ (5,394)
Unrealized gain (loss) on available-for-sale investments	(5)	(1)	—	23
Comprehensive loss	$ (7,975)	$ (7,913)	$ (3,412)	$ (5,417)
Reconciliation of net loss to net loss attributable to common stockholders:				
Net loss	$ (7,970)	$ (7,912)	$ (3,412)	$ (5,394)
Accretion of redeemable convertible preferred stock to redemption value	(6,133)	(6,119)	(3,039)	(3,409)
Net loss attributable to common stockholders	$ (14,103)	$ (14,031)	$ (6,451)	$ (8,803)
Net loss per share attributable to common stockholders—basic and diluted	$ (3.85)	$ (3.76)	$ (1.76)	$ (2.31)
Weighted-average number of common shares used in net loss per share attributable to common stockholders—basic and diluted	3,659,790	3,732,436	3,659,790	3,812,904
Pro forma net loss per share attributable to common stockholders—basic and diluted (unaudited)		$ (0.10)		$ (0.04)
Pro forma weighted-average number of common shares used in net loss per share attributable to common stockholders—basic and diluted (unaudited)		72,457,068		107,333,127

See accompanying notes to financial statements

Proteon Therapeutics, Inc.

Statements of Redeemable Convertible Preferred Stock and Stockholders' Equity (Deficit)

(in thousands, except share and per share data)

	Series A Redeemable Convertible Preferred Stock		Series A-1 Redeemable Convertible Preferred Stock		Series B Redeemable Convertible Preferred Stock		Series C Redeemable Convertible Preferred Stock		Series D Redeemable Convertible Preferred Stock		Common stock		Additional Paid-in Capital	Accumulated Deficit	Accumulated Other Comprehensive Income (Loss)	Total Stockholders' Deficit
	Shares	Amount	Shares	Amount	Shares	Amount	Shares	Amount	Shares	Amount	Shares	$0.001 Par Value				
	22,638,465	$ 31,031	10,909,091	$ 15,677	20,754,461	$ 22,446	13,202,932	$ 14,999			3,659,790	$ 4	$ —	$ (72,668)	$ 5	$ (72,6
Accretion of Series A, A-1, B and C redeemable convertible preferred stock to redemption value	—	1,602	—	849	—	2,480	—	1,202			—	—	(110)	(6,023)	—	(6,1
Stock-based compensation expense	—	—	—	—	—	—	—	—			—	—	110	—	—	1
Unrealized gain (loss) on short term investments	—	—	—	—	—	—	—	—			—	—	—	—	(4)	
Net loss	—	—	—	—	—	—	—	—			—	—	—	(7,970)	—	(7,9
Balance at December 31, 2012	22,638,465	$ 32,633	10,909,091	$ 16,526	20,754,461	$ 24,926	13,202,932	$ 16,201	—	$ —	3,659,790	$ 4	$ —	$ (86,661)	$ 1	$ (86,6
Accretion of Series A, A-1, B and C redeemable convertible preferred stock to redemption value	—	1,597	—	848	—	2,475	—	1,199			—	—	(174)	(5,945)	—	(6,1
Exercise of common stock options	—	—	—	—	—	—	—	—			147,566	—	19	—	—	
Stock-based compensation expense	—	—	—	—	—	—	—	—			—	—	155	—	—	1
Unrealized gain (loss) on short term investments	—	—	—	—	—	—	—	—			—	—	—	—	(1)	
Net loss	—	—	—	—	—	—	—	—			—	—	—	(7,912)	—	(7,9
Balance at December 31, 2013	22,638,465	$ 34,230	10,909,091	$ 17,374	20,754,461	$ 27,401	13,202,932	$ 17,400	—	$ —	3,807,356	$ 4	$ —	$ (100,518)	$ —	$ (100,5
Issuance of Series D redeemable convertible preferred stock net of $6,639 discount associated with investors rights and obligations and issuance costs of $437	—	—	—	—	—	—	—	—	52,813,827	24,090	—	—	—	—	—	
Accretion of Series A, A-1, B, C and D redeemable convertible preferred stock to redemption value	—	785	—	416	—	1,172	—	582		454	—	—	(50)	(3,359)	—	(3,4
Exercise of common stock options	—	—	—	—	—	—	—	—	—	—	7,500	0	1	—	—	
Stock-based compensation expense	—	—	—	—	—	—	—	—	—	—	—	—	49	—	—	
Unrealized gain (loss) on short term investments	—	—	—	—	—	—	—	—	—	—	—	—	—	—	(23)	(
Net loss	—	—	—	—	—	—	—	—	—	—	—	—	—	(5,394)	—	(5,3
Balance at June 30, 2014	22,638,465	$ 35,015	10,909,091	$ 17,790	20,754,461	$ 28,573	13,202,932	$ 17,982	52,813,827	$ 24,544	3,814,856	$ 4	$ —	$ 109,271	$ (23)	$ (109,2
Conversion of redeemable convertible preferred stock into common stock (unaudited)	(22,638,465)	(35,015)	(10,909,091)	(17,790)	(20,754,461)	(28,573)	(13,202,932)	(17,982)	(52,813,827)	(24,544)	134,918,694	135	123,769	—	—	123,9
Extinguishment of investors rights and obligations (unaudited)	—	—	—	—	—	—	—	—	—	—	—	—	—	6,580	—	6,5
Pro forma balance at June 30, 2014 (unaudited)	—	$ —	—	$ —	—	$ —	—	$ —	—	$ —	138,733,550	$ 139	$ 123,769	$ (102,691)	$ (23)	$ 21,1

See accompanying notes to financial statements.

Proteon Therapeutics, Inc.

Statements of Cash Flows

(in thousands)

	Year Ended December 31,		Six Months Ended June 30,	
	2012	2013	2013	2014
			(unaudited)	
Operating activities:				
Net loss	$ (7,970)	$ (7,912)	$ (3,412)	$ (5,394)
Reconciliation of net loss to net cash used in operating activities:				
Depreciation	57	27	15	13
Amortization of premium/discount on available-for-sale securities	138	30	20	6
Gain on sale of fixed assets	(5)	(65)	(4)	—
Accretion of discount & debt issuance cost of convertible notes payable	—	749	—	742
Stock-based compensation	110	155	105	49
Change in fair value of investor rights/obligations	—	—	—	18
Change in fair value of derivative liability	—	(2)	—	81
Changes in:				
Prepaid expenses and other assets	320	71	97	(1,480)
Interest receivable	28	1	8	(1)
Accounts payable and accrued expenses	(912)	177	(215)	1,617
Accrued interest payable	—	112	—	115
Net cash used in operating activities	(8,234)	(6,657)	(3,386)	(4,234)
Investing activities:				
Purchases of available-for-sale investments	(8,658)	(3,878)	(1,510)	(16,795)
Proceeds from maturities of available for sale investments	16,075	6,550	5,800	2,355
Purchase of property and equipment	(67)	(10)	—	(36)
Sale of property and equipment	33	65	4	—
Deposits	(1)	—	—	—
Net cash provided by investing activities	7,382	2,727	4,294	(14,476)
Financing activities:				
Proceeds from issuance of Series D preferred stock	—	—	—	25,000
Issuance costs for preferred stock	—	—	—	(437)
Proceeds from issuance of convertible notes payable	—	4,339	—	—
Payments for debt issuance costs	—	(46)	—	—
Exercise of stock options	—	19	—	0
Early exercise of stock options		2	—	—
Repayments of note payable	(9)	—	—	—
Net cash (used in) provided by financing activities	(9)	4,314	—	24,563
(Decrease) increase in cash and cash equivalents	(861)	384	908	5,853
Cash and cash equivalents, beginning of period	3,270	2,409	2,409	2,793
Cash and cash equivalents, end of period	$ 2,409	$ 2,793	$ 3,317	$ 8,646
Supplemental disclosure of non-cash investing and financing activities:				
Accretion of redeemable convertible preferred stock to redemption value	$ 6,133	$ 6,119	$ 1,515	$ 3,409
Fair value of embedded derivative contained within convertible notes payable	$ —	$ 1,445	$ —	$ —

See accompanying notes to financial statements.

1. Organization and operations

The Company

Proteon Therapeutics, Inc. is an early-stage biopharmaceutical company engaged in the development of elastases to treat the growing medical needs of renal and vascular disease patients.

Proteon Therapeutics, LLC (the "LLC" or the "Predecessor") was organized in June 2001. Proteon Therapeutics, Inc., a Delaware corporation ("the Company"), was incorporated on March 24, 2006. Effective March 27, 2006, the Predecessor and the Company merged, with the Company being the surviving entity. During 2013, the Company formed a wholly-owned subsidiary, organized in the United Kingdom. As of June 30, 2014 there has been no activity other than its formation. Since the inception of the Predecessor on June 1, 2001, the Company has been primarily involved in research and development activities.

The Company devotes substantially all of its efforts to product research and development, initial market development and raising capital. The Company has not generated any product revenue related to its primary business purpose to date and is subject to a number of risks similar to those of other development stage companies, including dependence on key individuals, competition from other companies, the need for development of commercially viable products and the need to obtain adequate additional financing to fund the development of its product candidates. The Company is also subject to a number of risks similar to other companies in the life sciences industry, including regulatory approval of products, uncertainty of market acceptance of products, competition from substitute products and larger companies, the need to obtain additional financing, compliance with government regulations, protection of proprietary technology, dependence on third parties, product liability and dependence on key individuals.

The Company had an accumulated deficit of $100.5 million as of December 31, 2013 and $109.3 million as of June 30, 2014 (unaudited) and will require substantial additional capital to fund its research and development and ongoing operating expenses.

Liquidity

The Company believes that its cash, cash equivalents and short-term investments of approximately $5.2 million as of December 31, 2013 and $25.4 million as of June 30, 2014 (unaudited) will be sufficient to allow the Company to fund its operations at least beyond December 31, 2014; however, the Company may be required to raise additional capital or obtain financing from other sources to fund operations in the future. As the Company continues to incur losses, a transition to profitability is dependent upon the successful development, approval and commercialization of its product candidate and the achievement of a level of revenues adequate to support the Company's cost structure. The Company may never achieve profitability, and unless and until it does, the Company will continue to need to raise additional capital or obtain financing from other sources, such as strategic partnerships or other sources. There can be no assurances, however, that additional funding will be available on terms acceptable to the Company, or at all.

2. Summary of Significant Accounting Policies

Basis of Presentation and Use of Estimates

The accompanying financial statements have been prepared in conformity with accounting principles generally accepted in the United States of America ("GAAP"). Any reference in these notes to applicable guidance is meant to refer to the authoritative United States generally accepted accounting principles as

2. Summary of Significant Accounting Policies (Continued)

found in the Accounting Standards Codification ("ASC") and Accounting Standards Update ("ASU") of the Financial Accounting Standards Board ("FASB"). The preparation of financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the amounts reported in the financial statements and accompanying notes. On an ongoing basis, the Company's management evaluates its estimates, which include, but are not limited to, estimates related to convertible notes, stock-based compensation expense, clinical trial accruals, and reported amounts of revenues and expenses during the reported period. The Company bases its estimates on historical experience and other market-specific or other relevant assumptions that it believes to be reasonable under the circumstances. Actual results may differ from those estimates or assumptions.

The Company utilizes significant estimates and assumptions in determining the fair value of its common stock ("Common Stock"). The Company utilized various valuation methodologies in accordance with the framework of the 2004 and 2013 American Institute of Certified Public Accountants Technical Practice Aids, *Valuation of Privately-Held Company Equity Securities Issued as Compensation*, to estimate the fair value of its Common Stock. Each valuation methodology includes estimates and assumptions that require the Company's judgment. These estimates and assumptions include a number of objective and subjective factors, including external market conditions affecting the biotechnology industry sector, the prices at which the Company sold shares of preferred stock, the superior rights and preferences of securities senior to the Company's Common Stock at the time and the likelihood of achieving a liquidity event, such as an initial public offering or a sale of the Company. Significant changes to the key assumptions used in the valuations could result in different fair values of Common Stock at each valuation date and materially affect the financial statements.

Recent Accounting Pronouncements

In June 2014, the FASB issued authoritative guidance regarding disclosure requirements of development stage companies in GAAP and International Financial Reporting Standards. This newly issued accounting standard removes all incremental financial reporting requirements, including inception-to-date information, for development stage entities. This guidance is effective for annual periods beginning after December 15, 2014. However, the Company early adopted this guidance effective with the publication of its 2013 financial statements.

In May 2014, the Financial Accounting Standards Board (FASB) issued a new standard on revenue recognition providing a single, comprehensive revenue recognition model for all contracts with customers. The new revenue standard is based on the principle that revenue should be recognized to depict the transfer of promised goods or services to customers in an amount that reflects the consideration to which the entity expects to be entitled in exchange for those goods or services. The new standard is effective beginning January 1, 2017, with no early adoption permitted. The amendments may be applied retrospectively to each prior period presented or retrospectively with the cumulative effect recognized as of the date of initial application. We are currently evaluating the impact of the new guidance on our financial statements, if any.

Unaudited Interim Financial Statements

The accompanying balance sheet as of June 30, 2014, the statements of operations and comprehensive loss and statements of cash flows for the six months ended June 30, 2013 and 2014, the statement of redeemable convertible preferred stock and stockholders' deficit for the six months ended June 30, 2014

2. Summary of Significant Accounting Policies (Continued)

and the related information contained within the notes to the financial statements are unaudited. These interim financial statements have been prepared on the same basis as the annual audited financial statements and, in the opinion of management, reflect all adjustments, consisting of normal and recurring adjustments, necessary for the fair presentation of the Company's financial position at June 30, 2014 and results of its operations and its cash flows for the six months ended June 30, 2013 and 2014. The results for the six months ended June 30, 2014 are not necessarily indicative of results to be expected for the year ending December 31, 2014 or any other interim or future period.

Unaudited Pro Forma Financial Information

On June 24, 2014, the Company's Board of Directors authorized the Company to file a registration statement with the Securities and Exchange Commission ("SEC") permitting the Company to sell shares of its Common Stock to the public. Upon the closing of a qualified (as defined in the Company's Articles of Incorporation) initial public offering ("IPO") or otherwise upon the election of the holders of the specified percentage of preferred stock, all of the Company's convertible notes plus accrued interest will convert into redeemable convertible preferred stock and the outstanding redeemable convertible preferred stock will automatically convert into Common Stock. The unaudited pro forma balance sheet and statement of redeemable convertible preferred stock and stockholders' (deficit) equity as of June 30, 2014 reflect the assumed conversion of: all of the outstanding shares of Series A Redeemable Convertible Preferred Stock ("Series A Preferred Stock"), the Series A-1 Redeemable Convertible Preferred Stock ("Series A-1 Preferred Stock"), the Series B Redeemable Convertible Preferred Stock ("Series B Preferred Stock"), the Series C Redeemable Convertible Preferred Stock ("Series C Preferred Stock") and the Series D Redeemable Convertible Preferred Stock ("Series D Preferred Stock") (collectively "Preferred Stock") into shares of common stock.

Unaudited pro forma net loss per share attributable to common stockholders is computed using the weighted-average number of common shares outstanding after giving effect to the conversion of all Preferred Stock and Convertible Notes and associated accrued interest into shares of the Common Stock as if such conversion had occurred at the beginning of the period presented, or the date of original issuance, if later, and excludes the accretion of Preferred Stock to its redemption value and interest expense of the Convertible Notes. Accordingly, the pro forma basic and diluted net loss per share attributable to common stockholders does not include the effects of the cumulative Preferred Stock dividends and extinguishment of Series B redeemable convertible Preferred Stock. As the years ended December 31, 2012 and December 31, 2013, the six months ended June 30, 2013 and 2014 (unaudited), resulted in net losses, there is no income allocation required under the two-class method or dilution attributed to pro forma weighted average shares outstanding in the calculation of pro forma diluted loss per share attributable to common stockholders.

As noted above, the unaudited pro forma information reflects the automatic conversion, at the closing of an IPO of the Company's Common Stock of Preferred Stock into shares of Common Stock. The conversion of Preferred Stock has been reflected assuming shares of Series D Preferred Stock Series C Preferred Stock, Series B Preferred Stock, Series A-1 Preferred Stock and Series A Preferred Stock convert into shares of fully paid Common Stock at the applicable conversion ratios. See Note 9 for further discussion of the Preferred Stock conversion features, as well as a discussion of the rights and preferences of the redeemable convertible Preferred Stock.

2. Summary of Significant Accounting Policies (Continued)

Segment Information

Operating segments are defined as components of an enterprise about which separate discrete information is available for evaluation by the chief operating decision maker, or decision-making group, in deciding how to allocate resources and in assessing performance. The Company and the Company's chief operating decision maker view the Company's operations and manage its business in one operating segment, which is the business of developing and commercializing products for the treatment of renal and vascular disease. The Company operates in only one geographic segment.

Cash and Cash Equivalents

The Company considers all highly liquid investments with maturities of 90 days or less from the purchase date to be cash equivalents. Cash and cash equivalents are held in depository and money market accounts and are reported at fair value.

Short-Term Investments

The Company classifies its investments as available-for-sale and records such assets at estimated fair value in the balance sheets, with unrealized gains and losses, if any, reported as a component of other comprehensive income (loss) within the statements of operations and comprehensive loss and as a separate component of stockholders' (deficit) equity. The Company invests its excess cash balances primarily in government debt securities and money market funds with strong credit ratings and maturities of less than one year. There have been no realized gains and losses for the years ended December 31, 2012 and 2013 and for the six months ended June 30, 2013 and 2014 (unaudited).

At each balance sheet date, the Company assesses available-for-sale securities in an unrealized loss position to determine whether the unrealized loss is other-than-temporary. The Company considers factors including: the significance of the decline in value compared to the cost basis, underlying factors contributing to a decline in the prices of securities in a single asset class, the length of time the market value of the security has been less than its cost basis, the security's relative performance versus its peers, sector or asset class, expected market volatility and the market and economy in general. When the Company determines that a decline in the fair value below its cost basis is other-than-temporary, the Company recognizes an impairment loss in the year in which the other-than-temporary decline occurred. There have been no other-than-temporary declines in value of short-term investments for the years ended December 31, 2012 and 2013, the six months ended June 30, 2013 and 2014 (unaudited), as it is more likely than not the Company will hold the securities until maturity or a recovery of the cost basis.

Concentrations of Credit Risk and Off-balance Sheet Risk

Financial instruments that potentially subject the Company to concentrations of credit risk are primarily cash, cash equivalents and short-term investments. The Company's cash and cash equivalents are held in accounts with financial institutions that management believes are creditworthy. The Company's investment policy includes guidelines on the quality of the institutions and financial instruments and defines allowable investments that the Company believes minimizes the exposure to concentration of credit risk. These amounts at times may exceed federally insured limits. The Company has not experienced any credit losses in such accounts and does not believe it is exposed to any significant credit risk on these funds. The Company has no financial instruments with off-balance sheet risk of loss.

2. Summary of Significant Accounting Policies (Continued)

Deferred Public Offering Costs

Deferred public offering costs, which primarily consist of direct, incremental legal and accounting fees relating to the IPO, are capitalized within other assets. The deferred issuance costs will be offset against IPO proceeds upon the consummation of the offering. In the event the offering is terminated, deferred offering costs will be expensed. The Company has incurred $1.2 million in IPO costs as of June 30, 2014 (unaudited).

Deferred Financing Costs

Deferred financing costs related to the Convertible Notes as of December 31, 2013 were included in prepaid expenses and other current assets and have been fully amortized as of June 30, 2014 (unaudited) (Note 5). Deferred financing costs are amortized over the life of the related debt using the effective interest method. For the years ended December 31, 2012 and 2013, and for the six months ended June 30, 2013 and 2014 (unaudited), deferred financing costs of $0, $18,000, $0 and $18,000, respectively, were amortized to interest expense.

As of June 30, 2014, the Company incurred $437,000 (unaudited) of costs related to the issuance of the Series D Preferred Stock. The Series D Preferred Stock issuance costs were allocated to the various tranches resulting in $360,000 allocated to the first tranche and $77,000 allocated to the second and third tranche rights. The amount allocated to the first tranche was offset against the proceeds upon closing of the issuance of the first tranche of Series D Preferred Stock (Note 9). The amount allocated to the future tranche rights has been recorded against the tranche right liability.

Fair Value of Financial Instruments

The Company's financial instruments consist of cash and cash equivalents, short-term investments, accounts payable, accrued liabilities, Convertible Notes and features embedded in the Convertible Notes (see Note 5). The Company is required to disclose information on all assets and liabilities reported at fair value that enables an assessment of the inputs used in determining the reported fair values. FASB ASC Topic 820, *Fair Value Measurement and Disclosures*, established a hierarchy of inputs used in measuring fair value that maximizes the use of observable inputs and minimizes the use of unobservable inputs by requiring that the observable inputs be used when available. Observable inputs are inputs that market participants would use in pricing the financial instrument based on market data obtained from sources independent of the Company. Unobservable inputs are inputs that reflect the Company's assumptions about the inputs that market participants would use in pricing the financial instrument and are developed based on the best information available in the circumstances. The fair value hierarchy applies only to the valuation inputs used in determining the reported or disclosed fair value of the financial instruments and is not a measure of the investment credit quality. Fair value measurements are classified and disclosed in one of the following three categories:

- Level 1—Valuations based on unadjusted quoted prices in active markets for identical assets or liabilities that the Company has the ability to access at the measurement date.
- Level 2—Valuations based on quoted prices for similar assets or liabilities in markets that are not active or for which all significant inputs are observable, either directly or indirectly.
- Level 3—Valuations that require inputs that reflect the Company's own assumptions that are both significant to the fair value measurement and unobservable.

2. Summary of Significant Accounting Policies (Continued)

To the extent that valuation is based on models or inputs that are less observable or unobservable in the market, the determination of fair value requires more judgment. Accordingly, the degree of judgment exercised by the Company in determining fair value is greatest for instruments categorized in Level 3. A financial instrument's level within the fair value hierarchy is based on the lowest level of any input that is significant to the fair value measurement.

Financial instruments measured at fair value on a recurring basis include cash equivalents, short-term investments (Note 3) and the derivative liability associated with the Convertible Notes (Note 5). The fair value of the derivative liability was determined based on Level 3 inputs as described in Note 5. An entity may elect to measure many financial instruments and certain other items at fair value at specified election dates. Subsequent unrealized gains and losses on items for which the fair value option has been elected will be reported in net loss. The Company did not elect to measure any additional financial instruments or other items at fair value. The Company is also required to disclose the fair value of financial instruments not carried at fair value. The carrying value of the Company's Convertible Notes approximates fair value considering their short-term maturity dates and considering that the stated interest rate is near current market rates for instruments with similar conversion and settlement features.

There have been no changes to the valuation methods utilized by the Company during the years ended December 31, 2012 and 2013, the six months ended June 30, 2013 and 2014 (unaudited). The Company evaluates transfers between levels at the end of each reporting period. There were no transfers of financial instruments between levels during the years ended December 31, 2012 and 2013, the six months ended June 30, 2013 and 2014 (unaudited).

Derivative Instruments

The Company occasionally issues financial instruments in which a derivative instrument is "embedded". Upon issuing the financial instrument, the Company assesses whether the economic characteristics of the embedded derivative are clearly and closely related to the economic characteristics of the remaining component of the financial instrument (i.e., the host contract) and whether a separate, non-embedded instrument with the same terms as the embedded instrument would meet the definition of a derivative instrument. When it is determined that (1) the embedded derivative possesses economic characteristics that are not clearly and closely related to the economic characteristics of the host contract and (2) a separate, stand-alone instrument with the same terms would qualify as a derivative instrument, the embedded derivative is separated from the host contract and carried at fair value with any changes in fair value recorded in current period earnings.

In connection with the issuance of the Convertible Notes in September 2013 and the Series D Preferred Stock in May 2014, the Company identified certain embedded features which require separation under ASC 815, *Derivatives and Hedging* ("ASC 815"). See Note 5 and Note 9 for further discussion of these instruments.

Property and Equipment

Property and equipment is stated at cost, less accumulated depreciation. Maintenance and repairs that do not improve or extend the lives of the respective assets are expensed to operations as incurred. Upon disposal, the related cost and accumulated depreciation is removed from the accounts and any resulting

2. Summary of Significant Accounting Policies (Continued)

gain or loss is included in the results of operations. Depreciation is recorded using the straight-line method over the estimated useful lives of the respective assets, which are as follows:

Asset	Estimated Useful Life
Computer equipment and software	3 years
Furniture, fixtures, and other	5 years
Laboratory equipment	7 years

Revenue

In general, the Company recognizes revenue when all of the following criteria are met: persuasive evidence of arrangement exists; delivery has occurred or services have been rendered; the Company's price to the customer is fixed or determinable and collectability is reasonably assured.

Research and Development Costs

Research and development costs are charged to expense as incurred in performing research and development activities. The costs include employee compensation costs, facilities and overhead, clinical study and related clinical manufacturing costs, regulatory and other related costs. Nonrefundable advanced payments for goods or services to be received in the future for use in research and development activities are deferred and capitalized. The capitalized amounts are expensed as the related goods are delivered or the services are performed.

Stock-based compensation expense

The Company accounts for its stock-based compensation awards to employees and directors in accordance with FASB ASC Topic 718, *Compensation-Stock Compensation* ("ASC 718"). ASC 718 requires all stock-based payments to employees, including grants of employee stock options and restricted stock, to be recognized in the statements of operations and comprehensive loss based on their grant date fair values. Compensation expense related to awards to employees is recognized on a straight-line basis based on the grant date fair value over the associated service period of the award, ASC 718 which is generally the vesting term. Share-based payments issued to non-employees are recorded at their fair values and are periodically revalued as the equity instruments vest and are recognized as expense over the related service period in accordance with the provisions of ASC 718 and FASB ASC Topic 505, *Equity,* and are expensed using an accelerated attribution model.

The Company estimates the fair value of its stock options using the Black-Scholes option pricing model, which requires the input of subjective assumptions, including (a) the expected stock price volatility, (b) the expected term of the award, (c) the risk-free interest rate, (d) expected dividends and (e) the estimated fair value of its Common Stock on the measurement date. Due to the lack of a public market for the trading of its Common Stock and a lack of company specific historical and implied volatility data, the Company has based its estimate of expected volatility on the historical volatility of a group of similar companies that are publicly traded. When selecting these public companies on which it has based its expected stock price volatility, the Company selected companies with comparable characteristics to it, including enterprise value, risk profiles, position within the industry and with historical share price information sufficient to meet the expected term of the stock based awards. The Company computes historical volatility data using the daily closing prices for the selected companies' shares during the

2. Summary of Significant Accounting Policies (Continued)

equivalent period of the calculated expected term of the stock-based awards. The Company will continue to apply this process until a sufficient amount of historical information regarding the volatility of its own stock price becomes available. Due to the lack of Company specific historical option activity, the Company has estimated the expected term of its employee stock options using the "simplified" method, whereby, the expected term equals the arithmetic average of the vesting term and the original contractual term of the option. The expected term for nonemployee awards is the remaining contractual term of the option. The risk-free interest rates are based on the U.S. Treasury securities with a maturity date commensurate with the expected term of the associated award. The Company has never paid, and does not expect to pay dividends in the foreseeable future. Refer to "Note 2," "*Basis of presentation and use of estimates*," for a discussion of the Company's estimated fair value of its Common Stock.

The Company is also required to estimate forfeitures at the time of grant and revise those estimates in subsequent periods if actual forfeitures differ from its estimates. The Company uses historical data to estimate forfeitures and records stock-based compensation expense only for those awards that are expected to vest. To the extent that actual forfeitures differ from the Company's estimates, the differences are recorded as a cumulative adjustment in the period the estimates were revised. Stock-based compensation expense recognized in the financial statements is based on awards that are ultimately expected to vest.

Income Taxes

Income taxes are recorded in accordance with FASB ASC Topic 740, "Income Taxes" ("ASC 740"), which provides for deferred taxes using an asset and liability approach. Under this method, deferred tax assets and liabilities are determined based on the difference between the financial reporting and tax reporting basis of assets and liabilities and are measured using enacted tax rates and laws that are expected to be in effect when the differences are expected to reverse. Valuation allowances are provided if, based upon the weight of available evidence, it is more likely than not that some or all of the deferred tax assets will not be realized. The Company has evaluated available evidence and concluded that the Company may not realize the benefit of its deferred tax assets; therefore a valuation allowance has been established for the full amount of the deferred tax assets.

The Company accounts for uncertain tax positions in accordance with the provisions of ASC 740. When uncertain tax positions exist, the Company recognizes the tax benefit of tax positions to the extent that the benefit will more likely than not be realized. The determination as to whether the tax benefit will more likely than not be realized is based upon the technical merits of the tax position as well as consideration of the available facts and circumstances. As of December 31, 2012 and 2013, and June 30, 2014 (unaudited), the Company does not have any significant uncertain tax positions. The Company's practice is to recognize interest and/or penalties related to income tax matters in income tax expense. See Note 13 for further details.

Net loss per share attributable to common stockholders

Basic net loss per share attributable to common stockholders is calculated by dividing net loss attributable to common stockholders by the weighted average shares outstanding during the period, without consideration for Common Stock equivalents. Net loss attributable to common stockholders is calculated by adjusting the net loss of the Company for cumulative preferred stock dividends and accretion of preferred stock issuance costs. During periods of income, the Company allocates participating securities

2. Summary of Significant Accounting Policies (Continued)

a proportional share of income determined by dividing total weighted average participating securities by the sum of the total weighted average common shares and participating securities (the "two class method"). The Company's redeemable convertible preferred stock participates in any dividends declared by the Company and are therefore considered to be participating securities. Participating securities have the effect of diluting both basic and diluted earnings per share during periods of income. During periods of loss, the Company allocates no loss to participating securities because they have no contractual obligation to share in the losses of the Company. Diluted net loss per share attributable to common stockholders is calculated by adjusting weighted average shares outstanding for the dilutive effect of Common Stock equivalents outstanding for the period, determined using the treasury-stock and if-converted methods. For purposes of the diluted net loss per share attributable to common stockholders calculation, preferred stock, stock options, warrants and the Convertible Notes are considered to be Common Stock equivalents but have been excluded from the calculation of diluted net loss per share attributable to common stockholders, as their effect would be anti-dilutive for all periods presented. Therefore, basic and diluted net loss per share were the same for all periods presented.

Comprehensive loss

Comprehensive loss consists of net income or loss and changes in equity during a period from transactions and other events and circumstances generated from non-owner sources. The Company's net loss equals comprehensive loss, net of any changes in the unrealized gains and losses of the Company's short-term investments, for all periods presented.

Subsequent events

The Company considers events or transactions that occur after the balance sheet date but prior to the date the financial statements are available to be issued for potential recognition or disclosure in the financial statements. The Company has completed an evaluation of all subsequent events after the audited balance sheet date of December 31, 2013 through June 25, 2014 and after the unaudited balance sheet date of June 30, 2014 through August 5, 2014, the dates the financial statements were available to be issued, to ensure that this filing includes appropriate disclosure of events both recognized in the financial statements as of December 31, 2013 and June 30, 2014 (unaudited), and events which occurred subsequently but were not recognized in the financial statements. See Note 15 for further details concerning events subsequent to the balance sheet dates.

3. Financial Instruments

Below is a summary of assets and liabilities measured at fair value as of December 31, 2012 and 2013, and June 30, 2014:

	As of December 31, 2012			
	Quoted Prices in Active Markets (Level 1)	Significant Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)	Total
	(in thousands)			
Financial assets				
Cash equivalents	$ 2,395	$ —	$ —	$ 2,395
Government securities	5,062	—	—	5,062
Total	$ 7,457	$ —	$ —	$ 7,457
Financial liabilities				
Derivative liability	$ —	$ —	$ —	$ —
Total	$ —	$ —	$ —	$ —

	As of December 31, 2013			
	Quoted Prices in Active Markets (Level 1)	Significant Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)	Total
	(in thousands)			
Financial assets				
Cash equivalents	$ 2,781	$ —	$ —	$ 2,781
Government securities	2,359	—	—	2,359
Total	$ 5,140	$ —	$ —	$ 5,140
Financial liabilities				
Derivative liability	$ —	$ —	$ 1,443	$ 1,443
Total	$ —	$ —	$ 1,443	$ 1,443

	As of June 30, 2014 (unaudited)			
	Quoted Prices in Active Markets (Level 1)	Significant Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)	Total
	(in thousands)			
Financial assets				
Cash equivalents	$ 8,486	$ —	$ —	$ 8,486
Government securities	16,770	—	—	16,770
Total	$ 25,256	$ —	$ —	$ 25,256
Financial liabilities				
Derivative liability	$ —	$ —	$ 6,580	$ 6,580
Total	$ —	$ —	$ 6,580	$ 6,580

3. Financial Instruments (Continued)

The Company's cash equivalents consist principally of money market funds. Short-term investments, consisting principally of government debt securities and money market funds, are classified as available-for-sale. Cash equivalents and short-term investments are stated at fair value and consist of Level 1 financial instruments in the fair value hierarchy. The Company determines the fair value of its debt security holdings based on pricing from a service provider. The service provider values the securities based on market prices from a variety of industry-standard independent data providers. Such market prices are quoted prices in active markets for identical assets (Level 1 inputs).

The derivative liability and investors rights and obligations are considered Level 3 inputs because their fair value measurement is based, in part, on significant inputs not observed in the market. The Company determined the fair value of both liabilities as described in Note 5 and Note 9. Any reasonable changes in the assumptions used in the valuation could materially affect the financial results of the Company.

Available-for-sale securities at December 31, 2012, 2013 and June 30, 2014 (unaudited) consist of the following (in thousands):

	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
December 31, 2012				
Government securities				
(Due within 1 year)	$ 5,061	$ 1	$ —	$ 5,062
	$ 5,061	$ 1	$ —	$ 5,062
December 31, 2013				
Government securities				
(Due within 1 year)	$ 2,359	$ —	$ —	$ 2,359
	$ 2,359	$ —	$ —	$ 2,359
June 30, 2014				
Government securities				
(Due within 1 year)	$ 16,793	$ —	$ 23	$ 16,770
	$ 16,793	$ —	$ 23	$ 16,770

4. Property and equipment, net

Property and equipment, net, consists of the following (in thousands):

	December 31, 2012	December 31, 2013	June 30, 2014 (unaudited)
Computer equipment and software	$ 86	$ 96	$ 124
Furniture, fixtures, and other	85	84	83
Laboratory equipment	410	236	245
	581	416	452
Accumulated depreciation	(502)	(354)	(367)
Property and equipment, net	$ 79	$ 62	$ 85

Depreciation expense for the years ended December 31, 2012 and 2013, and for the six months ended June 30, 2013 and 2014 (unaudited) was $57,000, $27,000, $15,000 and $13,000, respectively.

During 2013, the Company sold fully depreciated fixed assets with an original cost basis of $0.2 million and a net book value of $0, recognizing a gain on sale of $0.1 million, of which, $4,000 was recognized during the six months ended June 30, 2013. The Company did not sell or dispose of any fixed assets during 2012 or the six months ended June 30, 2014 (unaudited).

5. Convertible Notes

On April 29, 2013, the Company entered into a Convertible Note Purchase Agreement ("the Note Agreement") with certain existing Preferred Stockholders. Under the terms of the Note Agreement, the Company had the option, but not the obligation, to borrow up to $4.3 million from the issuance of the Convertible Notes, subject to meeting at least one of two pre-determined conditions. On September 4, 2013, upon satisfying one of the conditions, the Company issued the Convertible Notes with total aggregate proceeds of $4.3 million. All of the Convertible Notes were purchased by current Preferred Stockholders. The Convertible Notes accrue interest at 8% per annum and mature on or after March 31, 2014 upon written notice from a majority of the outstanding Convertible Note holders (the "Maturity Date").

In connection with the issuance of the Convertible Notes, the Company incurred $36,000 of financing costs which were recorded in other current assets. The Company also reimbursed the lenders $10,000 for financing costs which has been recorded as a discount on the Convertible Notes. The Convertible Notes included various embedded conversion and redemption features as further described below. The Company recorded approximately $1.4 million as the fair value of the combined embedded derivative liability on September 4, 2013, with a corresponding amount recorded as debt discount. The debt discount has been amortized to interest expense over the life of the Convertible Notes. As of December 31, 2013 and June 30, 2014 (unaudited), the fair value of the combined embedded derivative liability was $1.4 million and $0, respectively. Amounts recorded for issuance costs and embedded features are being amortized to interest expense over the life of the Convertible Notes, approximately seven months. Changes in the estimated fair value of the embedded features are recorded in earnings in the period in which they occur.

The Convertible Notes provide for conversion upon maturity at the holder's option and mandatory conversion upon a reverse acquisition. Both of these features provide for the conversion of the outstanding principal of the Convertible Notes, plus accrued interest into Series C Preferred Stock at $1.15 per share.

5. Convertible Notes (Continued)

In the event the Company issues or sells equity securities prior to the Maturity Date with aggregate proceeds of not less than $7.0 million, the Convertible Notes plus all accrued interest automatically convert into either (i) the newly issued equity securities at 75% of the cash price per share paid by the investors in the new equity securities; or (ii) shares of Series C Preferred Stock at $1.15 per share. In accordance with ASC 815, the Company determined that this embedded mandatory conversion feature should be separately accounted for as a freestanding financial instrument as the conversion feature was a substantial contingent call option.

In the event the Company issues or sells equity securities prior to the Maturity Date with aggregate proceeds less than $7.0 million, the Convertible Notes plus all accrued interest can be converted at the option of the holders into the newly issued equity securities at 75% of the cash price per share paid by the investors in the new equity securities. In accordance with ASC 815, the Company determined that this embedded conversion feature should be separately accounted for as a freestanding financial instrument as the conversion feature was a substantial contingent call option.

In the event of a change in control of the Company prior to the Maturity Date, the Company has the option to prepay the Convertible Notes at 1.5 times principal, plus accrued interest. In accordance with ASC 815, the Company determined that this embedded redemption feature should be separately accounted for as a free-standing financial instrument as the conversion feature was a substantial contingent call option.

The Convertible Notes include a call feature, at the issuer's option, whereby the Convertible Notes may be prepaid at 1.5 times principal, plus accrued interest. In accordance with ASC 815, the Company determined that this embedded redemption feature should be separately accounted for as a free-standing financial instrument.

The Convertible Notes include a put feature, at the option of the holders, whereby upon a breach of the Note Agreement, repayment of the Convertible Notes can be accelerated at 1.5 times principal, plus accrued interest. In accordance with ASC 815, the Company determined that this embedded redemption feature should be separately accounted for as a free-standing financial instrument. The Convertible Notes also include an additional put feature, at the option of the holders, whereby upon an event of default, the repayment of the Convertible Notes can be accelerated in the amount of the outstanding principal, plus accrued interest. In accordance with ASC 815, the Company determined that this embedded redemption feature does not require separate accounting as a free-standing financial instrument.

The embedded features requiring separate accounting were combined and valued upon issuance using a single income valuation approach. The Company estimated the fair value of the combined embedded derivative identified above using a "with and without" income valuation approach. Under this approach, the Company estimated the present value of the fixed interest rate debt based on the fair value of similar debt instruments excluding the embedded features. This amount was then compared to the fair value of the debt instrument including the embedded features using a probability weighted approach by assigning each embedded derivative feature a probability of occurrence, with consideration provided for the settlement amount including conversion discounts, prepayment penalties, the expected life of the liability and the applicable discount rate.

5. Convertible Notes (Continued)

As of September 4, 2013 and December 31, 2013, the Company ascribed a probability to the mandatory conversion feature upon a financing of not less than $7.0 million of 85% and 100%, respectively. As of September 4, 2013 and December 31, 2013 the Company ascribed a probability to the call feature upon a change in control of 15% and 0%, respectively. For all other features included in the combined embedded derivative, the Company estimated a 0% probability of occurrence as of September 4, 2013 and December 31, 2013. From December 31, 2013 to the conversion of the convertible notes into Series D Preferred Stock, as described below, the estimates of these probabilities did not change. The Company classified the liability within Level 3 of the fair value hierarchy as the probability factor is an unobservable input and significant to the valuation model.

On May 13, 2014, we received net proceeds of approximately $25.0 million from the issuance of Series D convertible preferred stock to new and existing investors at a price per share of $0.588656. In aggregate, we issued 52,813,827 shares of Series D preferred stock including 10,344,201 shares for the conversion of $4.6 million of convertible notes and accrued interest at a conversion price of $0.4414 per share. In connection with the conversion, the compound embedded derivative liability, which had a fair value of $1.5 million, was written-off. As a result, there was no gain or loss recognized upon conversion of the Convertible Notes.

6. Accrued expenses

Accrued expenses consist of the following (in thousands):

	December 31, 2012	December 31, 2013	June 30, 2014 (unaudited)
Payroll and employee-related costs	$ 81	$ 419	$ 291
Contracted service costs	544	360	773
Professional fees	95	202	940
Other	15	3	2
Total	$ 735	$ 984	$ 2,006

7. Option to Acquire Company

In March 2009, the Company entered into an option agreement with a major pharmaceutical entity that provides an exclusive option to acquire the Company under a pre-negotiated merger agreement. The Company received a $10.0 million non-refundable payment as consideration for the agreement. The fair value of the option to acquire the Company was estimated using the Black-Scholes option-pricing model with the following assumptions:

Expected volatility	76%
Expected option expiration date	June 30, 2013
Expected dividends	0%
Expected term (years)	4.34
Risk-free rate	1.80%

7. Option to Acquire Company (Continued)

Expected volatility was based on historical volatility of companies within the biotechnology industry. The exercise price of the option to acquire all outstanding shares of Company stock, prior to the payment of contingent program milestones, was $240.0 million. The fair value of the option to acquire all of the outstanding shares of the Company was estimated to be $7.1 million, which was recorded as additional paid-in capital during 2009. The $2.9 million difference between the $10.0 million non-refundable payment and the fair value of the option was recorded as deferred revenue during 2009, representing the value of certain residual rights in the event the acquisition option is not exercised (e.g., a right, under certain circumstances, to license the Company's underlying technology). The acquisition option expired unexercised in 2013. This amount will not be recognized as revenue until the residual rights lapse, which will occur during the second half of 2014.

8. Commitments and Contingencies

Significant Contracts and Agreements

In February 2002, the Company entered into an agreement to license certain intellectual property from Johns Hopkins University. The agreement calls for payments to be made by the Company upon the commencement of product sales, in the form of a royalty of 2.5% on net sales of the product. As the Company has not commenced product sales, during the years ended December 31, 2012 and 2013 and the six months ended June 30, 2014 (unaudited), the Company has recognized no royalties on product sales.

Operating Leases

The Company has various non-cancellable operating leases for facilities and office equipment that expire at various dates through 2018. The facility leases require the Company to pay all electricity costs. In August 2014, the Company amended the Massachusetts office lease to extend the term of the lease by 42 months. The lease expires in June 2018 with one optional one-year extension period. Rental expense for the years ended December 31, 2012 and 2013, and six months ended June 30, 2013 and 2014 (unaudited) was $0.3 million, $0.2 million, $0.1 million and $0.1 million, respectively.

Future minimum payments required under the leases as of June 30, 2014, are summarized as follows (in thousands):

Year Ending December 31:	
2014	$ 87

Restricted cash related to facilities leases

At December 31, 2012 and 2013, and June 30, 2014 (unaudited), the Company had $38,000 in an outstanding letter of credit to be used as collateral for leased premises. At December 31, 2012 and 2013 and June 30, 2014 (unaudited), the Company has pledged an aggregate of $39,000 to the bank as collateral for the letter of credit, which is included in short-term deposits.

9. Redeemable Convertible Preferred Stock

As of June 30, 2014 (unaudited), the total authorized capital stock of the Company was 364,568,592 shares, which included 22,638,465 shares of Series A Preferred Stock, $0.001 par value per share; 10,909,091 shares of Series A-1 Preferred Stock, $0.001 par value per share; 20,754,461 shares of

9. Redeemable Convertible Preferred Stock (Continued)

Series B Preferred Stock, $0.001 par value per share; 17,550,758 shares of Series C Preferred Stock, $0.001 par value per share; and 86,789,527 shares of Series D Preferred Stock, $0.001 par value per share.

On May 13, 2014, the Company issued 42,469,626 shares of Series D Preferred Stock to new and existing investors at a price of $0.588656 per share for gross proceeds of $25.0 million. Immediately upon closing this round of financing, $4.6 million of Convertible Notes, including $0.2 million of accrued and unpaid interest, automatically converted into 10,344,201 shares of Series D Preferred Stock at a conversion price of $0.4414 per share. (See Note 5).

The Series D Purchase Agreement contemplates the sale in two additional subsequent closings (the "second and third tranches") of up to 33,975,700 additional shares of the Company's Series D Preferred Stock for aggregate gross proceeds of $20.0 million. In addition, the Series D Purchase Agreement provides to the Series D investors party to the agreement certain individual purchase rights. The Company's right to cause the second and third tranche closings to occur will terminate at the closing of an initial public offering.

Individual Purchase Rights after the Closing of an Initial Public Offering. Following the closing of an initial public offering, the Series D investors will have individual purchase rights under the Series D Purchase Agreement, until May 13, 2024. The purchase price per share for the Common Stock purchasable pursuant to the individual purchase rights will be the lower of (i) $0.588656, the Series D conversion price immediately prior to an initial public offering, and (ii) the initial public offering price. If the Company or its underwriters offer to the Series D investors the opportunity to purchase shares of Common Stock in an initial public offering, which offer to purchase will be made only if so determined by the Company or its underwriters at the sole discretion of the Company or its underwriters, then the individual purchase rights under the Series D Purchase Agreement of the Series D investors shall terminate at the closing of the initial public offering to the extent of the number of shares of the Company's Common Stock that these investors are offered the opportunity to purchase in the initial public offering, regardless of whether these investors actually purchase any of such shares so offered in the initial public offering. For example, if the individual purchase rights are exercisable to purchase from the Company a certain number of shares of the Company's Common Stock, and if the Company or their underwriters offer to such investors the opportunity to purchase this number of shares of the Company's Common Stock in an initial public offering, then the individual purchase rights under the Series D Purchase Agreement of such investors shall terminate at the closing of such an initial public offering, regardless of whether these investors actually purchase any of the shares of the Company's Common Stock. On the other hand, if, for example, the individual purchase rights are exercisable to purchase from the Company a certain number of shares of the Company's Common Stock, and if the Company or their underwriters offer to such investors the opportunity to purchase an aggregate of less than this certain number of shares of the Company's Common Stock in an initial public offering, then, regardless of whether such investors actually purchase any of such shares so offered in such an initial public offering, the individual purchase rights under the Series D Purchase Agreement of such investors shall terminate at the closing of the initial public offering with respect to only the number of shares of the Company's Common Stock offered and the individual purchase rights shall remain exercisable after the initial public offering until May 13, 2024, for the amount of the difference between the number of shares the Series D investors had the right to purchase and the number of shares of the Company's Common Stock offered.

Anti-dilution Protection for Series D Preferred Stock. At the closing of an initial public offering, the Company's Series D Preferred Stock will automatically convert into a number of shares of the Company's

9. Redeemable Convertible Preferred Stock (Continued)

Common Stock determined by customary conversion formula, plus a potential incremental amount of shares. The incremental amount of shares will be applicable only if the Company or its underwriters offer to the Series D investors the opportunity to purchase shares in an initial public offering and these investors purchase shares in the initial public offering and the initial public offering price per share is greater than the purchase price per share of the Company's Series D Preferred Stock. The incremental amount of shares will be determined by multiplying (x) the number of shares of Common Stock purchased in the initial public offering by the holders of the Series D investors up to a maximum number of shares of the Company's Common Stock equal to the number of shares of the Company's Series D Preferred Stock that these Series D investors would have been entitled to purchase under the Series D Purchase Agreement at the second and third tranche closings if the second and third tranche closings had been consummated prior to the closing of the initial public offering, by (y) the remainder obtained by subtracting the number one from the quotient obtained by dividing the initial public offering price per share by the purchase price per share of the Company's Series D Preferred Stock.

As described above, in connection with the issuance of the Series D Preferred Stock, the holders received rights to purchase additional shares of Series D Preferred Stock at $0.588656 per share. These investor rights represent freestanding financial instruments, and are accounted for as liabilities. The Company adjusts the carrying value of such investor rights to its estimated fair value at each reporting date up to the closing of the tranche financing. Increases or decreases in the fair value of such investor rights are recorded as other income (expense) in the Statement of Operations and Comprehensive Loss. The estimated fair value of the tranche rights was determined upon issuance using a Black-Scholes option pricing model with the following inputs:

Expected term (in years)	1.84 - 3.50
Expected volatility	63.0% - 86.0%
Risk-free interest rate	0.44% - 1.12%
Expected dividend yield	0%

At the date of issuance, the investor rights obligation was recorded at its fair value of $6.6 million as a liability on the balance sheet. From the date of issuance to June 30, 2014 the change in fair value of the investor rights was $18,000 and was recorded as other expense in the Statement of Operations and Comprehensive Loss.

The Company incurred approximately $0.4 million in costs related to the issuance of the Series D Preferred Stock which have been allocated to the shares issued to date and the tranche right liability. The $360,000 of issuance costs allocated to the shares issued in May 2014 have been recorded as a discount on the Series D Preferred Stock and will be accreted over five years to the earliest redemption date of the Series D Preferred Stock. The remaining $77,000 of issuance costs have been allocated to the tranche right liability.

Conversion

Shares of Series D Preferred Stock, Series C Preferred Stock, Series B Preferred Stock, Series A-1 Preferred Stock and Series A Preferred Stock are convertible into Common stock at 1.00, 1.23, 1.23, 1.22 and 1.19, respectively, shares of common stock for each share of preferred stock. All outstanding shares of Preferred Stock are automatically convertible based on either: (i) stockholder approval, as defined in the Certificate of Incorporation, or (ii) the closing of a firm-commitment, underwritten IPO, in which the

9. Redeemable Convertible Preferred Stock (Continued)

aggregate proceeds are at least $40 million with an offering price of at least $3.45 per share of Common Stock. The Preferred Stock conversion prices are subject to adjustment in the event additional shares of Common Stock or certain securities convertible into Common Stock, are issued for consideration per share less than the respective Preferred Stock conversion price.

Dividends

Holders of Preferred Stock are entitled to two types of dividends:

Accruing Dividends

Holders of the Series D Preferred Stock Series C Preferred Stock, Series B Preferred Stock, Series A-1 Preferred Stock and Series A Preferred Stock are entitled to receive, when and if declared by the Board of Directors, dividends at the annual rate of $0.0412 $0.0805, $0.0805, $0.077 and $0.07 per share, subject to adjustment for stock dividends, stock splits, combinations, recapitalizations, or the like, with respect to such shares. The Preferred Stock Accruing Dividends are cumulative and non-compounding.

An aggregate of $22.5 million, $27.6 million, and $30.5 million of accruing dividends have been recorded for the Preferred Stock as of December 31, 2012 and 2013, and June 30, 2014 (unaudited), respectively.

Non-Cumulative Dividends

Holders of the Series D Preferred Stock Series C Preferred Stock, Series B Preferred Stock, Series A-1 Preferred Stock and Series A Preferred Stock are entitled to receive, when and if declared by the Board of Directors, dividends at the annual rate of 7% of the issue price per share, subject to adjustment for stock dividends, stock splits, combinations, recapitalizations, or the like, with respect to such shares. These dividends are non-cumulative and non-compounding.

The Company shall not declare, pay, or set aside any dividends on Common stock (other than those payable in shares of Common stock) unless the holders of the Preferred Stock then outstanding shall first receive, or simultaneously receive, a dividend on each outstanding share of Preferred Stock in an amount at least equal to or greater than the product of (i) the dividend payable on each share of Common stock and (ii) the number of shares of Common stock issuable upon conversion of a share of Preferred Stock calculated on the record date for determination of holders entitled to receive such a dividend.

Liquidation Preference

Holders of the Series D Preferred Stock have preference in the event of a liquidation or dissolution of the Company equal to $0.588656 per share, plus any declared dividends, but specifically excluding any Accruing Dividends. Holders of the Series C Preferred Stock have preference in the event of a liquidation or dissolution of the Company, which preference is junior to the liquidation preference for the Series D Preferred Stock, equal to $0.6242 per share, plus any declared dividends, but specifically excluding any Accruing Dividends. Holders of the Series B Preferred Stock have preference in the event of a liquidation or dissolution of the Company, which preference is junior to the liquidation preference for the Series C Preferred Stock, equal to $0.6242 per share, plus any declared dividends, but specifically excluding any Accruing Dividends. Holders of the Series A Preferred Stock and the Series A-1 Preferred Stock have

9. Redeemable Convertible Preferred Stock (Continued)

preference in the event of a liquidation or dissolution of the Company, which preference is junior to the liquidation preference for the Series B Preferred Stock, equal to $0.5428 per share and $0.5971 per share, respectively, plus any declared dividends but specifically excluding any Accruing Dividends,

After all preferred stockholders have received their respective initial preference amounts, any assets remaining for distribution shall be distributed to the holders of the Series D Preferred Stock, Series C Preferred Stock, Series B Preferred Stock, Series A-1 Preferred Stock, Series A Preferred Stock and Common Stock pro rata in proportion to the total number of shares of Series D Preferred Stock, Series C Preferred Stock, Series B Preferred Stock, Series A-1 Preferred Stock, Series A Preferred Stock and Common Stock, assuming conversion to Common Stock. As of June 30, 2014 (unaudited), the aggregate liquidation value for the Series D Preferred Stock, Series C Preferred Stock, Series B Preferred Stock, Series A-1 Preferred Stock and Series A Preferred Stock was $31.1 million $8.2 million, $13.0 million, $6.5 million and $12.3 million, respectively.

Voting Rights

Except for matters with specific voting rights, the holders of shares of Preferred Stock vote together with the holders of the Common Stock as a single class on any matter presented to the stockholders of the Company for their action or consideration at any meeting of the stockholders of the Company or by written consent of stockholders in lieu of meetings. The holders of the Preferred Stock are entitled to the number of votes equal to the number of shares of Common Stock into which each share of the Preferred Stock is convertible at the time of such vote. A vote of 80% of the Preferred Stockholders, voting as a single class, is required for events that would materially affect the business or change the rights of the Preferred Stock.

The number of directors of the Company constituting the entire Board of Directors shall be no less than five and no more than nine. The holders of Series A-1 Preferred Stock and Series A Preferred Stock have the right to elect three of the directors. The holders of Series B Preferred Stock have the right to elect one of the directors. The holders of Series D Preferred Stock have the right to elect two of the directors. The holders of the Common Stock and Designated Preferred Stock, exclusively and voting together as a single class, have the right to elect the balance of the total number of directors of the Company.

Redemption Rights

Each class of Preferred Stock is stated at its then current redemption value as of each balance sheet date presented.

The Preferred Stock may be redeemed upon written election of the holders of 80% of the Series D Preferred Stock, Series C Preferred Stock, Series B Preferred Stock, Series A-1 Preferred Stock and Series A Preferred Stock on or after May 13, 2019. The Series D Preferred Stock, Series C Preferred Stock, Series B Preferred Stock, Series A-1 Preferred Stock and Series A Preferred Stock will receive, through a series of three installments $0.588656, $1.15, $1.15, $1.10 and $1.00, respectively, per share (subject to certain adjustments) plus any Accruing Dividends accrued but unpaid thereon, whether or not declared, together with any other dividends declared but unpaid thereon.

If the Company does not have sufficient funds available to redeem all shares of Preferred Stock, then the Company shall redeem first, a pro rata portion of each holder's Series D Preferred Stock to the fullest extent of the funds available and shall redeem the remaining shares of Series D Preferred Stock as funds

9. Redeemable Convertible Preferred Stock (Continued)

become available until all shares of Series D Preferred Stock have been redeemed in full. Then, it shall redeem a pro rata portion of each holder's Series C Preferred Stock to the fullest extent of the funds available and shall redeem the remaining shares of Series C Preferred Stock as funds become available until all shares of Series C Preferred Stock have been redeemed in full. Then, it shall redeem a pro rata portion of each holder's Series B Preferred Stock to the fullest extent of the funds available and shall redeem the remaining shares of Series B Preferred Stock as soon as practicable as funds become available until all shares of Series B Preferred Stock have been redeemed in full. Then, it shall redeem a pro rata portion of each holder's Series A Preferred Stock and Series A-1 Preferred Stock out of funds available and shall redeem the remaining shares of Series A Preferred Stock and Series A-1 Preferred Stock as soon as funds become available for such purpose. Refer to Note 15 for further details.

10. Common Stock

General

The voting, dividend and liquidation rights of the holders of shares of Common Stock are subject to and qualified by the rights, powers and preferences of the holders of shares of Preferred Stock. The Common Stock has the following characteristics:

Voting

The holders of shares of Common stock are entitled to one vote for each share of Common Stock held at all meetings of stockholders and written action in lieu of meetings; there is no cumulative voting.

Dividends

The holders of shares of Common Stock are entitled to receive dividends, if and when declared by the Board of Directors. Cash dividends may not be declared or paid to holders of shares of Common Stock until paid on each series of outstanding Preferred Stock in accordance with their respective terms. As of June 30, 2014 (unaudited), no dividends have been declared or paid since the Company's inception.

Liquidation

After payment to the holders of shares of Preferred Stock of their liquidation preferences, the holders of the Common Stock are entitled to share ratably in the Company's assets available for distribution to stockholders, in the event of any voluntary or involuntary liquidation, dissolution or winding up of the Company or upon the occurrence of a deemed liquidation event.

10. Common Stock (Continued)

Reserve for future issuance

The Company has reserved for future issuances the following number of shares of Common Stock:

	December 31,		June 30,
	2012	2013	2014
			(unaudited)
Conversion of Series A Preferred Stock	22,638,465	22,638,465	26,989,109
Conversion of Series A-1 Preferred Stock	10,909,091	10,909,091	13,300,820
Conversion of Series B Preferred Stock	20,754,461	20,754,461	25,556,944
Conversion of Series C Preferred Stock	17,550,758	17,550,758	21,611,920
Conversion of Series D Preferred Stock	—	—	52,813,827
Stock-based compensation awards	10,036,341	9,888,775	18,019,231
Warrants to purchase Common Stock	10,471,282	10,471,282	10,471,282
Total	92,360,398	92,212,832	168,763,134

11. Stock-based Compensation

In March 2006, the Company adopted the 2006 Equity Incentive Plan (the "Plan"). Under the Plan, the Company has granted stock options to selected officers, employees and consultants of the Company. As of June 30, 2014 (unaudited), the Plan, as amended by the May 2014 Series D Preferred Stock and other Board of Director actions, provides for the issuance of up to 18,222,157 shares of Common Stock.

Terms of stock award agreements, including vesting requirements, are determined by the Board of Directors, subject to the provisions of the Plan. Option and share awards generally vest over three to four years. Certain option and share awards provide for accelerated vesting if there is a change in control as defined in the Plan. The options are exercisable from the date of grant for a period of ten years. For options granted to date, the exercise price equaled the fair value of the Common Stock as determined by the Board of Directors on the date of grant.

Stock options issued to non-employees are accounted for using the fair value method of accounting, are periodically revalued as the options vest and are recognized as expense over the related service period. The total expense related to all options granted to non-employees for the years ended December 31, 2012 and 2013 and the six months ended June 30, 2013 and 2014 (unaudited) was $9,000, $32,000, $20,000 and $2,000, respectively.

11. Stock-based Compensation (Continued)

Total stock-based compensation expense is recognized for stock options granted to employees and non-employees and has been reported in the Company's statements of operations as follows (in thousands):

	Years Ended December 31,		Six Months Ended June 30,	
	2012	2013	2013	2014
			(unaudited)	
Research and development	$ 46	$ 106	$ 84	$ 21
General and administrative	64	49	21	28
Total	$ 110	$ 155	$ 105	$ 49

A following table summarizes stock option activity for employees and non-employees (intrinsic value in thousands):

	Shares	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Term (years)	Aggregate Intrinsic Value
Outstanding at December 31, 2012	9,737,684	$ 0.13	6.2	$ 12,370
Granted	50,000	$ 1.40		
Exercised	(147,566)	$ 0.13		
Cancelled or forfeited	(6,748)	$ 0.16		
Outstanding at December 31, 2013	9,633,370	$ 0.14	5.2	$ 1,627
Granted (unaudited)	8,375,000	$ 0.31		
Exercised (unaudited)	(7,500)	$ 0.08		
Cancelled or forfeited (unaudited)	—	$ —		
Outstanding at June 30, 2014 (unaudited)	18,000,870	$ 0.22	7.2	$ 1,722
Exercisable at December 31, 2013	8,087,507	$ 0.14	4.7	$ 1,307
Vested or expected to vest at December 31, 2013(1)	9,262,144	$ 0.14	5.1	$ 1,561
Exercisable at June 30, 2014 (unaudited)	8,515,578	$ 0.14	4.4	$ 1,483
Vested or expected to vest at June 30, 2014 (unaudited)(1)	16,858,329	$ 0.21	7.0	$ 1,668

(1) This represents the number of vested options at December 31, 2013 and June 30, 2014 (unaudited), plus the number of unvested options expected to vest at December 31, 2013 and June 30, 2014 (unaudited), based on the unvested options outstanding at December 31, 2013 and June 30, 2014 (unaudited).

During the year ended December 31, 2013 and the six months ended June 30, 2013 (unaudited), the Company granted stock options to purchase an aggregate of 50,000 shares of its Common Stock with a weighted-average grant date fair value of $1.04. During the six months ended June 30, 2014 (unaudited) the Company granted stock options to purchase an aggregate of 8,375,000 shares of its Common Stock with a weighted-average grant date fair value of $0.21.

11. Stock-based Compensation (Continued)

The total intrinsic value of options exercised in the years ended December 31, 2012 and 2013 and six months ended June 30, 2013 and 2014 (unaudited), was $0, $0.1 million, $0 and $2,000, respectively. As of June 30, 2014 (unaudited), there was $1.7 million of total unrecognized compensation cost related to employee non-vested stock options granted under the Plan. As of June 30, 2014 (unaudited), the unrecognized compensation cost related to non-employee, non-vested stock options granted under the plan was $3,000.

The total unrecognized compensation cost for employee and non-employee awards will be adjusted for future forfeitures. The Company expects to recognize that cost over a remaining weighted-average period of four years.

During 2013, the Company modified the stock option awards of one employee upon the employee's termination. In accordance with ASC 718, the Company assessed the fair value of the unvested portion of the modified awards at $0.1 million, and recorded the amount as compensation cost on the date of termination.

The Company estimates the fair value of each employee stock award on the grant date using the Black-Scholes option-pricing model based on the following assumptions regarding the fair value of the underlying Common Stock on each measurement date:

	Year Ended December 31, 2013	Six Months Ended June 30,	
		2013	2014
Weighted average expected volatility	91.12%	91.1%	80.7% - 81.5%
Expected term (in years)	5.95	5.95	5.71 - 6.11
Risk free interest rate	1.03%	1.03%	1.87% - 1.97%
Expected dividend yield	0%	0%	0%

12. 401(k) Savings Plan

In October 2007, the Company adopted a tax-qualified employee savings and retirement 401(k) Plan, covering all qualified employees. Participants may elect a salary deferral of at least 1% as a contribution to the 401(k) Plan, up to the statutorily prescribed annual limit for tax-deferred contributions. The Company may elect to make a safe harbor contribution to the Plan equal to 3% of each eligible employee's salary. Safe harbor contributions are fully vested to plan participants at all times. The Company had no safe harbor contributions for the years ended 2012 and 2013 and the six months ended June 30, 2014 (unaudited).

13. Income Taxes

For the years ended December 31, 2012 and 2013, the six months ended June 30, 2013 and 2014 (unaudited) the Company has not recorded a provision for federal or state income taxes as it has had cumulative net operation losses since inception. The Company's losses before income taxes consist solely of domestic losses.

13. Income Taxes (Continued)

A reconciliation of income taxes computed using the U.S. federal statutory rate to that reflected in operations follows (in thousands):

	Years Ended December 31,	
	2012	2013
Income tax benefit using U.S. federal statutory rate	$ (2,710)	$ (2,690)
Permanent differences	38	299
State income taxes, net of federal benefit	(368)	(389)
Tax credits	(95)	(7,164)
Expiring net operating losses and tax credits	287	2,566
Change in the valuation allowance	2,988	7,286
Other	(140)	92
	$ —	$ —

The significant components of the Company's deferred tax assets are as follows (in thousands):

	Years Ended December 31,	
	2012	2013
Net operating loss carryforwards	$ 26,560	$ 26,304
Federal and state tax credits	2,777	9,941
Deferred revenue	1,139	1,147
Accrued expenses	155	332
Patents	692	612
Other	27	300
	31,350	38,636
Valuation allowance	(31,350)	(38,636)
Net deferred tax asset	$ —	$ —

Management of the Company has evaluated the positive and negative evidence bearing upon the realizability of its deferred tax assets. Based on the Company's history of operating losses, management of the Company has concluded that it is more likely than not that the benefit of its deferred tax assets will not be realized. Accordingly, the Company has provided a full valuation allowance for deferred tax assets as of December 31, 2012 and 2013.

The valuation allowance increased approximately $7.3 million during the year ended December 31, 2013, due primarily to the addition of Orphan Drug Tax credits for 2009 through 2012 as well as the generation of net operating losses during the year ended December 31, 2013, both of which are fully reserved. The valuation allowance increased approximately $3.0 million during the year ended December 31, 2012, due primarily to the generation of net operating losses during the period.

Subject to the limitations described below, as of December 31, 2012 and 2013, the Company has net operating loss carryforwards of approximately $70.3 million and $69.9 million, respectively, to offset future federal taxable income, which will expire at various times between 2026 and 2033. The Company does not have any net operating losses that are attributable to excess stock option deductions which would be

13. Income Taxes (Continued)

recorded as an increase in additional paid-in capital. As of December 31, 2012 and 2013, the Company has state net operating loss carryforwards of approximately $50.4 million and $45.4 million, respectively, to offset future state taxable income, which will expire at various times between 2014 and 2033. As of December 31, 2012 and 2013, the Company has tax credit carryforwards of approximately $3.1 million and $10.3 million, respectively, to offset future federal and state income taxes, which will expire at various times between 2022 and 2033.

Net operating loss and tax credit carryforwards are subject to review and possible adjustment by the Internal Revenue Service (the "IRS") and may become subject to an annual limitation in the event of certain cumulative changes in the ownership interest of significant shareholders over a three-year period in excess of 50% as defined under Sections 382 and 383 in the Internal Revenue Code. This could substantially limit the amount of tax attributes that can be utilized annually to offset future taxable income or tax liabilities. The amount of the annual limitation is determined based on the Company's value immediately prior to the ownership change. Subsequent ownership changes may further affect the limitation in future years.

The Company had no unrecognized tax benefits or related interest and penalties accrued during the years ended December 31, 2012 and 2013. The Company will recognize interest and penalties related to uncertain tax positions in income tax expense.

The Company is subject to U.S. federal income tax and primarily Massachusetts state income tax. The statute of limitations for assessment by the IRS and state tax authorities is open for tax years ending December 31, 2010 through 2013, although carryforward attributes that were generated prior to tax year 2010 may still be adjusted upon examination by the IRS or state tax authorities if they either have been or will be used in a future period. Currently, no federal or state income tax returns are under examination by the respective taxing authorities.

14. Net loss Per Share Attributable to Common Stockholders

As described in Note 2, *Summary of Significant Accounting Policies*, the Company computes basic and diluted earnings (loss) per share using a methodology that gives effect to the impact of outstanding participating securities (the "two-class method"). As the years ended December 31, 2012 and 2013 and the six months ended June 30, 2013 and 2014 (unaudited) resulted in net losses, there is no income allocation required under the two-class method or dilution attributed to weighted average shares outstanding in the calculation of diluted loss per share.

14. Net loss Per Share Attributable to Common Stockholders (Continued)

The following Common Stock equivalents, presented on an as converted basis, were excluded from the calculation of net loss per share for the periods presented, due to their anti-dilutive effect (in thousands):

	December 31,		June 30,	
	2012	2013	2013	2014
			(unaudited)	
Convertible preferred stock	67,505	67,505	67,505	120,319
Common stock warrants	10,471	10,471	10,471	10,471
Outstanding stock options	9,738	9,633	9,788	18,001
Convertible notes	—	3,870	—	—
	87,714	91,479	87,764	148,791

15. Subsequent Events (unaudited)

On August 4, 2014, the Company entered into an Amendment (the "Lease Amendment") to the existing Lease Agreement dated July 13, 2009 (the "Lease Agreement"), with Boston Properties Limited Partnership ("Lessor") pursuant to which the Company has agreed to extend the lease for approximately 5,000 square feet of property to be used for office space (the "Leased Property") located at 200 West St., Waltham, Massachusetts. The term of the Lease Amendment commences on January 1, 2015 (the "Commencement Date") and expires approximately three years and six months from the Commencement Date. The Company has the option to extend the term for one additional one-year period upon the Company's written notice to the Lessor at least nine months in advance of the extension.

The total cash obligation for the base rent over the three year and six month term of the Lease Agreement is approximately $0.6 million. In addition to the base rent, the Company is also responsible for its share of operating expenses and real estate taxes, in accordance with the terms of the Lease Agreement. The Company will provide a security deposit in the amount of $14,000 to the Lessor.

Shares

Common Stock

, 2014

Stifel

JMP Securities

Baird

Oppenheimer & Co.

Until , 2014 (25 days after the date of this prospectus), all dealers that effect buy, sell or trade shares of our common stock, whether or not participating in this offering, may be required to deliver a prospectus. This is in addition to the dealers' obligation to deliver a prospectus when acting as underwriter and with respect to their unsold allotments or subscriptions.

Neither we nor any of the underwriters have authorized anyone to provide information different from that contained in this prospectus. When you make a decision about whether to invest in our common stock, you should not rely upon any information other than the information in this prospectus. Neither the delivery of this prospectus nor the sale of our common stock means that information contained in this prospectus is correct after the date of this prospectus. This prospectus is not an offer to sell or solicitation of an offer to buy these shares of common stock in any circumstances under which the offer or solicitation is unlawful.

PART II

INFORMATION NOT REQUIRED IN PROSPECTUS

Item 13. Other Expenses of Issuance and Distribution.

The following table sets forth the fees and expenses in connection with the issuance and distribution of the securities being registered (excluding the underwriting discount). Except for the Securities and Exchange Commission registration fee and the FINRA filing fee, all amounts are estimates.

	Amount Paid or to be Paid
SEC registration fee	$ *
FINRA filing fee	*
NASDAQ listing fee	*
Legal fees and expenses	*
Accounting fees and expenses	*
Printing expenses	*
Transfer agent fees and expenses	*
Miscellaneous	*
Total	$ *

* To be filed by amendment.

Item 14. Indemnification of Directors and Officers.

Section 145 of the Delaware General Corporation Law authorizes a corporation's board of directors to grant, and authorizes a court to award, indemnity to officers, directors, and other corporate agents.

As permitted by Delaware law, our certificate of incorporation, which will be amended and restated and in effect upon the completion of the offering, provides that, to the fullest extent permitted by Delaware law, no director will be personally liable to us or our stockholders for monetary damages for breach of fiduciary duty as a director. Pursuant to Delaware law such protection would be not available for liability:

- for any breach of a duty of loyalty to us or our stockholders;
- for acts or omissions not in good faith or that involve intentional misconduct or a knowing violation of law;
- for any transaction from which the director derived an improper benefit; or
- for an act or omission for which the liability of a director is expressly provided by an applicable statute, including unlawful payments of dividends or unlawful stock repurchases or redemptions as provided in Section 174 of the Delaware General Corporation Law.

Our amended and restated certificate of incorporation also provides that if Delaware law is amended after the approval by our stockholders of the amended and restated certificate of incorporation to authorize corporate action further eliminating or limiting the personal liability of directors, then the liability of our directors will be eliminated or limited to the fullest extent permitted by Delaware law.

Our bylaws, which will be amended and restated and in effect upon the completion of the offering, further provide that we must indemnify our directors and officers to the fullest extent permitted by Delaware law. The amended and restated bylaws also authorize us to indemnify any of our employees or agents and permit us to secure insurance on behalf of any officer, director, employee or agent for any liability arising out of his or her action in that capacity, whether or not Delaware law would otherwise permit indemnification.

In addition, our amended and restated bylaws provide that we are required to advance expenses to our directors and officers as incurred in connection with legal proceedings against them for which they may be indemnified and that the rights conferred in the amended and restated bylaws are not exclusive.

At present, there is no pending litigation or proceeding involving any of our directors, officers or employees for which indemnification is sought, and we are not aware of any threatened litigation that may result in claims for indemnification.

We intend to enter into indemnification agreements with each of our directors and executive officers. These agreements, among other things, would require us to indemnify each director and officer to the fullest extent permitted by Delaware law, the amended and restated certificate of incorporation and amended and restated bylaws, for expenses such as, among other things, attorneys' fees, judgments, fines, and settlement amounts incurred by the director or executive officer in any action or proceeding, including any action by or in our right, arising out of the person's services as our director or executive officer or as the director or executive officer of any subsidiary of ours or any other company or enterprise to which the person provides services at our request. We also maintain directors' and officers' liability insurance.

The SEC has taken the position that personal liability of directors for violation of the federal securities laws cannot be limited and that indemnification by us for any such violation is unenforceable. The limitation of liability and indemnification provisions in our amended and restated certificate of incorporation and amended and restated bylaws may discourage stockholders from bringing a lawsuit against our directors and officers for breach of their fiduciary duty. They may also reduce the likelihood of derivative litigation against our directors and officers, even though an action, if successful, might benefit us and other stockholders. Further, a stockholder's investment may be adversely affected to the extent that we pay the costs of settlement and damage awards against directors and officers as required by these indemnification provisions.

Item 15. Recent Sales of Unregistered Securities

Set forth below is information regarding securities we have issued within the past three years that were not registered under the Securities Act:

(1) Issuances of Capital Stock

On August 2, 2011, the Registrant issued and sold to investors an aggregate of 13,202,932 shares of its Series C preferred stock and warrants to purchase 10,471,282 shares of its common stock, at a purchase price of $1.15 per share, for aggregate consideration of approximately $15,183,371, which was paid for in cash.

On May 13, 2014, the Registrant issued and sold to investors an aggregate of 52,813,827 shares of its Series D preferred stock, at a purchase price of $0.588656 per share, for aggregate consideration of $25,000,000. This included 10,344,201 shares of its Series D preferred stock in exchange for conversion of approximately $4,565,934 of principal indebtedness and unpaid accrued interest thereon under the promissory notes described in paragraph (2) below, at a conversion price of $0.4414 per share, which represented a 25% discount on the purchase price per share of the Registrant's Series D preferred stock issued and sold in the offering.

(2) Sale of Convertible Promissory Notes

On September 4, 2013, the Registrant issued and sold to investors convertible promissory notes in the aggregate principal amount of $4,338,660, which notes bore interest at the rate of 8% per annum.

(3) Stock Option Grants and Exercises

During the three-year period ended July 31, 2014, we have granted to employees, consultants and directors options to purchase 17,982,120 shares of our common stock under our 2006 Equity Incentive

Plan, as amended and in effect from time to time. The exercise price per share ranged from $0.08 to $1.40. Options to purchase shares of our common stock pursuant to our 2006 Equity Incentive Plan, as amended and in effect from time to time, generally vest either 25% on the first anniversary of the vesting start date, with the remainder vesting in 12 equal quarterly installments, or in 16 equal quarterly installments.

During the three year period ended July 31, 2014, an aggregate of 164,487 shares of our common stock were issued upon exercise of outstanding stock options granted under our 2006 Equity Incentive Plan, as amended and in effect from time to time, with exercise prices ranging from $0.08 to $0.20 per share.

No underwriters were involved in the foregoing issuances of securities. The offers, sales and issuances of the securities described above were deemed to be exempt from registration under the Securities Act in reliance upon Rule 701 or Section 4(a)(2) of the Securities Act. The offers, sales and issuances of the securities that were deemed to be exempt in reliance on Rule 701 were transactions under compensatory benefit plans and contracts relating to compensation as provided under Rule 701. The offers, sales and issuances of the securities that were deemed to be exempt in reliance upon Section 4(a)(2) were each transactions not involving any public offering, and all recipients of these securities were accredited investors within the meaning of Rule 501 of Regulation D of the Securities Act who were acquiring the applicable securities for investment and not distribution and had represented that they could bear the risks of the investment. Each of the recipients of securities in these transactions had adequate access, through employment, business or other relationships, to information about us.

Item 16. Exhibits and Financial Statement Schedules.

(a) Exhibits

Exhibit No.	Description
1.1*	Form of Underwriting Agreement.
3.1(1)	Fifth Amended and Restated Certificate of Incorporation of the Company, as currently in effect.
3.2*	Form of Amended and Restated Certificate of Incorporation of the Company, to be in effect upon completion of the offering.
3.3(1)	Bylaws of the Company, as currently in effect.
3.4*	Form of Amended and Restated Bylaws of the Company, to be in effect upon completion of the offering.
4.1*	Form of Common Stock Certificate.
4.2	Fourth Amended and Restated Investors' Rights Agreement, dated May 13, 2014, between the Company and certain investors named therein.
4.3	Series D Preferred Stock Purchase Agreement, dated May 13, 2014, between the Company and certain investors named therein.
5.1*	Form of Opinion of Bingham McCutchen LLP.
10.1†(1)	2006 Equity Incentive Plan, as amended on August 1, 2006, as further amended on June 25, 2007, as further amended on February 17, 2009, as further amended on February 25, 2009, as further amended on April 16, 2009, as further amended on August 2, 2011 and as further amended on May 8, 2014.
10.2*†	2014 Equity Incentive Plan.
10.3	Offer Letter by and between the Company and Daniel Gottlieb, dated July 19, 2007.

Exhibit No.	Description
10.4†	Employment Agreement by and between the Company and Timothy P. Noyes, dated April 14, 2006, as amended April 29, 2009.
10.5†	Employment Agreement by and between the Company and Steven Burke, dated July 25, 2006, as amended April 29, 2009.
10.6†	Employment Agreement by and between the Company and George Eldridge, dated September 9, 2013.
10.7†	Severance Agreement by and between the Company and Daniel Gottlieb, dated September 23, 2013.
10.8†*	Employment Agreement by and between the Company and F. Nicholas Franano, dated March 29, 2006, as amended by that Modification and Separation Agreement dated October 31, 2009.
10.9‡(1)	Process Development and Manufacturing Services Agreement by and between the Company and Lonza Ltd., dated September 1, 2009 (as amended by that Amendment No. 1 entered into as of February 21, 2012).
10.10	Lease Agreement by and between the Company and Boston Properties Limited Partnership, dated July 13, 2009, as amended by that Amendment No. 1 dated September 14, 2012, as amended by that Amendment No. 2 dated October 17, 2013, as amended by that Amendment No. 3 dated August 4, 2014.
10.11(1)	Assignment of Rights/License Agreement, effective as of February 4, 2002, by and between Johns Hopkins University and F. Nicholas Franano.
10.12(1)	Assignment of Patent made and entered into as of December 30, 2002, by and between F. Nicholas Franano and Proteon Therapeutics, L.L.C.
10.13	Letter agreement, dated October 1, 2010, among the National Institutes of Health, F. Nicholas Franano and the Company.
10.14	Letter agreement, dated January 12, 2009, by and between F. Nicholas Franano and the Company (as successor-in-interest to Proteon Therapeutics, L.L.C.).
10.15	Quitclaim Deed, dated January 17, 2011, by F. Nicholas Franano to the Company.
10.16‡(1)	Form of Stock Option Grant Notice and Stock Option Agreement under the Company's 2006 Equity Incentive Plan, as amended.
10.17(1)	Indemnification Agreement, dated as of March 29, 2006, by and between the Company and Brendan O'Leary.
10.18(1)	Indemnification Agreement, dated as of June 26, 2007, by and between the Company and Hubert Birner.
10.19(1)	Indemnification Agreement, dated as of September 12, 2012, by and between the Company and Todd Foley.
10.20	Indemnification Agreement, dated as of February 6, 2013, by and between the Company and F. Nicholas Franano.
10.21(1)	Indemnification Agreement, dated as of February 6, 2013, by and between the Company and Timothy P. Noyes.
10.22	Indemnification Agreement, dated as of February 6, 2013, by and between the Company and Gregory D. Phelps.

Exhibit No.	Description
10.23(1)	Indemnification Agreement, dated as of May 13, 2014, by and between the Company and Tim Haines.
10.24(1)	Indemnification Agreement, dated as of May 13, 2014, by and between the Company and Dmitry Kobyzev.
21.1(1)	List of Subsidiaries.
23.1*	Consent of Bingham McCutchen LLP (included in Exhibit 5.1).
23.2*	Consent of Ernst & Young LLP, independent registered public accounting firm.
24.1*	Power of Attorney (included on signature page).

* To be filed by amendment

† Indicates management contract or compensation plan

‡ Indicates confidential treatment has been requested with respect to specific portions of this exhibit. Omitted portions have been filed with the Securities and Exchange Commission pursuant to Rule 406 of the Securities Act of 1933, as amended.

(1) Indicates previously filed

(b) Financial Statement Schedules

All schedules have been omitted because they are not required or because the required information is given in the financial statements or notes to those statements.

Item 17. Undertakings.

The undersigned Registrant hereby undertakes to provide to the underwriters at the closing specified in the underwriting agreement certificates in such denominations and registered in such names as required by the underwriters to permit prompt delivery to each purchaser.

Insofar as indemnification for liabilities arising under the Securities Act may be permitted to directors, officers and controlling persons of the Registrant pursuant to the foregoing provisions, or otherwise, the Registrant has been advised that in the opinion of the Securities and Exchange Commission such indemnification is against public policy as expressed in the Act and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the Registrant of expenses incurred or paid by a director, officer or controlling person of the Registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the Registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Act and will be governed by the final adjudication of such issue.

The undersigned Registrant hereby undertakes that:

(1) For purposes of determining any liability under the Securities Act, the information omitted from the form of prospectus filed as part of this registration statement in reliance upon Rule 430A and contained in a form of prospectus filed by the Registrant pursuant to Rule 424(b)(1) or (4) or 497(h) under the Securities Act shall be deemed to be part of this registration statement as of the time it was declared effective.

(2) For the purpose of determining any liability under the Securities Act, each post-effective amendment that contains a form of prospectus shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial *bona fide* offering thereof.

SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, as amended, the Registrant has duly caused this Registration Statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the city of Waltham, Commonwealth of Massachusetts on , 2014.

PROTEON THERAPEUTICS, INC.

By: _____

Timothy P. Noyes
President & Chief Executive Officer

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Timothy P. Noyes and George Eldridge his true and lawful attorney-in-fact and agent with full power of substitution, for him and in his name, place and stead, in any and all capacities, to sign any and all amendments (including post-effective amendments) to this registration statement, and to sign any registration statement for the same offering covered by the registration statement that is to be effective upon filing pursuant to Rule 462(b) promulgated under the Securities Act, and all post-effective amendments thereto, and to file the same, with all exhibits thereto and all documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorney-in-fact and agent, full power and authority to do and perform each and every act and thing requisite and necessary to be done in and about the premises, as fully to all intents and purposes as he might or could do in person, hereby ratifying and confirming that all said attorneys-in-fact and agents or any of them, or his or their substitute or substitutes, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Act of 1933, as amended, this Registration Statement has been signed by the following persons in the capacities and on the dates indicated.

Name	Title	Date
Timothy P. Noyes	President, Chief Executive Officer and Director (*Principal Executive Officer*)	, 2014
George Eldridge	Chief Financial Officer (*Principal Financial Officer and Principal Accounting Officer*)	, 2014
Hubert Birner, Ph.D.	Director	, 2014
Todd Foley	Director	, 2014
F. Nicholas Franano, M.D.	Director	, 2014
John G. Freund, M.D.	Director	, 2014
Tim Haines	Director	, 2014
Dmitry Kobyzev, Ph.D.	Director	, 2014
Brendan M. O'Leary, Ph.D.	Director	, 2014
Gregory D. Phelps	Director	, 2014

EXHIBIT INDEX

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21.1(1)	List of Subsidiaries.
23.1*	Consent of Bingham McCutchen LLP (included in Exhibit 5.1).
23.2*	Consent of Ernst & Young LLP, independent registered public accounting firm.
24.1*	Power of Attorney (included on signature page).

* To be filed by amendment

† Indicates management contract or compensation plan

‡ Indicates confidential treatment has been requested with respect to specific portions of this exhibit. Omitted portions have been filed with the Securities and Exchange Commission pursuant to Rule 406 of the Securities Act of 1933, as amended.

(1) Indicates previously filed

Exhibit 4.2

Execution Version

FOURTH AMENDED AND RESTATED INVESTORS' RIGHTS AGREEMENT

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FOURTH AMENDED AND RESTATED INVESTORS' RIGHTS AGREEMENT

THIS FOURTH AMENDED AND RESTATED INVESTORS' RIGHTS AGREEMENT ("**Agreement**") is made as of the 13th day of May, 2014, by and between Proteon Therapeutics, Inc., a Delaware corporation (the "**Company**"), each of the investors listed on Schedule A hereto (the "**Series A Investors**"), each of the investors listed on Schedule B hereto (the "**Series A-1 Investors**"), each of the investors listed on Schedule C hereto (the "**Series B Investors**"), each of the investors listed on Schedule D hereto (the "**Series C Investors**") and each of the investors listed on Schedule E hereto (the "**Series D Investors**"), together with any persons or entities that become parties hereto pursuant to Section 6.9 (the Series A Investors, the Series A-1 Investors, the Series B Investors, the Series C Investors, the Series D Investors and such persons or entities, collectively, the "**Investors**").

RECITALS

WHEREAS, the Company and certain of the Investors are parties to an Third Amended and Restated Investor Rights Agreement dated as of August 2, 2011, as previously amended and in effect prior to the date hereof (the "**Prior Agreement**");

WHEREAS, the Company has entered into a Series D Preferred Stock Purchase Agreement dated as of May 13, 2014 (as amended and in effect from time to time, the "**Purchase Agreement**") with the Series D Investors, pursuant to which the Company will issue shares of Series D Preferred Stock (as defined below) to such Series D Investors;

WHEREAS, the Series D Investors have made it a condition precedent to their purchase of shares of Series D Preferred Stock pursuant to the Purchase Agreement that the parties enter into this Agreement;

WHEREAS, the Company and Series A Investors, Series A-1 Investors, Series B Investors and Series C Investors holding the requisite number of shares of Registrable Securities (as defined in the Prior Agreement) desire to amend and restate the Prior Agreement in the manner provided below; and

WHEREAS, in order to induce the Series D Investors to invest funds in the Company pursuant to the Purchase Agreement, the Investors and the Company hereby agree that this Agreement shall govern the rights of the Investors to cause the Company to register shares of Common Stock issuable to the Investors, to receive certain information from the Company, to participate in future equity offerings by the Company and certain other matters as set forth in this Agreement.

NOW, THEREFORE, the parties hereby agree as follows:

1. Definitions. For purposes of this Agreement:

"**Agreement**" shall have the meaning set forth in the Preamble.

"**Affiliate**" means, with respect to any specified Person, any other Person who or which, directly or indirectly, controls, is controlled by, or is under common control with such

specified Person, including without limitation any partner, officer, director, manager or employee of such Person and any venture capital fund now or hereafter existing that is controlled by or under common control with one or more general partners or managing members of, or shares the same management company with, such Person.

"**Charter**" means the Company's Fifth Amended and Restated Certificate of Incorporation, as amended and in effect from time to time.

"**Common Stock**" means shares of the Company's common stock, par value $0.001 per share.

"**Company**" shall have the meaning set forth in the Preamble.

"**Damages**" means any loss, claim, damage, or liability (joint or several) to which a party hereto may become subject under the Securities Act, the Exchange Act, or other federal or state law, insofar as such loss, claim, damage, or liability (or any action in respect thereof) arises out of or is based upon (i) any untrue statement or alleged untrue statement of a material fact contained in any registration statement of the Company, including any preliminary prospectus or final prospectus contained therein or any amendments or supplements thereto; (ii) an omission or alleged omission to state therein a material fact required to be stated therein, or necessary to make the statements therein not misleading; or (iii) any violation or alleged violation by any other party hereto of the Securities Act, the Exchange Act, any state securities law, or any rule or regulation promulgated under the Securities Act, the Exchange Act, or any state securities law.

"**Demand Notice**" shall have the meaning set forth in Section 2.1.

"**Derivative Securities**" means any securities or rights convertible into, or exercisable or exchangeable for, Preferred Stock or Common Stock, including options and warrants.

"**Exchange Act**" means the Securities Exchange Act of 1934, as amended, and the rules and regulations promulgated thereunder.

"**Excluded Registration**" means a registration relating either to the sale of securities to employees of the Company pursuant to a stock option, stock purchase, or similar plan or to an SEC Rule 145 transaction; a registration on any form that does not include substantially the same information as would be required to be included in a registration statement covering the sale of the Registrable Securities; or a registration in which the only Common Stock being registered is Common Stock issuable upon conversion of debt securities that are also being registered.

"**Final Prospectus**" shall have the meaning set forth in Section 2.9(d).

"**Form S-3**" means such form under the Securities Act as in effect on the date hereof or any registration form under the Securities Act subsequently adopted by the SEC that permits incorporation of substantial information by reference to other documents filed by the Company with the SEC.

"**Fully Exercising Investor**" shall have the meaning set forth in Section 4.1(c).

"**GAAP**" means generally accepted accounting principles in the United States.

"**Holder**" means any holder of Registrable Securities who is a party to this Agreement.

"Immediate Family Member" means a child, stepchild, grandchild, parent, stepparent, grandparent, spouse, sibling, mother-in-law, father-in-law, son-in-law, daughter-in-law, brother-in-law, or sister-in-law, including adoptive relationships, of a natural person referred to herein.

"**Initiating Holders**" means, collectively, Holders who properly initiate a registration request under this Agreement.

"**IPO"** means the Company's first underwritten public offering of its Common Stock under the Securities Act.

"**Investors**" shall have the meaning set forth in the Preamble.

"Key Person" means Timothy Noyes, Steven Burke, any executive-level employee (including division director and vice president-level positions) and any employee who, either alone or in concert with others, develops, invents, programs, or designs any Company Intellectual Property (as defined in the Purchase Agreement).

"**Major Holder**" means any Investor that, individually or together with such Investor's Affiliates, holds at least 2,000,000 shares of Registrable Securities (as adjusted for any stock split, stock dividend, combination, or other recapitalization or reclassification effected after the date hereof).

"**New Securities**" means, collectively, equity securities of the Company, whether or not currently authorized, as well as rights, options, or warrants to purchase such equity securities, or securities of any type whatsoever that are, or may become, convertible or exchangeable into or exercisable for such equity securities.

"**Offer Notice**" shall have the meaning set forth in Section 4.1(b).

"**Person**" means any individual**,** corporation**,** partnership, trust, limited liability company, association or other entity.

"**Preferred Director**" means each of (i) the directors of the Company that the holders of record of Series D Preferred Stock, exclusively, are entitled to elect, (ii) the director of the Company that the holders of record of Series B Preferred Stock, exclusively, are entitled to elect and (iii) the directors of the Company that the holders of record of Series A Preferred Stock and Series A-1 Preferred Stock, exclusively and voting together as single class, are entitled to elect, in each case pursuant to the Charter.

"**Preferred Stock**" means, collectively, shares of the Company's Series A Preferred Stock, Series A-1 Preferred Stock, Series B Preferred Stock, Series C Preferred Stock, and Series D Preferred Stock.

"**Prior Agreement**" shall have the meaning set forth in the Recitals.

"**Purchase Agreement**" shall have the meaning set forth in the Recitals.

"**Qualified Investors**" shall have the meaning set forth in Section 4.1.

"**Register**," "**registered**," and "**registration**" refer to a registration effected by preparing and filing a registration statement or similar document in compliance with the Securities Act, and the declaration or ordering of effectiveness of such registration statement or document.

"**Registrable Securities**" means (i) the Common Stock issuable or issued upon conversion of the Preferred Stock; (ii) Common Stock issuable or issued pursuant to the Purchase Agreement; (iii) the Warrant Shares; and (iv) any Common Stock issued as (or issuable upon the conversion or exercise of any warrant, right, or other security that is issued as) a dividend or other distribution with respect to, or in exchange for or in replacement of, the shares referenced in clauses (i)-(iii) above; excluding in all cases, however, any Registrable Securities sold by a Person in a transaction in which the rights under Section 2 hereof are not assigned or any shares for which registration rights have terminated pursuant to Section 2.15 of this Agreement.

"**Registrable Securities then outstanding**" means the number of shares of Registrable Securities determined by adding the shares of Common Stock outstanding that are Registrable Securities and the shares of Common Stock issuable pursuant to then exercisable or convertible securities that are Registrable Securities.

"**Restricted Securities**" means the securities of the Company required to bear the legend set forth in Section 2.14(b).

"**Right of First Refusal and Co-Sale Agreement**" means the Fourth Amended and Restated Right of First Refusal and Co-Sale Agreement dated as of the date hereof by and among the Company, the Investors and certain other holders of the Company's capital stock, as amended and in effect from time to time.

"**S-3 Notice**" shall have the meaning set forth in Section 2.3(a).

"**SEC**" means the Securities and Exchange Commission.

"**SEC Rule 144**" means Rule 144 promulgated by the SEC under the Securities Act.

"**SEC Rule 145**" means Rule 145 promulgated by the SEC under the Securities Act.

"**Securities Act**" means the Securities Act of 1933, as amended, and the rules and regulations promulgated thereunder.

"**Selling Expenses**" means all underwriting discounts, selling commissions, and stock transfer taxes applicable to the sale of Registrable Securities, and fees and disbursements of one counsel for the Holders, except as provided in Section 2.7.

"**Series A Investors**" shall have the meaning set forth in the Preamble.

"**Series A Preferred Stock**" means shares of the Company's Series A Preferred Stock, par value $0.001 per share.

"**Series A-1 Investors**" shall have the meaning set forth in the Preamble.

"**Series A-1 Preferred Stock**" means shares of the Company's Series A-1 Preferred Stock, par value $0.001 per share.

"**Series B Investors**" shall have the meaning set forth in the Preamble.

"**Series B Preferred Stock**" means shares of the Company's Series B Preferred Stock, par value $0.001 per share.

"**Series C Investors**" shall have the meaning set forth in the Preamble.

"**Series C Preferred Stock**" means shares of the Company's Series C Preferred Stock, par value $0.001 per share.

"**Series C Purchase Agreement**" means that certain Series C Preferred Stock and Warrant Purchase Agreement, dated as of August 2, 2011, by and among the Company and the Series C Investors, as amended and in effect from time to time.

"**Series D Investors**" shall have the meaning set forth in the Preamble.

"**Series D Preferred Stock**" means shares of the Company's Series D Preferred Stock, par value $0.001 per share.

"**Voting Agreement**" means the Fourth Amended and Restated Voting Agreement dated as of the date hereof by and among the Company, the Investors and certain other holders of the Company's capital stock, as amended and in effect from time to time.

"**Warrants**" means the warrants issued to the Series C Investors pursuant to, and in accordance with, the terms and conditions of the Series C Purchase Agreement.

"**Warrant Shares**" means the shares of Common Stock issued or issuable upon the exercise of the Warrants.

2. Registration Rights. The Company covenants and agrees as follows:

2.1. Demand Registration.

(a) If at any time after the earlier of (i) four (4) years after the date of this Agreement or (ii) one hundred eighty (180) calendar days after the effective date of the registration statement for the IPO, the Company receives a request from Holders of a majority of the Registrable Securities then outstanding that the Company effect a registration with respect to an amount of the Registrable Securities then outstanding, then the Company shall (i) within ten (10) calendar days after the date such request is given, give notice thereof (the "**Demand Notice**") to all Holders other than the Initiating Holders; and (ii) as soon as practicable, and in any event within sixty (60) calendar days after the date such request is given by the Initiating Holders, file a registration statement under the Securities Act covering all Registrable Securities that the Initiating Holders requested to be registered and any additional Registrable Securities requested to be included in such registration by any other Holders, as specified by notice given by each such Holder to the Company within twenty (20) calendar days of the date the Demand Notice is given, and in each case, subject to the limitations of Section 2.1(b).

(b) Notwithstanding the foregoing obligations, if the Company furnishes to Holders requesting a registration pursuant to this Section 2.1 a certificate signed by the Company's chief executive officer stating that in the good faith judgment of the Company's Board of Directors it would be materially detrimental to the Company and its stockholders for such registration statement to either become effective or remain effective for as long as such registration statement otherwise would be required to remain effective, because such action would (i) materially interfere with a significant acquisition, corporate reorganization, or other similar transaction involving the Company; (ii) require premature disclosure of material information that the Company has a bona fide business purpose for preserving as confidential; or (iii) render the Company unable to comply with requirements under the Securities Act or Exchange Act, then the Company shall have the right to defer taking action with respect to such filing, and any time periods with respect to filing or effectiveness thereof shall be tolled correspondingly, for a period of not more than sixty (60) calendar days after the request of the Initiating Holders is given; provided, however, that the Company may not invoke this right more than once in any twelve (12) month period; and provided further that the Company shall not register any securities for its own account or that of any other stockholder during such sixty (60) day period other than pursuant to a registration relating to the sale of securities to employees of the Company pursuant to a stock option, stock purchase, or similar plan; a registration on any form that does not include substantially the same information as would be required to be included in a registration statement covering the sale of the Registrable Securities; or a registration in which the only Common Stock being registered is Common Stock issuable upon conversion of debt securities that are also being registered.

(c) The Company shall not be obligated to effect, or to take any action to effect, any registration pursuant to this Section 2.1 (i) during the period that is sixty (60) calendar days before the Company's good faith estimate of the date of filing of, and ending on a date that is one hundred eighty (180) calendar days after the effective date of, a Company-initiated registration, provided, that the Company is actively employing in good faith commercially reasonable efforts to cause such registration statement to become effective; (ii)

after the Company has effected two registrations; (iii) if the Holders, together with the holders of any other securities of the Company entitled to and requesting inclusion in such registration, propose to sell Registrable Securities and such other securities (if any) at an aggregate price to the public (net of Selling Expenses) of less than $5,000,000; or (iv) if, in a distribution not underwritten, the Initiating Holders propose to dispose of shares of Registrable Securities that may be immediately registered on Form S-3 pursuant to a request made pursuant to Section 2.3. A registration shall not be counted as "effected" for purposes of this Section 2.1 until such time as the applicable registration statement has been declared effective by the SEC, unless the Initiating Holders withdraw their request for such registration, elect not to pay the registration expenses therefor, and forfeit their right to one demand registration statement pursuant to Section 2.7, in which case such withdrawn registration statement shall be counted as "effected" for purposes of this Section 2.1.

2.2. Company Registration. If the Company proposes to register (including, for this purpose, a registration effected by the Company for stockholders other than the Holders) any of its stock or other securities under the Securities Act in connection with the public offering of such securities solely for cash (other than an Excluded Registration), the Company shall, at such time, promptly give each Holder notice of such registration. Upon the request of each Holder given within twenty (20) calendar days after such notice is given by the Company, the Company shall, subject to the provisions of Section 2.4, cause to be registered all of the Registrable Securities that each such Holder has requested to be included in such registration. The Company shall have the right to terminate or withdraw any registration initiated by it under this Section 2.2 before the effective date of such registration, whether or not any Holder has elected to include Registrable Securities in such registration. The expenses of such withdrawn registration shall be borne by the Company in accordance with Section 2.7.

2.3. Form S-3 Registration. If the Company receives a request from one or more Holders of the Registrable Securities then outstanding that the Company effect a registration on Form S-3 with respect to all or a part of the Registrable Securities owned by such Initiating Holders, then the Company shall:

(a) within ten (10) calendar days after the date such request is given, give notice of the proposed registration to all Holders other than the Initiating Holders (the "**S-3 Notice**"); and

(b) as soon as practicable, use its commercially reasonable efforts to effect such registration as would permit or facilitate the sale and distribution of all or such portion of such Initiating Holders' Registrable Securities as are specified in such request, together with all or such portion of the Registrable Securities of any other

Holders joining in such request as are specified in a request given to the Company within fifteen (15) calendar days after the S-3 Notice is given; provided, however, that the Company shall not be obligated to effect any such registration pursuant to this Section 2.3 (i) if Form S-3 is not then available for such offering by the Holders; (ii) if the Holders, together with the holders of any other securities of the Company entitled to and requesting inclusion in such registration, propose to sell Registrable Securities and such other securities (if any) at an aggregate price to the public (without regard to Selling Expenses) of less than $1,000,000; (iii) if the Company furnishes to the Holders a certificate signed by the chief executive officer of the Company stating that in the

good-faith judgment of the Board of Directors of the Company, it would be materially detrimental to the Company and its stockholders for such Form S-3 registration to be effected at such time, in which event the Company shall have the right to defer the filing of the Form S-3 registration statement for a period of not more than sixty (60) calendar days after receipt of the request of the Initiating Holders under this Section 2.3; provided, however, that the Company shall not invoke this right more than once in any twelve (12) month period; and provided further that the Company shall not register any securities for its own account or that of any other stockholder during such sixty (60) day period other than pursuant to a registration relating to the sale of securities to employees of the Company pursuant to a stock option, stock purchase, or similar plan; a registration on any form that does not include substantially the same information as would be required to be included in a registration statement covering the sale of the Registrable Securities; or a registration in which the only Common Stock being registered is Common Stock issuable upon conversion of debt securities that are also being registered; or (iv) if the Company has, within the twelve (12) month period preceding the date of such request, already effected two registrations on Form S-3 for the Holders pursuant to this Section 2.3; or (v) during the period ending one hundred eighty (180) calendar days after the effective date of a registration made under Section 2.2 hereof.

(c) Registrations effected pursuant to this Section 2.3 shall not be counted as demands for registration or registrations effected pursuant to Section 2.1.

2.4. Underwriting Requirements.

(a) If, pursuant to Section 2.1 or Section 2.3, the Initiating Holders intend to distribute the Registrable Securities covered by their request by means of an underwriting, they shall so advise the Company as a part of their request made pursuant to Section 2.1(a) or Section 2.3, and the Company shall include such information in the Demand Notice or the S-3 Notice, as the case may be. The underwriter will be selected by the Company and shall be reasonably acceptable to a majority in interest of the Initiating Holders. In such event, the right of any Holder to include such Holder's Registrable Securities in such registration shall be conditioned upon such Holder's participation in such underwriting and the inclusion of such Holder's Registrable Securities in the underwriting to the extent provided herein. All Holders proposing to distribute their securities through such underwriting shall (together with the Company as provided in Section 2.5(e)) enter into an underwriting agreement in customary form with the underwriter(s) selected for such underwriting. Notwithstanding any other provision of this Section 2.4, if the underwriter(s) advise(s) the Initiating Holders in writing that marketing factors require a limitation on the number of shares to be underwritten, then the Initiating Holders shall so advise all Holders of Registrable Securities that otherwise would be underwritten pursuant hereto, and the number of Registrable Securities that may be included in the underwriting shall be allocated among all Holders of Registrable Securities, including the Initiating Holders, in proportion (as nearly as practicable) to the number of Registrable Securities of the Company owned by each Holder; provided, however, that the number of Registrable Securities held by the Holders to be included in such underwriting shall not be reduced unless all other securities are first entirely excluded from the underwriting. To facilitate the allocation of shares in accordance with the above provisions, the Company or the underwriters may round the number of shares allocated to any Holder to the nearest 100 shares.

(b) In connection with any offering involving an underwriting of shares of the Company's capital stock pursuant to Section 2.2, the Company shall not be required to include any of the Holders' Registrable Securities in such underwriting unless the Holders accept the terms of the underwriting as agreed upon between the Company and its underwriters, and then only in such quantity as the underwriters in their sole discretion determine will not jeopardize the success of the offering by the Company. If the total number of securities, including Registrable Securities, requested by stockholders to be included in such offering exceeds the number of securities to be sold (other than by the Company) that the underwriters in their reasonable discretion determine is compatible with the success of the offering, then the Company shall be required to include in the offering only that number of such securities, including Registrable Securities, which the underwriters and the Company in their sole discretion determine will not jeopardize the success of the offering. In no event shall any Registrable Securities be excluded from such offering unless all other stockholders' securities have been first excluded. If the underwriters determine that less than all of the Registrable Securities requested to be registered can be included in such offering, then the Registrable Securities that are included in such offering shall be apportioned pro rata among the selling Holders based on the number of Registrable Securities held by all selling Holders or in such other proportions as shall mutually be agreed to by all such selling Holders. Notwithstanding the foregoing, in no event shall the number of Registrable Securities included in the offering be reduced below thirty percent (30%) of the total number of securities included in such offering, unless such offering is the IPO, in which case the selling Holders may be excluded further if the underwriters make the determination described above and no other stockholder's securities are included in such offering. For purposes of the provision in this Section 2.4(b) concerning apportionment, for any selling stockholder that is a Holder and a partnership, limited liability company, or corporation, the partners, members, retired partners, retired members, stockholders, and Affiliates of such Holder, or the estates and Immediate Family Members of any such partners, retired partners, members, and retired members and any trusts for the benefit of any of the foregoing Persons, shall be deemed to be a single "selling Holder," and any pro rata reduction with respect to such "selling Holder" shall be based upon the aggregate number of Registrable Securities owned by all Persons included in such "selling Holder," as defined in this sentence.

(c) For purposes of Section 2.1 and Section 2.3, a registration shall not be counted as "effected" if, as a result of an exercise of the underwriter's cutback provisions in Section 2.4(a), fewer than seventy-five (75%) of the total number of Registrable Securities that Holders have requested to be included in such registration statement are actually included.

2.5. Obligations of the Company. Whenever required under this Section 2 to effect the registration of any Registrable Securities, the Company shall, as expeditiously as reasonably possible:

(a) prepare and file with the SEC a registration statement with respect to such Registrable Securities and use its commercially reasonable efforts to cause such registration statement to become effective and, upon the request of the Holders of a majority of the Registrable Securities registered thereunder, keep such registration statement effective for a period of up to one hundred twenty (120) calendar days or, if earlier, until the distribution contemplated in the registration statement has been completed; provided, however, that (i) such one hundred twenty (120) calendar day period shall be extended for a period of time equal to the

period the Holder refrains, at the request of an underwriter of Common Stock (or other securities) of the Company, from selling any securities included in such registration, and (ii) in the case of any registration of Registrable Securities on Form S-3 that are intended to be offered on a continuous or delayed basis, subject to compliance with applicable SEC rules, such one hundred twenty (120) calendar day period shall be extended for up to an additional one hundred twenty (120) calendar days, if necessary, to keep the registration statement effective until all such Registrable Securities are sold;

(b) prepare and file with the SEC such amendments and supplements to such registration statement, and the prospectus used in connection with such registration statement, as may be necessary to comply with the Securities Act in order to enable the disposition of all securities covered by such registration statement;

(c) furnish to the selling Holders such numbers of copies of a prospectus, including a preliminary prospectus, as required by the Securities Act, and such other documents as the Holders may reasonably request in order to facilitate their disposition of their Registrable Securities;

(d) use its commercially reasonable efforts to register and qualify the securities covered by such registration statement under such other securities or blue-sky laws of such jurisdictions as shall be reasonably requested by the selling Holders; provided that the Company shall not be required to qualify to do business or to file a general consent to service of process in any such states or jurisdictions, unless the Company is already subject to service in such jurisdiction and except as may be required by the Securities Act;

(e) in the event of any underwritten public offering, enter into and perform its obligations under an underwriting agreement, in usual and customary form, with the managing underwriter of such offering;

(f) use its commercially reasonable efforts to cause all such Registrable Securities covered by such registration statement to be listed on a national securities exchange or trading system and each securities exchange and trading system (if any) on which similar securities issued by the Company are then listed;

(g) provide a transfer agent and registrar for all Registrable Securities registered pursuant to this Agreement and provide a CUSIP number for all such Registrable Securities, in each case not later than the effective date of such registration;

(h) promptly make available for inspection by the selling Holders, any underwriter participating in any disposition pursuant to such registration statement, and any attorney or accountant or other agent retained by any such underwriter or selected by the selling Holders, all financial and other records, pertinent corporate documents, and properties of the Company, and cause the Company's officers, directors, employees, and independent accountants to supply all information reasonably requested by any such seller, underwriter, attorney, accountant, or agent in connection with any such registration statement;

(i) notify each selling Holder, promptly after the Company receives notice thereof, of the time when such registration statement has been declared effective or a supplement to any prospectus forming a part of such registration statement has been filed; and

(j) after such registration statement becomes effective, notify each selling Holder of any request by the SEC that the Company amend or supplement such registration statement or prospectus.

2.6. Furnish Information. It shall be a condition precedent to the obligations of the Company to take any action pursuant to this Section 2 with respect to the Registrable Securities of any selling Holder that such Holder shall furnish to the Company such information regarding itself, the Registrable Securities held by it, and the intended method of disposition of such securities as is reasonably required to effect the registration of such Holder's Registrable Securities.

2.7. Expenses of Registration. All expenses (other than Selling Expenses) incurred in connection with registrations, filings, or qualifications pursuant to Section 2, including all registration, filing, and qualification fees; printers' and accounting fees; fees and disbursements of counsel for the Company; and the reasonable fees and disbursements of one (1) counsel for the selling Holders, shall be borne and paid by the Company; provided, however, that the Company shall not be required to pay for any expenses of any registration proceeding begun pursuant to Section 2.1 or Section 2.3 if the registration request is subsequently withdrawn at the request of the Holders of a majority of the Registrable Securities to be registered (in which case all selling Holders shall bear such expenses pro rata based upon the number of Registrable Securities that were to be included in the withdrawn registration), unless the Holders of a majority of the Registrable Securities agree to forfeit their right to one (1) registration pursuant to Section 2.1 or Section 2.3, as the case may be; provided further that if, at the time of such withdrawal, the Holders have learned of a material adverse change in the condition, business, or prospects of the Company from that known to the Holders at the time of their request and have withdrawn the request with reasonable promptness after learning of such information, then the Holders shall not be required to pay any of such expenses and shall not forfeit their right to one registration pursuant to Section 2.1 or Section 2.3. All Selling Expenses relating to Registrable Securities registered pursuant to this Section 2 shall be borne and paid by the Holders pro rata on the basis of the number of Registrable Securities registered on their behalf.

2.8. Delay of Registration. No Holder shall have any right to obtain or seek an injunction restraining or otherwise delaying any registration pursuant to this Agreement as the result of any controversy that might arise with respect to the interpretation or implementation of this Section 2.

2.9. Indemnification. If any Registrable Securities are included in a registration statement under this Section 2:

(a) To the extent permitted by law, the Company will indemnify and hold harmless each selling Holder, and the partners, members, officers, directors, and stockholders of each such Holder; legal counsel and accountants for each such Holder; any underwriter (as defined in the Securities Act) for each such Holder; and each Person, if any, who

controls such Holder or underwriter within the meaning of the Securities Act or the Exchange Act, against any Damages, and the Company will pay to each such Holder, underwriter, controlling Person, or other aforementioned Person any legal or other expenses reasonably incurred thereby in connection with investigating any matter or defending any proceeding from which Damages may result, as such expenses are incurred; provided, however, that the indemnity agreement contained in this Section 2.9(a) shall not apply to amounts paid in settlement of any such investigation or proceeding if such settlement is effected without the consent of the Company, which consent shall not be unreasonably withheld, nor shall the Company be liable for any Damages to the extent that they arise out of or are based upon actions or omissions made in reliance upon and in conformity with written information furnished by or on behalf of any such Holder, underwriter, controlling Person, or other aforementioned Person expressly for use in connection with such registration.

(b) To the extent permitted by law, each selling Holder, severally and not jointly, will indemnify and hold harmless the Company, and each of its directors, each of its officers who has signed the registration statement, each Person (if any), who controls the Company within the meaning of the Securities Act, legal counsel and accountants for the Company, any underwriter (as defined in the Securities Act), any other Holder selling securities in such registration statement, and any controlling Person of any such underwriter or other Holder, against any Damages, in each case only to the extent that such Damages arise out of or are based upon actions or omissions made in reliance upon and in conformity with written information furnished by or on behalf of such selling Holder expressly for use in connection with such registration; and each such selling Holder will pay to the Company and each other aforementioned Person any legal or other expenses reasonably incurred thereby in connection with investigating any investigation or defending any proceeding from which Damages may result, as such expenses are incurred; provided, however, that the indemnity agreement contained in this Section 2.9(b) shall not apply to amounts paid in settlement of any such investigation or proceeding if such settlement is effected without the consent of the Holder, which consent shall not be unreasonably withheld; and provided further that in no event shall any indemnity under this Section 2.9(b) exceed the proceeds from the offering (net of any Selling Expenses) received by such Holder, except in the case of fraud or willful misconduct by such Holder.

(c) Promptly after receipt by an indemnified party under this Section 2.9 of notice of the commencement of any action (including any governmental action) for which a party may be entitled to indemnification hereunder, such indemnified party will, if a claim in respect thereof is to be made against any indemnifying party under this Section 2.9, give the indemnifying party notice of the commencement thereof. The indemnifying party shall have the right to participate in such action and, to the extent the indemnifying party so desires, participate jointly with any other indemnifying party to which notice has been given, and to assume the defense thereof with counsel mutually satisfactory to the parties; provided, however, that an indemnified party (together with all other indemnified parties that may be represented without conflict by one counsel) shall have the right to retain one (1) separate counsel, with the fees and expenses to be paid by the indemnifying party, if representation of such indemnified party by the counsel retained by the indemnifying party would be inappropriate due to actual or potential differing interests between such indemnified party and any other party represented by such counsel in such action. The failure to give notice to the indemnifying party within a reasonable time of the commencement of any such action shall relieve such indemnifying party of any

liability to the indemnified party under this Section 2.9, to the extent that such failure materially prejudices the indemnifying party's ability to defend such action. The failure to give notice to the indemnifying party will not relieve it of any liability that it may have to any indemnified party otherwise than under this Section 2.9.

(d) The foregoing indemnity agreements of the Company and the selling Holders are subject to the condition that, insofar as they relate to any Damages arising from any untrue statement or alleged untrue statement of a material fact contained in, or omission or alleged omission of a material fact from, a preliminary prospectus (or necessary to make the statements therein not misleading) that has been corrected in the form of prospectus included in the registration statement at the time it becomes effective, or any amendment or supplement thereto filed with the SEC pursuant to Rule 424(b) under the Securities Act (the "**Final Prospectus**"), such indemnity agreement shall not inure to the benefit of any Person if a copy of the Final Prospectus was furnished to the indemnified party and such indemnified party failed to deliver, at or before the confirmation of the sale of the shares registered in such offering, a copy of the Final Prospectus to the Person asserting the loss, liability, claim, or damage in any case in which such delivery was required by the Securities Act.

(e) To provide for just and equitable contribution to joint liability under the Securities Act in any case in which either (i) any party otherwise entitled to indemnification hereunder makes a claim for indemnification pursuant to this Section 2.9 but it is judicially determined (by the entry of a final judgment or decree by a court of competent jurisdiction and the expiration of time to appeal or the denial of the last right of appeal) that such indemnification may not be enforced in such case, notwithstanding the fact that this Section 2.9 provides for indemnification in such case, or (ii) contribution under the Securities Act may be required on the part of any party hereto for which indemnification is provided under this Section 2.9, then, and in each such case, such parties will contribute to the aggregate losses, claims, damages, liabilities, or expenses to which they may be subject (after contribution from others) in such proportion as is appropriate to reflect the relative fault of each of the indemnifying party and the indemnified party in connection with the statements, omissions, or other actions that resulted in such loss, claim, damage, liability, or expense, as well as to reflect any other relevant equitable considerations. The relative fault of the indemnifying party and of the indemnified party shall be determined by reference to, among other things, whether the untrue or allegedly untrue statement of a material fact, or the omission or alleged omission of a material fact, relates to information supplied by the indemnifying party or by the indemnified party and the parties' relative intent, knowledge, access to information, and opportunity to correct or prevent such statement or omission; provided, however, that, in any such case, (x) no Holder will be required to contribute any amount in excess of the public offering price of all such Registrable Securities offered and sold by such Holder pursuant to such registration statement, and (y) no Person guilty of fraudulent misrepresentation (within the meaning of Section 11(f) of the Securities Act) will be entitled to contribution from any Person who was not guilty of such fraudulent misrepresentation; and provided further that in no event shall a Holder's liability pursuant to this Section 2.9(e), when combined with the amounts paid or payable by such Holder pursuant to Section 2.9(b), exceed the proceeds from the offering (net of any Selling Expenses) received by such Holder, except in the case of willful misconduct or fraud by such Holder.

(f) Unless otherwise superseded by an underwriting agreement entered into in connection with the underwritten public offering, the obligations of the Company and Holders under this Section 2.9 shall survive the completion of any offering of Registrable Securities in a registration under this Section 2, and otherwise shall survive the termination of this Agreement.

2.10. Reports Under Exchange Act. With a view to making available to the Holders the benefits of SEC Rule 144 and any other rule or regulation of the SEC that may at any time permit a Holder to sell securities of the Company to the public without registration or pursuant to a registration on Form S-3, the Company shall:

(a) make and keep public information available, as those terms are understood and defined in SEC Rule 144, at all times after the effective date of the registration statement filed by the Company for the IPO;

(b) use commercially reasonable efforts to file with the SEC in a timely manner all reports and other documents required of the Company under the Securities Act and the Exchange Act (at any time after the Company has become subject to such reporting requirements); and

(c) furnish to any Holder, so long as the Holder owns any Registrable Securities, forthwith upon request (i) a written statement by the Company that it has complied with the reporting requirements of SEC Rule 144 (at any time after ninety (90) calendar days after the effective date of the registration statement filed by the Company for the IPO), the Securities Act, and the Exchange Act (at any time after the Company has become subject to such reporting requirements), or that it qualifies as a registrant whose securities may be resold pursuant to Form S-3 (at any time after the Company so qualifies); (ii) a copy of the most recent annual or quarterly report of the Company and such other reports and documents so filed by the Company; and (iii) such other information as may be reasonably requested in availing any Holder of any rule or regulation of the SEC that permits the selling of any such securities without registration (at any time after the Company has become subject to the reporting requirements under the Exchange Act) or pursuant to such Form S-3 (at any time after the Company so qualifies to use such form).

2.11. Limitations on Subsequent Registration Rights. From and after the date of this Agreement, the Company shall not, without the prior written consent of the Holders of at least seventy percent (70%) of the Registrable Securities then-outstanding and the holders of at least a majority of Registrable Securities issued or issuable upon conversion of the Series D Preferred Stock then-outstanding, enter into any agreement with any holder or prospective holder of any securities of the Company that would allow such holder or prospective holder (i) to include such securities in any registration unless, under the terms of such agreement, such holder or prospective holder may include such securities in any such registration only to the extent that the inclusion of such securities will not reduce the number of the Registrable Securities of the Holders that are included or (ii) to demand registration of any securities held by such holder or prospective holder; provided that this limitation shall not apply to any additional Holder who becomes a party to this Agreement in accordance with Section 6.9.

2.12. "Market Stand-off" Agreement. Each Holder hereby agrees that it will not, if such a request is made in writing by the managing underwriter, during the period commencing on the date of the final prospectus relating to the IPO and ending on the date specified by the Company and the managing underwriter (such period not to exceed one hundred eighty (180) calendar days) (i) lend; offer; pledge; sell; contract to sell; sell any option or contract to purchase; purchase any option or contract to sell; grant any option, right, or warrant to purchase; or otherwise transfer or dispose of, directly or indirectly, any shares of Common Stock or any securities convertible into or exercisable or exchangeable for Common Stock (whether such shares or any such securities are then owned by the Holder or are thereafter acquired); or (ii) enter into any swap or other arrangement that transfers to another, in whole or in part, any of the economic consequences of ownership of the Common Stock, whether any such transaction described in clause (i) or (ii) above is to be settled by delivery of Common Stock or other securities, in cash, or otherwise. The foregoing provisions of this Section 2.12 shall apply only to the IPO, shall not apply to the sale of any shares to an underwriter pursuant to an underwriting agreement, shall not apply to any shares issued under the Purchase Agreement after the closing of the IPO, shall not apply to any shares purchased by a Holder in the IPO, and shall be applicable to the Holders only if all officers, all directors, and all stockholders individually owning more than one percent (1%) of the Company's outstanding Common Stock are subject to the same restrictions. The underwriters in connection with the IPO are intended third-party beneficiaries of this Section 2.12 and shall have the right, power, and authority to enforce the provisions hereof as though they were a party hereto. Each Holder further agrees to execute such agreements as may be reasonably requested by the underwriters in the IPO that are consistent with this Section 2.12 or that are necessary to give further effect thereto. Any discretionary waiver or termination of the restrictions of any or all of such agreements by the Company or the underwriters shall apply pro rata to all Major Holders subject to such agreements, based on the number of shares held.

2.13. Assignment of Registration Rights. The rights to cause the Company to register Registrable Securities pursuant to this Section 2 may be assigned (but only with all related obligations) by a Holder to a transferee of such Registrable Securities that (i) is an Affiliate, partner, member, limited partner, retired partner, retired member, or stockholder of a Holder; (ii) is a Holder's Immediate Family Member or trust for the benefit of an individual Holder or one or more of such Holder's Immediate Family Members;

or (iii) after such transfer, holds at least 500,000 shares of Registrable Securities (subject to appropriate adjustment for stock splits, stock dividends, combinations, and other recapitalizations); provided, however, that (x) the Company is, within a reasonable time after such transfer, furnished with written notice of the name and address of such transferee and the Registrable Securities with respect to which such registration rights are being transferred; and (y) such transferee agrees in writing to be bound by and subject to the terms and conditions of this Agreement, including the provisions of Section 2.12. For the purposes of determining the number of shares of Registrable Securities held by a transferee, the holdings of a transferee (1) that is an Affiliate, limited partner, retired partner, member, retired member, or stockholder of a Holder; (2) who is a Holder's Immediate Family Member; or (3) that is a trust for the benefit of an individual Holder or such Holder's Immediate Family Member shall be aggregated together and with those of the transferring Holder; provided further that all transferees who would not qualify individually for assignment of registration rights shall have a single attorney-in-fact for the purpose of exercising any rights, receiving notices, or taking any action under this Section 2.

2.14. Restrictions on Transfer.

(a) The Preferred Stock and the Registrable Securities shall not be sold, pledged, or otherwise transferred, and the Company shall not recognize any such sale, pledge, or transfer, except upon the conditions specified in (i) the Right of First Refusal and Co-Sale Agreement; and (ii) this Agreement, which conditions are intended, among other things, to ensure compliance with the provisions of the Securities Act. A transferring Holder will cause any proposed purchaser, pledgee, or transferee of the Preferred Stock and the Registrable Securities held by such Holder to agree to take and hold such securities subject to the provisions and upon the conditions specified in the Right of First Refusal and Co-Sale Agreement and this Agreement.

(b) Each certificate representing (i) the Preferred Stock, (ii) the Registrable Securities, and (iii) any other securities issued in respect of the securities referenced in clauses (i) and (ii), upon any stock split, stock dividend, recapitalization, merger, consolidation, or similar event, shall (unless otherwise permitted by the provisions of Section 2.14(c)) be stamped or otherwise imprinted with a legend in the following form:

> THE SHARES REPRESENTED BY THIS CERTIFICATE HAVE NOT BEEN REGISTERED UNDER THE SECURITIES ACT OF 1933, AND HAVE BEEN ACQUIRED FOR INVESTMENT AND NOT WITH A VIEW TO, OR IN CONNECTION WITH, THE SALE OR DISTRIBUTION THEREOF. NO SUCH TRANSFER MAY BE EFFECTED WITHOUT AN EFFECTIVE REGISTRATION STATEMENT RELATED THERETO OR AN OPINION OF COUNSEL IN A FORM SATISFACTORY TO THE COMPANY THAT SUCH REGISTRATION IS NOT REQUIRED UNDER THE SECURITIES ACT OF 1933.
>
> THE SHARES REPRESENTED BY THIS CERTIFICATE MAY BE TRANSFERRED ONLY IN ACCORDANCE WITH THE TERMS OF A CERTAIN INVESTORS' RIGHTS AGREEMENT BETWEEN THE COMPANY AND THE STOCKHOLDER, A COPY OF WHICH IS ON FILE WITH THE SECRETARY OF THE COMPANY.

The Holders consent to the Company making a notation in its records and giving instructions to any transfer agent of the Restricted Securities in order to implement the restrictions on transfer set forth in this Section 2.14.

(c) The holder of each certificate representing Restricted Securities, by acceptance thereof, agrees to comply in all respects with the provisions of this Section 2. Before any proposed sale, pledge, or transfer of any Restricted Securities, unless there is in effect a registration statement under the Securities Act covering the proposed transaction, the Holder thereof shall give notice to the Company of such Holder's intention to effect such sale, pledge, or transfer. Each such notice shall describe the manner and circumstances of the proposed sale, pledge, or transfer in sufficient detail and, if reasonably requested by the Company, shall be accompanied at such Holder's expense by either (i) a written opinion of legal counsel who shall, and whose legal opinion shall, be reasonably satisfactory to the Company, addressed to the

Company, to the effect that the proposed transaction may be effected without registration under the Securities Act; (ii) a "no action" letter from the SEC to the effect that the proposed sale, pledge, or transfer of such Restricted Securities without registration will not result in a recommendation by the staff of the SEC that action be taken with respect thereto; or (iii) any other evidence reasonably satisfactory to counsel to the Company to the effect that the proposed sale, pledge, or transfer of the Restricted Securities may be effected without registration under the Securities Act, whereupon the Holder of such Restricted Securities shall be entitled to sell, pledge, or transfer such Restricted Securities in accordance with the terms of the notice given by the Holder to the Company. The Company will not require such a legal opinion or "no action" letter (x) in any transaction in compliance with Rule 144 or (y) in any transaction in which such Holder distributes Restricted Securities to an Affiliate of such Holder for no consideration; provided that each transferee agrees in writing to be subject to the terms of this Section 2.14(c). Each certificate evidencing the Restricted Securities transferred as above provided shall bear, except if such transfer is made pursuant to Rule 144, the appropriate restrictive legend set forth in Section 2.14(b), except that such certificate shall not bear such restrictive legend if, in the opinion of counsel for such Holder and the Company, such legend is not required in order to establish compliance with any provisions of the Securities Act.

2.15. Termination of Registration Rights. The right of any Holder to request registration or inclusion of Registrable Securities in any registration pursuant to Section 2.1, Section 2.2, or Section 2.3 shall terminate upon the earlier of:

(a) the closing of a Deemed Liquidation Event, as such term is defined in the Charter; or

(b) such time as all of such Holder's Registrable Securities constitute less than three percent (3%) of the outstanding Common Stock and could be sold without restriction under SEC Rule 144.

3. Information and Observer Rights.

3.1. Delivery of Financial Statements. The Company shall deliver to each Major Holder:

(a) as soon as practicable, but in any event within one hundred eighty (180) calendar days after the end of each fiscal year of the Company, (i) a balance sheet as of the end of such year; (ii) statements of income and of cash flows for such year; and (iii) a statement of stockholders' equity as of the end of such year, audited and certified by independent public accountants of a "Big Four" accounting firm or an accounting firm approved by the audit committee;

(b) as soon as practicable, but in any event within forty five (45) calendar days after the end of each of the first three (3) quarters of each fiscal year of the Company, unaudited statements of income and of cash flows for such fiscal quarter, and an unaudited balance sheet as of the end of such fiscal quarter, all prepared in accordance with GAAP (except that the financial report may (i) be subject to normal year-end audit adjustments and (ii) not contain all notes thereto that may be required in accordance with GAAP);

(c) as soon as practicable, but in any event within forty-five (45) calendar days after the end of each quarter of each fiscal year of the Company, a statement showing the number of shares of each class and series of capital stock and securities convertible into or exercisable for shares of capital stock outstanding at the end of the period, the Common Stock issuable upon conversion or exercise of any outstanding securities convertible or exercisable for Common Stock and the exchange ratio or exercise price applicable thereto, and the number of shares of issued stock options and stock options not yet issued but reserved for issuance, if any, all in sufficient detail as to permit the Major

Holders to calculate their respective percentage equity ownership in the Company, and certified by the chief financial officer or chief executive officer of the Company as being true, complete, and correct;

(d) as soon as practicable, but in any event within forty-five (45) calendar days of the end of each month, an unaudited income statement and statement of cash flows for such month, and an unaudited balance sheet as of the end of such month, all prepared in accordance with GAAP (except that the financial report may (i) be subject to normal year-end audit adjustments and (ii) not contain all notes thereto that may be required in accordance with GAAP);

(e) as soon as practicable, but in any event thirty (30) calendar days before the end of each fiscal year, a budget and business plan for the next fiscal year (collectively, the "Budget"), prepared on a monthly basis, including balance sheets, income statements, and statements of cash flow for such months and, promptly after prepared, any other budgets or revised budgets prepared by the Company;

(f) at the request of any Major Holder, as soon as practicable following the end of each fiscal year, an annual business plan and a management report covering all major events;

(g) with respect to the financial statements called for in Section 3.1(b) and Section 3.1(d), an instrument executed by the chief financial officer and chief executive officer of the Company certifying on behalf of the Company that such financial statements were prepared in accordance with GAAP consistently applied with prior practice for earlier periods (except as otherwise set forth in Section 3.1(b) and Section 3.1(d)) and fairly present the financial condition of the Company and its results of operation as of and for the periods specified therein; and

(h) such other information relating to the financial condition, business, prospects, or corporate affairs of the Company as any Major Holder may from time to time reasonably request; provided, however, that the Company shall not be obligated under this Section 3.1 to provide information (i) that the Company reasonably determines in good faith to be a trade secret or confidential information (unless covered by an enforceable confidentiality agreement, in form acceptable to the Company) or (ii) the disclosure of which would adversely affect the attorney-client privilege between the Company and its counsel.

If, for any period, the Company has any subsidiary whose accounts are consolidated with those of the Company, then in respect of such period the financial statements delivered pursuant to the

foregoing sections shall be the consolidated and consolidating financial statements of the Company and all such consolidated subsidiaries.

Notwithstanding anything else in this Section 3.1 to the contrary, the Company may cease providing the information set forth in this Section 3.1 during the period starting with the date sixty (60) calendar days before the Company's good-faith estimate of the date of filing a registration statement for an IPO; provided that the Company's covenants under this Section 3.1 shall be reinstated at such time as the Company is no longer actively employing its commercially reasonable efforts to cause such registration statement to become effective.

3.2. Inspection. The Company shall permit each Major Holder, at such Major Holder's expense, to visit and inspect the Company's properties; examine its books of account and records; and discuss the Company's affairs, finances, and accounts with its officers, during normal business hours of the Company as may be reasonably requested by the Major Holder upon reasonable advance notice; provided, however, that the Company shall not be obligated pursuant to this Section 3.2 to provide access to any information that it reasonably considers to be a trade secret or confidential information (unless covered by an enforceable confidentiality agreement, in form acceptable to the Company) or the disclosure of which would adversely affect the attorney-client privilege between the Company and its counsel.

3.3. Observer Rights. Devon Park Bioventures, L.P., Bessemer Venture Partners VII L.P., MPM Bio IV NVS Strategic Fund, LP, TVM Life Science Ventures VI, L.P., Skyline Venture Partners Qualified Purchaser Fund IV, L.P., Prism Venture Partners V, L.P., Intersouth Partners VI, L.P., Deerfield Private Design Fund III, L.P., Abingworth Bioventures VI LP, Pharmstandard International S.A., and the holders of a majority of the outstanding shares of capital stock held by the Key Holders (as defined in the Voting Agreement) shall each be entitled to designate one person to attend all meetings of the Company's Board of Directors in a nonvoting observer capacity and, in this respect, the Company shall give such designees copies of all notices, minutes, consents, and other materials that it provides to its directors at the same time and in the same manner as provided to such directors; provided, however, that each such designee shall agree to hold in confidence and trust and to act in a fiduciary manner with respect to all information so provided; and provided further, that the Company reserves the right to withhold any information and to exclude any such designee from any meeting or portion thereof if access to such information or attendance at such meeting could adversely affect the attorney-client privilege between the Company and its counsel or result in disclosure of trade secrets or a conflict of interest. The right of the holders of a majority of the outstanding shares of capital stock held by the Key Holders to designate a Board observer under this section shall terminate on the date on which the Key Holders, as of the effective date of this Agreement, hold collectively less than five percent (5%) of the total issued and outstanding voting capital stock of the Company.

3.4. Termination of Information and Observer Rights.

(a) The covenants set forth in Section 3.1, Section 3.2 and Section 3.3 shall terminate and be of no further force or effect (i) immediately before the consummation of the IPO, (ii) when the Company first becomes subject to the periodic reporting requirements of

Section 12(g) or 15(d) of the Exchange Act, or (iii) upon a Deemed Liquidation Event, as such term is defined in the Charter, whichever event occurs first.

(b) The rights, if any, of an Investor under Section 3.3 shall terminate on the date on which such Investor's shares of Series D Preferred Stock are converted to Common Stock pursuant to Section 5A of Division C of Article Fourth of the Charter. The rights, if any, of an Investor granted under any written agreement with the Company to designate one or more persons to attend all meetings of the Company's Board of Directors in a nonvoting observer capacity shall terminate on the date on which such Investor's shares of Series D Preferred Stock are converted to Common Stock pursuant to Section 5A of Division C of Article Fourth of the Charter.

(c) The covenants set forth in Section 3.1 (excluding Section 3.1(a)) and Section 3.2 with respect to an Investor shall terminate and be of no further force or effect with respect to such Investor on the date on which such Investor's shares of Series D Preferred Stock are converted to Common Stock pursuant to Section 5A of Division C of Article Fourth of the Charter.

3.5. Confidentiality. Each Investor agrees that such Investor will keep confidential and will not disclose, divulge, or use for any purpose (other than to monitor its investment in the Company) any confidential information obtained from the Company pursuant to the terms of this Agreement (including notice of the Company's intention to file a registration statement), unless such confidential information (a) is known or becomes known to the public in general (other than as a result of a breach of this Section 3.5 by such Investor), (b) is or has been independently developed or conceived by the Investor without use of the Company's confidential information, or (c) is or has been made known or disclosed to the Investor by a third party without a breach of any obligation of confidentiality such third party may have to the Company; provided, however, that an Investor may disclose confidential information (i) to its attorneys, accountants, consultants, and other professionals to the extent necessary to obtain their services in connection with monitoring its investment in the Company; (ii) to any prospective purchaser of any Registrable Securities from such Investor, if such prospective purchaser agrees to be bound by the provisions of this Section 3.5; (iii) to any Affiliate, partner, member, stockholder, or wholly owned subsidiary of such Investor in the ordinary course of business, provided that such Investor informs such Person that such information is confidential and directs such Person to maintain the confidentiality of such information; or (iv) as may otherwise be required by law, provided that the Investor promptly notifies the Company of such disclosure and takes reasonable steps to minimize the extent of any such required disclosure.

The Company acknowledges that certain of the Investors are in the business of venture capital investing and therefore review the business plans and related proprietary information of many enterprises, including enterprises that may have products or services that compete directly or indirectly with those of the Company. The Company further acknowledges that certain of the Investors may engage in the research, development or commercialization of products or services that compete directly or indirectly with those of the Company. Nothing in this Agreement shall preclude or in any way restrict the Investors from investing or participating in any particular enterprise, or from engaging in such research, development or commercialization activities, regardless of whether such enterprise or activities are competitive with respect to the Company, so long as such activities do not result in a violation of the confidentiality provisions of this Agreement.

3.6. Management Rights Letter. At Closing under and as defined in the Purchase Agreement, the Company shall deliver to each Investor that participates in such Closing and who makes such a request, a Management Rights Letter (as defined in the Purchase Agreement) in a form reasonably acceptable to the Investors.

4. Rights to Future Stock Issuances.

4.1. Right of First Offer.

(a) Subject to the terms and conditions of this Section 4.1 and applicable securities laws, if the Company proposes to offer or sell any New Securities, the Company shall first offer such New Securities to each Investor: (i) that holds at least 150,000 shares of Preferred Stock (subject to appropriate adjustment for stock splits, stock dividends, combinations, and other recapitalizations); and (ii) which is an "Accredited Investor" as defined in Rule 501 under the Securities Act ("**Qualified Investors**"). A Qualified Investor shall be entitled to apportion the right of first offer hereby granted to it among itself and its Affiliates in such proportions as it deems appropriate."

(b) The Company shall give notice (the "**Offer Notice**") to each Qualified Investor, stating (i) its bona fide intention to offer such New Securities, (ii) the number of such New Securities to be offered, and (iii) the price and terms, if any, upon which it proposes to offer such New Securities.

(c) By notification to the Company within twenty (20) calendar days after the Offer Notice is given, each Qualified Investor may elect to purchase or otherwise acquire, at the price and on the terms specified in the Offer Notice, up to that portion of such New Securities which equals the proportion that the Common Stock issued and held, or issuable upon conversion of the Preferred Stock and any other Derivative Securities then held, by such Qualified Investor bears to the total Common Stock of the Company then outstanding (assuming full conversion and exercise of all Derivative Securities). At the expiration of such twenty (20) day period, the Company shall promptly notify each Qualified Investor that elects to purchase or acquire all the shares available to it (each, a "**Fully Exercising Investor**") of any other Qualified Investor's failure to do likewise. During the ten (10) day period commencing after the Company has given such notice, each Fully Exercising Investor may, by giving notice to the Company, elect to purchase or acquire, in addition to the number of shares specified above, up to that portion of the New Securities for which Qualified Investors were entitled to subscribe but that were not subscribed for by the Qualified Investors which is equal to the proportion that the Common Stock issued and held, or issuable upon conversion of Preferred Stock then held, by such Fully Exercising Investor bears to the Common Stock issued and held, or issuable upon conversion of the Preferred Stock then held, by all Fully Exercising Investors who wish to purchase such unsubscribed shares. The closing of any sale pursuant to this Section 4.1(c) shall occur within sixty (60) calendar days of the date that the Offer Notice is given.

(d) If all New Securities referred to in the Offer Notice are not elected to be purchased or acquired as provided in Section 4.1(c)the Company may, during the ninety (90) day period following the expiration of the periods provided in Section 4.1(c)offer and sell the remaining unsubscribed portion of such New Securities to any Person or Persons at a price

not less than, and upon terms no more favorable to the offeree than, those specified in the Offer Notice. If the Company does not enter into an agreement for the sale of the New Securities within such period, or if such agreement is not consummated within thirty (30) calendar days of the execution thereof, the right provided hereunder shall be deemed to be revived and such New Securities shall not be offered unless first reoffered to the Qualified Investors in accordance with this Section 4.1.

(e) The right of first offer in this Section 4.1 shall not be applicable to (i) shares of Common Stock or Derivative Securities issued as a dividend or distribution on Preferred Stock; (ii) shares of Common Stock or Derivative Securities issued by reason of a dividend, stock split, split-up or other distribution on shares of Common Stock that is covered by the Charter Article Fourth Part C Sections 4.5, 4.6, 4.7 or 4.8; (iii) shares of Common Stock or Derivative Securities issued to employees or directors of, or consultants or advisors to, the Company or any of its subsidiaries pursuant to a plan, agreement or arrangement approved by the Board of Directors of the Company; (iv) shares of Common Stock or Derivative Securities actually issued upon the exercise of Derivative Securities or shares of Common Stock actually issued upon the conversion or exchange of Derivative Securities, in each case provided such issuance is pursuant to the terms of such Derivative Security; (v) shares of Common Stock or Derivative Securities issued to banks, equipment lessors or other financial institutions, or to real property lessors, pursuant to a debt financing, equipment leasing or real property leasing transaction approved by the Board of Directors of the Company including a majority of the Preferred Directors; (vi) shares of Common Stock or Derivative Securities issued or issuable to a contracting party in connection with a licensing, corporate partnering, merger, acquisition or similar strategic or combination transaction approved by a majority of the Board of Directors of the Company, including a majority of the Preferred Directors; (vii) the Warrants and/or shares of Common Stock issued or issuable upon exercise of the Warrants; or (viii) shares of Series D Preferred Stock or Common Stock issued or issuable pursuant to the Purchase Agreement (including, without limitation, any right granted under the Purchase Agreement to purchase shares of Series D Preferred Stock or Common Stock) and/or shares of Common Stock issued or issuable upon conversion of such shares of Series D Preferred Stock.

4.2. Termination. The covenants set forth in Section 4.1 shall terminate and be of no further force or effect immediately before the consummation of the IPO. The covenants set forth in Section 4.1 shall terminate and be of no further force and effect upon a Deemed Liquidation Event, as such term is defined in the Charter. The covenants set forth in Section 4.1 with respect to an Investor shall terminate with respect to such Investor on the date on which such Investor's shares of Series D Preferred Stock are converted to Common Stock pursuant to Section 5A of Division C of Article Fourth of the Charter.

5. Additional Covenants.

5.1. Insurance. The Company shall use its commercially reasonable efforts to obtain, to the extent it has not already done so, within ninety (90) calendar days of the date hereof, from financially sound and reputable insurers Directors and Officers Errors and Omissions insurance in an amount satisfactory to the Board of Directors, and will use commercially reasonable efforts to cause such insurance policies to be maintained until such time as the Board of Directors determines that such insurance should be discontinued.

5.2. Employee Agreements. The Company will cause (i) each Person now or hereafter employed by it or by any subsidiary (or engaged by the Company or any subsidiary as a consultant/independent contractor) with access to confidential information and/or trade secrets, or who works on technical matters, to enter into a nondisclosure and proprietary rights assignment agreement which provides, among other things, for the protection of confidential information of the Company and the assignment to and ownership by the Company of patents, patent applications, and other intellectual property rights conceived of or developed during such Person's employment with the Company and (ii) each Key Person to enter into a non-competition and nonsolicitation agreement, in a form acceptable to the Major Holders, which provides that such Key Person will not compete with the Company or solicit employees of the Company while employed and for a period of one (1) year following termination of such Key Person's employment. In

addition, the Company shall not amend, modify, terminate, waive, or otherwise alter, in whole or in part, any of the above-referenced agreements or any restricted stock agreement between the Company and any employee, without the unanimous consent of the Preferred Directors.

5.3. Employee Vesting. Unless otherwise approved by the Board of Directors, all future employees and consultants of the Company who purchase, receive options to purchase, or receive awards of shares of the Company's capital stock after the date hereof shall be required to execute restricted stock or option agreements, as applicable, providing for (i) vesting of shares over a four (4) year period, with the first twenty-five percent (25%) of such shares vesting following twelve (12) months of continued employment or service, and the remaining shares vesting in equal quarterly installments over the following twelve (12) quarters, and (ii) a one hundred eighty (180) day lockup period in connection with the IPO. The Company shall retain a "right of first refusal" on employee transfers until the Company's IPO and shall have the right to repurchase unvested shares at cost upon termination of employment of a holder of restricted stock.

5.4. Matters Requiring Preferred Director Approval. So long as at least 10% of the shares of Preferred Stock issued as of the date hereof remain outstanding, the Company hereby covenants and agrees with each of the Investors that it shall not, without approval of the Board of Directors, which approval must include the affirmative vote of a majority of the Preferred Directors:

(a) make, or permit any subsidiary to make, any loan or advance to, or own any stock or other securities of, any subsidiary or other corporation, partnership, or other entity unless it is wholly owned by the Company;

(b) make, or permit any subsidiary to make, any loan or advance to any Person, including, without limitation, any employee or director of the Company or any subsidiary, except advances and similar expenditures in the ordinary course of business or under the terms of an employee stock or option plan approved by the Board of Directors;

(c) guarantee, directly or indirectly, or permit any subsidiary to guarantee, directly or indirectly, any indebtedness except for trade accounts of the Company or any subsidiary arising in the ordinary course of business;

(d) make any investment other than investments in prime commercial paper, money market funds, certificates of deposit in any United States bank having a net worth in excess of $100,000,000 or obligations issued or guaranteed by the United States of America, in each case having a maturity not in excess of two (2) years;

(e) incur any aggregate indebtedness in excess of $1,000,000 that is not already included in a budget approved or modified by the Board of Directors, other than trade credit incurred in the ordinary course of business;

(f) otherwise enter into or be a party to any transaction with any director, officer, or employee of the Company or any "associate" (as defined in Rule 12b-2 promulgated under the Exchange Act) of any such Person, except for transactions contemplated by this Agreement, the Purchase Agreement, or transactions made in the ordinary course of business and pursuant to reasonable requirements of the Company's business and upon fair and reasonable terms;

(g) hire, terminate, or change the compensation of the executive officers, including approving any option grants or stock awards to executive officers;

(h) change the principal business of the Company, enter new lines of business, or exit the current line of business;

(i) sell, assign, license, pledge, or encumber material technology or intellectual property, other than licenses, material transfer agreements, or other similar agreements granted in the ordinary course of business; or

(j) make any material investments, joint ventures or acquisitions.

5.5. Meetings of the Board of Directors. Unless otherwise determined by the vote of a majority of the directors then in office, the Board of Directors shall meet at least four (4) times per year in accordance with an agreed-upon schedule.

5.6. Successor Indemnification. If the Company or any of its successors or assignees (i) consolidates with or merges into any other Person and is not the continuing or surviving corporation or entity of such consolidation or merger or (ii) transfers or conveys all or substantially all of its properties and assets to any Person, then, and in each such case, to the extent necessary, proper provision shall be made so that the successors and assignees of the Company assume the obligations of the Company with respect to indemnification of members of the Board of Directors as in effect immediately before such transaction, whether such obligations are contained in the Company's Bylaws, its Charter, the Indemnification Agreements (as defined in the Purchase Agreement) or elsewhere, as the case may be.

5.7. Board Expenses. The Company shall reimburse the nonemployee directors for all reasonable out-of-pocket travel expenses incurred in connection with attending meetings of the Board of Directors.

5.8. Board Committees. The MPM Director, the Prism Director, the TVM Director, the Skyline Director, the Abingworth Director and the Pharmstandard Director (each as

defined in the Voting Agreement) shall have the right to join any committee of the Board of Directors.

5.9. Termination of Covenants. The covenants set forth in this Section 5, except for Section 5.6, shall terminate and be of no further force or effect (i) immediately before the consummation of the IPO or (ii) upon a Deemed Liquidation Event, as such term is defined in the Charter, whichever event occurs first.

5.10. Annual Review of Science and Technology and Business. Each Major Holder shall have the right to have the science and technology and the business of the Company reviewed once a calendar year by one or more representatives of the Major Holder, which may include third party consultants, and at the Major Holder's expense.

5.11. Scientific Advisory Board. If the Company forms a scientific advisory board or any board or committee with similar functions, each Major Holder shall have the right to designate up to one individual to serve on such board or committee.

6. Miscellaneous.

6.1. Successors and Assigns. Each Investor hereby agrees that it shall not, and may not, assign any of its rights and obligations hereunder, unless such rights and obligations are assigned by such Investor to (i) any Person to which Registrable Securities are transferred by such Investor pursuant to Section 2.13 or (ii) with respect to the right of first offer set forth in Section 4.1, to any Major Holder or any Affiliate of a Major Holder, and, in each case, such assignee shall be deemed an "Investor" for purposes of this Agreement; provided that such assignment of rights shall be contingent upon the assignee providing a written instrument to the Company notifying the Company of such assignment and agreeing in writing to be bound by the terms of this Agreement. The terms and conditions of this Agreement inure to the benefit of and are binding upon the

respective successors and permitted assignees of the parties. Nothing in this Agreement, express or implied, is intended to confer upon any party other than the parties hereto or their respective successors and permitted assignees any rights, remedies, obligations or liabilities under or by reason of this Agreement, except as expressly provided herein.

6.2. Governing Law. This Agreement shall be governed by and construed in accordance with the General Corporation Law of the State of Delaware as to matters within the scope thereof, and as to all other matters shall be governed by and construed in accordance with the internal laws of the Commonwealth of Massachusetts, without regard to its principles of conflicts of laws.

6.3. Counterparts. This Agreement may be executed in two or more counterparts, each of which shall be deemed an original, but all of which together shall constitute one and the same instrument. This Agreement may also be executed and delivered by facsimile signature and in two or more counterparts, each of which shall be deemed an original, but all of which together shall constitute one and the same instrument.

6.4. Titles and Subtitles. The titles and subtitles used in this Agreement are for convenience only and are not to be considered in construing or interpreting this Agreement.

6.5. Notices. All notices, requests, and other communications given or made pursuant to this Agreement shall be in writing and shall be deemed effectively given (i) upon personal delivery to the party to be notified; (ii) when sent by confirmed electronic mail or facsimile if sent during normal business hours of the recipient, and if not so confirmed, then on the next business day; (iii) five (5) calendar days after having been sent by registered or certified mail, return receipt requested, postage prepaid; or (iv) one (1) day after deposit with a nationally recognized overnight courier, specifying next-day delivery, with written verification of receipt. All communications shall be sent to the respective parties at their addresses as set forth on the signature pages, or to such email address, facsimile number, or address as subsequently modified by written notice given in accordance with this Section 6.5. If notice is given to the Company, a copy shall also be sent to:

Julio E. Vega
Bingham McCutchen LLP
One Federal Street
Boston, MA 02110
e-mail: julio.vega@bingham.com
fax: 617-951-8736

and if notice is given to the Investors, a copy shall also be given to:

Lowell A. Segal
Ropes & Gray LLP
1900 University Avenue, 6th Floor
East Palo Alto, CA 94303
e-mail: Lowell.Segal@ropesgray.com
fax: 650-566-4244

6.6. Amendments and Waivers. Any term of this Agreement may be amended and the observance of any term of this Agreement may be waived (either generally or in a particular instance, and either retroactively or prospectively) only with the written consent of the Company and the holders of at least seventy percent (70%) of the Registrable Securities then-outstanding and the holders of at least a majority of Registrable Securities issued or issuable upon conversion of the Series D Preferred Stock then-outstanding; provided that the Company may in its sole discretion waive compliance with Section 2.14(c) (and the Company's failure to object promptly in writing to a proposed assignment allegedly in violation of Section 2.14(c) shall be deemed to be a waiver). Notwithstanding the foregoing, (a) this Agreement may not be amended or terminated and the observance of any term hereof may not be waived with respect to any Investor without the written consent of such Investor, unless such amendment, termination, or waiver applies to all Investors in the same fashion, subject to clause (b) below (it being agreed that (i) a waiver of the provisions of Section 4 with respect to a particular transaction shall be deemed to apply to all Investors in the same fashion if such waiver does so by its terms, notwithstanding the fact that certain Investors may nonetheless, by agreement with the Company, purchase securities in such transaction and (ii) in the event that any Major Holder purchases securities in such transaction, the Company shall offer to each Qualified Investor, with reasonable advance notice, the opportunity to purchase their respective pro rata percentage of any New Securities that the Board of Directors of the Company determines, in good faith, to be

available for purchase by Investors in such transaction (such pro rata percentage being the ratio of shares of the Corporation's capital stock (on an as-converted basis) held by each Investor purchasing New Securities in such transaction to the sum of the total number of shares of the Corporation's capital stock (on an as-converted basis) held by all Investors purchasing New Securities in such transaction)), and (b) the exception to the "market stand-off" provision contained in Section 2.12 for shares purchased by an Investor in the IPO may not be amended or waived in an adverse manner with respect to any Investor without the written consent of such Investor. The Company shall give prompt notice of any amendment or termination hereof or waiver hereunder to any party hereto that did not consent in writing to such amendment, termination, or waiver. Any amendment, termination, or waiver effected in accordance with this Section 6.6 shall be binding on all parties hereto, regardless of whether any such party has consented thereto, except as otherwise provided in clause (b) above. No waivers of or exceptions to any term, condition, or provision of this Agreement, in any one or more instances, shall be deemed to be or construed as a further or continuing waiver of any such term, condition, or provision.

6.7. Severability. In case any one or more of the provisions contained in this Agreement is for any reason held to be invalid, illegal or unenforceable in any respect, such invalidity, illegality, or unenforceability shall not affect any other provision of this Agreement, and such invalid, illegal, or unenforceable provision shall be reformed and construed so that it will be valid, legal, and enforceable to the maximum extent permitted by law.

6.8. Aggregation of Stock. All shares of Registrable Securities held or acquired by Affiliates shall be aggregated together for the purpose of determining the availability of any rights under this Agreement.

6.9. Additional Investors. Notwithstanding anything to the contrary contained herein, if the Company issues additional shares of the Company's Preferred Stock after the date hereof, whether pursuant to the Purchase Agreement or otherwise, any purchaser of such shares of Preferred Stock may become a party to this Agreement by executing and delivering an additional counterpart signature page to this Agreement, and thereafter shall be deemed an "Investor" for all purposes hereunder. No action or consent by the Investors shall be required for such joinder to this Agreement by such additional Holder, so long as such additional Holder has agreed in writing to be bound by all of the obligations as an "Investor" hereunder.

6.10. Entire Agreement. This Agreement (including the Exhibits hereto) supersedes the Prior Agreement, and together with the Charter and the other Transaction Agreements (as defined in the Purchase Agreement) constitutes the full and entire understanding and agreement between the parties with respect to the subject matter hereof, and any other written or oral agreements relating to the subject matter hereof existing between the parties are expressly canceled.

6.11. Dispute Resolution. The parties (a) hereby irrevocably and unconditionally submit to the jurisdiction of the state courts of Massachusetts and to the jurisdiction of the United States District Court for the District of Massachusetts for the purpose of any suit, action or other proceeding arising out of or based upon this Agreement, (b) agree not to commence any suit, action or other proceeding arising out of or based upon this Agreement

except in the state courts of Massachusetts or the United States District Court for the District of Massachusetts, and (c) hereby waive, and agree not to assert, by way of motion, as a defense, or otherwise, in any such suit, action or proceeding, any claim that it is not subject personally to the jurisdiction of the above-named courts, that its property is exempt or immune from attachment or execution, that the suit, action or proceeding is brought in an inconvenient forum, that the venue of the suit, action or proceeding is improper or that this Agreement or the subject matter hereof may not be enforced in or by such court. Each party will bear its own costs in respect of any disputes arising under this Agreement. Each of the parties to this Agreement consents to personal jurisdiction for any equitable action sought in the U.S. District Court for the District of Massachusetts or any court of the Commonwealth of Massachusetts having subject matter jurisdiction.

6.12. Delays or Omissions. No delay or omission to exercise any right, power, or remedy accruing to any party under this Agreement, upon any breach or default of any other party under this Agreement, shall impair any such right, power, or remedy of such nonbreaching or nondefaulting party, nor shall it be construed to be a waiver of or acquiescence to any such breach or default, or to any similar breach or default thereafter occurring, nor shall any waiver of any single breach or default be deemed a waiver of any other breach or default theretofore or thereafter occurring. All remedies, whether under this Agreement or by law or otherwise afforded to any party, shall be cumulative and not alternative.

[Remainder of Page Intentionally Left Blank]

IN WITNESS WHEREOF, the parties have executed this Fourth Amended and Restated Investors' Rights Agreement as of the date first written above.

PROTEON THERAPEUTICS, INC.

By: /s/ Timothy Noyes
Timothy Noyes
President and Chief Executive Officer

Address:
200 West Street
Waltham, MA 02451

Email:
Fax:

**[SIGNATURE PAGE TO THE PROTEON THERAPEUTICS, INC.
FOURTH AMENDED AND RESTATED INVESTORS' RIGHTS AGREEMENT]**

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EXECUTED this 13th day of May, 2014.

Abingworth Bioventures VI, LP

By:
By: [ILLEGIBLE]

By: [ILLEGIBLE]

Title: Partner

Address: 38 Jermyn Street

London SW1Y 6DN

United Kingdom

Email:

Fax:

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EXECUTED this 13th day of May, 2014.

Pharmstandard International S.A.

By: /s/ Ericks Martinovsky /s/ Gerard Birchen

Title: Director Director

Address: 65 Boulevard Grande Duchesse

Charlotte

L-1331 Luxembourg

Grand-Duchey of Luxembourg

Email:

Fax:

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EXECUTED this 13th day of May, 2014.

Deerfield Special Situations International Master Fund, L.P.

By: Deerfield Mgmt, L.P.
General Partner
By: J.E. Flynn Capital LLC
General Partner

By: /s/ David J. Clark
Name: David J. Clark
Title: Authorized Signatory

Address: 780 Third Avenue, 37th Floor

New York, NY 10017

Email:

Fax:

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EXECUTED this 13th day of May, 2014.

Deerfield Special Situations Fund, L.P.

By: Deerfield Mgmt, L.P.
General Partner
By: J.E. Flynn Capital LLC
General Partner

By: /s/ David J. Clark
Name: David J. Clark
Title: Authorized Signatory

Address: 780 Third Avenue, 37th Floor

New York, NY 10017

Email:

Fax:

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EXECUTED this 13th day of May, 2014.

Deerfield Private Design Fund III, L.P.

By: Deerfield Mgmt, L.P.
General Partner
By: J.E. Flynn Capital LLC
General Partner

By: /s/ David J. Clark
Name: David J. Clark
Title: Authorized Signatory

Address: 780 Third Avenue, 37th Floor

New York, NY 10017

Email:

Fax:

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parties named therein, (ii) that he, she or it is a party to the Investors' Rights Agreement for all purposes and (iii) that he, she or it is bound by all terms and conditions of the Investors' Rights Agreement.

EXECUTED this 13th day of May, 2014.

TVM Life Science Ventures VI GmbH & Co. KG

By: /s/ Josef Moosholzer /s/ Stefan Fischer

By: Josef Moosholzer (and) Stefan Fischer

Title: Authorized Officers

Address: Ottostrasse 4, 80333 Munich

Germany

Email:

Fax:

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EXECUTED this 13th day of May, 2014.

TVM Life Science Ventures VI LP
By: its General Partner TVM Life Science Ventures VI (Cayman) Ltd.

By: /s/ Josef Moosholzer /s/ Stefan Fischer

By: Josef Moosholzer (and) Stefan Fischer

Title: Authorized Officers

Address: 75 Arlington St. Suite 500
Boston, MA 02116, U.S.A.

Email:

Fax:

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EXECUTED this 13th day of May, 2014.

Skyline Venture Partners Qualified Purchaser Fund IV, L.P.

By: Skyline Venture Management IV, LLC, its General Partner

By: /s/ John G. Freund

Title: John G. Freund, Managing Director

Address: 525 University Ave., Suite 610

Palo Alto, CA 94301

Email:

Fax:

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EXECUTED this 13th day of May, 2014.

Prism Venture Partners V, L.P.
By: Prism Investment Partners V, L.P.
its General Partner

By: Prism Venture Partners V, L.L.C.
its General Partner

By: /s/ Brendan O'Leary

Title: Managing Director

NOTE NEW ADDRESS:
75 Second Avenue, Suite 210
Needham, MA 02494

Address: 117 Kendrick Street, Suite 200

Needham, MA 02494

Email:

Fax:

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EXECUTED this 13th day of May, 2014.

Prism Venture Partners V-A, L.P.
By: Prism Investment Partners V, L.P.
its General Partner

By: Prism Venture Partners V, L.L.C.
its General Partner

By: /s/ Brendan O'Leary

NOTE NEW ADDRESS:
75 Second Avenue, Suite 210
Needham, MA 02494

Title: Managing Director

Address: 117 Kendrick Street, Suite 200

Needham, MA 02494

Email:

Fax:

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EXECUTED this 13th day of May, 2014.

Intersouth Partners VI, L.P.
By: Intersouth Associates VI, LLC
its General Partner

By: [ILLEGIBLE]

Title: PARTNER

Address: 102 City Hall Plaza, Suite 200

Durham, NC 27701

Email:

Fax:

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EXECUTED this 13th day of May, 2014.

MPM Bio IV NVS Strategic Fund, L.P.
By: MPM Bioventures IV GP LLC
its General Partner
By: MPM Bioventures IV LLC.
its Managing Member

By: /s/ Todd Foley

Title: Member

Address: 200 Clarendon Street, 54th Floor

Boston, MA 02116

Email:

Fax:

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EXECUTED this 13th day of May, 2014.

Vectis Healthcare & Life Sciences Fund II, L.P.

By: Vectis II GP, LP
its General Partner
By: Vectis II GP, LLC
General Partner

By: [ILLEGIBLE]

Title: Authorized Person

Address: 84 State Street, Suite 320

Boston, MA 02109

Email:

Fax:

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EXECUTED this 13th day of May, 2014.

Devon Park Bioventures, L.P.
By: Devon Park Associates, L.P.
its General Partner

By: /s/ Marc J. Ostro

Title: General Partner

Address: 1400 Liberty Ridge Drive

Suite 103

Wayne, PA 19087

Email:

Fax:

PROTEON THERAPEUTICS, INC.

Fourth Amended and Restated Investors' Rights Agreement

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EXECUTED this 13th day of May, 2014.

BVP VII Special Opportunity Fund LP
By: Deer VII & Co. L.P., their General Partner
By: Deer VII & Co. Ltd., its General Partner

By: [ILLEGIBLE]

Title: Director

Address: c/o Bessemer Venture Partners

1865 Palmer Avenue, Suite 104

Larchmont, NY 10538

Email:

Fax:

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EXECUTED this 13th day of May, 2014.

Bessemer Venture Partners VII, L.P.
By: Deer VII & Co. L.P., their General Partner
By: Deer VII & Co. Ltd., its General Partner

By: [ILLEGIBLE]

Title: Director

Address: c/o Bessemer Venture Partners

1865 Palmer Avenue, Suite 104

Larchmont, NY 10538

Email:

Fax:

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FOURTH AMENDED AND RESTATED INVESTORS' RIGHTS AGREEMENT]**

Exhibit 4.3

Execution Version

SERIES D PREFERRED STOCK
PURCHASE AGREEMENT

TABLE OF CONTENTS

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(continued)

SERIES D PREFERRED STOCK PURCHASE AGREEMENT

THIS SERIES D PREFERRED STOCK PURCHASE AGREEMENT (the "**Agreement**") is made as of the 13th day of May, 2014 by and among Proteon Therapeutics, Inc., a Delaware corporation (the "**Company**"), and the investors listed on Exhibit A attached to this Agreement, as the same may be amended from time to time (each a "**Purchaser**" and together the "**Purchasers**"). The parties hereby agree as follows:

1. Purchase and Sale of Preferred Stock.

1.1. Sale and Issuance of Series D Preferred Stock.

(a) Authorization. The Company shall adopt and file with the Secretary of State of the State of Delaware on or before the Initial Tranche Closing (as defined in Section 1.2(a)(i) hereof) the Fifth Amended and Restated Certificate of Incorporation in the form of Exhibit B attached to this Agreement (the "**Restated Certificate**").

(b) Initial Tranche.

(i) Subject to the terms and conditions of this Agreement, each Purchaser (a "**Noteholder Purchaser**") that is a holder of one or more outstanding convertible promissory notes previously issued by the Company as reflected opposite such Purchaser's name under the heading "Convertible Notes Amount Owed" on Exhibit A (in the case of such Noteholder Purchaser, the "**Applicable Convertible Note(s)**") hereby agrees that, at the Initial Tranche Closing, the full amount owed by the Company to such Noteholder Purchaser through and including the date of the Initial Tranche Closing under such Noteholder Purchaser's Applicable Convertible Note(s), which full amount owed is set forth opposite such Noteholder Purchaser's name under the heading "Convertible Notes Amount Owed" on Exhibit A, shall convert into that number of shares of the Company's Series D Preferred Stock, par value $0.001 per share ("**Series D Preferred Stock**"), set forth opposite such Noteholder Purchaser's name under the heading "Note Conversion Shares" on Exhibit A (in the case of each Noteholder Purchaser, the "**Note Conversion Shares**" and, collectively with the Note Conversion Shares of all other Noteholder Purchasers, the "**Total Note Conversion Shares**"), at a conversion price per share equal to $0.4414 (the "**Note Conversion Price**"). Subject to the terms and conditions of this Agreement, the Company hereby agrees that, at the Initial Tranche Closing, the Company shall sell and issue to each Noteholder Purchaser the Note Conversion Shares to which such Noteholder Purchaser is entitled pursuant to the foregoing provisions of this Section 1.1(b)(i) upon conversion of the full amount owed by the Company to such Noteholder Purchaser through and including the date of the Initial Tranche Closing under such Noteholder Purchaser's Applicable Convertible Notes. The number of Total Note Conversion Shares to be issued to the Noteholder Purchasers at the Initial Tranche Closing shall be 10,344,201. Notwithstanding anything to the contrary express or implied in the Applicable Convertible Note(s) of each Noteholder Purchaser, each Noteholder Purchaser hereby agrees that interest shall accrue under the Applicable Convertible Note(s) of such Noteholder Purchaser only through and including April 30, 2014. Upon the sale and issuance of the Note Conversion Shares by the Company to each Noteholder Purchaser at the Initial Tranche Closing pursuant to, and in accordance with, the

terms and conditions of this Agreement (including, without limitation, this Section 1.1(b)(i)), the Applicable Convertible Note(s) of such Noteholder Purchaser shall be deemed satisfied in full and the Company shall not owe any amount or have any other obligation of any kind under such Applicable Convertible Note(s), and such Applicable Convertible Note(s) shall be deemed cancelled, terminated and of no further force or effect whatsoever. Each Noteholder Purchaser hereby agrees that, in the event that any provision of this Agreement (including, without limitation, this Section 1.1(b)(i)) conflicts with or is inconsistent with the terms and provisions of the Applicable Convertible Note(s) of any

Noteholder Purchaser, then the conflicting or inconsistent terms and provisions of this Agreement (including, without limitation, this Section 1.1(b)(i)) (1) shall be deemed to constitute an amendment or modification of the conflicting or inconsistent terms and provisions of the Applicable Convertible Note(s) of any Noteholder Purchaser and (2) shall be deemed to supersede and control any such conflicting or inconsistent terms and provisions of the Applicable Convertible Note(s).

(ii) Subject to the terms and conditions of this Agreement, at the Initial Tranche Closing, the Company shall issue and sell to each Purchaser, and each Purchaser, acting severally and not jointly, shall purchase from the Company, that number of shares of the Company's Series D Preferred Stock set forth opposite each such Purchaser's name under the heading "Initial Tranche Shares" on Exhibit A, at a purchase price per share equal to $0.588656 (such purchase price per share, subject to proportionate and equitable adjustment upon any stock split, stock dividend, reverse stock split or other similar event that affects or involves the Series D Preferred Stock, being hereinafter referred to as the "**Series D Price**"). The aggregate number of shares of Series D Preferred Stock issued to the Purchasers at the Initial Tranche Closing pursuant to this Section 1.1(b)(ii) shall be 42,469,626 and the aggregate purchase price payable by the Purchasers at the Initial Tranche Closing for such aggregate number of shares shall be $25,000,000.27. For purposes of this Agreement, the term "**Initial Tranche Shares**" shall mean, collectively, (1) the Total Note Conversion Shares and (2) the aggregate number of shares of Series D Preferred Stock issued to the Purchasers at the Initial Tranche Closing pursuant to this Section 1.1(b)(ii), subject to, in the case of clauses (1) and (2), proportionate and equitable adjustment upon any stock split, stock dividend, reverse stock split or other similar event that affects or involves the Series D Preferred Stock.

(c) Second Tranche.

(i) Subject to the terms and conditions of this Agreement (including, without limitation, the terms and conditions set forth below in this Section 1.1(c)), at the Second Tranche Closing (as defined in Section 1.2(b)(i) hereof), the Company shall issue and sell to each Purchaser, and each Purchaser, acting severally and not jointly, shall purchase from the Company, that number of shares of Series D Preferred Stock set forth opposite each such Purchaser's name under the heading "Second Tranche Shares" on Exhibit A, at a purchase price per share equal to the Series D Price. Subject to the provisions of this Section 1.1(c), the aggregate number of shares of Series D Preferred Stock issued to the Purchasers at the Second Tranche Closing shall be 8,493,925 (such aggregate number of shares, subject to proportionate and equitable adjustment upon any stock split, stock dividend, reverse stock split or other similar event that affects or involves the Series D Preferred Stock, being hereinafter referred to as the "**Second Tranche Shares**") and the aggregate purchase price payable by the Purchasers at the Second Tranche Closing for all of the Second Tranche Shares shall be $5,000,000.03.

(ii) The sale and purchase of the Second Tranche Shares pursuant to this Section 1.1(c) shall be consummated only if (1) the Company delivers a written notice to all of the Purchasers (the "**Second Tranche Closing Notice**") stating that the Company desires to consummate such sale and purchase of the Second Tranche Shares pursuant to this Section 1.1(c) and setting forth a proposed date for the Second Tranche Closing that is consistent with the applicable requirements of Section 1.1(c)(iii) below, (2) at any time during the period commencing on the date of the Second Tranche Closing Notice and ending immediately prior to the Second Tranche Closing, those Purchasers that hold at least sixty five percent (65%) of the Tranche Shares (as defined in Section 1.7 hereof) issued and outstanding consent to the consummation of the sale and purchase of the Second Tranche Shares pursuant to this Section 1.1(c) and (3) all other applicable conditions precedent set forth in this Agreement to the consummation of the Second Tranche Closing shall have been satisfied or properly waived in accordance with the terms of this Agreement. Notwithstanding the foregoing or the provisions of clause (C) of Section 1.1(c)(iii) below, if the sale and purchase of the Second Tranche Shares pursuant to this Section 1.1(c) has not been consummated prior to the consummation of the sale and purchase of the Third Tranche Shares (as defined in Section 1.1(d)(i) below) pursuant to Section 1.1(d) hereof, then the sale and purchase of the Second Tranche Shares pursuant to this Section 1.1(c) shall be consummated simultaneously with the sale and purchase of the Third Tranche Shares pursuant to Section 1.1(d) hereof, and compliance with the provisions of clauses (1) and (2) above in this Section 1.1(c)(ii) and clause (C) of Section 1.1(c)(iii) below shall not be required in connection with such sale and purchase of the Second Tranche Shares.

(iii) Notwithstanding anything express or implied in the foregoing provisions of this Section 1.1(c) to the contrary: (A) the Company shall send the Second Tranche Closing Notice at least fifteen (15) business days before the Second Tranche Closing and the Company shall not send the Second Tranche Closing Notice at any time during the Restricted Period; (B) the sale and purchase of the Second Tranche Shares pursuant to this Section 1.1(c) shall not be consummated at any time during the Restricted Period; (C) the sale and purchase of the Second Tranche Shares pursuant to this Section 1.1(c) also shall not be consummated at any time prior to December 31, 2015 or at any time after March 31, 2017, except that the provisions of this clause (C) shall not apply to the sale and purchase of the Second Tranche Shares that, in accordance with the provisions of Section 1.1(c)(ii) above, is consummated simultaneously with the sale and purchase of the Third Tranche Shares; (D) in the event that the sale and purchase of the Second Tranche Shares pursuant to this Section 1.1(c) is to be consummated at any time within thirty (30) days prior to the consummation of a Deemed Liquidation Event (as defined in the Restated Certificate), each Purchaser shall have the right to make a Net Issue Election pursuant to which such Purchaser shall be issued pursuant to this Section 1.1(c), at the Second Tranche Closing, a smaller number of the Second Tranche Shares determined in accordance with such Net Issue Election and without having to make payment to the Company of any cash purchase price in connection with such smaller number of the Second Tranche Shares, in lieu of purchasing and paying the purchase price for the full number of the Second Tranche Shares that such Purchaser would otherwise have the right and obligation to purchase and pay for pursuant to this Section 1.1(c); and (E) the Company shall have no right or obligation to sell any shares of Series D Preferred Stock to a Purchaser pursuant to this Section 1.1(c), and such Purchaser shall have no right or obligation to purchase any shares of Series D Preferred Stock from the Company pursuant to this Section 1.1(c), if the Company has previously sold to such Purchaser, and such Purchaser has previously purchased from the

Company, shares of Series D Preferred Stock pursuant to Section 2.1(a) hereof. In the event that the provisions of clause (E) of the immediately preceding sentence are applicable with respect to one or more Purchasers, then (1) the rights and obligations of the Purchasers to purchase Second Tranche Shares pursuant to this Section 1.1(c) shall continue to apply only with respect to those Purchasers that have not previously purchased shares of Series D Preferred Stock from the Company pursuant to Section 2.1(a) hereof, (2) the rights and obligations of the Company to sell Second Tranche Shares pursuant to this Section 1.1(c) shall continue to apply only with respect to those Purchasers that have not previously purchased shares of Series D Preferred Stock from the Company pursuant to Section 2.1(a) hereof and (3) the aggregate purchase price payable by the Purchasers at the Second Tranche Closing for all of the Second Tranche Shares shall be automatically reduced to reflect the reduction in the number of Second Tranche Shares.

(iv) The rights and obligations of the Company and the Purchasers to consummate the sale and purchase of the Second Tranche Shares pursuant to this Section 1.1(c) shall automatically terminate on the earlier of (1) the sixteenth (16th) business day after September 30, 2017, (2) the consummation of a Deemed Liquidation Event, (3) the closing of the IPO (as defined in Section 1.4 hereof) and (4) the date on which all Purchasers have purchased shares of Series D Preferred Stock pursuant to, and in accordance with, Section 2.1(a) hereof. In addition, if one or more Purchasers is or are in material breach of any representation, warranty, covenant or provision under this Agreement that is applicable to such Purchaser or Purchasers (which material breach remains uncured for at least thirty (30) days after written notice thereof), then the obligation of the Company to consummate the sale of any number of the Second Tranche Shares to such Purchaser or Purchasers pursuant to this Section 1.1(c), and the right of such Purchaser or Purchasers to consummate the purchase of such number of the Second Tranche Shares from the Company pursuant to this Section 1.1(c), may be terminated by the Company by giving written notice of termination to the breaching Purchaser or Purchasers. Any termination pursuant to this Section 1.1(c)(iv) of the rights and/or obligations of the Company and/or the Purchasers to consummate the sale and purchase of the Second Tranche Shares pursuant to this Section 1.1(c) shall not relieve or release any party to this Agreement from any material breach by such party of any representation, warranty, covenant or provision under this Agreement that is applicable to such party if and to the extent that such material breach occurred prior to such termination.

(d) Third Tranche.

(i) Subject to the terms and conditions of this Agreement (including, without limitation, the terms and conditions set forth below in this Section 1.1(d)), at the Third Tranche Closing (as defined in section 1.2(c)(i)), the Company shall issue and sell to each Purchaser, and each Purchaser, acting severally and not jointly, shall purchase from the Company, that number of shares of Series D Preferred Stock set forth opposite each such Purchaser's name under the heading "Third Tranche Shares" on Exhibit A, at a purchase price per share equal to the Series D Price. Subject to the provisions of this Section 1.1(d), the aggregate number of shares of Series D

Preferred Stock issued to the Purchasers at the Third Tranche Closing shall be 25,481,775 (such aggregate number of shares, subject to proportionate and equitable adjustment upon any stock split, stock dividend, reverse stock split or other similar event that affects or involves the Series D Preferred Stock, being hereinafter referred to as the

"**Third Tranche Shares**") and the aggregate purchase price payable by the Purchasers at the Third Tranche Closing for all of the Third Tranche Shares shall be $14,999,999.85.

(ii) The sale and purchase of the Third Tranche Shares pursuant to this Section 1.1(d) shall be consummated only if (1) either the Board of Directors of the Company determines that the Milestones (as defined in Section 1.4 below) have been achieved or those Purchasers that hold at least seventy-five percent (75%) of the Tranche Shares issued and outstanding agree in writing to waive the requirement that the Milestones be achieved as a condition precedent to such sale and purchase of the Third Tranche Shares pursuant to this Section 1.1(d), (2) the Company delivers a written notice to all of the Purchasers (the "**Third Tranche Closing Notice**") stating that (A) the Board of Directors of the Company has determined that the Milestones have been achieved or that the requirement that the Milestones be achieved as a condition precedent to such sale and purchase of the Third Tranche Shares pursuant to this Section 1.1(d) has been waived in accordance with the provisions of the foregoing clause (1) of this Section 1.1(d)(ii) and (B) the Company desires to consummate such sale and purchase of the Third Tranche Shares pursuant to this Section 1.1(d), and setting forth a proposed date for the Third Tranche Closing that is consistent with the applicable requirements of Section 1.1(d)(iii) below, (3) those Purchasers that hold at least seventy-five percent (75%) of the Tranche Shares issued and outstanding do not elect in writing, within ten (10) business days after the date of the Third Tranche Closing Notice, to abandon the consummation of the sale and purchase of the Third Tranche Shares pursuant to this Section 1.1(d) and (4) all other applicable conditions precedent set forth in this Agreement to the consummation of the Third Tranche Closing shall have been satisfied or properly waived in accordance with the terms of this Agreement. Upon request by any Purchaser, the Company shall promptly provide such Purchaser with reasonable evidence supporting achievement of the Milestones, as applicable, which evidence shall be subject to the confidentiality provisions set forth in Section 3.5 of the Investors' Rights Agreement.

(iii) Notwithstanding anything express or implied in this Section 1.1(d) or elsewhere in this Agreement to the contrary: (A) the Company shall send the Third Tranche Closing Notice at least fifteen (15) business days before the Third Tranche Closing and the Company shall not send the Third Tranche Closing Notice at any time during the Restricted Period; (B) the sale and purchase of the Third Tranche Shares pursuant to this Section 1.1(d) shall not be consummated at any time during the Restricted Period and also shall not be consummated at any time prior to December 31, 2015 or after the fifteenth (15th) business day after September 30, 2017; (C) in the event that the sale and purchase of the Third Tranche Shares pursuant to this Section 1.1(d) is to be consummated at any time within thirty (30) days prior to the consummation of a Deemed Liquidation Event, each Purchaser shall have the right to make a Net Issue Election pursuant to which such Purchaser shall be issued pursuant to this Section 1.1(d), at the Third Tranche Closing, a smaller number of the Third Tranche Shares determined in accordance with such Net Issue Election and without having to make payment to the Company of any cash purchase price in connection with such smaller number of the Third Tranche Shares, in lieu of purchasing and paying the purchase price for the full number of the Third Tranche Shares that such Purchaser would otherwise have the right and obligation to purchase and pay for pursuant to this Section 1.1(d); and (D) the Company shall have no right or obligation to sell any shares of Series D Preferred Stock to a Purchaser pursuant to this Section 1.1(d), and such Purchaser shall have no right or obligation to purchase any shares of Series D Preferred Stock

from the Company pursuant to this Section 1.1(d), if the Company has previously sold to such Purchaser, and such Purchaser has previously purchased from the Company, shares of Series D Preferred Stock pursuant to Section 2.1(b) hereof. In the event that the provisions of clause (D) of the immediately preceding sentence are applicable with respect to one or more Purchasers, then (1) the rights and obligations of the Purchasers to purchase Third Tranche Shares pursuant to this Section 1.1(d) shall continue to apply only with respect to those Purchasers that have not previously purchased shares of Series D Preferred Stock from the Company pursuant to Section 2.1(b) hereof, (2) the rights and obligations of the Company to sell Third Tranche Shares pursuant to this Section 1.1(d) shall continue to apply only with respect to those Purchasers that have not previously purchased shares of Series D Preferred Stock from the Company pursuant to Section 2.1(b) hereof and (3) the aggregate purchase price payable by the Purchasers at the Third Tranche Closing for all of the Third Tranche Shares shall be automatically reduced to reflect the reduction in the number of Third Tranche Shares.

(iv) The rights and obligations of the Company and the Purchasers to consummate the sale and purchase of the Third Tranche Shares pursuant to this Section 1.1(d) shall automatically terminate on the earlier of (1) the sixteenth (16th) business day after September 30, 2017, (2) the consummation of a Deemed Liquidation Event, (3) the closing of the IPO and (4) the date on which all Purchasers have purchased shares of Series D Preferred Stock pursuant to, and in accordance with, Section 2.1(b) hereof. In addition, if one or more Purchasers is or are in material breach of any representation, warranty, covenant or provision under this Agreement that is applicable to such Purchaser or Purchasers (which material breach remains uncured for at least thirty (30) days after written notice thereof), then the obligation of the Company to consummate the sale of any number of the Third Tranche Shares to such Purchaser or Purchasers pursuant to this Section 1.1(d), and the right of such Purchaser or Purchasers to consummate the purchase of such number of the Third Tranche Shares from the Company pursuant to this Section 1.1(d), may be terminated by the Company by giving written notice of termination to the breaching Purchaser or Purchasers. Any termination pursuant to this Section 1.1(d)(iv) of the rights and/or obligations of the Company and/or the Purchasers to consummate the sale and purchase of the Third Tranche Shares pursuant to this Section 1.1(d) shall not relieve or release any party to this Agreement from any material breach by such party of any representation, warranty, covenant or provision under this Agreement that is applicable to such party if and to the extent that such material breach occurred prior to such termination.

1.2. Closings; Delivery.

(a) Initial Tranche Closing.

(i) The closing of (1) the conversion of the Applicable Convertible Note(s) of each Noteholder Purchaser and the issuance and sale the Total Note Conversion Shares in connection with such conversion, all pursuant to Section 1.1(b)(i) hereof and (2) the sale and purchase of the shares of Series D Preferred Stock pursuant to Section 1.1(b)(ii) hereof shall take place remotely via the exchange of documents and signatures either (i) at 11:00 am Eastern Standard Time on the fifth (5th) business day after the date of this Agreement or (ii) at such other time and/or date (whether prior or after such fifth (5th) business date) as the Company and the Purchasers mutually agree upon, orally or in writing, which may be on the date hereof (the "**Initial Tranche Closing**").

(ii) At the Initial Tranche Closing: (1) the Company shall deliver to each Noteholder Purchaser a certificate representing the Note Conversion Shares of such Noteholder Purchaser, against delivery by such Noteholder Purchaser of the original Applicable Convertible Note(s) of such Noteholder Purchaser or, in the event that such original Applicable Convertible Note(s) have been lost, stolen or destroyed an affidavit of loss, in form and substance satisfactory to the Company, duly executed by such Noteholder Purchaser pursuant to which such Noteholder Purchaser certifies that such original Applicable Convertible Note(s) have been lost, stolen or destroyed and agreeing to customary indemnification of the Company in the event of any claims pertaining to such original Applicable Convertible Note(s); and (2) the Company shall deliver to each Purchaser a certificate representing the shares of Series D Preferred Stock being purchased by such Purchaser pursuant to Section 1.1(b)(ii) hereof, against payment by such Purchaser of the purchase price for such shares of Series D Preferred Stock by check payable to the Company, by wire transfer to a bank account designated by the Company or by any combination of such methods.

(b) Second Tranche Closing.

(i) The closing of the purchase and sale of the Second Tranche Shares pursuant to Section 1.1(c) hereof shall take place remotely via the exchange of documents and signatures on either the date specified in the Second Tranche Closing Notice delivered pursuant to Section 1.1(c)(ii) hereof, which date specified must

be consistent with the applicable requirements of Section 1.1(c)(iii), or on such other date as the Company and those Purchasers that hold at least sixty five percent (65%) of the Initial Tranche Shares then outstanding mutually agree (the "**Second Tranche Closing**").

(ii) At the Second Tranche Closing, the Company shall deliver to each Purchaser a certificate representing the number of the Second Tranche Shares being purchased by such Purchaser pursuant to Section 1.1(c) hereof, against either (1) payment by such Purchaser of the purchase price for such number of the Second Tranche Shares by check payable to the Company, by wire transfer to a bank account designated by the Company or by any combination of such methods or (2) delivery by such Purchaser of a Net Issue Election Form that has been properly completed and duly executed by such Purchaser if such Purchaser is entitled to make a Net Issue Election pursuant to Section 1.1(c)(iii) in connection with the number of the Second Tranche Shares being purchased by such Purchaser pursuant to Section 1.1(c) hereof.

(c) Third Tranche Closing.

(i) The closing of the purchase and sale of the Third Tranche Shares pursuant to Section 1.1(d) hereof shall take place remotely via the exchange of documents and signatures on either the date specified in the Third Tranche Closing Notice delivered pursuant to Section 1.1(c)(ii) hereof, which date specified must be consistent with the applicable requirements of Section 1.1(d)(iii), or on such other date as the Company and those Purchasers that hold at least sixty five percent (65%) of the Initial Tranche Shares and Second Tranche Shares, if any, then outstanding mutually agree (the "**Third Tranche Closing**").

(ii) At the Third Tranche Closing, the Company shall deliver to each Purchaser a certificate representing the number of the Third Tranche Shares being purchased by such Purchaser pursuant to Section 1.1(d) hereof, against either (1) payment by such Purchaser of the purchase price for such number of the Third Tranche Shares by check payable to the Company, by wire transfer to a bank account designated by the Company or by any combination of such methods or (2) delivery by such Purchaser of a Net Issue Election Form that has been properly completed and duly executed by such Purchaser if such Purchaser is entitled to make a Net Issue Election pursuant to Section 1.1(d)(iii) in connection with the number of the Third Tranche Shares being purchased by such Purchaser pursuant to Section 1.1(d) hereof.

(d) Definition of Closing. Each of the Initial Tranche Closing, the Second Tranche Closing (if any) and the Third Tranche Closing (if any), is sometimes referred to herein, individually, as a "**Closing.**" The Initial Tranche Closing, the Second Tranche Closing (if any) and the Third Tranche Closing (if any) are sometimes referred to in this Agreement, collectively, as the "**Closings**."

1.3. Updates to Disclosure Schedule. The Company shall have the right to deliver to the Purchasers at each of the Initial Tranche Closing, the Second Tranche Closing and the Third Tranche Closing an amended and restated Disclosure Schedule consisting of the Disclosure Schedule as modified, revised and updated to make such disclosures concerning matters or events occurring or arising since the date hereof or the prior Closing, as the case may be, as are required in order for the representations and warranties of the Company under Section 3 hereof to be true and correct as of each of the Initial Tranche Closing, the Second Tranche Closing or the Third Tranche Closing, as applicable, provided, however, that no such Updated Disclosure Schedule (as defined below) shall cure any breach, inaccuracy, default or non-compliance existing as of the date hereof or any previous Closing, as the case may be. For purposes of this Agreement, the term "**Updated Disclosure Schedule**" shall mean the last amended and restated Disclosure Schedule delivered pursuant to this Section 1.3.

1.4. Use of Proceeds. In accordance with the directions of the Company's Board of Directors, as it shall be constituted in accordance with the Voting Agreement, the Company will use the proceeds from the sale of the Tranche Shares to advance the Company's lead product, PRT-201, through Phase III clinical studies, as provided for in the Proposed Budgets (as defined in Section 5.1(n)), and for other general corporate purposes, subject to Section 5.4 of the Investors' Rights Agreement.

1.5. Special Mandatory Conversion; Limitation on Remedies.

(a) Special Mandatory Conversion. Each Purchaser hereby acknowledges and agrees that if such Purchaser fails to purchase (i) all of the Second Tranche Shares that such Purchaser is obligated to purchase at the Second Tranche Closing pursuant to, and in accordance with, Section 1.1(c) hereof or (ii) all of the Third Tranche Shares that such Purchaser is obligated to purchase at the Third Tranche Closing pursuant to, and in accordance with, Section 1.1(d) hereof, then, in each case, (x) all of the shares of the Company's Series D Preferred Stock owned by such Purchaser shall be subject to a special mandatory conversion, such special mandatory conversion to be pursuant to, and in accordance with, the terms and

provisions of Section 5A of Division C of Article Fourth of the Restated Certificate and (y) any right that such Purchaser may have to designate a nominee for election to the Board of Directors of the Company shall terminate in accordance with the provisions of Section 1.7 of the Voting Agreement (as defined in Section 1.7 hereof).

(b) Limitation on Remedies. The parties hereby acknowledge that, if a Purchaser fails to purchase (i) all of the Second Tranche Shares that such Purchaser is obligated to purchase at the Second Tranche Closing pursuant to, and in accordance with, Section 1.1(c) hereof or (ii) all of the Third Tranche Shares that such Purchaser is obligated to purchase at the Third Tranche Closing pursuant to, and in accordance with, Section 1.1(d) hereof, then, in each case, the only remedies available against such Purchaser are (w) the special mandatory conversion of Series D Preferred Stock owned by the Purchaser pursuant to the Restated Certificate, (x) termination, pursuant to Section 1.7 of the Voting Agreement, of the Purchaser's right, if any, to designate a nominee for election to the Board of Directors of the Company, (y) termination, pursuant to Section 3.4(b) and Section 3.4(c) of the Investors' Rights Agreement (as defined in Section 1.7 hereof), of the Purchaser's information and observer rights, if any, and (z) termination, pursuant to Section 4.2 of the Investors' Rights Agreement, of the Purchaser's preemptive rights, if any.

1.6. Waiver of Preemptive Rights. Certain of the Purchasers, acting for themselves and on behalf of all other stockholders of the Company that have preemptive rights under that certain Third Amended and Restated Investors' Rights Agreement, dated August 2, 2011, among the Company, certain of the Purchasers and those other stockholders of the Company that are parties thereto, as previously amended and in effect prior to the date of this Agreement (the "**Prior Investors' Rights Agreement**"), hereby waive any and all preemptive rights, if any, under Section 4.1 of the Prior Investors' Rights Agreement with respect to the offer, sale and/or issuance by the Company of the Shares pursuant to this Agreement and the Common Stock issuable upon conversion of the Series D Preferred Stock issued pursuant to this Agreement.

1.7. Defined Terms Used in this Agreement. In addition to the terms defined above, the following terms used in this Agreement shall be construed to have the meanings set forth or referenced below.

"**Abingworth**" means Abingworth Bioventures VI, LP.

"**Affiliate**" means, with respect to any specified Person, any other Person who or which, directly or indirectly, controls, is controlled by, or is under common control with such specified Person, including, without limitation, any partner, officer, director, member or employee of such Person and any venture capital fund now or hereafter existing that is controlled by or under common control with one or more general partners or managing members of, or shares the same management company with, such Person.

"**Applicable Convertible Notes**" shall have the meaning set forth in Section 1.1(b)(i) hereto.

"**Bessemer**" means Bessemer Venture Partners VII L.P., Bessemer Venture Partners VII Institutional L.P. and BVP VII Special Opportunity Fund LP, collectively.

"**Code**" means the Internal Revenue Code of 1986, as amended.

"**Common Stock**" means the Company's common stock, par value $0.001 per share.

"**Company Intellectual Property**" means all Intellectual Property Rights as are necessary to or actually used in the conduct of the Company's business as now conducted and as presently proposed to be conducted.

"**Deerfield**" means Deerfield Private Design Fund III, L.P., Deerfield Special Situations Fund, L.P. and Deerfield Special Situations International Master Fund, L.P.

"**Devon Park**" means Devon Park Bioventures, L.P.

"**Initial Tranche Closing**" shall have the meaning set forth in Section 1.2(a) hereof.

"**Initial Tranche Shares**" shall have the meaning set forth in Section 1.1(b) hereof.

"**Intellectual Property Rights**" means patents, patent applications, trademarks, trademark applications, trademark registrations, service marks, service mark applications, service mark registrations, tradenames, copyrights, trade secrets, licenses, domain names, mask works, biological materials, formulae, know how, information, proprietary rights and processes and other intellectual property rights of any kind.

"**Intersouth**" means Intersouth Partners VI, L.P.

"**Investors' Rights Agreement**" means the agreement between the Company, the Purchasers and the other stockholders of the Company party thereto dated as of the Initial Tranche Closing, in the form of Exhibit D attached to this Agreement.

"**IPO**" means the initial public offering of the Common Stock pursuant to a registration statement filed with the Securities and Exchange Commission under the Securities Act.

"**Key Employee**" means Timothy Noyes, George Eldridge and Steven Burke, any executive-level employee (including division director and vice president-level positions), any employee who either alone or in concert with others develops, invents, programs or designs any Company Intellectual Property and any other employee whose responsibilities consist primarily of being the leader or head of the Company's clinical, regulatory or manufacturing operations.

"Knowledge," including the phrase **"to the Company's knowledge,"** shall mean the actual knowledge of any Key Employee; provided, however, that, solely for the purposes of

Section 3.8 hereof, "Knowledge", including the phrase "to the Company's knowledge" shall mean the actual knowledge of any Key Employee, F. Nicholas Franano and Marco Wong.

"**Major Investor"** means each of (i) MPM; (ii) TVM LSV VI GmbH and TVM LSV VI LP collectively, except that for purposes of Section 5.1(m) each of TVM LSV VI GmbH and TVM LSV VI LP individually shall be considered a Major Investor; (iii) Skyline IV; (iv) Prism V LP and Prism V-A LP, collectively; (v) Intersouth; (vi) Devon Park; (vii) Bessemer; (viii) Abingworth; (ix) Pharmstandard; and (x) Deerfield.

"**Management Rights Letter**" means the agreement between the Company and each Major Investor, dated as of the Initial Tranche Closing, in the form of Exhibit E attached to this Agreement or such other form as the Company and a Major Investor shall agree upon.

"**Material Adverse Effect**" means a material adverse effect on the business, assets (including intangible assets), liabilities, financial condition, property, prospects or results of operations of the Company; provided, however, that none of the following shall be deemed in themselves, either alone or in combination, to constitute, and none of the following shall be taken into account in determining whether there has been or will be, a Material Adverse Effect: (a) any failure by the Company to meet internal projections, forecasts or predictions on or after the date of this Agreement (provided that the underlying causes of such failure shall not be excluded from the determination of whether a Material Adverse Effect has occurred); (b) any adverse change, effect, event, occurrence, state of facts or development attributable to conditions affecting the industries in which Company participates as a whole or the U.S. economy as a whole, unless such change, effect, event, occurrence, state of facts or development affects the Company in a disproportionate manner; (c) any adverse change, effect, event, occurrence, state of facts or development attributable or relating to (i) out-of-pocket fees and expenses (including legal, accounting, investment banking and other fees and expenses) incurred in connection with the transactions contemplated by any of the Transaction Agreements or (ii) the payment of any amounts due to, or the provision of any other benefits (including benefits relating to acceleration of stock options) to, any officers or employees under employment contracts, non-competition agreements, employee benefit plans, severance arrangements or other arrangements in existence as of the date of this Agreement; (d) any adverse change, effect, event, occurrence, state of facts or development resulting from or relating to compliance with the terms of, or the taking of any action required by, any of the Transaction Agreements; or (e) any adverse change or effect on the business, assets, liabilities, financial condition or results of operations of the Company resulting from the conduct of the Company's business in the ordinary course of business in accordance with budgets approved by the Board of Directors of the Company from time to time, including, without limitation, (1) any reduction of the Company's cash balance as a result of incurring expenses in the ordinary course of business and the reduction of the Company's cash balance, (2) any increase in the Company's liabilities in the ordinary course of business or (3) any deterioration of the financial condition of the Company as a result of the activities contemplated in the foregoing clauses (1) and (2).

"**Milestones**" means the following milestones achieved in a Phase 3 clinical trial with NCT No. 02110901, enrolling no less than 285 patients, and which has been designed based upon FDA's guidance in the end-of-Phase 2 meeting with the Company to satisfy FDA's requirements of an adequate, well-controlled trial in support of a BLA filing: (i) statistically

significant effect of PRT-201 compared to placebo on primary patency loss in radiocephalic arteriovenous fistula ("**RC-AVF**") patients; and (ii) statistically significant effect of PRT-201 compared to placebo on fistula maturation according to the KDOQI criteria in RC-AVF patients.

"**MPM**" means MPM Bio IV NVS Strategic Fund, LP.

"**Net Issue Election**" means the following: (i) in the case of a Purchaser's right and obligation to purchase Shares pursuant to Section 1.1(c) hereof or Section 1.1(d) hereof, as applicable, by making payment of the applicable cash purchase price therefor in accordance with the provisions of Section 1.1(c) or Section 1.1(d), as applicable, Purchaser's election to have the Company issue to such Purchaser a smaller number of the class or series of Shares than the Purchaser would be required to purchase pursuant to Section 1.1(c) or Section 1.1(d), as applicable, absent such election, which smaller number of such class or series of Shares shall be determined in accordance with the formula provided below and shall be issued by the Company to such Purchaser without such Purchaser being required to make payment to the Company of any cash purchase price therefor;

and (ii) in the case of a Purchaser's right to purchase Shares pursuant to Section 2.1(a) hereof or Section 2.1(b) hereof, as applicable, by making payment of the applicable cash purchase price therefor in accordance with the provisions of Section 2.1(a) hereof or Section 2.1(b) hereof, as applicable, such Purchaser's election to have the Company issue to such Purchaser a smaller number of the class or series of Shares that such Purchaser would be entitled to purchase pursuant to Section 2.1(a) hereof or Section 2.1(b) hereof, as applicable, absent such election, which smaller number of such class or series of Shares shall be determined in accordance with the formula provided below and shall be issued by the Company to such Purchaser without such Purchaser being required to make payment to the Company of any cash purchase price therefor. The smaller number of the applicable class or series of Shares to be issued by the Company to any Purchaser that makes a Net Issue Election shall be determined as follows:

$$X = \frac{Y (A - B)}{A}$$

Where: X = The smaller number of the applicable class or series of Shares to be issued to the Purchaser as a result of such Purchaser's Net Issue Election;

Y = The number of the applicable class or series of Shares that the Purchaser making the Net Issue Election would have purchased if such Purchaser had not made such Net Issue Election;

A = The fair market value of one Share of the same class or series as the Shares with respect to which the Net Issue Election is made, such fair market value to be determined at the time such Net Issue Election is made as determined in good faith by the Board of Directors based upon (i) if such Net Issue Election is made in connection with a Deemed Liquidation Event, the consideration per Share payable in connection with such Deemed Liquidation Event or (ii) if such Net Issue Election is made after the closing of an IPO, the average closing price per Share quoted on the national securities exchange on which the Shares are listed as published in the Wall Street Journal for the ten

(10) trading day period ending five (5) trading days prior to the date of determination of fair market value;

B = The cash purchase price per share that the Purchaser is required to pay pursuant to this Agreement in connection with the purchase of the applicable class or series of Shares with respect to which the Net Issue Election is made.

"**Net Issue Election Form**" means the Net Issue Election Form attached as Exhibit I hereto.

"**Note Conversion Price**" shall have the meaning set forth in Section 1.1(b)(i) hereto.

"**Note Conversion Shares**" shall have the meaning set forth in Section 1.1(b)(i) hereto.

"**Noteholder Purchaser**" shall have the meaning set forth in Section 1.1(b)(i) hereto.

"**Novartis**" means Novartis International Pharmaceutical Limited.

"**Option Agreement**" means that certain Option Agreement between the Company and Novartis, dated as of March 27, 2009.

"**Person**" means any individual, corporation, partnership, trust, limited liability company, association or other entity.

"**Pharmstandard**" means Pharmstandard International S.A., with registered address 65, Boulevard Grande-Duchesse Charlotte L - 1331 Luxembourg.

"Preferred Stock" means the Series A Preferred Stock, the Series A-1 Preferred Stock, the Series B Preferred Stock, the Series C Preferred Stock and the Series D Preferred Stock.

"**Prism V LP**" means Prism Venture Partners V, L.P.

"**Prism V-A LP**" means Prism Venture Partners V-A, L.P.

"**Prior Investors' Rights Agreement**" shall have the meaning set forth in Section 1.6.

"**Proposed Budgets**" shall have the meaning set forth in Section 5.1(n).

"**Purchaser**" shall have the meaning set forth in the Preamble.

"**Restated Certificate**" shall have the meaning set forth in Section 1.1(a) hereof.

"**Restricted Period**" means the period commencing on the date on which the Company either submits a registration statement on Form S-1 to the United States Securities and Exchange Commission on a confidential basis pursuant to Jumpstart Our Business Startups Act or files a registration statement on Form S-1 with the United States Securities and Exchange Commission pursuant to the Securities Act and ending on the earlier of (i) the third business day

following the withdrawal of such registration statement on Form S-1 in connection with any abandonment of the IPO and (ii) the closing of the IPO.

"**Right of First Refusal and Co-Sale Agreement**" means the agreement among the Company, the Purchasers, and certain other stockholders of the Company, dated as of the Initial Tranche Closing, in the form of Exhibit F attached to this Agreement.

"**Second Tranche Closing**" shall have the meaning set forth in Section 1.2(b)(i) hereof.

"**Second Tranche Closing Notice**" shall have the meaning set forth in Section 1.1(c)(ii) hereof.

"**Second Tranche Individual Purchase Exercise Notice**" shall have the meaning set forth in Section 2.1(a)(i) hereto.

"**Second Tranche Individual Purchase Right**" shall have the meaning set forth in Section 2.1(a)(i) hereto.

"**Second Tranche Individual Purchase Shares**" shall have the meaning set forth in Section 2.1(a)(i) hereto.

"**Second Tranche Shares**" shall have the meaning set forth in Section 1.1(c)(i) hereof.

"**Section 2.1(a) Closing**" shall have the meaning set forth in Section 2.2(a)(i) hereto.

"**Section 2.1(b) Closing**" shall have the meaning set forth in Section 2.2(b)(i) hereto.

"**Securities Act**" means the Securities Act of 1933, as amended, and the rules and regulations promulgated thereunder.

"**Series A Preferred Stock**" means the Company's Series A Preferred Stock, par value $0.001 per share.

"**Series A-1 Preferred Stock**" means the Company's Series A-1 Preferred Stock, par value $0.001 per share.

"**Series B Preferred Stock**" means the Company's Series B Preferred Stock, par value $0.001 per share.

"**Series C Preferred Stock**" means the Company's Series C Preferred Stock, par value $0.001 per share.

"**Series D Preferred Stock**" shall have the meaning set forth in Section 1.1(b) hereof.

"**Series D Price**" shall have the meaning set forth in Section 1.1(b) hereof.

"**Shares**" shall mean, collectively, (i) any shares of Series D Preferred Stock or Common Stock sold or issued pursuant to this Agreement and (ii) any shares of Common Stock issued or issuable upon conversion of any shares of Series D Preferred Stock sold or issued pursuant to this Agreement.

"**Skyline IV**" means Skyline Venture Partners Qualified Purchaser Fund IV, L.P.

"**Third Tranche Closing**" shall have the meaning set forth in Section 1.2(c)(i) hereof.

"**Third Tranche Closing Notice**" shall have the meaning set forth in Section 1.2(c)(i) hereof.

"**Third Tranche Individual Purchase Exercise Notice**" shall have the meaning set forth in Section 2.1(b)(i) hereto.

"**Third Tranche Individual Purchase Right**" shall have the meaning set forth in Section 2.1(b)(i) hereto.

"**Third Tranche Individual Purchase Shares**" shall have the meaning set forth in Section 2.1(b)(i) hereto

"**Third Tranche Shares**" shall have the meaning set forth in Section 1.1(d)(i) hereof.

"**Total Note Conversion Shares**" shall have the meaning set forth in Section 1.1(b)(i) hereto.

"**Tranche Shares**" shall mean, as of the relevant time of reference thereto, those shares of Series D Preferred Stock sold by the Company, and purchased by Purchasers, prior to such time pursuant to Section 1.1(b), Section 1.1(c) and/or Section 1.1(d) hereof, as applicable.

"**Transaction Agreements**" means this Agreement, the Investors' Rights Agreement, the Management Rights Letter, the Right of First Refusal and Co-Sale Agreement and the Voting Agreement.

"**TVM LSV VI GmbH**" means TVM Life Science Ventures VI GmbH & Co. KG.

"**TVM LSV VI LP**" means TVM Life Science Ventures VI, L.P.

"**Updated Disclosure Schedule**" shall have the meaning set forth in Section 1.3 hereof.

"**Voting Agreement**" means the agreement among the Company, the Purchasers and certain other stockholders of the Company, dated as of the Initial Tranche Closing, in the form of Exhibit G attached to this Agreement.

1.8. Conversion Price Adjustment. The parties acknowledge that, in the event that Shares are issued and sold pursuant to Section 1.1(c) or Section 1.1(d) hereof, the Conversion Price (as defined in the Restated Certificate) applicable to each of the Series A Preferred Stock, the Series A-1 Preferred Stock, the Series B Preferred Stock and the Series C Preferred Stock (but not Series D Preferred Stock) shall adjust in accordance with the provisions of Section 4.4.4 of Division C of Article Fourth of the Restated Certificate.

2. Individual Purchase Rights of each Purchaser.

2.1. Exercise of Individual Purchase Rights.

(a) Second Tranche Individual Purchase Right.

(i) Subject to the terms and conditions of this Agreement (including, without limitation, the terms and conditions set forth below in this Section 2.1(a)), each Purchaser shall have the right under this Section 2.1(a) to purchase from the Company all (but not less than all) of the number of shares of Series D Preferred Stock set forth opposite such Purchaser's name under the heading "Second Tranche Shares" on Exhibit A (such number of shares of Series D Preferred Stock subject to such Purchaser's rights under this Section 2.1(a) being hereinafter referred to, subject to the provisions of Section 2.1(a)(iii) below, as such Purchaser's "**Second Tranche Individual Purchase Shares**"), at a purchase price per share equal to the Series D Price. The right of each Purchaser to purchase such Purchaser's Second Tranche Individual Purchase Shares pursuant to this Section 2.1(a) shall be referred to in this Agreement as such Purchaser's "**Second Tranche Individual Purchase Right**." Subject to the terms and conditions of this Agreement (including, without limitation, the terms and conditions set forth below in this Section 2.1(a)), each Purchaser may exercise such Purchaser's Second Tranche Individual Purchase Right by delivering a written notice of exercise to the Company (a "**Second Tranche Individual Purchase Exercise Notice**") setting forth a proposed date for the closing of such Purchaser's Second Tranche Individual Purchase Right (such closing being referred to in this Agreement as a "**Section 2.1(a) Closing**") that is consistent with the applicable requirements of Section 2.1(a)(ii) below. If a Purchaser delivers to the Company a Second Tranche Individual Purchase Exercise Notice in accordance with the provisions of this Section 2.1(a)(i) and Section 2.1(a)(ii) below, then, subject to the terms and conditions of this Agreement (including, without limitation, the terms and conditions set forth below in this Section 2.1(a)), at the applicable Section 2.1(a) Closing, the Company shall issue and sell to such Purchaser, and such Purchaser shall purchase from the Company, all (but not less than all) of such Purchaser's Second Tranche Individual Purchase Shares, at a purchase price per share equal to the Series D Price.

(ii) Notwithstanding anything express or implied in the foregoing provisions of this Section 2.1(a) to the contrary: (A) no Purchaser shall send the Second Tranche Individual Purchase Exercise Notice at any time during the Restricted Period; (B) the sale and purchase of any Purchaser's Second Tranche Individual Purchase Shares

pursuant to this Section 2.1(a) shall not be consummated at any time during the Restricted Period; and (C) in the event that the sale and purchase of a Purchaser's Second Tranche Individual Purchase Shares pursuant to this Section 2.1(a) is to be consummated at any time within thirty (30) days prior to the consummation of a Deemed Liquidation Event or at any time after the closing of the IPO, such Purchaser shall have the right to make a Net Issue Election pursuant to which such Purchaser shall be issued pursuant to this Section 2.1(a), at the applicable Section 2.1(a) Closing, a smaller number of such Purchaser's Second Tranche Individual Purchase Shares determined in accordance with such Net Issue Election and without having to make payment to the Company of any cash purchase price in connection with such smaller number of such Purchaser's Second Tranche Individual Purchase Shares, in lieu of purchasing and paying the purchase price for the full number of such Purchaser's Second Tranche Individual Purchase Shares that such Purchaser would otherwise purchase and pay for pursuant to this Section 2.1(a).

(iii) In the event that (1) the Company consummates the IPO, (2) the sale and purchase of a Purchaser's Second Tranche Individual Purchase Shares has not been consummated pursuant to this Section 2.1(a) prior to the closing of the IPO and (3) the rights and obligations of the Company and such Purchaser to consummate the sale and purchase of such Purchaser's Second Tranche Individual Purchase Shares pursuant to this Section 2.1(a) have not terminated in accordance with Section 2.1(a)(iv) prior to the closing of the IPO, then upon the exercise by such Purchaser of such Purchaser's Second Tranche Individual Purchase Right by sending such Purchaser's Second Tranche Individual Purchase Notice in accordance with the provisions of this Section 2.1(a) at any time from and after the closing of the IPO, the Company shall issue and sell to such Purchaser, and such Purchaser shall purchase from the Company, in lieu of the number of shares of Series D Preferred Stock set forth opposite such Purchaser's name under the heading "Second Tranche Shares" on Exhibit A, all (but not less than all) of that number of whole shares of Common Stock that is equal to (A) the quotient (rounded down to the nearest whole number) obtained by dividing (x) the total purchase price that such Purchaser would have been required to pay to the Company for the purchase pursuant to Section 2.1(a)(i) above of such number of shares of Series D Preferred Stock, by (y) the price per share at which the Company sold Common Stock to the public in the IPO, less (B) the number of shares of Common Stock, if any, that are offered to such Purchaser for purchase in the IPO by the Company or the underwriters in connection with the IPO and that such Purchaser could have purchased in the IPO at the time of the closing of the IPO (regardless of whether or not such Purchaser actually purchases in the IPO such number of shares of Common Stock so offered and made available for purchase by such Purchaser at the time of the closing of the IPO); provided, however, that in no event shall such number of shares of Common Stock subject to purchase and sale pursuant to this Section 2.1(a)(iii) be less than zero. The purchase price per share payable by such Purchaser to the Company for any shares of Common Stock sold and purchased pursuant to this Section 2.1(a)(iii) shall be the lower of (I) the Conversion Price (as defined in the Restated Certificate) per share of the Series D Preferred Stock immediately prior to the IPO and (II) the price per share at which the Company sold Common Stock to the public in the IPO. Upon request by a Purchaser, the Company shall request from the underwriter or underwriters of the IPO written confirmation as to (x) the number of shares of Common Stock offered in connection with the IPO that such Purchaser could have purchased at the time of the closing of the IPO and (y) the number of shares of Common Stock that such Purchaser purchased in the IPO or entered into a legally binding agreement to purchase at the time of the closing of

the IPO. The Company shall provide to such Purchaser a copy of such written confirmation received from the underwriter or underwriters of the IPO. From and after the closing of the IPO, any reference in this Agreement (including, without limitation, this Section 2.1(a)) to any Purchaser's Second Tranche Individual Purchase Shares shall be a reference to the shares of Common Stock, if any, that the Company is required to issue and sell to such Purchaser, and such Purchaser is entitled to purchase from the Company, pursuant to this Section 2.1(a)(iii) upon the exercise by such Purchaser of such Purchaser's Second Tranche Individual Purchase Right in accordance with the provisions of this Section 2.1(a), and such Purchaser's Second Tranche Individual Purchase Shares shall no longer be a reference to the number of shares of Series D Preferred Stock set forth opposite such Purchaser's name under the heading "Second Tranche Shares" on Exhibit A that the Company was required to issue and sell to such Purchaser, and such Purchaser had the right to purchase from the Company, pursuant to Section 2.1(a)(i) prior to the closing of the IPO.

(iv) The rights and obligations of the Company and each Purchaser to consummate the sale and purchase of such Purchaser's Second Tranche Individual Purchase Shares pursuant to this Section 2.1(a) shall automatically terminate on the earlier of (1) the date of the Second Tranche Closing (if any), (2) the date of the Third Tranche Closing (if any), (3) the closing of the IPO if there are no shares of Common Stock that the Company is required to issue and sell to such Purchaser, and such Purchaser is entitled to purchase from the Company, pursuant to, and in accordance with, Section 2.1(a)(iii) hereof upon the exercise by such Purchaser of such Purchaser's Second Tranche Individual Purchase Right at any time from and after the closing of the IPO, (4) the tenth (10^{th}) anniversary of the Initial Tranche Closing and (5) the consummation of a Deemed Liquidation Event. In addition, if a Purchaser is in material breach of any representation, warranty, covenant or provision under this Agreement that is applicable to such Purchaser (which material breach remains uncured for at least thirty (30) days after written notice thereof), then the obligation of the Company to consummate the sale of such Purchaser's Second Tranche Individual Purchase Shares to such Purchaser pursuant to this Section 2.1(a), and the right of such Purchaser to consummate the purchase of such Purchaser's Second Tranche Individual Purchase Shares from the Company pursuant to this Section 2.1(a), may be terminated by the Company by giving written notice of termination to such Purchaser. Any termination pursuant to this Section 2.1(a)(iv) of the rights and/or obligations of the Company and/or any Purchaser to consummate the sale and purchase of such Purchaser's Second Tranche Individual Purchase Shares pursuant to this Section 2.1(a) shall not relieve or release any party to this Agreement from any material breach by such party of any representation, warranty, covenant or provision under this Agreement that is applicable to such party if and to the extent that such material breach occurred prior to such termination.

(b) Third Tranche Individual Purchase Right.

(i) Subject to the terms and conditions of this Agreement (including, without limitation, the terms and conditions set forth below in this Section 2.1(b)), each Purchaser shall have the right under this Section 2.1(b) to purchase from the Company all (but not less than all) of the number of shares of Series D Preferred Stock set forth opposite such Purchaser's name under the heading "Third Tranche Shares" on Exhibit A (such number of shares of Series D Preferred Stock subject to such Purchaser's rights under this Section 2.1(b) being hereinafter referred to, subject to the provisions of Section 2.1(b)(iii) below, as such

Purchaser's "**Third Tranche Individual Purchase Shares**"), at a purchase price per share equal to the Series D Price. The right of each Purchaser to purchase such Purchaser's Third Tranche Individual Purchase Shares pursuant to this Section 2.1(b) shall be referred to in this Agreement as such Purchaser's "**Third Tranche Individual Purchase Right**." Subject to the terms and conditions of this Agreement (including, without limitation, the terms and conditions set forth below in this Section 2.1(b)), each Purchaser may exercise such Purchaser's Third Tranche Individual Purchase Right by delivering a written notice of exercise to the Company (a "**Third Tranche Individual Purchase Exercise Notice**") setting forth a proposed date for the closing of such Purchaser's Third Tranche Individual Purchase Right (such closing being referred to in this Agreement as a "**Section 2.1(b) Closing**") that is consistent with the applicable requirements of Section 2.1(b)(ii) below. If a Purchaser delivers to the Company a Third Tranche Individual Purchase Exercise Notice in accordance with the provisions of this Section 2.1(b)(i) and Section 2.1(b)(ii) below, then, subject to the terms and conditions of this Agreement (including, without limitation, the terms and conditions set forth below in this Section 2.1(b)), at the applicable Section 2.1(b) Closing, the Company shall issue and sell to such Purchaser, and such Purchaser shall purchase from the Company, all (but not less than all) of such Purchaser's Third Tranche Individual Purchase Shares, at a purchase price per share equal to the Series D Price. Notwithstanding anything express or implied in this Agreement to the contrary (including, without limitation, any of the foregoing provisions of this Section 2.1(b)(i)), if a Purchaser has not exercised such Purchaser's Second Tranche Individual Purchase Right and consummated the sale and purchase of all of such Purchaser's Second Tranche Individual Purchase Shares pursuant to Section 2.1(a) hereof and if such Purchaser's Second Tranche Individual Purchaser Right has not terminated pursuant to, and in accordance with, the provisions of Section 2.1(a)(iv) hereof, then, simultaneously with such Purchaser's exercise of such Purchaser's Third Tranche Individual Purchase Right and the consummation of the sale and purchase of all of such Purchaser's Third Tranche Individual Purchase Shares pursuant to, and in accordance with, this Section 2.1(b), such Purchaser

shall be obligated to exercise such Purchaser's Second Tranche Individual Purchase Right and to consummate the sale and purchase of all of such Purchaser's Second Tranche Individual Purchase Shares pursuant to, and in accordance with, the provisions of Section 2.1(a) hereof.

(ii) Notwithstanding anything express or implied in the foregoing provisions of this Section 2.1(b) to the contrary: (A) no Purchaser shall send the Third Tranche Individual Purchase Exercise Notice at any time during the Restricted Period; (B) the sale and purchase of any Purchaser's Third Tranche Individual Purchase Shares pursuant to this Section 2.1(b) shall not be consummated at any time during the Restricted Period; and (C) in the event that the sale and purchase of a Purchaser's Third Tranche Individual Purchase Shares pursuant to this Section 2.1(b) is to be consummated at any time within thirty (30) days prior to the consummation of a Deemed Liquidation Event or at any time after the closing of the IPO, such Purchaser shall have the right to make a Net Issue Election pursuant to which such Purchaser shall be issued pursuant to this Section 2.1(b), at the applicable Section 2.1(b) Closing, a smaller number of such Purchaser's Third Tranche Individual Purchase Shares determined in accordance with such Net Issue Election and without having to make payment to the Company of any cash purchase price in connection with such smaller number of such Purchaser's Third Tranche Individual Purchase Shares, in lieu of purchasing and paying the purchase price for the full number of such Purchaser's Third Tranche Individual Purchase Shares that such Purchaser would otherwise purchase and pay for pursuant to this Section 2.1(b).

(iii) In the event that (1) the Company consummates the IPO, (2) the sale and purchase of a Purchaser's Third Tranche Individual Purchase Shares has not been consummated pursuant to this Section 2.1(b) prior to the closing of the IPO and (3) the rights and obligations of the Company and such Purchaser to consummate the sale and purchase of such Purchaser's Third Tranche Individual Purchase Shares pursuant to this Section 2.1(b) have not terminated in accordance with Section 2.1(b)(iv) prior to the closing of the IPO, then upon the exercise by such Purchaser of such Purchaser's Third Tranche Individual Purchase Right by sending such Purchaser's Third Tranche Individual Purchase Notice in accordance with the provisions of this Section 2.1(b) at any time from and after the closing of the IPO, the Company shall issue and sell to such Purchaser, and such Purchaser shall purchase from the Company, in lieu of the number of shares of Series D Preferred Stock set forth opposite such Purchaser's name under the heading "Third Tranche Shares" on Exhibit A, all (but not less than all) of that number of whole shares of Common Stock that is equal to (A) the quotient (rounded down to the nearest whole number) obtained by dividing (x) the total purchase price that such Purchaser would have been required to pay to the Company for the purchase pursuant to Section 2.1(b)(i) above of such number of shares of Series D Preferred Stock, by (y) the price per share at which the Company sold Common Stock to the public in the IPO, less (B) the number of shares of Common Stock, if any, that are offered to such Purchaser for purchase in the IPO by the Company or the underwriters in connection with the IPO and that such Purchaser could have purchased in the IPO at the time of the closing of the IPO (regardless of whether or not such Purchaser actually purchases in the IPO such number of shares of Common Stock so offered and made available for purchase by such Purchaser at the time of the closing of the IPO); provided, however, that (i) the reduction or deduction pursuant to the foregoing clause (B) shall be implemented only to the extent that the shares of Common Stock referred to in such clause (B) have not been taken into account to effect a reduction or deduction pursuant clause (B) of Section 2.1(a)(iii) hereof and (ii) in no event shall the number of shares of Common Stock subject to purchase and sale pursuant to this Section 2.1(b)(iii) be less than zero. The purchase price per share payable by such Purchaser to the Company for any shares of Common Stock sold and purchased pursuant to this Section 2.1(b)(iii) shall be the lower of (I) the Conversion Price (as defined in the Restated Certificate) per share of the Series D Preferred Stock immediately prior to the IPO and (II) the price per share at which the Company sold Common Stock to the public in the IPO. Upon request by a Purchaser, the Company shall request from the underwriter or underwriters of the IPO written confirmation as to (x) the number of shares of Common Stock offered in connection with the IPO that such Purchaser could have purchased at the time of the closing of the IPO and (y) the number of shares of Common Stock that such Purchaser purchased in the IPO or entered into a legally binding agreement to purchase at the time of the closing of the IPO. The Company shall provide to such Purchaser a copy of such written confirmation received from the underwriter or underwriters of the IPO. From and after the closing of the IPO, any reference in this Agreement (including, without limitation, this Section 2.1(b)) to any Purchaser's Third Tranche Individual Purchase Shares shall be a reference to the shares of Common Stock, if any, that the Company is required to issue and sell to such Purchaser, and such Purchaser is entitled to purchase from the Company, pursuant to this Section 2.1(b)(iii) upon the exercise by such Purchaser of such Purchaser's Third Tranche Individual Purchase Right in accordance with the provisions of this Section 2.1(b), and such Purchaser's Third Tranche Individual Shares shall no longer be a reference to the number of shares of Series D Preferred Stock set forth opposite such Purchaser's name under the heading "Third Tranche

Shares" on Exhibit A that the Company was required to issue and sell to such Purchaser, and such Purchaser had the right to purchase from the Company, pursuant to Section 2.1(b)(i) prior to the closing of the IPO.

(iv) The rights and obligations of the Company and each Purchaser to consummate the sale and purchase of such Purchaser's Third Tranche Individual Purchase Shares pursuant to this Section 2.1(b) shall automatically terminate on the earlier of (1) the date of the Third Tranche Closing (if any), (2) the closing of the IPO if there are no shares of Common Stock that the Company is required to issue and sell to such Purchaser, and such Purchaser is entitled to purchase from the Company, pursuant to, and in accordance with, Section 2.1(b)(iii) hereof upon the exercise by such Purchaser of such Purchaser's Third Tranche Individual Purchase Right at any time from and after the closing of the IPO, (3) the tenth (10^{th}) anniversary of the Initial Tranche Closing and (4) the consummation of a Deemed Liquidation Event. In addition, if a Purchaser is in material breach of any representation, warranty, covenant or provision under this Agreement that is applicable to such Purchaser (which material breach remains uncured for at least thirty (30) days after written notice thereof), then the obligation of the Company to consummate the sale of such Purchaser's Third Tranche Individual Purchase Shares to such Purchaser pursuant to this Section 2.1(b), and the right of such Purchaser to consummate the purchase of such Purchaser's Third Tranche Individual Purchase Shares from the Company pursuant to this Section 2.1(b), may be terminated by the Company by giving written notice of termination to such Purchaser. Any termination pursuant to this Section 2.1(b)(iv) of the rights and/or obligations of the Company and/or any Purchaser to consummate the sale and purchase of such Purchaser's Third Tranche Individual Purchase Shares pursuant to this Section 2.1(b) shall not relieve or release any party to this Agreement from any material breach by such party of any representation, warranty, covenant or provision under this Agreement that is applicable to such party if and to the extent that such material breach occurred prior to such termination.

2.2. Closings; Delivery.

(a) Second Tranche Individual Purchase Right Closings.

(i) The closing of the purchase and sale of a Purchaser's Second Tranche Individual Purchase Shares pursuant to Section 2.1(a) hereof shall take place remotely via the exchange of documents and signatures on either the date specified in such Purchaser's Second Tranche Individual Purchase Exercise Notice delivered pursuant to Section 2.1(a)(i) hereof, which date specified must be consistent with the applicable requirements of Section 2.1(a)(ii), or on such other date as the Company and such Purchaser mutually agree (such closing, a "**Section 2.1(a) Closing**").

(ii) At each Section 2.1(a) Closing, the Company shall deliver to the Purchaser participating in such Section 2.1(a) Closing a certificate representing such Purchaser's Second Tranche Individual Purchase Shares, against either (1) payment by such Purchaser of the purchase price for such Purchaser's Second Tranche Individual Purchase Shares by check payable to the Company, by wire transfer to a bank account designated by the Company or by any combination of such methods or (2) delivery by such Purchaser of a Net Issue Election Form that has been properly completed and duly executed by such Purchaser if

such Purchaser is entitled to make a Net Issue Election pursuant to Section 2.1(a)(ii) in connection with the purchase of such Purchaser's Second Tranche Individual Purchase Shares at such Section 2.1(a) Closing.

(b) Third Tranche Individual Purchase Right Closings.

(i) The closing of the purchase and sale of a Purchaser's Third Tranche Individual Purchase Shares pursuant to Section 2.1(b) hereof shall take place remotely via the exchange of documents and signatures on either the date specified in such Purchaser's Third Tranche Individual Purchase Exercise Notice delivered pursuant to Section 2.1(b)(i) hereof, which date specified must be consistent with the applicable requirements of Section 2.1(b)(ii), or on such other date as the Company and such Purchaser mutually agree (such closing, a "**Section 2.1(b) Closing**").

(ii) At each Section 2.1(b) Closing, the Company shall deliver to the Purchaser participating in such Section 2.1(b) Closing a certificate representing such Purchaser's Third Tranche Individual Purchase Shares, against either (1) payment by such Purchaser of the purchase price for such Purchaser's Third Tranche Individual Purchase Shares by check payable to the Company, by wire transfer to a bank account designated by the Company or by any combination of such methods or (2) delivery by such Purchaser of a Net Issue Election Form that has been properly completed and duly executed by such Purchaser if such Purchaser is entitled to make a Net Issue Election pursuant to Section 2.1(b)(ii) in connection with the purchase of such Purchaser's Third Tranche Individual Purchase Shares at such Section 2.1(b) Closing.

3. Representations and Warranties of the Company. The Company hereby represents and warrants to each Purchaser that, except as set forth on the Disclosure Schedule attached as Exhibit C to this Agreement (as updated by the Updated Disclosure Schedule pursuant to Section 1.3), which exceptions shall be deemed to be a part of the representations and warranties made hereunder, the following representations are true and complete as of the date of the hereof and as of the applicable Closing (unless the particular statement speaks expressly as of another date, in which case as of such other date).

The Disclosure Schedule (including each update thereto) shall be arranged in sections corresponding to the numbered and lettered sections and subsections contained in this Section 3, and the disclosures in any section or subsection of the Disclosure Schedule shall qualify other sections and subsections in this Section only to the extent it is readily apparent from a reading of the disclosure that such disclosure is applicable to such other sections and subsections. For purposes of these representations and warranties (other than those in Sections 3.2, 3.3, 3.4, 3.5 and 3.6), the term "the Company" shall include any subsidiaries of the Company unless otherwise noted herein:

3.1. Organization, Good Standing, Corporate Power and Qualification. The Company is a corporation duly organized, validly existing and in good standing under the laws of the State of Delaware and has all requisite corporate power and authority to carry on its business as presently conducted and as proposed to be conducted. The Company is duly qualified to transact business and is in good standing in the State of Missouri, Commonwealth of

Massachusetts and in each other jurisdiction in which the failure to so qualify would have a Material Adverse Effect.

3.2. Capitalization.

(a) (i) Immediately prior to the Initial Tranche Closing after giving effect to the filing of the Restated Certificate with the Secretary of State of the State of Delaware, the authorized capital of the Company consists of: (i) 205,926,290 shares of Common Stock, of which 3,833,606 shares are issued and outstanding, (ii) 158,642,302 shares of Preferred Stock, of which (A) 22,638,465 shares are designated Series A Preferred Stock and are issued and outstanding, (B) 10,909,091 shares are designated Series A-1 Preferred Stock and are issued and outstanding, (C) 20,754,461 shares are designated as Series B Preferred Stock and are issued and outstanding, (D) 17,550,758 shares are designated as Series C Preferred Stock, of which 13,202,932 shares are issued and outstanding and (E) 86,789,527 shares are designated as Series D Preferred Stock, none of which are issued and outstanding. At the time of the Closing, (i) all of the outstanding shares of Common Stock and Preferred Stock will have been duly authorized, will be fully paid and nonassessable and will have been issued in compliance with all applicable federal and state securities laws; (ii) the Company will hold no shares of Common Stock or Preferred Stock in its treasury; and (iii) the rights, privileges and preferences of the Preferred Stock will be as stated in the Restated Certificate and as provided by the General Corporation Law of the State of Delaware.

(b) As of immediately prior to the Initial Tranche Closing, The Company has reserved 18,222,157 shares of Common Stock for issuance to officers, directors, employees and consultants of the Company pursuant to its 2006 Equity Incentive Plan duly adopted by the Board of Directors and approved by the Company stockholders (as amended and in effect from time to time, the "**Stock Plan**"). Of such reserved shares, options to purchase 9,607,120 shares are currently outstanding, 221,676 shares have been issued upon exercise and 8,393,361 shares remain available for issuance to officers, directors, employees and consultants pursuant to the Stock Plan. The Company has furnished to the Purchasers complete and accurate copies of the Stock Plan and forms of agreements used thereunder.

(c) Section 3.2(c) of the Disclosure Schedule sets forth the capitalization of the Company immediately prior to the Initial Tranche Closing including the number of shares of the following: (i) issued and outstanding Common Stock, including, with respect to restricted Common Stock, if any, vesting schedule and repurchase price; (ii) issued stock options, if any; (iii) stock options, if any, not yet issued but reserved for issuance, including vesting schedule and exercise price; (iv) each series of Preferred Stock; and (v) warrants or stock purchase rights, if any. Except for (A) the conversion privileges of the Preferred Stock, (B) the rights provided in Section 5 of the Investors' Rights Agreement, and (C) the securities and rights described in Sections 3.2(a) and 3.2(b) of this Agreement and Section 3.2(c) of the Disclosure Schedule, there are no outstanding options, warrants (other than warrants to purchase Common Stock, issued pursuant to that certain Series C Preferred Stock Purchase Agreement, dated as of August 2, 2011, by and among the Company and the investors named therein, as amended), rights (including conversion or preemptive rights and rights of first refusal or similar rights) or agreements, orally or in writing, to purchase or acquire from the Company any shares of Common Stock or Preferred Stock, or any securities convertible into or exchangeable for shares

of Common Stock or Preferred Stock. Outstanding shares of the Company's Common Stock and shares of the Company's Common Stock underlying outstanding options that, in each case, are held by holders that hold 1% or more of the Company's then outstanding capital stock (treating for this purpose all shares of Common Stock issuable upon exercise or conversion of outstanding options, warrants or convertible securities, as if exercised and/or converted), if any, are subject to (i) a right of first refusal in favor of the Company upon any proposed transfer (other than transfers for estate planning purposes); and (ii) a lock-up or market standoff agreement of not less than 180 days following the IPO.

(d) None of the Company's stock purchase agreements or stock option documents contains a provision for acceleration of vesting (or lapse of a repurchase right) or other changes in the vesting provisions or other terms of such agreement or understanding upon the occurrence of any event or combination of events. The Company has never adjusted or amended the exercise price of any stock options previously awarded, whether through amendment, cancellation, replacement grant, repricing, or any other means. No stock options, stock appreciation rights or other equity-based awards issued or granted by the Company are subject to the requirements of Section 409A of the Code. Except as set forth in the Restated Certificate, the Company has no obligation (contingent or otherwise) to purchase or redeem any of its capital stock.

3.3. Subsidiaries. The Company does not currently own or control, directly or indirectly, any interest in any other corporation, partnership, trust, joint venture, limited liability company, association, or other business entity. The Company is not a participant in any joint venture, partnership or similar arrangement.

3.4. Authorization. All corporate action required to be taken by the Company's Board of Directors and stockholders in order to authorize the Company to enter into the Transaction Agreements, and to issue the Shares pursuant to this Agreement and the Common Stock issuable upon conversion of the Series D Preferred Stock issued pursuant to this Agreement, has been taken or will be taken prior to the Initial Tranche Closing. All action on the part of the officers of the Company necessary for the execution and delivery of the Transaction Agreements, the performance of all obligations of the Company under the Transaction Agreements and the issuance and delivery of the Shares has been taken or will be taken prior to the Initial Tranche Closing. The Transaction Agreements, when executed and delivered by the Company, shall constitute valid and legally binding obligations of the Company, enforceable against the Company in accordance with their respective terms except (i) as limited by applicable bankruptcy, insolvency, reorganization, moratorium, fraudulent conveyance, or other laws of general application relating to or affecting the enforcement of creditors' rights generally, (ii) as limited by laws relating to the availability of specific performance, injunctive relief, or other equitable remedies, or (iii) to the extent the indemnification provisions contained in the Investors' Rights Agreement may be limited by applicable federal or state securities laws.

3.5. Valid Issuance of Shares. The Shares, when issued, sold and delivered in accordance with the terms and for the consideration set forth in this Agreement, will be validly issued, fully paid and nonassessable and free of restrictions on transfer other than restrictions on transfer under the Transaction Agreements, applicable state and federal securities laws and liens or encumbrances created by or imposed by a Purchaser. Assuming the accuracy of the

representations of the Purchasers in Section 4 of this Agreement and subject to the filings described in Section 3.6(ii) below, the Shares will be issued in compliance with all applicable federal and state securities laws. The Common Stock issuable upon conversion of the Series D Preferred Stock issued pursuant to this Agreement have been duly reserved for issuance, and upon issuance in accordance with the terms of the Restated Certificate, will be validly issued, fully paid and nonassessable and free of restrictions on transfer other than restrictions on transfer under the Transaction Agreements, applicable federal and state securities laws and liens or encumbrances created by or imposed by a Purchaser. Based in part upon the representations of the Purchasers in Section 4 of this Agreement, and subject to Section 3.6 below, the Common Stock issuable upon conversion of the Series D Preferred Stock issued pursuant to this Agreement will be issued in compliance with all applicable federal and state securities laws.

3.6. Governmental Consents and Filings. Assuming the accuracy of the representations made by the Purchasers in Section 4 of this Agreement, no consent, approval, order or authorization of, or registration, qualification, designation, declaration or filing with, any federal, state or local governmental authority is required on the part of the Company in connection with the consummation of the transactions contemplated by this Agreement, except for (i) the filing of the Restated Certificate, and (ii) filings pursuant to Regulation D of the Securities Act, and applicable state securities laws, which have been made or will be made in a timely manner.

3.7. Litigation. There is no claim, action, suit, proceeding, arbitration, complaint, charge or investigation pending or, to the Company's knowledge, currently threatened (i) against the Company, or to the Company's knowledge, any officer, director, consultant or Key Employee of the Company or (ii) that questions the validity of the Transaction Agreements or the right of the Company to enter into them, or to consummate the transactions contemplated by the Transaction Agreements. Neither the Company nor, to the Company's knowledge, any of its officers or directors, is a party or is named as subject to the provisions of any order, writ, injunction, judgment or decree of any court or government agency or instrumentality (in the case of officers or directors, such as would have a Material Adverse Effect on the Company). There is no action, suit, proceeding or investigation by the Company pending or which the Company intends to initiate. The foregoing includes, without limitation, actions, suits, proceedings or investigations pending or threatened in writing (or any basis therefor known to the Company) involving the prior employment of any of the Company's employees, their services provided in connection with the Company's business, or any information or techniques allegedly proprietary to any of their former employers, or their obligations under any agreements with prior employers.

3.8. Intellectual Property.

(a) The Company owns or possesses sufficient legal rights to all Company Intellectual Property without, to the Company's knowledge, any conflict with, or infringement of, the rights of others. To the Company's knowledge, no product or service marketed or sold (or proposed to be marketed or sold) by the Company violates or will violate any license or infringes or will infringe any Intellectual Property Rights of any other party, except as indicated in Section 3.8.5 of the Disclosure Schedule.

(b) Other than the inventions made by F. Nicholas Franano that are the subject of the JHU Assignment Documents identified in Section 3.8.9 of the Disclosure Schedule, and subject to Section 3.8.10 of the Disclosure Schedule, the Company has not developed or invented any Company Intellectual Property using any government funding or third party grant funding

(c) Other than with respect to (i) commercially available software products under standard end-user object code license agreements, (ii) the agreement between Johns Hopkins University and Nicholas Franano, dated February 4, 2002, which agreement subsequently was assigned by Franano to Company, and (iii) U. S. government rights pursuant to the Bayh-Dole Act, and subject to Sections 3.8.7, 3.8.9(a) and 3.8.9(d) of the Disclosure Schedule, there are no outstanding options, licenses, agreements, claims, encumbrances of any kind relating to the Company Intellectual Property, nor is the Company bound by or a party to any options, licenses or agreements of any kind with respect to the Intellectual Property Rights of any other Person. In addition, there are no shared ownership interests of any kind relating to the Company Intellectual Property identified in Sections 3.8.1 through 3.8.4 of the Disclosure Schedule.

(d) The Company has not received any communications alleging that the Company has violated or, by conducting its business, would violate any of the Intellectual Property Rights of any other Person.

(e) The Company has obtained and possesses valid licenses to use all of the software programs present on the computers and other software-enabled electronic devices that it owns or leases or that it has otherwise provided to its employees for their use in connection with the Company's business.

(f) To the Company's knowledge, the Company's business as presently conducted, or as is currently planned to be conducted, does not and will not use any inventions of any of its employees or consultants (or Persons it currently intends to hire) made prior to their employment by the Company other than the inventions made by F. Nicholas Franano that are the subject of the JHU Assignment Documents as set forth in Section 3.8.9 of the Disclosure Schedule. Each Key Employee has assigned to the Company all patents, patent applications, and other Intellectual Property Rights he or she owns that are related to the Company's business as now conducted and as presently proposed to be conducted. Each employee and consultant has assigned to the Company all patents, patent applications, and other Intellectual Property Rights he or she owns that were developed by such person within the scope of his/her employment.

(g) Sections 3.8.1 through 3.8.4 of the Disclosure Schedule list all registered Intellectual Property owned by the Company; the Company is the sole owner of such registered Intellectual Property; except as indicated in Section 3.8.1 of the Disclosure Schedule all necessary registration, maintenance, annuity and renewal fees currently due in connection with such registered Intellectual Property have been paid and all necessary documents and certificates in connection with such registered Intellectual Property have been filed with the relevant patent, copyright, trademark or other authorities in the United States or foreign jurisdictions, as the case may be, for the purposes of maintaining such registered Intellectual

Property; and each patent application included in such registered Intellectual Property that has issued as a patent or is currently pending has been prosecuted in accordance with applicable law.

(h) The Company has not embedded any open source, copyleft or community source code in any of its products generally available or in development, including but not limited to any libraries or code licensed under any General Public License, Lesser General Public License or similar license arrangement.

(i) For purposes of this Section 3.8, the Company shall be deemed to have knowledge of a patent right if the Company has actual knowledge of the patent right or would be found to be on notice of such patent right for the purposes of willful infringement as determined by reference to United States patent laws.

3.9. Compliance with Other Instruments. The Company is not in violation or default (i) of any provisions of its Restated Certificate or Bylaws, (ii) of any instrument, judgment, order, writ or decree, (iii) under any note, indenture or mortgage, or (iv) under any lease, agreement, contract or purchase order to which it is a party or by which it is bound that is required to be listed on the Disclosure Schedule, or of any provision of federal or state statute, rule or regulation applicable to the Company, the violation of

which would have a Material Adverse Effect. The execution, delivery and performance of the Transaction Agreements and the consummation of the transactions contemplated by the Transaction Agreements will not result in any such violation or be in conflict with or constitute, with or without the passage of time and giving of notice, either (i) a default under any such provision, instrument, judgment, order, writ, decree, contract or agreement or (ii) an event which results in the creation of any lien, charge or encumbrance upon any assets of the Company (other than any lien, charge, or encumbrance contemplated or created by the terms of the Option Agreement) or the suspension, revocation, forfeiture, or nonrenewal of any material permit or license applicable to the Company.

3.10. Agreements; Actions.

(a) Except for the Transaction Agreements or the Option Agreement, there are no agreements, understandings, instruments, contracts or proposed transactions to which the Company is a party or by which it is bound that involve (i) obligations (contingent or otherwise) of, or payments to, the Company in excess of $50,000 per annum, (ii) the license of any patent, copyright, trademark, trade secret or other proprietary right to or from the Company, (iii) the grant of rights to manufacture, produce, assemble, license, market, or sell its products to any other Person that limit the Company's exclusive right to develop, manufacture, assemble, distribute, market or sell its products, or (iv) indemnification by the Company with respect to infringements of proprietary rights.

(b) The Company has not (i) declared or paid any dividends, or authorized or made any distribution upon or with respect to any class or series of its capital stock, (ii) incurred any indebtedness for money borrowed or incurred any other liabilities individually in excess of $50,000 per annum or in excess of $100,000 in the aggregate, (iii) made any loans or advances to any Person, other than ordinary advances for travel expenses, or (iv) sold, exchanged or otherwise disposed of any of its assets or rights, other than the sale of its

inventory in the ordinary course of business. For the purposes of subsections (b) and (c) of this Section 3.10, all indebtedness, liabilities, agreements, understandings, instruments, contracts and proposed transactions involving the same Person (including Persons the Company has reason to believe are affiliated with each other) shall be aggregated for the purpose of meeting the individual minimum dollar amounts of such subsection.

(c) The Company is not a guarantor or indemnitor of any indebtedness of any other Person.

(d) Novartis' option to acquire the Company, granted to Novartis under the Option Agreement and that certain Agreement and Plan of Merger, dated as of February 27, 2009, by and among the Company and Novartis, Novartis PR Sub, Inc. and the Stockholders' Representative referenced therein, terminated on August 3, 2013, and the Company has provided Ropes & Gray LLP with all correspondence in the Company's possession regarding the termination thereof. The transactions contemplated by the Transaction Agreements do not constitute an Acquisition Proposal as defined under and for purposes of the Option Agreement.

3.11. Certain Transactions.

(a) Other than (i) standard employee benefits generally made available to all employees, (ii) standard director and officer indemnification agreements approved by the Board of Directors, and (iii) the purchase of shares of the Company's capital stock and the issuance of options to purchase shares of the Company's Common Stock, in each instance, approved in the written minutes of the Board of Directors (previously provided to the Purchasers or their counsel), there are no agreements, understandings or proposed transactions between the Company and any of its officers, directors, consultants, or Key Employees, or any Affiliate thereof.

(b) The Company is not indebted, directly or indirectly, to any of its directors, officers or employees or to their respective spouses or children or to any Affiliate of any of the foregoing, other than in connection with expenses or advances of expenses incurred in the ordinary course of business or employee relocation expenses and for other customary employee benefits made generally available to all employees. None of the Company's directors, officers or employees, or any members of their immediate families, or any Affiliate of the foregoing (i) are, directly or indirectly, indebted to the Company or, (ii) to the Company's knowledge, have any direct or indirect ownership interest in any firm or corporation with which the Company is affiliated or with which the Company has a business relationship, or any firm or corporation which competes with the Company except that directors, officers or employees or stockholders of the Company may own stock in (but not exceeding two percent (2%) of the outstanding capital stock of) publicly traded companies that may compete with the Company. None of the Company's Key Employees or directors or any members of their immediate families or any Affiliate of any of the foregoing are, directly or indirectly, interested in any contract with the Company. None of the directors or officers, or any members of their immediate families, has any material commercial, industrial, banking, consulting, legal, accounting, charitable or familial relationship with any of the Company's customers, suppliers, service providers, joint venture partners, licensees and competitors.

3.12. Rights of Registration and Voting Rights. Except as provided in the Investors' Rights Agreement, the Company is not under any obligation to register under the Securities Act any of its currently outstanding securities or any securities issuable upon exercise or conversion of its currently outstanding securities. To the Company's knowledge, except as contemplated in the Voting Agreement, no stockholder of the Company has entered into any agreements with respect to the voting of capital shares of the Company.

3.13. Absence of Liens. The property and assets that the Company owns are free and clear of all mortgages, deeds of trust, liens, loans and encumbrances, except for any encumbrances contemplated or created by the terms of the Option Agreement and except for any statutory liens for the payment of current taxes that are not yet delinquent and encumbrances and liens that arise in the ordinary course of business and do not materially impair the Company's ownership or use of such property or assets. With respect to the property and assets it leases, the Company is in compliance with such leases and, to its knowledge, holds a valid leasehold interest free of any liens, claims or encumbrances other than those of the lessors of such property or assets.

3.14. Financial Statements. The Company has delivered to each Purchaser the Company's audited financial statements as of December 31, 2012 and for the fiscal year then ended and its unaudited financial statements (including balance sheet, income statement and statement of cash flows) as of December 31, 2013 and for the fiscal year then ended and its unaudited financial statements (including balance sheet, income statement and statement of cash flows) as of March 31, 2014 (the "**Balance Sheet Date**") and for the three-month period then ended (collectively, the "**Financial Statements**"). The Financial Statements have been prepared in accordance with generally accepted accounting principles applied on a consistent basis throughout the periods indicated, except that the unaudited Financial Statements may not contain all footnotes required by generally accepted accounting principles. The Financial Statements fairly present in all material respects the financial condition and operating results of the Company as of the dates, and for the periods, indicated therein, subject in the case of the unaudited Financial Statements to normal year-end audit adjustments and the omitted footnote disclosures. Except as set forth in the Financial Statements, the Company has no material liabilities or obligations, contingent or otherwise, other than (i) liabilities incurred in the ordinary course of business subsequent to the Balance Sheet Date and (ii) liabilities and obligations under contracts and commitments incurred in the ordinary course of business and of a type or nature not required under generally accepted accounting principles to be reflected in the Financial Statements, which, in all such cases, individually and in the aggregate would not have a Material Adverse Effect. The Company maintains and will continue to maintain a standard system of accounting established and administered in accordance with generally accepted accounting principles.

3.15. Changes. Since the Balance Sheet Date there has not been:

(a) any change in the assets, liabilities, financial condition or operating results of the Company from that reflected in the Financial Statements, except changes in the ordinary course of business that have not caused, in the aggregate, a Material Adverse Effect;

(b) any damage, destruction or loss, whether or not covered by insurance, that would have a Material Adverse Effect;

(c) any waiver or compromise by the Company of a valuable right or of a material debt owed to it;

(d) any satisfaction or discharge of any lien, claim, or encumbrance or payment of any obligation by the Company, except in the ordinary course of business and the satisfaction or discharge of which would not have a Material Adverse Effect;

(e) any material change to a material contract or agreement by which the Company or any of its assets is bound or subject;

(f) any material change in any compensation arrangement or agreement with any employee, officer, director or stockholder;

(g) any resignation or termination of employment of any officer or Key Employee of the Company, or of a consultant of the Company that would have a Material Adverse Effect;

(h) any mortgage, pledge, transfer of a security interest in, or lien, created by the Company, with respect to any of its material properties or assets, except liens for taxes not yet due or payable and liens that arise in the ordinary course of business and do not materially impair the Company's ownership or use of such property or assets and except for any encumbrances contemplated or created by the terms of the Option Agreement;

(i) any loans or guarantees made by the Company to or for the benefit of its employees, officers or directors, or any members of their immediate families, other than travel advances and other advances made in the ordinary course of its business;

(j) any declaration, setting aside or payment or other distribution in respect of any of the Company's capital stock, or any direct or indirect redemption, purchase, or other acquisition of any of such stock by the Company;

(k) any sale, assignment or transfer of any Company Intellectual Property that could reasonably be expected to result in a Material Adverse Effect;

(l) receipt of notice that there has been a loss of, or material order cancellation by, any major customer of the Company;

(m) to the Company's knowledge, any other event or condition of any character, other than events affecting the economy or the Company's industry generally, that could reasonably be expected to result in a Material Adverse Effect; or

(n) any arrangement or commitment by the Company to do any of the things described in this Section 3.15.

3.16. Employee Matters.

(a) The Company has provided to the Major Investors a written description of all compensation, including salary, bonus, severance obligations and deferred compensation paid or payable for each officer, employee, consultant and independent contractor of the Company who received compensation in excess of $100,000 for the fiscal year ended December 31, 2013 or is anticipated to receive compensation in excess of $100,000 for the fiscal year ending December 31, 2014.

(b) To the Company's knowledge, none of its employees is obligated under any contract (including licenses, covenants or commitments of any nature) or other agreement, or subject to any judgment, decree or order of any court or administrative agency, that would materially interfere with such employee's ability to promote the interest of the Company or that would conflict with the Company's business. Neither the execution or delivery of the Transaction Agreements, nor the carrying on of the Company's business by the employees of the Company, nor the conduct of the Company's business as now conducted and as presently proposed to be conducted, will, to the Company's knowledge, conflict with or result in a breach of the terms, conditions, or provisions of, or constitute a default under, any contract, covenant or instrument under which any such employee is now obligated.

(c) The Company is not delinquent in payments to any of its employees, consultants, or independent contractors for any wages, salaries, commissions, bonuses, or other direct compensation for any service performed for it or amounts required to be reimbursed to such employees, consultants, or independent contractors. The Company has complied in all material respects with all applicable state and federal equal employment opportunity laws and with other laws related to employment, including those related to wages, hours, worker classification, and collective bargaining. The Company has withheld and paid to the appropriate governmental entity or is holding for payment not yet due to such governmental entity all amounts required to be withheld from employees of the Company and is not liable for any arrears of wages, taxes, penalties, or other sums for failure to comply with any of the foregoing.

(d) To the Company's knowledge, no Key Employee or consultants of the Company intends to terminate employment with the Company or is otherwise likely to become unavailable to continue as a Key Employee or consultant, nor does the Company have a present intention to terminate the employment of any of the foregoing. The employment of each employee of the Company is terminable at the will of the Company. Except as set forth in Section 3.16(d) of the Disclosure Schedule or as required by law, upon termination of the employment of any such employees, no severance or other payments will become due. Except as set forth in Section 3.16(d) of the Disclosure Schedule, the Company has no policy, practice, plan, or program of paying severance pay or any form of severance compensation in connection with the termination of employment services.

(e) The Company has not made any representations regarding equity incentives to any officer, employees, director or consultant that are inconsistent with the share amounts and terms set forth in the Company's board minutes.

(f) Each former Key Employee whose employment was terminated by the Company has entered into an agreement with the Company providing for the full release of any claims against the Company or any related party arising out of such employment.

(g) Section 3.16(g) of the Disclosure Schedule lists each employee benefit plan maintained, established or sponsored by the Company, or which the Company participates in or contributes to, which is subject to the Employee Retirement Income Security Act of 1974, as amended ("**ERISA**"). The Company has made all required contributions and has no liability to any such employee benefit plan, other than liability for health plan continuation coverage described in Part 6 of Title I(B) of ERISA, and has complied in all material respects with all applicable laws for any such employee benefit plan.

(h) The Company is not bound by or subject to (and none of its assets or properties is bound by or subject to) any written or oral, express or implied, contract, commitment or arrangement with any labor union, and no labor union has requested or, to the knowledge of the Company, has sought to represent any of the employees, representatives or agents of the Company. There is no strike or other labor dispute involving the Company pending, or to the Company's knowledge, threatened, which could have a Material Adverse Effect, nor is the Company aware of any labor organization activity involving its employees.

(i) To the Company's knowledge, none of the Key Employees or directors of the Company has been (i) subject to voluntary or involuntary petition under the federal bankruptcy laws or any state insolvency law or the appointment of a receiver, fiscal agent or similar officer by a court for his business or property; (ii) convicted in a criminal proceeding or named as a subject of a pending criminal proceeding (excluding traffic violations and other minor offenses); (iii) subject to any order, judgment, or decree (not subsequently reversed, suspended, or vacated) of any court of competent jurisdiction permanently or temporarily enjoining him from engaging, or otherwise imposing limits or conditions on his engagement in any securities, investment advisory, banking, insurance, or other type of business or acting as an officer or director of a public company; or (iv) found by a court of competent jurisdiction in a civil action or by the Securities and Exchange Commission or the Commodity Futures Trading Commission to have violated any federal or state securities, commodities, or unfair trade practices law, which such judgment or finding has not been subsequently reversed, suspended, or vacated.

3.17. **Tax Returns and Payments**. There are no federal, state, county, local or foreign taxes dues and payable by the Company which have not been timely paid. There are no accrued and unpaid federal, state, country, local or foreign taxes of the Company which are due, whether or not assessed or disputed. There have been no examinations or audits of any tax returns or reports by any applicable federal, state, local or foreign governmental agency. The Company has duly and timely filed all federal, state, county, local and foreign tax returns required to have been filed by it and there are in effect no waivers of applicable statutes of limitations with respect to taxes for any year.

3.18. **Insurance**. The Company has in full force and effect fire and casualty insurance policies with extended coverage, sufficient in amount (subject to reasonable deductions) to allow it to replace any of its properties that might be damaged or destroyed.

3.19. **Confidential Information and Invention Assignment Agreements**.

(a) Each current and former employee, consultant and officer of the Company has executed an agreement with the Company regarding confidentiality and proprietary information in the form or forms delivered to the Major Investors (the "**Employee/Consulting Agreements**"). Except as set forth in Section 3.19(a) of the Disclosure Schedule, no current or former Key Employee or consultant of the Company has excluded works or inventions from his or her assignment of inventions pursuant to such person's Employee/Consulting Agreement. The Company is not aware that any of its Key Employees or consultants is in violation thereof.

(b) Each Key Employee has entered into non-competition and non-solicitation covenants as set forth in the Employee/Consulting Agreements.

3.20. **Permits**. The Company and each of its subsidiaries has all franchises, permits, licenses and any similar authority (each a "**Permit**") necessary for the conduct of its business, the lack of which could reasonably be expected to have a Material Adverse Effect. The Company is not in default in any material respect under any of such Permits.

3.21. **Corporate Documents**. The Restated Certificate and Bylaws of the Company are in the form provided to the Purchasers. The copy of the minute books of the Company provided to the Purchasers contains minutes of all meetings of directors and stockholders and all actions by written consent without a meeting by the directors and stockholders since the date of incorporation and accurately reflects in all material respects all actions by the directors (and any committee of directors) and stockholders with respect to all transactions referred to in such minutes.

3.22. **Real Property Holding Corporation**. The Company is not now and has never been a "United States real property holding corporation" as defined in the Code and any applicable regulations promulgated thereunder. The Company has filed with the Internal Revenue Service all statements, if any, with its United States income tax returns which are required under such regulations.

3.23. **Environmental and Safety Laws**. Except as could not reasonably be expected to have a Material Adverse Effect: (a) the Company is and has been in compliance with all Environmental Laws; (b) there has been no release or threatened release of any pollutant, contaminant or toxic or hazardous material, substance or waste, or petroleum or any fraction thereof, (each a "**Hazardous Substance**") on, upon, into or from any site currently or heretofore owned, leased or otherwise used by the Company; (c) there have been no Hazardous Substances generated by the Company that have been disposed of or come to rest at any site that has been included in any published U.S. federal, state or local "superfund" site list or any other similar list of hazardous or toxic waste sites published by any governmental authority in the United States; and (d) there are no underground storage tanks located on, no polychlorinated biphenyls ("**PCBs**") or PCB-containing equipment used or stored on, and no hazardous waste as defined by the Resource Conservation and Recovery Act, as amended, stored on, any site owned or operated by the Company, except for the storage of hazardous waste in compliance with Environmental Laws. The Company has made available to the Purchasers true and complete copies of all

material environmental records, reports, notifications, certificates of need, permits, pending permit applications, correspondence, engineering studies, and environmental studies or assessments.

For purposes of this Section 3.23, "**Environmental Laws**" means any law, regulation, or other applicable requirement relating to (a) releases or threatened release of Hazardous Substance; (b) pollution or protection of employee health or safety, public health or the environment; or (c) the manufacture, handling, transport, use, treatment, storage, or disposal of Hazardous Substances.

3.24. **No General Solicitation**. Neither the Company, nor any of is officers, directors, employees, agents, managers, stockholders or other equity holders has either directly or indirectly, including through a broker or finder (a) engaged in any general solicitation, or (b) published any advertisement in connection with the offer and sale of the Shares.

3.25. **Disclosure**. The Company has made available to the Purchasers all the information reasonably available to the Company that the Purchasers have requested for deciding whether to acquire the Shares. No representation or warranty of the Company contained in this Agreement, as qualified by the Disclosure Schedule, and no certificate furnished or to be furnished to Purchasers at the Closings contains or will contain any untrue statement of a material fact or omits or will omit to state a material fact necessary in order to make the statements contained herein or therein not misleading in light of the circumstances under which they were made.

3.26. **Regulatory Compliance**.

(a) The Company, and to the Company's knowledge, the Company's agents, are in material compliance with all statutes, rules and regulations of the Federal Food and Drug Administration (the "**FDA**") with respect to the evaluation, testing, manufacturing, and distribution of each of the Company s products, in whatever stage of development, to the extent that the same are applicable to the Company's business as it is currently conducted and proposed to be conducted, including, but not limited to, those relating to investigational use, current "Good Manufacturing Practices," current "Good Laboratory Practice," current "Good Clinical Practice," labeling, record keeping, reporting of adverse events and filing of reports.

(b) Section 3.26(b) of the Disclosure Schedule sets forth a true, complete and accurate list of the material products that are currently being developed, tested, manufactured, distributed or licensed in or out by the Company as of the date of this Agreement.

(c) Section 3.26(c) of the Disclosure Schedule sets forth a true, complete and accurate list of each of the Company s pending and approved Investigational New Drug Applications ("**INDs**") and similar state and foreign regulatory filings as of the date of this Agreement. As to each drug for which such an IND

application has become effective, and to the extent applicable, the Company is in substantial compliance with 21 U.S.C. § 355 or 21 C.F.R. Parts 312 and 600, respectively, and similar state and foreign laws and regulations and all terms and conditions of such applications.

(d) Neither the Company nor, to the Company's knowledge, any of its officers, employees or agents has made an untrue statement of a material fact or fraudulent statement to the FDA or other governmental entity, failed to disclose a material fact required to be disclosed to the FDA or other governmental entity, or committed an act, made a statement, or failed to make a statement that, at the time such disclosure was made, could reasonably be expected to provide a basis for the FDA to invoke its policy respecting "Fraud, Untrue Statements of Material Facts, Bribery, and Illegal Gratuities", set forth in 56 Fed. Reg. 46191 (September 10, 1991) or any similar policy. Neither the Company nor any of its officers, employees or agents has been convicted of any crime or engaged in any conduct for which debarment is mandated by 21 U.S.C. § 335a(a) or any similar state or foreign law or regulation or for which debarment is authorized by 21 U.S.C. § 335a(b) or any similar state or foreign law or regulation.

3.27. Studies.

(a) The clinical, pre-clinical, safety and other studies and tests conducted by or on behalf of or sponsored by the Company were and, if still pending, are being conducted in material compliance with standard medical and scientific research procedures. The Company has operated within, and currently is in material compliance with, all applicable rules, regulations and policies of the FDA for such studies. The Company has not received any notices or other correspondence from the FDA or any other governmental entity requiring the termination, suspension or modification of any clinical, pre-clinical, safety or other studies or tests.

4. Representations and Warranties of the Purchasers. Each Purchaser hereby represents and warrants to the Company, severally and not jointly, that:

4.1. Authorization. The Purchaser has full power and authority to enter into the Transaction Agreements. The Transaction Agreements to which such Purchaser is a party, when executed and delivered by the Purchaser, will constitute valid and legally binding obligations of the Purchaser, enforceable in accordance with their terms, except (a) as limited by applicable bankruptcy, insolvency, reorganization, moratorium, fraudulent conveyance, and any other laws of general application affecting enforcement of creditors' rights generally, and as limited by laws relating to the availability of specific performance, injunctive relief, or other equitable remedies, or (b) to the extent the indemnification provisions contained in the Investors' Rights Agreement may be limited by applicable federal or state securities laws.

4.2. Purchase Entirely for Own Account. This Agreement is made with the Purchaser in reliance upon the Purchaser's representation to the Company, which by the Purchaser's execution of this Agreement, the Purchaser hereby confirms, that the Shares to be acquired by the Purchaser will be acquired for investment for the Purchaser's own account, not as a nominee or agent, and not with a view to the resale or distribution of any part thereof, and that the Purchaser has no present intention of selling, granting any participation in, or otherwise distributing the same. By executing this Agreement, the Purchaser further represents that the Purchaser does not presently have any contract, undertaking, agreement or arrangement with any Person to sell, transfer or grant participations to such Person or to any third Person, with respect

to any of the Shares. The Purchaser has not been formed for the specific purpose of acquiring the Shares.

4.3. Disclosure of Information. The Purchaser has had an opportunity to: (a) discuss with the Company's management the Company's business, management and financial affairs, the terms and conditions of the offering of the Shares; and (b) review the Company's facilities. The foregoing, however, does not limit or modify the representations and warranties of the Company in Section 3 of this Agreement or the right of the Purchasers to rely thereon.

4.4. Restricted Securities. The Purchaser understands that the Shares have not been, and will not be, registered under the Securities Act, by reason of a specific exemption from the registration provisions of the Securities Act which depends upon, among other things, the bona fide nature of the investment intent and the accuracy of the Purchaser's representations as expressed herein. The Purchaser understands that the Shares are "restricted securities" under applicable U.S. federal and state securities laws and that, pursuant to these laws, the Purchaser must hold the Shares indefinitely unless they are registered with the Securities and Exchange Commission and qualified by state authorities, or an exemption from such registration and qualification requirements is available. The Purchaser acknowledges that the Company has no obligation to register or qualify the Shares for resale except if and to the extent set forth in the Investors' Rights Agreement. The Purchaser further acknowledges that if an exemption from registration or qualification is available, it may be conditioned on various requirements including, but not limited to, the time and manner of sale, the holding period for the Shares and on requirements relating to the Company which are outside of the Purchaser's control, and which the Company is under no obligation and may not be able to satisfy.

4.5. No Public Market. The Purchaser understands that no public market now exists for the Shares, and that the Company has made no assurances that a public market will ever exist for the Shares.

4.6. Legends. The Purchaser understands that the Shares may bear one or all of the following legends:

(a) "THE SHARES REPRESENTED BY THIS CERTIFICATE HAVE NOT BEEN REGISTERED UNDER THE SECURITIES ACT OF 1933, AND HAVE BEEN ACQUIRED FOR INVESTMENT AND NOT WITH A VIEW TO, OR IN CONNECTION WITH, THE SALE OR DISTRIBUTION THEREOF. NO SUCH TRANSFER MAY BE EFFECTED WITHOUT AN EFFECTIVE REGISTRATION STATEMENT RELATED THERETO OR AN OPINION OF COUNSEL IN A FORM SATISFACTORY TO THE COMPANY THAT SUCH REGISTRATION IS NOT REQUIRED UNDER THE SECURITIES ACT OF 1933."

(b) Any legend set forth in, or required by, any of the other Transaction Agreements.

(c) Any legend required by the securities laws of any state to the extent such laws are applicable.

4.7. Accredited Investor. The Purchaser is an accredited investor as defined in Rule 501(a) of Regulation D promulgated under the Securities Act.

4.8. Foreign Investors. If the Purchaser is not a United States person (as defined by Section 7701(a)(30) of the Code), such Purchaser hereby represents that it has satisfied itself as to the full observance of the laws of its jurisdiction in connection with any invitation to subscribe for the Shares or any use of this Agreement, including (i) the legal requirements within its jurisdiction for the purchase of the Shares, (ii) any foreign exchange restrictions applicable to such purchase, (iii) any governmental or other consents that may need to be obtained, and (iv) the income tax and other tax consequences, if any, that may be relevant to the purchase, holding, redemption, sale, or transfer of the Shares. Such Purchaser's subscription and payment for and/or continued beneficial ownership of the Shares will not violate any applicable securities or other laws of the Purchaser's jurisdiction.

4.9. No General Solicitation. Neither the Purchaser, nor any of its officers, directors, employees, agents, stockholders or partners has either directly or indirectly, including through a broker or finder (a) engaged in any general solicitation, or (b) published any advertisement, in connection with the offer and sale of the Shares.

4.10. Exculpation Among Purchasers. Each Purchaser acknowledges that it is not relying upon any Person, other than the Company and its officers and directors, in making its investment or decision to invest in the Company. Each Purchaser agrees that no Purchaser nor the respective controlling Persons, officers, directors,

partners, agents, or employees of any Purchaser shall be liable to any other Purchaser for any action heretofore or hereafter taken or omitted to be taken by any of them in connection with the purchase of the Shares.

4.11. Residence. If the Purchaser is an individual, then the Purchaser resides in the state or province identified in the address of the Purchaser set forth on Exhibit A; if the Purchaser is a partnership, corporation, limited liability company or other entity, then the office or offices of the Purchaser in which its principal place of business is identified is the address or addresses of the Purchaser set forth on Exhibit A.

5. Closing Conditions

5.1. Conditions to the Purchasers' Obligations at Initial Tranche Closing. The obligations of each Purchaser to purchase Shares at the Initial Tranche Closing are subject to the fulfillment, on or before the Initial Tranche Closing, of each of the following conditions, unless otherwise waived:

(a) **Representations and Warranties**. The representations and warranties of the Company contained in Section 3, as modified by the Updated Disclosure Schedule delivered at the Initial Tranche Closing, shall be true and correct as of the Initial Tranche Closing except for those representations and warranties which address matters only as of a particular date (which representations shall have been true and correct as of such particular date).

(b) **Performance**. The Company shall have performed and complied with all covenants, agreements, obligations and conditions contained in this Agreement that are

required to be performed or complied with by the Company on or before the Initial Tranche Closing.

(c) **Compliance Certificate**. The President of the Company shall have delivered to the Purchasers at the Initial Tranche Closing a certificate certifying that the conditions specified in Sections 5.1(a) and 5.1(b) have been fulfilled.

(d) **Qualifications**. All authorizations, approvals or permits, if any, of any governmental authority or regulatory body of the United States or of any state that are required in connection with the lawful issuance and sale of the Shares pursuant to this Agreement at the Initial Tranche Closing shall be obtained and effective as of the Initial Tranche Closing.

(e) **Opinion of Company Counsel**. The Purchasers shall have received from Bingham McCutchen LLP, counsel for the Company, an opinion, dated as of the Initial Tranche Closing, in substantially the form of Exhibit H-1 attached to this Agreement.

(f) **Board of Directors**. As of the Initial Tranche Closing, the Company's Board of Directors shall be comprised of Todd Foley, Hubert Birner, John G. Freund, Brendan O'Leary, Timothy Noyes, F. Nicholas Franano, Greg Phelps, Tim Haines and Dmitry Kobyzev. In addition, as of the Initial Tranche Closing, the Company's Board of Directors shall have an Audit Committee comprised of Brendan O'Leary, Hubert Birner, Todd Foley and Dmitry Kobyzev, a Compensation Committee comprised of Brendan O'Leary, Hubert Birner, Greg Phelps and Tim Haines, a Nominating and Governance Committee comprised of Hubert Birner, Todd Foley, Tim Haines and Dmitry Kobyzev and no other committees.

(g) **Investors' Rights Agreement**. The Company, each other Purchaser and any other stockholder of the Company that is required to sign the Investors' Rights Agreement in order for it to be an effective and legally binding agreement on all parties thereto, shall have executed and delivered the Investors' Rights Agreement.

(h) **Right of First Refusal and Co-Sale Agreement**. The Company, each other Purchaser that is a Major Investor, and any other stockholder of the Company that is required to sign the Right of First Refusal and Co-Sale Agreement in order for it to be an effective and legally binding agreement on all parties thereto, shall have executed and delivered the Right of First Refusal and Co-Sale Agreement.

(i) **Voting Agreement**. The Company, each other Purchaser, and any other stockholder of the Company that is required to sign the Voting Agreement in order for it to be an effective and legally binding agreement on all parties thereto, shall have executed and delivered the Voting Agreement.

(j) **Restated Certificate**. The Company shall have filed the Restated Certificate with the Secretary of State of Delaware on or prior to the Initial Tranche Closing.

(k) **Secretary's Certificate**. The Secretary of the Company shall have delivered to the Purchasers at the Initial Tranche Closing a certificate certifying (i) the Bylaws of the Company, (ii) resolutions of the Board of Directors of the Company approving the

Transaction Agreements and the transactions contemplated under the Transaction Agreements, and (iii) resolutions of the stockholders of the Company approving the Restated Certificate.

(l) **Proceedings and Documents**. All corporate and other proceedings in connection with the transactions contemplated at the Initial Tranche Closing and all documents incident thereto shall be reasonably satisfactory in form and substance to each Purchaser, and each Purchaser (or its counsel) shall have received all such counterpart original and certified or other copies of such documents as reasonably requested. Such documents may include good standing certificates.

(m) **Management Rights**. A Management Rights Letter shall have been executed by the Company and delivered to each Major Investor that makes a request for such Management Rights Letter.

(n) **Delivery of Operating Budgets**. The Company shall have delivered to the Major Investors proposed operating budgets for the years 2014, 2015 and 2016 reasonably acceptable to the Major Investors (collectively, the "**Proposed Budgets**").

(o) **Indemnification Agreements**. The Company shall have executed and delivered an Indemnification Agreement with each of Tim Haines and Dmitry Kobyzev in substantially the form of Exhibit J attached to this Agreement.

(p) **Minimum Aggregate Purchase Price at Initial Tranche Closing**. The aggregate purchase price of the Shares issued and sold at the Initial Tranche Closing shall be at least $22,500,000.

(q) **Increase in Shares Reserved under Stock Plan**. The Stock Plan shall have been amended to reserve 18,222,157 shares of Common Stock for issuance to officers, directors, employees and consultants of the Company.

(r) **No Material Adverse Effect**. There shall not have been any event or series of events that has caused a Material Adverse Effect.

5.2. Conditions to the Purchasers' Obligations at Second Tranche Closing. The obligations of each Purchaser to purchase Shares at the Second Tranche Closing, if any, are subject to the fulfillment, on or before the Second Tranche Closing, of each of the following conditions, unless otherwise waived:

(a) **Representations and Warranties**. The representations and warranties of the Company contained in Section 3, as modified by the Updated Disclosure Schedule delivered at the Second Tranche Closing, shall be true and correct as of the Second Tranche Closing except for those representations and warranties which address matters only as of a particular date (which representations shall have been true and correct as of such particular date).

(b) **Performance**. The Company shall have performed and complied with all covenants, agreements, obligations and conditions contained in this Agreement that are

required to be performed or complied with by the Company on or before the Second Tranche Closing.

(c) **Compliance Certificate**. The President of the Company shall have delivered to the Purchasers at the Second Tranche Closing a certificate certifying that the conditions specified in Sections 5.2(a) and 5.2(b) have been fulfilled.

(d) **Opinion of Company Counsel**. The Purchasers shall have received from Bingham McCutchen LLP, counsel for the Company, an opinion, dated as of the Second Tranche Closing, in substantially the form of Exhibit H-2 attached to this Agreement.

(e) **No Material Adverse Effect**. There shall not have been any event or series of events that has caused a Material Adverse Effect.

(f) **Minimum Aggregate Purchase Price at Second Tranche Closing**. The aggregate purchase price of the Shares issued and sold at the Second Tranche Closing shall be at least $4,500,000.

5.3. Conditions to the Purchasers' Obligations at Third Tranche Closing. The obligations of each Purchaser to purchase Shares at the Third Tranche Closing, if any, are subject to the fulfillment, on or before the Third Tranche Closing, of each of the following conditions, unless otherwise waived:

(a) **Representations and Warranties**. The representations and warranties of the Company contained in Section 3, as modified by the Updated Disclosure Schedule delivered at the Third Tranche Closing, shall be true and correct as of the Third Tranche Closing except for those representations and warranties which address matters only as of a particular date (which representations shall have been true and correct as of such particular date).

(b) **Performance**. The Company shall have performed and complied with all covenants, agreements, obligations and conditions contained in this Agreement that are required to be performed or complied with by the Company on or before the Third Tranche Closing.

(c) **Compliance Certificate**. The President of the Company shall have delivered to the Purchasers at the Third Tranche Closing a certificate certifying that the conditions specified in Sections 5.3(a) and 5.3(b) have been fulfilled.

(d) **Opinion of Company Counsel**. The Purchasers shall have received from Bingham McCutchen LLP, counsel for the Company, an opinion, dated as of the Third Tranche Closing, in substantially the form of Exhibit H-3 attached to this Agreement.

(e) **No Material Adverse Effect**. There shall not have been any event or series of events that has caused a Material Adverse Effect.

(f) **Minimum Aggregate Purchase Price at Third Tranche Closing**. The aggregate purchase price of the Shares issued and sold at the Third Tranche Closing shall be at least $13,500,000.

5.4. Conditions to the Company's Obligations at Initial Tranche Closing. The obligations of the Company to sell Shares to the Purchasers at the Initial Tranche Closing are subject to the fulfillment, on or before the Initial Tranche Closing, of each of the following conditions, unless otherwise waived:

(a) **Representations and Warranties**. The representations and warranties of each Purchaser contained in Section 4 shall be true and correct as of the Initial Tranche Closing.

(b) **Performance**. The Purchasers shall have performed and complied with all covenants, agreements, obligations and conditions contained in this Agreement that are required to be performed or complied with by them on or before the Initial Tranche Closing.

(c) **Qualifications**. All authorizations, approvals or permits, if any, of any governmental authority or regulatory body of the United States or of any state that are required in connection with the lawful issuance and sale of the Shares pursuant to this Agreement at the Initial Tranche Closing shall be obtained and effective as of the Initial Tranche Closing.

(d) **Investors' Rights Agreement**. Each Purchaser, as well as any other stockholder of the Company that is required to sign the Investors' Rights Agreement in order for it to be an effective and legally binding agreement on all parties thereto, shall have executed and delivered the Investors' Rights Agreement.

(e) **Right of First Refusal and Co-Sale Agreement**. Each Purchaser who is a Major Investor, as well as any other stockholder of the Company that is required to sign the Right of First Refusal and Co-Sale Agreement in order for it to be an effective and legally binding agreement on all parties thereto, shall have executed and delivered the Right of First Refusal and Co-Sale Agreement.

(f) **Voting Agreement**. Each Purchaser, as well as any other stockholder of the Company that is required to sign the Voting Agreement in order for it to be an effective and legally binding agreement on all parties thereto, shall have executed and delivered the Voting Agreement.

(g) **Increase in Shares Reserved under Stock Plan**. The Stock Plan shall have been amended to reserve 18,222,157 shares of Common Stock for issuance to officers, directors, employees and consultants of the Company.

5.5. Conditions to the Company's Obligations at Second Tranche Closing. The obligations of the Company to sell Shares at the Second Tranche Closing are subject to the fulfillment, on or before the Second Tranche Closing, of each of the following conditions, unless otherwise waived:

(a) **Representations and Warranties**. The representations and warranties of each Purchaser contained in Section 4 shall be true and correct as of the Second Tranche Closing.

(b) **Performance**. The Purchasers shall have performed and complied with all covenants, agreements, obligations and conditions contained in this Agreement that are required to be performed or complied with by them on or before the Second Tranche Closing.

(c) **Qualifications**. All authorizations, approvals or permits, if any, of any governmental authority or regulatory body of the United States or of any state that are required in connection with the lawful issuance and sale of the Shares pursuant to this Agreement at the Second Tranche Closing shall be obtained and effective as of the Second Tranche Closing.

5.6. Conditions to the Company's Obligations at Third Tranche Closing. The obligations of the Company to sell Shares at the Third Tranche Closing are subject to the fulfillment, on or before the Third Tranche Closing, of each of the following conditions, unless otherwise waived:

(a) **Representations and Warranties**. The representations and warranties of each Purchaser contained in Section 4 shall be true and correct as of the Third Tranche Closing.

(b) **Performance**. The Purchasers shall have performed and complied with all covenants, agreements, obligations and conditions contained in this Agreement that are required to be performed or complied with by them on or before the Third Tranche Closing.

(c) **Qualifications**. All authorizations, approvals or permits, if any, of any governmental authority or regulatory body of the United States or of any state that are required in connection with the lawful issuance and sale of the Shares pursuant to this Agreement at the Third Tranche Closing shall be obtained and effective as of the Third Tranche Closing.

6. Miscellaneous.

6.1. Survival of Warranties. Unless otherwise set forth in this Agreement, the representations and warranties of the Company and the Purchasers contained in or made pursuant to this Agreement shall survive the execution and delivery of this Agreement and the Closing and shall in no way be affected by any investigation or knowledge of the subject matter thereof made by or on behalf of the Purchasers or the Company.

6.2. Successors and Assigns. The terms and conditions of this Agreement shall inure to the benefit of and be binding upon the respective successors and assigns of the parties. Nothing in this Agreement, express or implied, is intended to confer upon any party other than the parties hereto or their respective successors and assigns any rights, remedies, obligations, or liabilities under or by reason of this Agreement, except as expressly provided in this Agreement.

6.3. Governing Law. This Agreement shall be governed by and construed in accordance with the General Corporation Law of the State of Delaware as to matters within the scope thereof, and as to all other matters shall be governed by and construed in accordance with the internal laws of the Commonwealth of Massachusetts, without regard to its principles of conflicts of laws.

6.4. Counterparts; Facsimile. This Agreement may be executed and delivered by facsimile signature and in two or more counterparts, each of which shall be deemed an original, but all of which together shall constitute one and the same instrument.

6.5. Titles and Subtitles. The titles and subtitles used in this Agreement are used for convenience only and are not to be considered in construing or interpreting this Agreement.

6.6. Notices. All notices and other communications given or made pursuant to this Agreement shall be in writing and shall be deemed effectively given: (a) upon personal delivery to the party to be notified, (b) when sent by confirmed electronic mail or facsimile if sent during normal business hours of the recipient, and if not so confirmed, then on the next business day, (c) five (5) days after having been sent by registered or certified mail, return receipt requested, postage prepaid, or (d) one (1) day after deposit with a nationally recognized overnight courier, specifying next day delivery, with written verification of receipt. All communications shall be sent to the respective parties at their address as set forth on the signature pages or to such e-mail address, facsimile number or address as subsequently modified by written notice given in accordance with this Section 6.6. If notice is given to the Company, a copy shall also be sent to:

Julio E. Vega
Bingham McCutchen LLP
One Federal Street
Boston, MA 02110
e-mail: julio.vega@bingham.com
fax: 617-951-8736

and if notice is given to the Purchasers, a copy shall also be given to:

Lowell A. Segal
Ropes & Gray LLP
1900 University Avenue, 6th Floor
East Palo Alto, CA 94303
e-mail: Lowell.Segal@ropesgray.com
fax: 650-566-4244

6.7. No Finder's Fees. Each party represents that it neither is nor will be obligated for any finder's fee or commission in connection with this transaction. Each Purchaser agrees to indemnify and to hold harmless the Company from any liability for any commission or compensation in the nature of a finder's or broker's fee arising out of this transaction (and the costs and expenses of defending against such liability or asserted liability) for which each

Purchaser or any of its officers, employees, or representatives is responsible. The Company agrees to indemnify and hold harmless each Purchaser from any liability for any commission or compensation in the nature of a finder's or broker's fee arising out of this transaction (and the costs and expenses of defending against such liability or asserted liability) for which the Company or any of its officers, employees or representatives is responsible.

6.8. Fees and Expenses. At the Closing, the Company shall pay or reimburse Abingworth and Pharmstandard, collectively, for their reasonable expenses in connection with their due diligence investigation with respect to financial and tax matters performed by The Brenner Group, Inc., in an amount not to exceed $11,000, and the reasonable fees and expenses of Ropes & Gray LLP, special transaction legal counsel for Abingworth and Pharmstandard, in an amount not to exceed $79,000 in the aggregate, in

connection with due diligence and the review and negotiation of the Transaction Agreements and the consummation of the transactions contemplated under the Transaction Agreements.

6.9. Amendments and Waivers. Any term of this Agreement may be amended, terminated or waived only with the written consent of the Company and the holders of sixty five percent (65%) of the then-outstanding Shares, except that any amendment, termination or waiver of any provision in Section 1.1(d)(ii) requiring approval or waiver by Purchasers that hold at least seventy-five percent (75%) of the Tranche Shares then issued and outstanding must also be approved by Purchasers that hold at least seventy-five percent (75%) of the Tranche Shares then issued and outstanding; provided, however, that no amendment to this Agreement that increases or adds to a Purchaser's obligations or commitments under this Agreement, shall be effective against such Purchaser without the prior written consent of such Purchaser; further provided that this Agreement may not be amended, modified or terminated and the observance of any term hereof may not be waived with respect to any Purchaser without such Purchaser's consent unless such amendment, modification, termination or waiver applies to all Purchasers in the same fashion. Any amendment or waiver effected in accordance with this Section 6.9 shall be binding upon the Purchasers and each transferee of the Shares, and each future holder of any or all such securities, and the Company.

6.10. Severability. The invalidity or unenforceability of any provision hereof shall in no way affect the validity or enforceability of any other provision.

6.11. Delays or Omissions. No delay or omission to exercise any right, power or remedy accruing to any party under this Agreement, upon any breach or default of any other party under this Agreement, shall impair any such right, power or remedy of such non-breaching or non-defaulting party nor shall it be construed to be a waiver of any such breach or default, or an acquiescence therein, or of or in any similar breach or default thereafter occurring; nor shall any waiver of any single breach or default be deemed a waiver of any other breach or default theretofore or thereafter occurring. Any waiver, permit, consent or approval of any kind or character on the part of any party of any breach or default under this Agreement, or any waiver on the part of any party of any provisions or conditions of this Agreement, must be in writing and shall be effective only to the extent specifically set forth in such writing. All remedies, either under this Agreement or by law or otherwise afforded to any party, shall be cumulative and not alternative.

6.12. Entire Agreement. This Agreement (including the Exhibits hereto), the Restated Certificate and the other Transaction Agreements constitute the full and entire understanding and agreement between the parties with respect to the subject matter hereof, and any other written or oral agreements relating to the subject matter hereof existing between the parties are expressly cancelled as of the Initial Tranche Closing.

6.13. Dispute Resolution. The parties (a) hereby irrevocably and unconditionally submit to the jurisdiction of the state courts of Massachusetts and to the jurisdiction of the United States District Court for the District of Massachusetts for the purpose of any suit, action or other proceeding arising out of or based upon this Agreement, (b) agree not to commence any suit, action or other proceeding arising out of or based upon this Agreement except in the state courts of Massachusetts or the United States District Court for the District of Massachusetts, and (c) hereby waive, and agree not to assert, by way of motion, as a defense, or otherwise, in any such suit, action or proceeding, any claim that it is not subject personally to the jurisdiction of the above-named courts, that its property is exempt or immune from attachment or execution, that the suit, action or proceeding is brought in an inconvenient forum, that the venue of the suit, action or proceeding is improper or that this Agreement or the subject matter hereof may not be enforced in or by such court. Each party will bear its own costs in respect of any disputes arising under this Agreement. Each of the parties to this Agreement consents to personal jurisdiction for any equitable action sought in the U.S. District Court for the District of Massachusetts or any court of the Commonwealth of Massachusetts having subject matter jurisdiction.

6.14. No Commitment for Additional Financing. The Company acknowledges and agrees that no Purchaser has made any representation, undertaking, commitment or agreement to provide or assist the Company in obtaining any financing, investment or other assistance, other than the purchase of the Shares as set forth herein, subject to the conditions set forth herein. In addition, the Company acknowledges and agrees that, subject to the terms and conditions set forth herein, (x) no statements, whether written or oral, made by any Purchaser or its representatives on or after the date of this Agreement shall create an obligation, commitment or agreement to provide or assist the Company in obtaining any financing or investment, (y) the Company shall not rely on any such statement by any Purchaser or its representatives and (z) an obligation, commitment or agreement to provide or assist the Company in obtaining any financing or investment may only be created by a written agreement, signed by such Purchaser and the Company, setting forth the terms and conditions of such financing or investment and stating that the parties intend for such writing to be a binding obligation or agreement. Subject to the terms and conditions set forth herein, each Purchaser shall have the right, in it sole and absolute discretion, to refuse or decline to participate in any other financing of or investment in the Company, and shall have no obligation to assist or cooperate with the Company in obtaining any financing, investment or other assistance.

6.15. Covenant Relating to Registration. The Company shall use commercially reasonable efforts to file a registration statement on Form S-1 with the Securities and Exchange Commission with respect to a firm commitment underwritten initial public offering of the Company's Common Stock and to cause such registration statement to become effective within eighteen (18) months after the Initial Tranche Closing.

[Remainder of Page Intentionally Left Blank]

IN WITNESS WHEREOF, the parties have executed this Series D Preferred Stock Purchase Agreement as of the date first written above.

PROTEON THERAPEUTICS, INC.

By: /s/ Timothy Noyes
Timothy Noyes
President and Chief Executive Officer

Address:
200 West Street
Waltham, MA 02451

Email:
Fax:

**[SIGNATURE PAGE TO THE PROTEON THERAPEUTICS, INC.
SERIES D PREFERRED STOCK PURCHASE AGREEMENT]**

Purchase Agreement

Purchaser Signature Page

By executing this page in the space provided, the undersigned hereby agrees (i) that he, she or it is a "Purchaser" as defined in the Series D Preferred Stock Purchase Agreement dated as of May 13, 2014, by and among Proteon Therapeutics, Inc. and the parties named therein (the "Purchase Agreement"), (ii) that he, she or it is a party to the Purchase Agreement for all purposes and (iii) that he, she or it is bound by all terms and conditions of the Purchase Agreement.

EXECUTED this 13th day of May, 2014.

Abingworth Bioventures VI, LP

By:
By: [ILLEGIBLE]

By:

Title: Partner

Address: 38 Jermyn Street

London SWIY 6DN

United Kingdom

Email:

Fax:

**[SIGNATURE PAGE TO THE PROTEON THERAPEUTICS, INC.
SERIES D PREFERRED STOCK PURCHASE AGREEMENT]**

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Series D Preferred Stock
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EXECUTED this 13th day of May, 2014.

Pharmstandard International S.A.

By: /s/ Eriks Martinovsky /s/ Gerard Birchen

Title: Director Director

Address: 65 Boulevard Grande Duchesse Charlotte

L-1331 Luxembourg

Grand-Duchy of Luxembourg

Email:

Fax:

**[SIGNATURE PAGE TO THE PROTEON THERAPEUTICS, INC.
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Purchase Agreement for all purposes and (iii) that he, she or it is bound by all terms and conditions of the Purchase Agreement.

EXECUTED this 13th day of May, 2014.

Deerfield Special Situations International Master Fund, L.P.

By: Deerfield Mgmt, L.P.
General Partner
By: J.E. Flynn Capital, LLC
General Partner

By: /s/ David J. Clark
Name: David J. Clark
Title: Authorized Signatory

Address: 780 Third Avenue, 37th Floor

New York, NY 10017

Email:

Fax:

**[SIGNATURE PAGE TO THE PROTEON THERAPEUTICS, INC.
SERIES D PREFERRED STOCK PURCHASE AGREEMENT]**

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EXECUTED this 13th day of May, 2014.

Deerfield Special Situations Fund, L.P.

By: Deerfield Mgmt, L.P.
General Partner
By: J.E. Flynn Capital, LLC
General Partner

By: /s/ David J. Clark
Name: David J. Clark
Title: Authorized Signatory

Address: 780 Third Avenue, 37th Floor

New York, NY 10017

Email:

Fax:

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EXECUTED this 13th day of May, 2014.

Deerfield Private Design Fund III, L.P.

By: Deerfield Mgmt III, L.P.
General Partner
By: J.E. Flynn Capital III, LLC
General Partner

By: /s/ David J. Clark
Name: David J. Clark
Title: Authorized Signatory

Address: 780 Third Avenue, 37th Floor

New York, NY 10017

Email:

Fax:

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EXECUTED this 13th day of May, 2014.

TVM Life Science Ventures VI GmbH & Co. KG

/s/ Josef Moosholzer /s/ Stefan Fischer

By: Josef Moosholzer (and) Stefan Fischer

Title: Authorized Officers

Address: Ottostrasse 4, 80333 Munich

Germany

Email:

Fax:

**[SIGNATURE PAGE TO THE PROTEON THERAPEUTICS, INC.
SERIES D PREFERRED STOCK PURCHASE AGREEMENT]**

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EXECUTED this 13th day of May, 2014.

TVM Life Science Ventures VI LP
By: its General Partner TVM Life Science Ventures VI (Cayman) Ltd.

/s/ Josef Moosholzer /s/ Stefan Fischer

By: Josef Moosholzer (and) Stefan Fischer

Title: Authorized Officers

Address: 75, Arlington St. Suite 500,
Boston, MA 02116, U.S.A.

Email:

Fax:

**[SIGNATURE PAGE TO THE PROTEON THERAPEUTICS, INC.
SERIES D PREFERRED STOCK PURCHASE AGREEMENT]**

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EXECUTED this 13th day of May, 2014.

Skyline Venture Partners Qualified Purchaser Fund IV, LP
By: Skyline Venture Management IV, LLC, its General Partner

By: /s/ John G. Freund

Title: John G. Freund, Managing Director

Address: 525 University Ave., Suite 610

Palo Alto, CA 94301

Email:

Fax:

**[SIGNATURE PAGE TO THE PROTEON THERAPEUTICS, INC.
SERIES D PREFERRED STOCK PURCHASE AGREEMENT]**

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EXECUTED this 13th day of May, 2014.

Prism Venture Partners V, LP
By: Prism Investment Partners V, L.P.
its General Partner

By: Prism Venture Partners V, L.L.C.
its General Partner

By: /s/ Brendan O'Leary

Title: Manging Director

Address: 75 Second Avenue, Suite 210

Needham, MA 02494

Email:

Fax:

**[SIGNATURE PAGE TO THE PROTEON THERAPEUTICS, INC.
SERIES D PREFERRED STOCK PURCHASE AGREEMENT]**

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EXECUTED this 13th day of May, 2014.

Prism Venture Partners V-A, LP
By: Prism Investment Partners V, L.P.
its General Partner

By: Prism Venture Partners V, L.L.C.
its General Partner

By: /s/ Brendan O'Leary

Title: Managing Director

Address: 75 Second Avenue, Suite 210

Needham, MA 02494

Email:

Fax:

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EXECUTED this 13th day of May, 2014.

Intersouth Partners VI, L.P.
By: Intersouth Associates VI, LLC
its General Partners

By: [ILLEGIBLE]

Title: Partner

Address: 102 City Hall Plaza, Suite 200

Durham, NC 27701

Email:

Fax:

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EXECUTED this 13th day of May, 2014.

MPM Bio IV NVS Strategic Fund, L.P.
By: MPM Bioventures IV GP LLC
its General Partner

By: MPM Bioventures IV LLC,
its General Partner

By: /s/ Toddy Foley

Title: Member

Address: 200 Clarendon Street, 54th Floor

Boston, MA 02116

Email:

Fax:

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EXECUTED this 13th day of May, 2014.

Vectis Healthcare & Life Sciences Fund II, L.P.
By: Vectis II GP, LP
Its: General Partner
By: Vectis II GP, LLC
Its: General Partner

By: [ILLEGIBLE]

Title: Authorized Person

Address: 84 State Street, Suite 320

Boston, MA 02109

Email:

Fax:

**[SIGNATURE PAGE TO THE PROTEON THERAPEUTICS, INC.
SERIES D PREFERRED STOCK PURCHASE AGREEMENT]**

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EXECUTED this 13th day of May, 2014.

Devon Park Bioventures, L.P.
By: Devon Park associates, L.P.
its General Partner

By: /s/ Marc J. Ostro

Title: General Partner

Address: 1400 Liberty Ridge Drive

Suite 103

Wayne, PA 19087

Email:

Fax:

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EXECUTED this 13th day of May, 2014.

BVP VII Special Opportunity Fund, L.P.
By: Deer VII & Co. L.P., their General Partner
By: Deer VII & Co., Ltd., its General Partner

By: [ILLEGIBLE]

Title: Director

Address: c/o Bessemer Venture Partners

1865 Palmer Avenue, Suite 104

Larchmont, NY 10538

Email:

Fax:

**[SIGNATURE PAGE TO THE PROTEON THERAPEUTICS, INC.
SERIES D PREFERRED STOCK PURCHASE AGREEMENT]**

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EXECUTED this 13th day of May, 2014.

Bessemer Venture Partners VII L.P.
By: Deer VII & Co. L.P., their General Partner
By: Deer VII & Co., Ltd., its General Partner

By: [ILLEGIBLE]

Title: Director

Address: c/o Bessemer Venture Partners

1865 Palmer Avenue, Suite 104

Larchmont, NY 10538

Email:

Fax: _____

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EXECUTED this 13th day of May, 2014.

Bessemer Venture Partners VII Institutional L.P.
By: Deer VII & Co. L.P., their General Partner
By: Deer VII & Co., Ltd., its General Partner

By: [ILLEGIBLE]

Title: Director

Address: c/o Bessemer Venture Partners

1865 Palmer Avenue, Suite 104

Larchmont, NY 10538

Email: _____

Fax: _____

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EXECUTED this 13th day of May, 2014.

Rockhill Partners, LLC

By: /s/ James G. Clarke

Title: Vice President

Address: [ILLEGIBLE]

Kansas City, MO 64154

Email: _____

Fax: _____

**[SIGNATURE PAGE TO THE PROTEON THERAPEUTICS, INC.
SERIES D PREFERRED STOCK PURCHASE AGREEMENT]**

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EXECUTED this 13th day of May, 2014.

Christena A. Gautreaux Trust u/t/a 3-8-04

By: /s/ Christena Gautreauk

Title: Trustee

Address: 200 W. 54th Street

Kansas City, MO 64112

Email:

Fax:

**[SIGNATURE PAGE TO THE PROTEON THERAPEUTICS, INC.
SERIES D PREFERRED STOCK PURCHASE AGREEMENT]**

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EXECUTED this 13th day of May, 2014.

**DeMars Pension Consulting Services, Inc.
Profit Sharing 401(k) Plan**

By: [ILLEGIBLE]

Title: Trustee

Address: Attn. Jim DeMars

8700 Indian Creek Parkway

Suite 185

Overland Park, KS 66210

Email:

Fax:

**[SIGNATURE PAGE TO THE PROTEON THERAPEUTICS, INC.
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EXECUTED this 13th day of May, 2014.

William P. Whitaker Trustee u/t/a 3-1-1994

By: /s/ William P. Whitaker

Title: Trustee

Address: 9825 Overbrook Court

Leawood, KS 66206

Email: [ILLEGIBLE]

Fax:

**[SIGNATURE PAGE TO THE PROTEON THERAPEUTICS, INC.
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EXECUTED this 13th day of May, 2014.

Patricia A. Heary Trust

By: /s/ Patricia A. Heary

Title:

Address: 5735 Ward Parkway

Kansas City, MO 64113

Email:

Fax:

**[SIGNATURE PAGE TO THE PROTEON THERAPEUTICS, INC.
SERIES D PREFERRED STOCK PURCHASE AGREEMENT]**

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EXECUTED this 13th day of May, 2014.

Sudarshan Hebbar Trust U.T.A., dated October 30, 2011

/s/ Sudarshan Hebbar

Title: Sudarshan Hebbar, Trustee

Address: 4342 Rockhill Rd. #3

Kansas City, MO 64110

Email:

Fax:

**[SIGNATURE PAGE TO THE PROTEON THERAPEUTICS, INC.
SERIES D PREFERRED STOCK PURCHASE AGREEMENT]**

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EXECUTED this 13th day of May, 2014.

Robert F. Eltonhead Trust

By: /s/ Robert F. Eltonhead

Title:

Address: 57 Sugar Mill Drive

Osprey, FL 34229

Email:

Fax:

**[SIGNATURE PAGE TO THE PROTEON THERAPEUTICS, INC.
SERIES D PREFERRED STOCK PURCHASE AGREEMENT]**

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EXECUTED this 13th day of May, 2014.

Darcy A. Howe Trust

By: /s/ Darcy A. Howe
Name:
Title:
Address: 434 W. 56th St.

Kanas City, MO 64113

Email: darcy_howe@ml.com

Fax:

**[SIGNATURE PAGE TO THE PROTEON THERAPEUTICS, INC.
SERIES D PREFERRED STOCK PURCHASE AGREEMENT]**

EXHIBITS

Exhibit H-3 Form of Legal Opinion of Company Counsel Delivered at Third Tranche Closing

Exhibit I Net Issue Election Form

Exhibit J Form of Indemnification Agreement

EXHIBIT A

Schedule of Purchasers

Investor	Note Conversion Shares	Convertible Notes Amount Owed ($)	Initial Tranche Shares	Initial Tranche Purchase Price ($)	Second Tranche Shares	Second Tranche Purchase Price ($)	Third Tranche Shares	Third Tranche Purchase Price ($)	Aggregate Shares	Aggregate Purchase Price ($)
Abingworth Bioventures VI, LP 38 Jermyn Street London SW1Y 6DN United Kingdom	0	0	16,044,081	9,444,444.55	3,208,816	1,888,888.80	9,626,448	5,666,666.38	28,879,345	16,999,999.73
Pharmstandard International S.A. 65, Boulevard Grande Duchesse Charlotte L-1331 Luxembourg Grand-Duchy of Luxembourg	0	0	8,493,925	4,999,999.92	1,698,785	999,999.99	5,096,355	2,999,999.95	15,289,065	8,999,999.86
Deerfield Private Design Fund III, L.P. 780 Third Avenue, 37th Floor New York, NY 10017	0	0	6,134,501	3,611,110.83	1,226,900	722,222.05	3,680,701	2,166,666.73	11,042,102	6,499,999.61
Deerfield Special Situations Fund, L.P. 780 Third Avenue, 37th Floor New York, NY 10017	0	0	1,311,840	772,222.49	262,368	154,444.50	787,104	463,333.50	2,361,312	1,390,000.49
Deerfield Special Situations International Master Fund, L.P. 780 Third Avenue, 37th Floor New York, NY 10017	0	0	1,047,584	616,666.61	209,517	123,333.44	628,550	369,999.73	1,885,651	1,109,999.78
TVM Life Science Ventures VI GmbH & Co. KG c/o TVM Capital GmbH TVM Life Science Management GmbH Ottostrasse 4 (Palais am Lenbachplatz) 80333 Munich / Germany Attn:	2,081,969	918,981.32	1,645,854	968,841.84	329,171	193,768.49	987,512	581,304.87	5,044,506	2,662,896.52

Investor	Note Conversion Shares	Convertible Notes Amount Owed ($)	Initial Tranche Shares	Initial Tranche Purchase Price ($)	Second Tranche Shares	Second Tranche Purchase Price ($)	Third Tranche Shares	Third Tranche Purchase Price ($)	Aggregate Shares	Aggregate Purchase Price ($)
Stefan Fischer General Partner Chief Financial Officer T +49 (89) 998 992 36 F +49 (89) 998 992 55										
TVM Life Science Ventures VI, L.P. 75 Arlington St. Suite 500 Boston, MA 02116 U.S.A With copies to: c/o TVM Capital GmbH TVM Life Science Management GmbH Ottostrasse 4 (Palais am Lenbachplatz) 80333 Munich / Germany Attn: Stefan Fischer General Partner Chief Financial Officer T +49 (89) 998 992 36 F +49 (89) 998 992 55	713,568	314,968.93	564,095	332,057.91	112,819	66,411.59	338,457	199,234.75	1,728,939	912,673.18
Skyline Venture Partners Qualified Purchaser Fund IV, L.P. 525 University Avenue Suite 520 Palo Alto, CA 94301	2,196,417	969,498.88	1,736,330	1,022,101.08	347,266	204,420.22	1,041,798	613,260.65	5,321,811	2,809,280.83
Prism Venture Partners V, L.P. 117 Kendrick Street, Suite 200 Needham, MA 02494	1,534,975	677,538.22	1,213,475	714,319.34	242,695	142,863.87	728,085	428,591.61	3,719,230	1,963,313.04
Prism Venture Partners V-A,	699,014	308,545.18	552,606	325,294.84	110,521	65,058.85	331,564	195,177.14	1,693,705	894,076.01

Investor	Note Conversion Shares	Convertible Notes Amount Owed ($)	Initial Tranche Shares	Initial Tranche Purchase Price ($)	Second Tranche Shares	Second Tranche Purchase Price ($)	Third Tranche Shares	Third Tranche Purchase Price ($)	Aggregate Shares	Aggregate Purchase Price ($)
L.P. 117 Kendrick Street, Suite 200 Needham, MA 02494										
Intersouth Partners VI, L.P. 102 City Hall Plaza, Suite 200 Durham, NC 27701	1,559,144	688,206.23	760,662	447,768.26	152,132	89,553.42	456,397	268,660.84	2,928,335	1,494,188.75
MPM Bio IV NVS Strategic Fund, LP 200 Clarendon Street, 54th Floor Boston, MA 02116	0	0	1,765,137	1,039,058.49	353,027	207,811.47	1,059,082	623,434.98	3,177,246	1,870,304.94
Vectis Healthcare & Life Sciences Fund II, L.P. c/o Brooke Private Equity Advisors 84 State Street, Suite 320 Boston, MA 02109	50,337	22,218.97	141,917	83,540.30	28,383	16,707.83	85,150	50,124.06	305,787	172,591.16
Devon Park Bioventures, L.P. 1400 Liberty Ridge Drive, Suite 103 Wayne, PA 19087	501,789	221,489.91	396,679	233,507.48	79,336	46,701.62	238,007	140,104.25	1,215,811	641,803.26
BVP VII Special Opportunity Fund LP c/o Bessemer Venture Partners 1865 Palmer Avenue, Suite 104 Larchmont, NY 10538	270,145	119,242.42	213,558	125,712.20	42,712	25,142.68	128,135	75,427.44	654,550	345,524.74
Bessemer Venture Partners VII, L.P. c/o Bessemer Venture Partners 1865 Palmer Avenue, Suite 104 Larchmont, NY 10538	160,086	70,662.29	126,553	74,496.19	25,311	14,899.48	75,932	44,697.83	387,882	204,755.79

Investor	Note Conversion Shares	Convertible Notes Amount Owed ($)	Initial Tranche Shares	Initial Tranche Purchase Price ($)	Second Tranche Shares	Second Tranche Purchase Price ($)	Third Tranche Shares	Third Tranche Purchase Price ($)	Aggregate Shares	Aggregate Purchase Price ($)
Bessemer Venture Partners VII Institutional L.P. c/o Bessemer Venture Partners 1865 Palmer Avenue, Suite 104 Larchmont, NY 10538	70,038	30,914.82	55,367	32,592.12	11,073	6,518.19	33,220	19,555.16	169,698	89,580.29
Rockhill Partners, LLC c/o James G. Clarke 6005 NW 101st Terrace Kansas City, Missouri 64154-1764	120,714	53,283.23	95,428	56,174.27	19,086	11,235.09	57,257	33,704.68	292,485	154,397.27
Christena A. Gautreaux, Trustee of the Christena A. Gautreaux Revocable Trust u/t/a 3/8/04 200 W. 54th St. Kansas City, Missouri 64112	93,081	41,086.11	73,583	43,315.08	14,717	8,663.26	44,150	25,989.17	225,531	119,053.62
DeMars Pension Consulting Services, Inc. 8700 Indian Creek Pkwy Suite 185 Overland Park, KS 66210	88,091	38,883.47	0	0	0	0	0	0	88,091	38,883.47
William P. Whitaker Trust u/t/a 3-1-1994 9825 Overbrook Ct., Leawood, KS 66206	82,013	36,200.94	64,835	38,165.52	12,967	7,633.11	38,901	22,899.31	198,716	104,898.88
Robert F. Eltonhead Trust u/t/a 12-14-95 57 Sugar Mill Drive Osprey, Florida 34229	65,822	29,054.21	0	0	0	0	0	0	65,822	29,054.21
Patricia A. Henry, Trustee for Patricia A. Henry Trust 5735 Ward Parkway Kansas City, Missouri 64113	56,998	25,159.33	0	0	0	0	0	0	56,998	25,159.33
Sudarshan Hebbar Trust U.T.A. dated 10-3-11	0	0.00	23,594	13,888.75	4,719	2,777.87	14,157	8,333.61	42,470	25,000.23

Investor	Note Conversion Shares	Convertible Notes Amount Owed ($)	Initial Tranche Shares	Initial Tranche Purchase Price ($)	Second Tranche Shares	Second Tranche Purchase Price ($)	Third Tranche Shares	Third Tranche Purchase Price ($)	Aggregate Shares	Aggregate Purchase Price ($)
4342 Rockhill Rd #3 Kansas City, MO 64110										
Darcy A. Howe Trust 434 W. 56th St. Kansas City, MO 64113	0	0.00	8,022	4,722.20	1,604	944.21	4,813	2,833.21	14,439	8,499.62
Total	**10,344,201**	**4,565,934.46**	**42,469,626**	**25,000,000.27**	**8,493,925**	**5,000,000.03**	**25,481,775**	**14,999,999.85**	**86,789,527**	**49,565,934.61**

Exhibit 10.3

[Proteon Therapeutics Letterhead]

To: Daniel Gottlieb

From: Timothy P. Noyes
CEO

Date: July 19, 2007

RE: Letter of Intent for Employment Terms

Dear Daniel,

I am looking forward to having you come to work for Proteon Therapeutics, Inc. The company and I have agreed on employment and compensation terms for you which shall take effect upon your start date. These terms include:

1) Position:	Director of Business Development, reporting directly to Timothy Noyes, President & CEO.
2) Base Salary:	$160,000 annually. You will be paid monthly.
3) Bonus:	Participation in the company's incentive bonus plan with a target bonus of up to 20% of Base Salary. This bonus will be based ¾ on your performance against goals set for you annually and agreed upon by the Board, and ¼ on subjective performance evaluation by the Board.
4) Vacation, Medical, and other Benefits	You will be entitled to 3 weeks of vacation annually, which is pro-rated in 2007. You will participate in all the standard benefit programs offered by the company for which you qualify. If you require time off associated with your relocation the company will grant you up to three additional days to be used within the first 6 months of your employment.

5) Options	Subject to Board approval at their next meeting you shall be entitled to a grant of options in Proteon amounting to 84,000 shares at an exercise price equal to the fair market value of the Company's common stock on the date of grant as determined by the Board and supported by an external common stock valuation to be completed in September. In no event will the exercise price of the option be less than $0.12 per share. One fourth (1/4) of the granted options will vest one year after the grant date and the remainder will vest at the rate of 1/12 each calendar quarter thereafter.

The Company is also prepared to pay for the following aspects of your relocation to the Boston area:

- Transportation of your household goods and automobiles and up to three months storage. The Company will gross up the second and third month of storage if required
- A lump sum payment in the amount of $20,000 for temporary housing. This includes a 40% gross up
- A lump sum payment of $2,000 (based on a $500 ticket on American Airlines, direct from SFO to Boston) for the final transportation for you and your family from California to the Boston area

Your first day of employment with Proteon will be September 4, 2007. It is understood that you are not being offered employment for a definite period of time and that either you or the company may terminate the employment relationship at any time and for any reason without prior notice and without any severance obligations.

As a condition to your employment you will be required to sign Proteon's standard "Employee Confidentiality and Inventions Assignment Agreement." Under separate cover I will send you a copy of this agreement for your review.

We are very pleased with your decision to join Proteon. Please indicate your acceptance of this offer by signing and dating a copy of this letter and returning it to me.

Sincerely,

/s/ Timothy Noyes
Timothy P. Noyes
President and Chief Executive Officer
Proteon Therapeutics, Inc.

ACCEPTED AND AGREED:

/s/ Daniel Gottlieb	7-26-07
Daniel Gottlieb	Date

[Proteon Therapeutics Letterhead]

April 14, 2006

Mr. Timothy P. Noyes
5 Brigham Road
Lexington, Massachusetts 02420

Re: Employment with Proteon Therapeutics, Inc.

Dear Tim,

Proteon Therapeutics, Inc. (the "Company" or "Proteon") is very pleased to offer you employment as its President & Chief Executive Officer. This letter contains the basic terms of your employment with the Company (the "Agreement"). If you agree to the terms and conditions set forth in this offer letter, please sign at the end of this letter in the space indicated.

1. **Duties**. Effective April 19, 2006, you will be employed as the Company's President & Chief Executive Officer. In this capacity, you will be responsible for all aspects of the Company and shall perform such duties as are ordinary, customary and necessary in your role as President & Chief Executive Officer. You will report directly to the Board of Directors ("Board") of the Company who will be responsible for evaluating your performance. In addition, pursuant to the Voting Agreement dated March 29, 2006 as it may be amended from time to time (the "Voting Agreement"), you shall serve as a Director on the Board.

2. **Place of Performance**. You shall be based no more than twenty (20) miles outside of the Boston, Massachusetts area, although reasonable travel may be expected.

3. **Compensation**. During the first year of your employment with the Company, you will be compensated at a base rate of $320,000 per year ("Base Salary"), payable and due in accordance with the regular payroll of the Company for its executives. Upward adjustments to your Base Salary will be made at the discretion of the Board with such increases typically made annually as part of the Company's annual compensation review process.

4. **Annual Bonus**. You will have an annual target bonus of 25% ("Bonus") of your Base Salary. The actual amount of this Bonus, if any and up to the full 25% target shall be determined by the Board, based on its assessment, in its discretion, of your and the Company's performance. This bonus will be based 3/4 on your performance against goals set for you annually and agreed upon by the Board, and 1/4 on subjective performance evaluation by the Board. The Bonus shall be paid in one lump sum following the completion of Company's annual compensation review process and shall be paid at the same time that other employees'

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annual bonuses are paid, but in no event later than March 15th of the calendar year immediately following the end of the annual performance review process.

5. **Options**. You will receive an option to purchase 1,329,000 shares of Proteon Therapeutics common stock (which represents 4.5% of the total equity that will be outstanding after all money from Series A investors has been paid into the Company) subject to adjustment for stock splits, combinations, recapitalizations and the like after the date of grant pursuant, and subject to the Company's **Proteon Therapeutics, Inc 2006 Equity Incentive Plan** ("Plan") and the Company's standard form of Stock Option Grant Notice and related Stock Option Agreement (collectively "Stock Agreement") between you and the Company. The option will be an incentive stock option (ISO) to the extent permissible under Section 422 of the Internal Revenue Code and will have an exercise price equal to the Board's estimate of the current fair market value of Proteon's common stock at the time of the grant. The option will vest 25% upon the first anniversary of the date of grant and 1/12 of the remaining amount quarterly thereafter.

6. **Benefits**. You will be entitled to participate in any and all employee benefit plans, programs and perquisites from time to time in effect for executives of the Company generally, on terms no less favorable than those provided to any other such executive.

7. **Vacation**. In the year that this Agreement becomes effective and in each year of employment thereafter, you will accrue vacation per standard Company policy. However, your vacation benefit shall not be less than four (4) weeks and it shall be taken at such times and intervals as shall be determined by you, subject to the reasonable business needs of the Company. Carry-over privileges for unused vacation time shall be consistent with Company policy.

8. **Business Expenses**. The Company shall pay or reimburse you for all reasonable business expenses incurred or paid by you in the performance of your duties and responsibilities hereunder, subject to such reasonable documentation as may be specified by the Company.

9. **Termination of Employment and Severance Benefits**.

(a) By the Company for Cause. The Company may terminate your employment hereunder for Cause, as defined below, provided that the Company has given written notice to you setting forth in reasonable detail the nature of such Cause. The following, as determined by the Board in its reasonable judgment, shall constitute Cause for Termination:

(i) Your commission of any felony or any crime involving moral turpitude;

(ii) Your willful failure to perform, or gross negligence in the performance

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of, your duties and responsibilities to the Company which, if capable of being cured, is not cured within 30 days after written notice by the Company specifying in reasonable detail the nature of such failure or negligence;

(iii) Your material breach of this Agreement which, if capable of being cured, is not cured within 30 days after written notice by the Company specifying in reasonable detail the nature of such breach; or

(iv) Your material breach of any agreements between you and the Company relating to confidentiality or inventions, including, without limitation, the Employee Confidentiality and Inventions Assignment Agreement between you and the Company that you are executing concurrently with this Agreement, which, if capable of being cured, is not cured within 30 days after written notice by the Company specifying in reasonable detail the nature of such breach.

Upon giving written notice to you that your employment with the Company has been terminated for Cause, the Company shall have no further obligation to you, other than for Final Compensation, as defined below.

(b) By Reason of Constructive Termination. Provided you have not previously been notified of the Company's intention to terminate your employment, you may resign from employment by reason of Constructive Termination within thirty (30) days after the occurrence of one of the events specified in 9(b) (i-v) below, by giving notice of your resignation in accordance with Paragraph 19 below. In the event of your death or disability as provided in 9(b) (vi & vii) below your employment will terminate by reason of Constructive Termination as of the date of your death or as of the end of the 180 day period.

In the event of such termination, in addition to Final Compensation, you shall be entitled to the following: (i) provided that no benefits are payable to you under a separate severance agreement as a result of such termination, an amount equal to twelve (12) months of your Base Salary at the rate in effect on the date of termination, less applicable withholdings and deductions, paid in a lump sum as provided below (the "Severance Payment"); (ii) if you are participating in the Company's group health insurance plans on the effective date of termination, and you timely elect and remain eligible for continued coverage under COBRA, or, if applicable, state insurance laws, the Company shall pay that portion of your COBRA premiums that the Company was paying prior to the effective date of termination for twelve months following or for the continuation period for which Employee is eligible, whichever is shorter and in the event the continuation period is provided by state law and is less than twelve months, pay to you the premium payments it would have made for the remainder of the twelve month period (the "COBRA Premiums"); (iii) fifty percent (50%) of any unvested stock options or unvested restricted shares held by you shall vest in full upon the occurrence of the Constructive Termination, accelerated to one hundred percent (100%) vesting in the event Constructive Termination occurs within thirty days prior to or **one hundred eighty** days following a Corporate Transaction (as defined below); (iv) at your request, the post-termination exercise grace period set forth in your stock option agreements shall be extended to provide for an exercise period of up to 180 days following the Constructive Termination; *provided*, *however*, that such post-termination exercise grace period shall not be extended beyond the period of time that would enable the stock option to remain exempt under IRS Regulation 409A.

Any obligation of the Company to you in Paragraph 9(b) is conditioned upon you signing and returning to the Company a timely and effective release of claims in the form provided by the Company (the "Release of Claims"). The Release of Claims required for separation benefits in accordance with this Section 9(b) creates legally binding obligations on your part and the Company and its Affiliates therefore advise you to seek the advice of an attorney before signing it. The Severance Payments shall be payable and due as a lump sum thirty (30) days following the later of the effective date of the Release of Claims or the date the Release of Claims, signed by you, is received by the Company, and the COBRA Premiums shall commence upon the effective date of your termination of employment; provided, however, that the Company has the right to terminate the payment of COBRA Premiums if a Release of Claims has not been delivered by you within thirty (30) days following the effective date of your termination of

employment.

The following shall constitute Constructive Termination:

(i) failure of the Company to provide you Base Salary and benefits in accordance with the terms of this Agreement, excluding an inadvertent failure which is cured within ten (10) business days following written notice from you to the Company specifying in detail the nature of such failure;

(ii) failure of the Company, or a successor to the Company, to provide you with a position that is equivalent in title, total compensation (salary and bonus), benefits or responsibilities to your then current position within ninety (90) days of a Corporate Transaction, as defined below, *provided further*, that a change in your duties or responsibilities following the Company becoming a subsidiary or division of a surviving entity after a Corporate Transaction shall be deemed to be a Constructive Termination (i.e., a change from President of the Company to President of a subsidiary or division shall be deemed to constitute a Constructive Termination);

(iii) material diminution in the nature or scope of your responsibilities, duties or authority;

(iv) relocation of your employment by more than twenty (20) miles outside of the Boston, Massachusetts area;

(v) failure of the Company to materially comply with the terms of this Agreement;

(vi) termination of your employment as a result of your death; or

(vii) termination of your employment as a result of the fact that you become disabled during your employment with an illness, injury, accident or condition of either a physical or psychological nature, and, as a result, you are unable to perform substantially all of your duties and responsibilities hereunder, with or without a reasonable accommodation, for 180 consecutive days in any 365 consecutive calendar days.

(c) By the Company Without Cause. The Company may terminate your employment hereunder without Cause. In the event of such termination, in addition to Final

Compensation, you shall be entitled to the following: (i) provided that no benefits are payable to you under a separate severance agreement as a result of such termination, an amount equal to twelve (12) months of your Base Salary at the rate in effect on the date of termination, *provided however*, that in the event of your termination Without Cause occurs at such time as the Company's business is being discontinued because rendered impracticable by substantial financial losses, lack of funding, legal decisions, administrative rulings, declaration of war, dissolution, national or local economic depression or crisis or any reasons beyond the control of the Company this amount shall be reduced to five (5) months of your Base Salary at the rate in effect on the date of termination, in either case less applicable withholdings and deductions, paid in a lump sum as provided below (the "Severance Payment"); (ii) if you are participating in the Company's group health insurance plans on the effective date of termination, and you timely elect and remain eligible for continued coverage under COBRA, or, if applicable, state insurance laws, the Company shall pay that portion of your COBRA premiums that the Company was paying prior to the effective date of termination for twelve months following or for the continuation period for which Employee is eligible, whichever is shorter and in the event the continuation period is provided by state law and is less than twelve months, pay to you the premium payments it would have made for the remainder of the twelve month period (the "COBRA Premiums"); (iii) fifty percent (50%) of any unvested stock options or unvested restricted shares held by you shall vest in full upon the occurrence of the Termination Without Cause, accelerated to one hundred percent (100%) vesting in the event Termination Without Cause occurs within thirty days prior to or **one hundred eighty** days following a Corporate Transaction (as defined below); (iv) at your request, the post-termination exercise grace period set forth in your stock option agreements shall be extended to provide for an exercise period of up to 180 days following the Termination Without Cause; *provided*, *however*, that such post-termination exercise grace period shall not be extended beyond the period of time that would enable the stock option to remain exempt under IRS Regulation 409A.

Any obligation of the Company to you in Paragraph 9(c) is conditioned upon you signing and returning to the Company a timely and effective release of claims in the form provided by the Company (the "Release of Claims"). The Release of Claims required for separation benefits in accordance with this Section 9(c) creates legally binding obligations on your part and the Company and its Affiliates therefore advise you to seek the advice of an attorney before signing it. The Severance Payments shall be payable and due as a lump sum thirty (30) days following the later of the effective date of the Release of Claims or the date the Release of Claims, signed by you, is received by the Company, and the COBRA Premiums shall commence upon the effective date of your termination of employment; provided, however, that the Company has the right to terminate the payment of COBRA Premiums if a Release of Claims has not been delivered by you within thirty (30) days following the effective date of your termination of employment.

(d) If any payment or benefit you would receive under this Agreement, when

combined with any other payment or benefit you receive pursuant to the termination or Constructive Termination of your employment with the Company ("Payment") would (i) constitute a "parachute payment" within the meaning of Section 280G of the Internal Revenue Code of 1986, as amended (the "Code"), and (ii) but for this sentence, be subject to the excise tax imposed by Section 4999 of the Code (the "Excise Tax"), then such Payment shall be either (x) the full amount of such Payment or (y) such lesser amount (with your choice of whether to reduce cash payments or stock option compensation or both) as would result in no portion of the Payment being subject to the Excise Tax, whichever of the foregoing amounts, taking into account the applicable federal, state and local employment taxes, income taxes and the Excise Taxes results in your receipt, on an after-tax basis, of the greater amount of the Payment notwithstanding that all or some portion of the Payment may be subject to the Excise Tax.

10. **At-Will Employment**. Please understand your employment is "**at will**," voluntarily entered into and is for no specific period. As a result, you are free to resign at any time, for any reason or for no reason, with two (2) months written notice. Similarly, the Company is free to conclude its at-will employment relationship with you at any time, with or without cause. Any contrary representations or agreements, which may have been made to you, are superseded by this offer letter. This at-will relationship cannot be altered unless specifically set forth in writing and signed by both you and an authorized member of the Board.

11. **Definitions**. Words or phrases which are initially capitalized or are within quotation marks shall have the meanings provided in this Section and as provided elsewhere herein. For purposes of this Agreement, the following definitions apply:

(a) "Affiliates" means all persons and entities directly or indirectly controlling, controlled by or under common control with the Company, where control may be by either management authority, contract or equity interest.

(b) "Corporate Transaction" as used herein shall mean any (i) consolidation or merger of the Company with or into any other corporation or other entity or person, or any other corporate reorganization in which the stockholders of the Company prior to such consolidation, merger or reorganization shall own less than fifty percent (50%) of the voting stock of the continuing or surviving entity after such consolidation, merger or reorganization, (ii) any transaction or series of related transactions to which the Company is a party, in which in excess of fifty percent (50%) of the Company's voting stock is transferred, except for bona fide sales of the Company's equity securities to venture investors for primarily fundraising purposes, or (iii) a sale of substantially all of the assets of the Company.

(c) "Final Compensation" means (1) any Base Salary earned but not paid through the date of termination; (2) pay for any vacation time earned but not used through the date of termination, and (3) any business expenses incurred by you but un-reimbursed on the date

of termination, provided that such expenses and required substantiation and documentation are submitted within thirty (30) days of termination and that such expenses are reimbursable under Company policy.

(d) "Person" means an individual, a corporation, a limited liability company, an association, a partnership, an estate, a trust and any other entity or organization, other than the Company or any of its Affiliates.

12. **Timing of Payments**. In the event that at the time your employment with the Company terminates the Company is publicly traded (as defined in Section 409A of the Internal Revenue Code), any amounts payable and due under Section 9 that would otherwise be considered deferred compensation subject to the additional twenty percent (20%) tax imposed by Section 409A if paid within six (6) months following the date of termination of Company employment shall be paid at the later of the time otherwise provided in Section 9 or the time that will prevent such amounts from being considered deferred compensation.

13. **Noncompetition Covenant**. You agree that during the term of your employment by Company and for twelve (12) months thereafter, you will not, without Company's express written consent, participate, whether as owner, stockholder, director, officer, manager, employee, agent or consultant or otherwise in any business, firm or corporation that is competitive with, or, with respect to action during the term of your employment by the Company, that would otherwise conflict with your employment by the Company. For the purposes of this section, a "business, firm or corporation that is competitive with" the Company means a business, firm or corporation that sells, or is developing for sale, Company Products or products that may be used in direct substitution for Company Products and would compete directly in the marketplace with such Company Products. "Company Products" means the specific products that the Company is, at the applicable time, developing or selling. Your obligations under this Paragraph 13 survive any termination of your employment.

14. **Indemnification**. The Company shall indemnify you against any and all losses, liabilities, damages, expenses (including attorneys' fees) judgments, fines and amounts incurred by you in connection with any claim, action, suit or proceeding (whether civil, criminal, administrative or investigative), including any action by or in the right of the Company, by reason of any act or omission to act in connection with the performance of your duties hereunder to the fullest extent that the Company is permitted to indemnify you against the foregoing under applicable law. The Company shall at all times cause you to be included, in your capacities hereunder, under all liability insurance coverage (or similar insurance coverage), including directors' and officers' liability insurance, maintained by the Company.

15. **Withholding**. All payments made by the Company under this Agreement shall be reduced by any tax or other amounts required to be withheld by the Company under applicable

law.

16. **Assignment and Successors**. The Company shall assign this Agreement and its rights and obligations hereunder in whole, but not in part, to any Company or other entity with or into which the Company may hereafter merge or consolidate, or to which the Company may transfer all or substantially all of its assets, if in any such case said Company or other entity shall by operation of law or expressly in writing assume all obligations of the Company hereunder as fully as if it had been originally made a party hereto, and may not otherwise assign this Agreement or its rights and obligations hereunder. You may not assign or transfer this Agreement or any rights or obligations hereunder.

17. **Severability**. If any portion or provision of this Agreement shall to any extent be declared illegal or unenforceable by a court of competent jurisdiction, then the remainder of this Agreement, or the application of such portion or provision in circumstances other than those as to which it is so declared illegal or unenforceable, shall not be affected thereby, and each portion and provision of this Agreement shall be valid and enforceable to the fullest extent permitted by law.

18. **Waiver**. No waiver of any provision hereof shall be effective unless made in writing and signed by the waiving party. The failure of either party to require the performance of any term or obligation of this Agreement, or the waiver by either party of any breach of this Agreement, shall not prevent any subsequent enforcement of such term or obligation or be deemed a waiver of any subsequent breach.

19. **Notices**. Any and all notices, requests, demands and other communications provided for by this Agreement shall be in writing and shall be effective when delivered in person, consigned to a reputable national courier service or deposited in the United States mail, postage prepaid, registered or certified, and addressed to you at your last known address on the books of the Company or, in the case of the Company, at its principal place of business, attention of the Chair of the Board, or to such other address as either party may specify by notice to the other actually received.

20. **Entire Agreement**. This letter, the Employee Confidentiality and Inventions Assignment Agreement that you are executing with the Company on the date hereof and the Stock Agreement constitute the entire agreement between the parties and amend and supersede all prior communications, agreements and understandings, written or oral, with respect to the terms and conditions of your employment.

21. **Miscellaneous**. This Agreement may not be modified or amended, and no breach shall be deemed to be waived, unless agreed to in writing by you and the Company. This is a Missouri contract and shall be governed and construed in accordance with the laws of the State of Missouri, without regard to the conflict of laws principles thereof.

Best Regards,

/s/ Stephen J. Hoffman
Stephen J. Hoffman, Ph.D., M.D.
Chairman of the Board

I have read, understand and accept the enclosed offer of employment with Proteon Therapeutics, Inc.

/s/ Timothy P. Noyes	April 17, 2006
Timothy P. Noyes	Date

[Proteon Therapeutics Letterhead]

FIRST AMENDMENT TO EMPLOYMENT AGREEMENT

This First Amendment to the Employment Agreement (the "Amendment") is made and entered into as of this 29th day of April, 2009 by and between Proteon Therapeutics, Inc., with offices located at 200 West Street, Waltham, Massachusetts 02451 (the "Company") and Timothy P. Noyes ("Noyes").

WHEREAS, Company and Noyes entered into an Employment Agreement (the "Agreement") dated April 14, 2006, and pursuant to the terms contained in Section 21 of the Agreement, Noyes and the Company desire to amend and modify the Agreement.

NOW, THEREFORE, in consideration of the mutual covenants contained in this Amendment, the parties, intending to be legally bound, mutually agree as follows:

1. The following defined term shall be added to Section 11 as part (e):

"Series B Second Tranche Grant" — shall be those incentive stock options granted by the Company to Noyes to purchase shares of Company Common Stock, $.001 par value, which options do not commence vesting by its terms until the closing date of the Series B second tranche.

2. Section 9.(b) Termination of Employment and Severance Benefits — By Reason of Constructive Termination, the second paragraph of such section is hereby deleted and replaced with the following:

In the event of such termination, in addition to Final Compensation, you shall be entitled to the following: (i) provided that no benefits are payable to you under a separate severance agreement as a result of such termination, an amount equal to twelve (12) months of your Base Salary at the rate in effect on the date of termination, less applicable withholdings and deductions, paid in a lump sum as provided below (the "Severance Payment"); (ii) if you are participating in the Company's group health insurance plans on the effective date of termination, and you timely elect and remain eligible for continued coverage under COBRA, or, if applicable, state insurance laws, the Company shall pay that portion of your COBRA premiums that the Company was paying prior to the effective date of termination for twelve (12) months following or for the continuation period for which Employee is eligible, whichever is shorter and in the event the continuation period is provided by state law and is less than twelve months, pay to you the premium payments it would have made for the remainder of the twelve (12) month period (the "COBRA Premiums"); (iii) fifty percent (50%) of any unvested stock options or unvested restricted shares held by you (excluding the Series B Second Tranche Grant, unless the date of such termination by reason of Constructive Termination occurs after either: (i) the closing date of the Series B Second Tranche, or (ii) the date the Board of Directors or Compensation Committee thereof has otherwise determined that the vesting

under the Series B Second Tranche Grant has commenced) shall vest in full upon the occurrence of the Constructive Termination, accelerated to one hundred percent (100%) vesting in the event Constructive Termination occurs within thirty days prior to or **one hundred eighty** days following a Corporate Transaction (as defined below); (iv) at your request, the post-termination exercise grace period set forth in your stock option agreements shall be extended to provide for an exercise period of up to 180 days following the Constructive Termination; *provided*, *however*, that such post-termination exercise grace period shall not be extended beyond the period of time that would enable the stock option to remain exempt under IRS Regulation 409A.

3. Section 9.(c) Termination of Employment and Severance Benefits — By the Company Without Cause, the first paragraph of such section is hereby deleted and replaced with the following:

The Company may terminate your employment hereunder without Cause. In the event of such termination, in addition to Final Compensation, you shall be entitled to the following: (i) provided that no benefits are payable to you under a separate severance agreement as a result of such termination, an amount equal to twelve (12) months of your Base Salary at the rate in effect on the date of termination, *provided however*, that in the event of your termination Without Cause occurs at such time as the Company's business is being discontinued because rendered impracticable by substantial financial losses, lack of funding, legal decisions, administrative rulings, declaration of war, dissolution, national or local economic depression or crisis or any reasons beyond the control of the Company this amount shall be reduced to five (5) months of your Base Salary at the rate in effect on the date of termination, in either case less applicable withholdings and deductions, paid in a lump sum as provided below (the "Severance Payment"); (ii) if you are participating in the Company's group health insurance plans on the effective date of termination, and you timely elect and remain eligible for continued coverage under COBRA, or, if applicable, state insurance laws, the Company shall pay that portion of your COBRA premiums that the Company was paying prior to the effective date of termination for twelve (12) months following or for the continuation period for which Employee is eligible, whichever is shorter and in the event the continuation period is provided by state law and is less than twelve (12) months, pay to you the premium payments it would have made for the remainder of the twelve (12) month period (the "COBRA Premiums"); (iii) fifty percent (50%) of any unvested stock options or unvested restricted shares held by you (excluding the Series B Second Tranche Grant, unless the date of such termination without Cause occurs after either (i) the closing date of the Series B Second Tranche, or (ii) the date that the Board of Directors or Compensation Committee thereof has otherwise determined that the vesting

under the Series B Second Tranche Grant has commenced) shall vest in full upon the occurrence of your termination without Cause, accelerated to one hundred percent (100%) vesting in the event your termination without Cause occurs within thirty (30) days prior to or One hundred eighty (180) days following a Corporate Transaction (as defined below); (iv) at your request, the post-termination exercise grace period set forth in your stock option agreements shall be extended to provide for an exercise period of up to 180 days following the Termination Without Cause; *provided, however*, that such post-termination exercise grace period shall

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not be extended beyond the period of time that would enable the stock option to remain exempt under IRS Regulation 409A.

4. Section 21. Miscellaneous. The last sentence of such section is hereby deleted and replaced with the following:

This is a Massachusetts contract and shall be governed and construed in accordance with the laws of the Commonwealth of Massachusetts, without regard to the conflict of laws principles thereof.

This Amendment sets forth the entire amendment and modification to the Agreement intended by the parties. Further, this Amendment and the Agreement constitute the entire agreement and understanding of the parties relating to the subject matter contained therein. The amendments and modifications to the Agreement are specifically limited to the terms and conditions discussed herein. The remainder of the terms and conditions of the Agreement, as agreed to by the parties, remains in full force and effect.

THIS AMENDMENT IS EXECUTED by the parties as of the date first written above.

Proteon Therapeutics, Inc. ("Company"):

/s/ Brendan O'Leary
Brendan O'Leary
Chairman, Compensation Committee of the Board of Directors

Date: 6/30/09

Timothy P. Noyes

/s/ Timothy P. Noyes
Timothy P. Noyes
President and CEO

Date: 6-22-09

Exhibit 10.5

[Proteon Therapeutics Letterhead]

July 25, 2006

Mr. Steven K. Burke
82 Willis Road
Sudbury, Massachusetts 01776

Re: Employment with Proteon Therapeutics, Inc.

Dear Steve,

Proteon Therapeutics, Inc. (the "Company" or "Proteon") is very pleased to offer you employment as its Senior Vice President & Chief Medical Officer. This letter contains the basic terms of your employment with the Company (the "Agreement"). If you agree to the terms and conditions set forth in this offer letter, please sign at the end of this letter in the space indicated.

1. **Duties**. Effective August 1, 2006, you will be employed as the Company's Senior Vice President & Chief Medical Officer. In this capacity, you will be responsible for all aspects of the Company and shall perform such duties as are ordinary, customary and necessary in your role as Senior Vice President & Chief Medical Officer. You will report directly to the President and Chief Executive Office of the Company who will be responsible for evaluating your performance.

2. **Place of Performance**. You shall be based no more than fifty (50) miles outside of the Boston, Massachusetts area, although reasonable travel may be expected.

3. **Compensation**. During the first year of your employment with the Company, you will be compensated at a base rate of $292,000 per year ("Base Salary"), payable and due in accordance with the regular payroll of the Company for its executives. Upward adjustments to your Base Salary will be made at the discretion of the Board with such increases typically made annually as part of the Company's annual compensation review process.

4. **Annual Bonus**. You will have an annual target bonus of 25% ("Bonus") of your Base Salary. The actual amount of this Bonus, if any and up to the full 25% target shall be determined by the Board, based on its assessment, in its discretion, of your and the Company's performance. This bonus will be based ¾ on your performance against goals set for you annually and agreed upon by the Board, and ¼ on subjective performance evaluation by the Board. The Bonus shall be paid in one lump sum following the completion of Company's annual compensation review process and shall be paid at the same time that other employees' annual bonuses are paid, but in no event later than March 15th of the calendar year immediately following the end of the annual performance review process.

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5. **Options**. You will receive an option to purchase 482,632 shares of Proteon Therapeutics common stock (which represents 1.6% of the total equity that will be outstanding after all money from Series A investors has been paid into the Company) subject to adjustment for stock splits, combinations, recapitalizations and the like after the date of grant pursuant, and subject to the Company's **Proteon Therapeutics, Inc 2006 Equity Incentive Plan** ("Plan") and the Company's standard form of Stock Option Grant Notice and related Stock Option Agreement (collectively "Stock Agreement") between you and the Company. The option will be an incentive stock option (ISO) to the extent permissible under Section 422 of the Internal Revenue Code and will have an exercise price equal to $.12 per share at the time of the grant. The option will vest 25% upon the first anniversary of the date of grant and 1/12 of the remaining amount quarterly thereafter.

6. **Benefits**. You will be entitled to participate in any and all employee benefit plans, programs and perquisites from time to time in effect for executives of the Company generally, on terms no less favorable than those provided to any other such executive.

7. **Vacation**. In the year that this Agreement becomes effective and in each year of employment thereafter, you will accrue vacation per standard Company policy. However, your vacation benefit shall not be less than three (3) weeks and it shall be taken at such times and intervals as shall be determined by you, subject to the reasonable business needs of the Company. Carry-over privileges for unused vacation time shall be consistent with Company policy.

8. **Business Expenses**. The Company shall pay or reimburse you for all reasonable business expenses incurred or paid by you in the performance of your duties and responsibilities hereunder, subject to such reasonable documentation as may be specified by the Company.

9. **Termination of Employment and Severance Benefits**.

(a) By the Company for Cause. The Company may terminate your employment hereunder for Cause, as defined below, provided that the Company has given written notice to you setting forth in reasonable detail the nature of such Cause. The following, as determined by the Board in its reasonable judgment, shall constitute Cause for Termination:

(i) Your conviction of any crime involving a felony or any crime involving moral turpitude;

(ii) Your willful failure to perform, or gross negligence in the performance of, your duties and responsibilities to the Company which, if capable of

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being cured, is not cured within 30 days after written notice by the Company specifying in reasonable detail the nature of such failure or negligence;

(iii) Your material breach of this Agreement which, if capable of being cured, is not cured within 30 days after written notice by the Company specifying in reasonable detail the nature of such breach;

(iv) Your material breach of any agreements between you and the Company relating to confidentiality or inventions, including, without limitation, the Employee Confidentiality and Inventions Assignment Agreement between you and the Company that you are executing concurrently with this Agreement, which, if capable of being cured, is not cured within 30 days after written notice by the Company specifying in reasonable detail the nature of such breach;

(v) The Company's business is being discontinued because rendered impracticable by substantial financial losses, lack of funding, legal decisions, administrative rulings, declaration of war, dissolution, national or local economic depression or crisis or any reasons beyond the control of the Company.

Upon giving written notice to you that your employment with the Company has been terminated for Cause, the Company shall have no further obligation to you, other than for Final Compensation, as defined below.

(b) By Reason of Constructive Termination. Provided you have not previously been notified of the Company's intention to terminate your employment, you may resign from employment by reason of Constructive Termination within thirty (30) days after the occurrence of one of the events specified in 9(b) (i-iv) below, by giving notice of your resignation in accordance with Paragraph 19 below. In the event of your death or disability as provided in 9(b) (v & vi) below your employment will terminate by reason of Constructive Termination as of the date of your death or as of the end of the 180 day period.

In the event of such termination, in addition to Final Compensation, you shall be entitled to the following: (i) provided that no benefits are payable to you under a separate severance agreement as a result of such termination, an amount equal to twelve (12) months of your Base Salary at the rate in effect on the date of termination, less applicable withholdings and deductions, paid in a lump sum as provided below (the "Severance Payment"); (ii) if you are participating in the Company's group health insurance plans on the effective date of termination, and you timely elect and remain eligible for continued coverage under COBRA,

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or, if applicable, state insurance laws, the Company shall pay that portion of your COBRA premiums that the Company was paying prior to the effective date of termination for twelve (12) months following or for the continuation period for which Employee is eligible, whichever is shorter and in the event the continuation period is provided by state law and is less than twelve (12) months, pay to you the premium payments it would have made for the remainder of the twelve (12) month period (the "COBRA Premiums"); (iii) fifty percent (50%) of any unvested stock options or unvested restricted shares held by you shall vest in full upon the occurrence of the Constructive Termination, accelerated to one hundred percent (100%) vesting in the event Constructive Termination occurs within thirty (30) days prior to or One hundred eighty)180) days following a Corporate Transaction (as defined below); (iv) at your request, the post-termination exercise grace period set forth in your stock option agreements shall be extended to provide for an exercise period of up to 180 days following the Constructive Termination; *provided, however*, that such post-termination exercise grace period shall not be extended beyond the period of time that would enable the stock option to remain exempt under IRS Regulation 409A.

Any obligation of the Company to you in Paragraph 9(b) is conditioned upon you signing and returning to the Company a timely and effective release of claims in the form provided by the Company (the "Release of Claims"). The Release of Claims required for separation benefits in accordance with this Section 9(b) creates legally binding obligations on your part and the Company and its Affiliates therefore advise you to seek the advice of an attorney before signing it. The Severance Payments shall be payable and due as a lump sum and COBRA Premiums will commence thirty (30) days following the later of the effective date of the Release of Claims or the date the Release of Claims, signed by you, is received by the Company.

The following shall constitute Constructive Termination:

(i) failure of the Company to provide you Base Salary and benefits in accordance with the terms of this Agreement, excluding an inadvertent failure which is cured within ten (10) business days following written notice from you to the Company specifying in detail the nature of such failure;

(ii) failure of the Company, or a successor to the Company, to provide you with a position that is equivalent in title, total compensation (salary and bonus), benefits or responsibilities to your then current position within ninety (90) days of a Corporate Transaction resulting in a material diminution of your responsibilities, duties or authority. Diminution of your responsibilities shall NOT, however, include having the same general responsibilities in a division/business unit/subsidiary of any entity

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surviving the Corporate Transaction.

(iii) material diminution in the nature or scope of your responsibilities, duties or authority;

(iv) relocation of your employment by more than fifty (50) miles outside of the Boston, Massachusetts area;

(v) failure of the Company to materially comply with the terms of this Agreement;

(vi) termination of your employment as a result of your death; or

(vii) termination of your employment as a result of the fact that you become disabled during your employment with an illness, injury, accident or condition of either a physical or psychological nature, and, as a result, you are unable to perform substantially all of your duties and responsibilities hereunder, with or without a reasonable accommodation, for 180 consecutive days in any 365 consecutive calendar days.

(c) By the Company Without Cause. The Company may terminate your employment hereunder without Cause. In the event of such termination, in addition to Final Compensation, you shall be entitled to the following: (i) provided that no benefits are payable to you under a separate severance agreement as a result of such termination, an amount equal to twelve (12) months of your Base Salary at the rate in effect on the date of termination, less applicable withholdings and deductions, paid in a lump sum as provided below (the "Severance Payment"); (ii) if you are participating in the Company's group health insurance plans on the effective date of termination, and you timely elect and remain eligible for continued coverage under COBRA, or, if applicable, state insurance laws, the Company shall pay that portion of your COBRA premiums that the Company was paying prior to the effective date of termination for twelve (12) months following or for the continuation period for which Employee is eligible, whichever is shorter and in the event the continuation period is provided by state law and is less than twelve (12) months, pay to you the premium payments it would have made for the remainder of the twelve (12) month period (the "COBRA Premiums"); (iii) at your request, the post-termination exercise grace period set forth in your stock option agreements shall be extended to provide for an exercise period of up to 180 days following the Termination Without Cause; *provided, however*, that such post-termination exercise grace period shall not be extended beyond the period of time that would enable the stock option to remain exempt under IRS Regulation 409A.

Any obligation of the Company to you in Paragraph 9(c) is conditioned upon you signing and returning to the Company a timely and effective release of claims in the form provided by the Company (the "Release of Claims"). The Release of Claims required for separation benefits in accordance with this Section 9(c) creates legally binding obligations on your part and the Company and its Affiliates therefore advise you to seek the advice of an attorney before signing it. The Severance Payments shall be payable and due as a lump sum and COBRA Premiums will commence thirty (30) days following the later of the effective date of the Release of Claims or the date the Release of Claims, signed by you, is received by the Company.

(d) If any payment or benefit you would receive under this Agreement, when combined with any other payment or benefit you receive pursuant to the termination or Constructive Termination of your employment with the Company ("Payment") would (i) constitute a "parachute payment" within the meaning of Section 280G of the Internal Revenue Code of 1986, as amended (the "Code"), and (ii) but for this sentence, be subject to the excise tax imposed by Section 4999 of the Code (the "Excise Tax"), then such Payment shall be either (x) the full amount of such Payment or (y) such lesser amount (with your choice of whether to reduce cash payments or stock option compensation or both) as would result in no portion of the Payment being subject to the Excise Tax, whichever of the foregoing amounts, taking into account the applicable federal, state and local employment taxes, income taxes and the Excise Taxes results in your receipt, on an after-tax basis, of the greater amount of the Payment notwithstanding that all or some portion of the Payment may be subject to the Excise Tax.

10. **At-Will Employment**. Please understand your employment is "**at will,**" voluntarily entered into and is for no specific period. As a result, you are free to resign at any time, for any reason or for no reason, with thirty (30) days written notice. Similarly, the Company is free to conclude its at-will employment relationship with you at any time, with or without cause. Any contrary representations or agreements, which may have been made to you, are superseded by this offer letter. This at-will relationship cannot be altered unless specifically set forth in writing and signed by both you and an authorized member of the Board.

11. **Definitions**. Words or phrases which are initially capitalized or are within quotation marks shall have the meanings provided in this Section and as provided elsewhere herein. For purposes of this Agreement, the following definitions apply:

(a) "Affiliates" means all persons and entities directly or indirectly controlling, controlled by or under common control with the Company, where control may be by either management authority, contract or equity interest.

(b) "Corporate Transaction" as used herein shall mean any (i) consolidation or merger of the Company with or into any other corporation or other entity or person, or any other corporate reorganization in which the stockholders of the Company prior to such consolidation,

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merger or reorganization shall own less than fifty percent (50%) of the voting stock of the continuing or surviving entity after such consolidation, merger or reorganization, (ii) any transaction or series of related transactions to which the Company is a party, in which in excess of fifty percent (50%) of the Company's voting stock is transferred, except for bona fide sales of the Company's equity securities to venture investors for primarily fundraising purposes, or (iii) a sale of substantially all of the assets of the Company.

(c) "Final Compensation" means (1) any Base Salary earned but not paid through the date of termination; (2) pay for any vacation time earned but not used through the date of termination, and (3) any business expenses incurred by you but un-reimbursed on the date of termination, provided that such expenses and required substantiation and documentation are submitted within thirty (30) days of termination and that such expenses are reimbursable under Company policy.

(d) "Person" means an individual, a corporation, a limited liability company, an association, a partnership, an estate, a trust and any other entity or organization, other than the Company or any of its Affiliates.

12. **Timing of Payments**. In the event that at the time your employment with the Company terminates the Company is publicly traded (as defined in Section 409A of the Internal Revenue Code), any amounts payable and due under Section 9 that would otherwise be considered deferred compensation subject to the additional twenty percent (20%) tax imposed by Section 409A if paid within six (6) months following the date of termination of Company employment shall be paid at the later of the time otherwise provided in Section 9 or the time that will prevent such amounts from being considered deferred compensation.

13. **Noncompetition Covenant**. You agree that during the term of your employment by Company and for twelve (12) months thereafter, you will not, without Company's express written consent, participate, whether as owner, stockholder (excluding holding of less than 1% of the stock of a public company), director, officer, manager, employee, agent or consultant or otherwise in any business, firm or corporation that is competitive with, or, with respect to action during the term of your employment by the Company, that would otherwise conflict with your employment by the Company. For the purposes of this section, a "business, firm or corporation that is competitive with" the Company means a business, firm or corporation that sells, or is developing for sale, Company Products or products that may be used in direct substitution for Company Products and would compete directly in the marketplace with such Company Products. "Company Products" means the specific products that the Company is, at the applicable time, developing or selling. Your obligations under this Paragraph 13 survive any termination of your employment.

14. **Indemnification**. The Company shall indemnify you against any and all losses,

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liabilities, damages, expenses (including attorneys' fees) judgments, fines and amounts incurred by you in connection with any claim, action, suit or proceeding (whether civil, criminal, administrative or investigative), including any action by or in the right of the Company, by reason of any act or omission to act in connection with the performance of your duties hereunder to the fullest extent that the Company is permitted to indemnify you against the foregoing under applicable law. The Company shall at all times cause you to be included, in your capacities hereunder, under all liability insurance coverage (or similar insurance coverage), including directors' and officers' liability insurance, maintained by the Company.

15. **Withholding**. All payments made by the Company under this Agreement shall be reduced by any tax or other amounts required to be withheld by the Company under applicable law.

16. **Assignment and Successors**. The Company may assign this Agreement and its rights and obligations hereunder in whole, but not in part, to any Company or other entity with or into which the Company may hereafter merge or consolidate, or to which the Company may transfer all or substantially all of its assets, if in any such case said Company or other entity shall by operation of law or expressly in writing assume all obligations of the Company hereunder as fully as if it had been originally made a party hereto, and may not otherwise assign this Agreement or its rights and obligations hereunder. You may not assign or transfer this Agreement or any rights or obligations hereunder.

17. **Severability**. If any portion or provision of this Agreement shall to any extent be declared illegal or unenforceable by a court of competent jurisdiction, then the remainder of this Agreement, or the application of such portion or provision in circumstances other than those as to which it is so declared illegal or unenforceable, shall not be affected thereby, and each portion and provision of this Agreement shall be valid and enforceable to the fullest extent permitted by law.

18. **Waiver**. No waiver of any provision hereof shall be effective unless made in writing and signed by the waiving party. The failure of either party to require the performance of any term or obligation of this Agreement, or the waiver by either party of any breach of this Agreement, shall not prevent any subsequent enforcement of such term or obligation or be deemed a waiver of any subsequent breach.

19. **Notices**. Any and all notices, requests, demands and other communications provided for by this Agreement shall be in writing and shall be effective when delivered in person, consigned to a reputable national courier service or deposited in the United States mail, postage prepaid, registered or certified, and addressed to you at your last known address on the books of the Company or, in the case of the Company, at its principal place of business, attention of the Chair of the Board, or to such other address as either party may specify by notice to the other actually received.

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20. **Entire Agreement**. This letter, the Employee Confidentiality and Inventions Assignment Agreement that you are executing with the Company on the date hereof and the Stock Agreement constitute the entire agreement between the parties and amend and supersede all prior communications, agreements and understandings, written or oral, with respect to the terms and conditions of your employment.

21. **Miscellaneous**. This Agreement may not be modified or amended, and no breach shall be deemed to be waived, unless agreed to in writing by you and the Company. This is a Massachusetts contract and shall be governed and construed in accordance with the laws of the Commonwealth of Massachusetts, without regard to the conflict of laws principles thereof.

Best Regards,

/s/ Timothy P. Noyes

Timothy P. Noyes
President and Chief Executive Officer

I have read, understand and accept the enclosed offer of employment with Protean Therapeutics, Inc.

/s/ Steven K. Burke — July 28, 2006

Steven K. Burke — Date

[Proteon Therapeutics Letterhead]

FIRST AMENDMENT TO EMPLOYMENT AGREEMENT

This First Amendment to the Employment Agreement (the "Amendment") is made and entered into as of this 29th day of April, 2009 by and between Proteon Therapeutics, Inc., with offices located at 200 West Street, Waltham, Massachusetts 02451 (the "Company") and Steven K. Burke ("Burke").

WHEREAS, Company and Burke entered into an Employment Agreement (the "Agreement") dated July 25, 2006, and pursuant to the terms contained in Section 21 of the Agreement, Burke and the Company desire to amend and modify the Agreement.

NOW, THEREFORE, in consideration of the mutual covenants contained in this Amendment, the parties, intending to be legally bound, mutually agree as follows:

1. **Clause 9.(a)(v) shall be deleted in its entirety.**

2. **The following defined term shall be added to Section 11 as part (e):**

"Series B Second Tranche Grant" — shall be those incentive stock options granted by the Company to Burke to purchase shares of Company Common Stock, $.001 par value, which options do not commence vesting by its terms until the closing date of the Series B second tranche.

3. **Section 9.(b) Termination of Employment and Severance Benefits — By Reason of Constructive Termination, the second paragraph of such section is hereby deleted and replaced with the following:**

In the event of such termination, in addition to Final Compensation, you shall be entitled to the following: (i) provided that no benefits are payable to you under a separate severance agreement as a result of such termination, an amount equal to twelve (12) months of your Base Salary at the rate in effect on the date of termination, less applicable withholdings and deductions, paid in a lump sum as provided below (the "Severance Payment"); (ii) if you are participating in the Company's group health insurance plans on the effective date of termination, and you timely elect and remain eligible for continued coverage under COBRA, or, if applicable, state insurance laws, the Company shall pay that portion of your COBRA premiums that the Company was paying prior to the effective date of termination for twelve (12) months following or for the continuation period for which Employee is eligible, whichever is shorter and in the event the continuation period is provided by state law and is less than twelve months, pay to you the premium payments it would have made for the remainder of the twelve (12) month period (the "COBRA Premiums"); (iii) fifty percent (50%) of any unvested stock options or unvested restricted shares held by you (excluding the Series B Second Tranche Grant, unless the date of such termination by reason of Constructive Termination occurs after

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either: (i) the closing date of the Series B Second Tranche, or (ii) the date the Board of Directors or Compensation Committee thereof has otherwise determined that the vesting under the Series B Second Tranche Grant has commenced) shall vest in full upon the occurrence of the Constructive Termination, accelerated to one hundred percent (100%) vesting in the event Constructive Termination occurs within thirty (30) days prior to or one hundred eighty (180) days following a Corporate Transaction (as defined below); (iv) at your request, the post-termination exercise grace period set forth in your stock option agreements shall be extended to provide for an exercise period of up to 180 days following the Constructive Termination; *provided*, *however*, that such post-termination exercise grace period shall not be extended beyond the period of time that would enable the stock option to remain exempt under IRS Regulation 409A.

4. **Section 9.(c) Termination of Employment and Severance Benefits — By the Company Without Cause, the first paragraph of such section is hereby deleted and replaced with the following:**

The Company may terminate your employment hereunder without Cause. In the event of such termination, in addition to Final Compensation, you shall be entitled to the following: (i) provided that no benefits are payable to you under a separate severance agreement as a result of such termination, an amount equal to twelve (12) months of your Base Salary at the rate in effect on the date of termination, *provided however*, that in the event of your termination Without Cause occurs at such time as the Company's business is being discontinued because rendered impracticable by substantial financial losses, lack of funding, legal decisions, administrative rulings, declaration of war, dissolution, national or local economic depression or crisis or any reasons beyond the control of the Company this amount shall be reduced to four (4) months of your Base Salary at the rate in effect on the date of termination, in either case less applicable withholdings and deductions, paid in a lump sum as provided below (the "Severance Payment"); (ii) if you are participating in the Company's group health insurance plans on the effective date of termination, and you timely elect and remain eligible for continued coverage under COBRA, or, if applicable, state insurance laws, the Company shall pay that portion of your COBRA premiums that the Company was paying prior to the effective date of termination for twelve (12) months following or for the continuation period for which Employee is eligible, whichever is shorter and in the event the continuation period is provided by state law and is less than twelve (12) months, pay to you the premium payments it would have made for the remainder of the twelve (12) month period (the "COBRA Premiums"); (iii) fifty percent (50%) of any unvested stock options or unvested restricted shares held by you (excluding the Series B Second Tranche Grant, unless the date of such termination without Cause occurs after either (i) the closing date of the Series B Second Tranche, or (ii) the date that the Board of Directors or Compensation Committee thereof has otherwise determined that the vesting under the Series B Second Tranche Grant has commenced) shall vest in full upon the occurrence of your termination without Cause, accelerated to one hundred percent (100%) vesting in the event your termination without Cause occurs within thirty (30) days prior to or One hundred eighty (180) days following a Corporate Transaction (as defined below); (iv) at your request, the post-termination exercise grace period set forth in your stock option

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agreements shall be extended to provide for an exercise period of up to 180 days following the termination without Cause; *provided*, *however*, that such post-termination exercise grace period shall not be extended beyond the period of time that would enable the stock option to remain exempt under IRS Regulation 409A.

This Amendment sets forth the entire amendment and modification to the Agreement intended by the parties. Further, this Amendment and the Agreement constitute the entire agreement and understanding of the parties relating to the subject matter contained therein. The amendments and modifications to the Agreement are specifically limited to the terms and conditions discussed herein. The remainder of the terms and conditions of the Agreement, as agreed to by the parties, remains in full force and effect.

THIS AMENDMENT IS EXECUTED by the parties as of the date first written above.

Proteon Therapeutics, Inc. ("Company"):

/s/ Timothy P. Noyes
Timothy P. Noyes
President & CEO

Date: 6-22-09

Steven K. Burke

/s/ Steven K. Burke
Steven K. Burke
SVP and CMO

Date: 6-26-09

Exhibit 10.6

[Proteon Therapeutics Letterhead]

September 9, 2013

Mr. George Eldridge
64 Damien Road
Wellesley, Massachusetts 02481

Re: Employment with Proteon Therapeutics, Inc.

Dear George,

Proteon Therapeutics, Inc. (the "Company" or "Proteon") is very pleased to offer you employment as its Senior Vice President and Chief Financial Officer. This letter contains the basic terms of your employment with the Company (the "Agreement"). If you agree to the terms and conditions set forth in this Agreement, please sign at the end of this letter in the space indicated.

1. **Duties**. Effective September 9, 2013 ("Start Date"), you will be employed as the Company's Senior Vice President and Chief Financial Officer. In this capacity, you will be responsible for all financial aspects of the Company and shall perform such duties as are ordinary, customary and necessary in your role as Senior Vice President and Chief Financial Officer. You will report directly to the President and Chief Executive Officer of the Company who will be responsible for evaluating your performance.

2. **Place of Performance**. You shall be based no more than fifty (50) miles outside of the Boston, Massachusetts area, although reasonable travel may be expected.

3. **Compensation**. During the first year of your employment with the Company, you will be compensated at a base rate of $275,000 per year ("Base Salary"), payable and due in accordance with the regular payroll of the Company for its executives. Upward adjustments to your Base Salary will be made at the discretion of the Board of Directors of the Company (the "Board") with such increases typically made annually as part of the Company's annual compensation review process. Following the time the Company's common stock is registered pursuant to Section 12 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), and becomes publicly traded on any national securities exchange or the OTC Buletting Board (or a successor), your salary will be reviewed by the Board and may be adjusted, if appropriate, to be consistent with the salaries of your peers in other similar publicly traded companies.

4. **Annual Bonus**. You will have an annual target bonus of 25% of your Base Salary ("Bonus"). The actual amount of this Bonus, if any and up to the full 25% target shall be determined by the Board, based on its assessment, in its discretion, of your and the Company's performance. This bonus will be based 3/4 on your performance against goals set for you

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annually and agreed upon by the Board, and 1/4 on subjective performance evaluation by the Board. The Bonus shall be paid in one lump sum following the completion of Company's annual compensation review process and shall be paid at the same time that other employees' annual bonuses are paid, but in no event later than March 15th of the calendar year immediately following the end of the annual performance review process, provided that you remain employed by the Company on the date of any such payment. Base Salary earned from your Start Date through December 31, 2013 is bonus eligible compensation and such Bonus will be determined and paid in accordance with this Section 4.

5. **Options**. It is the Board's intention to grant you an option as soon as practicable after your Start Date to purchase 250,000 shares of Proteon's common stock (the "Initial Option") subject to the Company's **2006 Equity Incentive Plan** (as amended and in effect from time to time, the "Plan") and the Company's standard form of Stock Option Grant Notice and related Stock Option Agreement (collectively "Stock Agreement") between you and the Company. The Initial Option will be an incentive stock option (ISO) to the extent permissible under Section 422 of the Internal Revenue Code and will have an exercise price equal to $1.40 per share or the then-current fair market value of the common stock as determined by the Board, whichever is greater. The Initial Option will vest as follows: 62,500 shares of common stock upon the first anniversary of your Start Date and 15,625 shares of common stock quarterly thereafter. In addition, you may be eligible for a grant, at the Board's discretion, after the next financing that raises in excess of $10 million, but no later than the date on which the Company's common stock becomes publicly traded on any national securities exchange or the OTC Buletting Board (or a successor), of an additional option to purchase a number of shares of Proteon's common stock (the "Additional Option") such that the Initial Option and the Additional Option, collectively, would equal one percent (1%) of the fully diluted shares outstanding at the time of grant of the Additional Option. The Additional Option (i) will be an ISO to the extent permissible under Section 422 of the Internal Revenue Code, (ii) will have an exercise price equal to the then-current fair market value of common stock as determined by the Board, and (iii) will be subject to the Plan and the Company's Stock Agreement.

6. **Benefits**. You will be entitled to participate in any and all employee benefit plans, programs and perquisites from time to time in effect for employees of the Company generally, on terms no less favorable than those provided to any other employee.

7. **Vacation**. In the year that this Agreement becomes effective and in each year of employment thereafter, you will accrue vacation on a monthly basis per standard Company policy. However, your vacation benefit shall not be less than three (3) weeks per annum and it shall be taken at such times and intervals as shall be determined by you, subject to the reasonable business needs of the Company. Carry-over privileges for unused vacation time shall be consistent with Company policy.

8. **Business Expenses**. The Company shall pay or reimburse you for all reasonable business expenses incurred or paid by you in the performance of your duties and responsibilities hereunder, subject to such reasonable documentation as may be specified by the Company.

9. **Termination of Employment and Severance Benefits**.

(a) By the Company for Cause. The Company may terminate your employment

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hereunder for Cause, as defined below, provided that the Company has given written notice to you setting forth in reasonable detail the nature of such Cause. The following, as determined by the Board in its reasonable judgment, shall constitute Cause for Termination:

(i) Your conviction of any crime involving a felony or any crime involving moral turpitude;

(ii) Your willful failure to perform, or gross negligence in the performance of, your duties and responsibilities to the Company which, if capable of being cured, is not cured within 30 days after written notice by the Company specifying in reasonable detail the nature of such failure or negligence;

(iii) Your material breach of this Agreement which, if capable of being cured, is not cured within 30 days after written notice by the Company specifying in reasonable detail the nature of such breach; or

(iv) Your material breach of any agreements between you and the Company relating to confidentiality or inventions, including, without limitation, the Employee Confidentiality and Inventions Assignment Agreement between you and the Company that you are executing concurrently with this

Agreement, which, if capable of being cured, is not cured within 30 days after written notice by the Company specifying in reasonable detail the nature of such breach.

Upon giving written notice to you that your employment with the Company has been terminated for Cause, the Company shall have no further obligation to you, other than for Final Compensation, as defined below.

(b) By Reason of Constructive Termination. Provided you have not previously been notified of the Company's intention to terminate your employment, you may resign from employment by reason of Constructive Termination within thirty (30) days after the occurrence of one of the events specified in 9(b) (i-vi) below, by giving notice of your resignation in accordance with Paragraph 19 below. In the event of your death or disability as provided in 9(b) (vii & viii) below your employment will terminate by reason of Constructive Termination as of the date of your death or as of the end of the 180 day period, in the case of disability.

In the event of such termination, in addition to Final Compensation, you shall be entitled to the following: (i) provided that no benefits are payable to you under a separate severance agreement as a result of such termination, an amount equal to six (6) months of your Base Salary or, in the event Constructive Termination occurs within thirty (30) days prior to or three hundred sixty-five (365) days following a Corporate Transaction, twelve (12) months of your Base Salary, as applicable, at the rate in effect on the date of termination, less applicable withholdings and deductions, paid in a lump sum as provided below (the "Severance Payment"); (ii) if you are participating in the Company's group health insurance plans on the effective date of termination, and you timely elect and remain eligible for continued coverage under COBRA, or, if applicable, state insurance laws, the Company shall pay that portion of your COBRA premiums that the Company was paying prior to the effective date of termination for six (6) months following (the "6-Month Tail Period") or, in the event Constructive Termination occurs within thirty (30) days

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prior to or three hundred sixty-five (365) days following a Corporate Transaction, twelve (12) months following (the "12-Month Tail Period" and, collectively with the 6-Month Tail Period, the "Tail Period"), as applicable, or for the continuation period for which Employee is eligible, whichever is longer and in the event the continuation period is provided by state law and is less than the applicable Tail Period, pay to you the premium payments it would have made for the remainder of the applicable Tail Period (the "COBRA Premiums"); (iii) fifty percent (50%) of any unvested stock options or unvested restricted shares held by you shall vest in full upon the occurrence of the Constructive Termination within thirty (30) days prior to or three hundred sixty-five (365) days following a Corporate Transaction (as defined below) that is consummated on or prior to December 31, 2013, accelerated to one hundred percent (100%) vesting in the event Constructive Termination occurs within thirty (30) days prior to or three hundred sixty-five (365) days following a Corporate Transaction that is consummated on or after January 1, 2014; (iv) at your request, the post-termination exercise grace period set forth in your stock option agreements shall be extended to provide for an exercise period of up to 180 days following the Constructive Termination; *provided*, *however*, that such post-termination exercise grace period shall not be extended beyond the period of time that would enable the stock option to remain exempt under IRS Regulation 409A.

Any obligation of the Company to you in Paragraph 9(b) is conditioned upon you signing and returning to the Company a timely and effective release of claims, in the form attached hereto as Exhibit A (the "Release of Claims"). The Release of Claims required for separation benefits in accordance with this Section 9(b) creates legally binding obligations on your part and the Company and its Affiliates therefore advise you to seek the advice of an attorney before signing it. The Severance Payments shall be payable and due as a lump sum and COBRA Premiums will commence thirty (30) days following the later of the effective date of the Release of Claims or the date the Release of Claims, signed by you, is received by the Company, subject to Paragraph 12(d) hereof.

The following shall constitute Constructive Termination:

(i) failure of the Company to provide you Base Salary and benefits in accordance with the terms of this Agreement, excluding an inadvertent failure which is cured within ten (10) business days following written notice from you to the Company specifying in detail the nature of such failure;

(ii) failure of the Company, or a successor to the Company, to provide you with a position that is equivalent in title, total compensation (salary and bonus), benefits or responsibilities to your then current position within ninety (90) days of a Corporate Transaction resulting in a material diminution of your responsibilities, duties or authority. Diminution of your responsibilities shall NOT, however, include having the same general responsibilities in a division/business unit/subsidiary of any entity surviving the Corporate Transaction.

(iii) material diminution in the nature or scope of your responsibilities, duties or authority, or a reduction in your Base Salary without your prior written consent;

(iv) relocation of your employment by more than fifty (50) miles outside of the Boston, Massachusetts area;

(v) failure of the Company to materially comply with the terms of this Agreement;

(vi) The Company's business is being discontinued because rendered impracticable by substantial financial losses, lack of funding, legal decisions, administrative rulings, declaration of war, dissolution, national or local economic depression or crisis;

(vii) termination of your employment as a result of your death; or

(viii) termination of your employment as a result of the fact that you become disabled during your employment with an illness, injury, accident or condition of either a physical or psychological nature, and, as a result, you are unable to perform substantially all of your duties and responsibilities hereunder, with or without a reasonable accommodation, for 180 consecutive days in any 365 consecutive calendar days.

(c) By the Company Without Cause. The Company may terminate your employment hereunder without Cause. In the event of such termination, in addition to Final Compensation, you shall be entitled to the following: (i) provided that no benefits are payable to you under a separate severance agreement as a result of such termination, an amount equal to six (6) months of your Base Salary at the rate in effect on the date of termination, or, in the event termination without Cause occurs within thirty (30) days prior to or three hundred sixty-five (365) days following a Corporate Transaction, twelve (12) months of your Base Salary at the rate in effect on the date of termination, as applicable, *provided however*, that in the event of your termination without Cause occurs at such time as the Company's business is being discontinued because rendered impracticable by substantial financial losses, lack of funding, legal decisions, administrative rulings, declaration of war, dissolution, national or local economic depression or crisis or any reasons beyond the control of the Company this amount shall be reduced to four (4) months of your Base Salary at the rate in effect on the date of termination, in either case less applicable withholdings and deductions, paid in a lump sum as provided below (the "Severance Payment"); (ii) if you are participating in the Company's group health insurance plans on the effective date of termination, and you timely elect and remain eligible for continued coverage under COBRA, or, if applicable, state insurance laws, the Company shall pay that portion of your COBRA premiums that the Company was paying prior to the effective date of termination for six (6) months following (the "6-Month Tail Period") or, in the event termination without Cause occurs within thirty (30) days prior to or three hundred sixty-five (365) days following a Corporate Transaction, twelve (12) months following (the "12-Month Tail Period" and, collectively with the 6-Month Tail Period, the "Tail Period"), as applicable, or for the continuation period for which Employee is eligible, whichever is longer and in the event the continuation period is provided by state law and is less than the applicable Tail Period, pay to you the premium payments it would have made for the remainder of the applicable Tail Period (the "COBRA Premiums"); (iii) fifty percent (50%) of any unvested stock options or unvested restricted shares held by you shall vest in full upon the occurrence of your termination without

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Cause within thirty (30) days prior to or three hundred sixty-five (365) days following a Corporate Transaction that is consummated on or prior to December 31, 2013, accelerated to one hundred percent (100%) vesting in the event your termination without Cause occurs within thirty (30) days prior to or three hundred sixty-five (365) days following a Corporate Transaction that is consummated on or after January 1, 2014; (iv) at your request, the post-termination exercise grace period set forth in your stock option agreements shall be extended to provide for an exercise period of up to 180 days following the termination without Cause; *provided*, *however*, that such post-termination exercise grace period shall not be extended beyond the period of time that would enable the stock option to remain exempt under IRS Regulation 409A.

Any obligation of the Company to you in Paragraph 9(c) is conditioned upon you signing and returning to the Company a timely and mutually agreeable effective release of claims (the "Release of Claims") which the form is attached as Exhibit A. The Release of Claims required for separation benefits in accordance with this Section 9(c) creates legally binding obligations on your part and the Company and its Affiliates therefore advise you to seek the advice of an attorney before signing it. The Severance Payments shall be payable and due as a lump sum and COBRA Premiums will commence thirty (30) days following the later of the effective date of the Release of Claims or the date the Release of Claims, signed by you, is received by the Company, subject to Paragraph 12(d) hereof.

(d) If any payment or benefit you would receive under this Agreement, when combined with any other payment or benefit you receive pursuant to the termination or Constructive Termination of your employment with the Company ("Payment") would (i) constitute a "parachute payment" within the meaning of Section 280G of the Internal Revenue Code of 1986, as amended (the "Code"), and (ii) but for this sentence, be subject to the excise tax imposed by Section 4999 of the Code (the "Excise Tax"), then such Payment shall be either (x) the full amount of such Payment or (y) such lesser amount (with your choice of whether to reduce cash payments or stock option compensation or both) as would result in no portion of the Payment being subject to the Excise Tax, whichever of the foregoing amounts, taking into account the applicable federal, state and local employment taxes, income taxes and the Excise Taxes results in your receipt, on an after-tax basis, of the greater amount of the Payment notwithstanding that all or some portion of the Payment may be subject to the Excise Tax.

10. **At-Will Employment**. Please understand your employment is **"at will,"** voluntarily entered into and is for no specific period. As a result, you are free to resign at any time, for any reason or for no reason, with thirty (30) days written notice. Similarly, the Company is free to conclude its at-will employment relationship with you at any time, with or without cause, subject to all terms and conditions of this Agreement. Any contrary representations or agreements, which may have been made to you, are superseded by this Agreement. This at-will relationship cannot be altered unless specifically set forth in writing and signed by both you and an authorized member of the Board.

11. **Definitions**. Words or phrases which are initially capitalized or are within quotation marks shall have the meanings provided in this Section and as provided elsewhere herein. For purposes of this Agreement, the following definitions apply:

(a) "Affiliates" means all persons and entities directly or indirectly controlling, controlled by or under common control with the Company, where control may be by either management

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authority, contract or equity interest.

(b) "Corporate Transaction" as used herein shall mean any (i) consolidation or merger of the Company with or into any other corporation or other entity or person, or any other corporate reorganization in which the stockholders of the Company prior to such consolidation, merger or reorganization shall own less than fifty percent (50%) of the voting stock of the continuing or surviving entity after such consolidation, merger or reorganization, (ii) any transaction or series of related transactions to which the Company is a party, in which in excess of fifty percent (50%) of the Company's voting stock is transferred, except for bona fide sales of the Company's equity securities to venture investors for primarily fundraising purposes, or (iii) a sale of substantially all of the assets of the Company.

(c) "Final Compensation" means (1) any Base Salary earned but not paid through the date of termination; (2) pay for any vacation time earned but not used through the date of termination, and (3) any business expenses incurred by you but un-reimbursed on the date of termination, provided that such expenses and required substantiation and documentation are submitted within thirty (30) days of termination and that such expenses are reimbursable under Company policy.

(d) "Person" means an individual, a corporation, a limited liability company, an association, a partnership, an estate, a trust and any other entity or organization, other than the Company or any of its Affiliates.

12. **Tax Matters**.

(a) Subsections (a) through (e) of this section are intended to help ensure that compensation paid or delivered to you pursuant to this Agreement either is paid in compliance with, or is exempt from, Section 409A of the Internal Revenue Code of 1986, as amended and the rules and regulations promulgated thereunder (collectively, "Section 409A"). However, the Company does not warrant to you that all compensation paid or delivered to you for your services will be exempt from, or paid in compliance with, Section 409A. You bear the entire risk of any adverse federal, state or local tax consequences and penalty taxes which may result from payment of compensation for your services on a basis contrary to the provisions of Section 409A or comparable provisions of any applicable state or local income tax laws.

(b) For the purposes determining when amounts of otherwise payable on account of your termination of employment will be paid, "termination of employment" or words of similar import, as used in this Agreement, shall mean the date as of which the Company and you reasonably anticipate that no further services will be performed by you and shall be construed as the date that you first incur a "separation from service" for purposes of Section 409A on or following termination of employment. Furthermore, if you are a "specified employee" of a public company as determined pursuant to Section 409A as of your termination of employment, any amounts payable on account of your termination of employment which constitute deferred compensation within the meaning of Section 409A and which are otherwise payable during the first six months following your termination of employment shall be paid or provided to you in a lump sum on the earlier of (1) the date of your death and (2) the first business day of the seventh calendar month immediately following the month in which your termination of employment occurs.

(c) Any taxable reimbursement of business or other expenses, or any provision of taxable in-kind benefits to you, as specified under this Agreement, shall be subject to the following conditions: (1) the expenses eligible for reimbursement or the amount of in-kind benefits provided in one taxable year shall not affect the expenses eligible for reimbursement or the amount of in-kind benefits provided in any other taxable year, except for any medical reimbursement arrangement providing for the reimbursement of expenses referred to in Section 105(b) of the Code (and, as a result, if there is a maximum dollar amount of expense reimbursement specified in this Agreement, only expenses in the first taxable year in which you could incur eligible expenses shall be eligible for reimbursement, to the limitation specified); (2) the reimbursement of an eligible expense shall be made no later than the end of the year after the year in which such expense was incurred; and (3) the right to reimbursement or in-kind benefits shall not be subject to liquidation or exchange for another benefit.

(d) Any amounts otherwise payable on account of your termination of employment under this Agreement which (i) are conditioned in any part on a release of claims and (ii) would otherwise be paid (assuming the release is given) prior to the last day on which the release could become irrevocable assuming your latest possible execution and delivery of the release (such last day, the "Release Deadline") shall be paid, if ever, only on the Release Deadline, even if your release becomes irrevocable before that date. The Employer may elect to make such payment up to thirty (30) days prior to the Release Deadline, however. If no such last day is specified in this Agreement, then such last day will be the sixtieth (60th) day after your termination of employment.

(e) In applying Section 409A to compensation paid pursuant to this Agreement, any right to a series of installment payments under this Agreement shall be treated as a right to a series of separate payments.

(f) The Company makes no representation or warranty as to the tax treatment to you of your receipt or exercise of any options granted to you in connection with this Agreement or upon your sale or other disposition of the shares underlying any such options. You should rely on your own tax advisors for such advice. In particular, you acknowledge that in any event an option will not be treated as an ISO as to any shares acquired under any such option

(i) more than twelve months after your employment ends, if your employment ends on account of your death or total and permanent disability, or

(ii) more than three months after your employment ends, if your employment ends in any other circumstance.

13. **Noncompetition Covenant**. You agree that during the term of your employment by Company and during the Tail Period, you will not, without Company's express written consent, participate, whether as owner, stockholder (excluding holding of less than 1% of the stock of a public company), director, officer, manager, employee, agent or consultant or otherwise in any business, firm or corporation that is competitive with, or, [with respect to action during the term of your employment by the Company], that would otherwise conflict with your employment by the Company. For the purposes of this section, a "business, firm or corporation that is competitive with" the Company means a business, firm or corporation that sells, or is developing

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for sale, Company Products or products that may be used in direct substitution for Company Products and would compete directly in the marketplace with such Company Products. "Company Products" means PRT-201 that the Company is developing for the reduction of vascular access failure in patients receiving hemodialysis. Your obligations under this Paragraph 13 survive any termination of your employment.

14. **Indemnification**. The Company shall indemnify you against any and all losses, liabilities, damages, expenses (including attorneys' fees) judgments, fines and amounts incurred by you in connection with any claim, action, suit or proceeding (whether civil, criminal, administrative or investigative), including any action by or in the right of the Company, by reason of any act or omission to act in connection with the performance of your duties hereunder to the fullest extent that the Company is permitted to indemnify you against the foregoing under applicable law. The Company shall at all times cause you to be included, in your capacities hereunder, under all liability insurance coverage (or similar insurance coverage), including directors' and officers' liability insurance, maintained by the Company.

15. **Withholding**. All payments made by the Company under this Agreement shall be reduced by any tax or other amounts required to be withheld by the Company under applicable law.

16. **Assignment and Successors**. The Company may assign this Agreement and its rights and obligations hereunder in whole, but not in part, to any Company or other entity with or into which the Company may hereafter merge or consolidate, or to which the Company may transfer all or substantially all of its assets, if in any such case said Company or other entity shall by operation of law or expressly in writing assume all obligations of the Company hereunder as fully as if it had been originally made a party hereto, and may not otherwise assign this Agreement or its rights and obligations hereunder. You may not assign or transfer this Agreement or any rights or obligations hereunder.

17. **Severability**. If any portion or provision of this Agreement shall to any extent be declared illegal or unenforceable by a court of competent jurisdiction, then the remainder of this Agreement, or the application of such portion or provision in circumstances other than those as to which it is so declared illegal or unenforceable, shall not be affected thereby, and each portion and provision of this Agreement shall be valid and enforceable to the fullest extent permitted by law.

18. **Waiver**. No waiver of any provision hereof shall be effective unless made in writing and signed by the waiving party. The failure of either party to require the performance of any term or obligation of this Agreement, or the waiver by either party of any breach of this Agreement, shall not prevent any subsequent enforcement of such term or obligation or be deemed a waiver of any subsequent breach.

19. **Notices**. Any and all notices, requests, demands and other communications provided for by this Agreement shall be in writing and shall be effective when delivered in person, consigned to a reputable national courier service or deposited in the United States mail, postage prepaid, registered or certified, and addressed to you at your last known address on the books of the Company or, in the case of the Company, at its principal place of business, attention of the Chair of the Board, or to such other address as either party may specify by notice to the other

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actually received.

20. **Entire Agreement**. This letter, the Employee Confidentiality and Inventions Assignment Agreement that you are executing with the Company on the date hereof and the Stock Agreement constitute the entire agreement between the parties and amend and supersede all prior communications, agreements and understandings, written or oral, with respect to the terms and conditions of your employment.

21. **Miscellaneous**. This Agreement may not be modified or amended, and no breach shall be deemed to be waived, unless agreed to in writing by you and the Company. This is a Massachusetts contract and shall be governed and construed in accordance with the laws of the Commonwealth of Massachusetts, without regard to the conflict of laws principles thereof.

Best Regards,

/s/ Timothy P. Noyes
Timothy P. Noyes
President and Chief Executive Officer

I have read, understand and accept the enclosed offer of employment with Proteon Therapeutics, Inc.

/s/ George Eldridge	Sept 9, 2013
George Eldridge	Date

EXHIBIT A

Release of Claims

In consideration of the promises and covenants recited in the Employment Agreement dated as of September 9, 2013 by and between Proteon Therapeutics, Inc. (the "Company") and George Eldridge (the "Executive"), the Executive enters into this Release of Claims.

The Executive hereby releases, waives and discharges his right to assert any legal claim or right, known or unknown, that arose on or before the Effective Date (as defined below), against the Company arising from any conduct by the Company or any of the Company's affiliates, parents, subsidiaries, directors, officers, shareholders, creditors, insurers, representatives, agents, or employees.

The claims the Executive is releasing include, without limitation, any and all claims arising out of or related to his employment with the Company and his separation from employment with the Company. Such claims include, without limitation, any claims under the Massachusetts Fair Employment Practices Act, M. GL c. 151B, the Massachusetts Wage Act, M GL c. 149 § 148, and any federal, state and local statutes, common law, orders, and regulations prohibiting discrimination or harassment on the basis of age, sex, sexual orientation, race, color, disability, religion, national origin, and any other protected characteristic, as well as any common law claims, including without limitation claims arising out of agreements, representations or policies related to his employment, and claims for wrongful termination, misrepresentation, personal injury, emotional distress, breach of contract, interference with contractual or advantageous relations, and violation of the covenant of good faith and fair dealing.

The Executive acknowledges that he is waiving and releasing any rights he may have under the Age Discrimination in Employment Act ("ADEA") and the Older Workers Benefit Protection Act ("OWBPA"). The Executive is advised that this is an important legal document, and is further advised to consult with an attorney before entering into it. The Executive affirms that he understands the terms of this Agreement and that he knowingly and voluntarily is entering into this Agreement.

The Executive acknowledges that this release releases claims under the Massachusetts Wage Act, M GL c. 149 §148, and further that he has been paid all compensation owed for services performed for the Company. The Executive acknowledges that he has not been denied any leave under the FMLA, and that he has not been retaliated against for taking such leave. The Executive agrees that these terms represent a full and final settlement of any and all claims he may have arising out of his employment with the Company, except that this Agreement shall not release or affect any vested rights he may have (1) under the Company's 401 (k) plan, (2) under the terms of this Agreement, (3) to continue health insurance coverage under COBRA, and (4) which by law cannot be released in this manner.

Nothing in this Agreement shall be construed to waive claims that cannot be waived under applicable law. Nothing in this Agreement shall be construed to affect the Equal Employment Opportunity Commission's, or any local agency's, independent rights and

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responsibilities to enforce the law. The Executive recognizes and agrees, however, that while this Agreement does not affect his right to file a charge or participate in an investigation or proceeding conducted by a Commission, it does bar any claim he might have to receive monetary damages in connection with any Commission proceeding concerning matters covered by this Agreement.

The Executive understands that he has until forty five (45) days after receiving this Agreement to consider this Agreement. The Executive further understands that if he executes and returns the Agreement prior to the expiration of this forty five (45) day period, he has waived any right he may have to additional time within which to consider the Agreement.

The Executive has seven (7) days after the day he signs this agreement to revoke it. To revoke this agreement after signing it, he must deliver a written notice of revocation to Timothy Noyes at the Company's offices before the seven day period expires. This Agreement shall not become effective until the eighth (8th) day after the day the Executive signs the Agreement (the "Effective Date"). If the Executive revokes this Agreement it will not become enforceable and he will not receive the benefits described in the Employment Agreement and this Agreement.

IN WITNESS WHEREOF, the Executive has duly executed this Agreement.

George Eldridge

_____

George Eldridge
Date:

[Proteon Therapeutics Letterhead]

September 23, 2013

Mr. Daniel Gottlieb
25 Suffolk Road
Sudbury, Massachusetts 01776

Re: Severance Agreement with Proteon Therapeutics, Inc.

Dear Daniel,

The purpose of this letter agreement (the "Agreement"), which shall be effective as of the date you sign this Agreement, is to set forth the terms of your severance benefits should your employment with Proteon be terminated prior to or following a Corporate Transaction (as defined below).

1. **Termination of Employment and Severance Benefits**.

(a) By the Company Without Cause. The Company may terminate your employment hereunder without Cause. In the event of such termination, in addition to Final Compensation (as defined below), you shall be entitled to the following:

(i) provided that no benefits are payable to you under a separate severance agreement as a result of such termination, in the event termination without Cause occurs within thirty (30) days prior to or three hundred sixty-five (365) days following a Corporate Transaction (as defined below), six (6) months of your Base Salary at the rate in effect on the date of termination, as applicable, less applicable withholdings and deductions, paid in a lump sum as provided below (the "Severance Payment");

(ii) if you are participating in the Company's group health insurance plans on the effective date of termination, and you timely elect and remain eligible for continued coverage under COBRA, or, if applicable, state insurance laws, the Company shall pay, in the event termination without Cause occurs within thirty (30) days prior to or three hundred sixty-five (365) days following a Corporate Transaction, that portion of your COBRA premiums that the Company was paying prior to the effective date of termination for six (6) months following (the "Tail Period") pay to you the premium payments it would have made for the remainder of the applicable Tail Period (the "COBRA Premiums");

(iii) one hundred percent (100%) of any unvested stock options or unvested restricted shares held by you shall vest in full in the event your termination without Cause occurs within thirty (30) days prior to or three hundred sixty-five (365) days following a Corporate Transaction (as defined below);

(iv) at your request, the post-termination exercise grace period set forth in your stock option agreements shall be extended to provide for an exercise period of up to 180 days following the termination without Cause; *provided, however*, that such post-termination exercise grace period shall not be extended beyond the period of time that would enable the stock option to remain exempt under IRS Regulation 409A.

Any obligation of the Company to you in Section 1(a) is conditioned upon you signing and returning to the Company a timely and mutually agreeable effective release of claims (the "Release of Claims") which form is attached as Exhibit A. The Release of Claims required for separation benefits in

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accordance with this Section 1(a) creates legally binding obligations on your part and the Company and its Affiliates therefore advise you to seek the advice of an attorney before signing it. The Severance Payments shall be payable and due as a lump sum and COBRA Premiums will commence thirty (30) days following the later of the effective date of the Release of Claims or the date the Release of Claims, signed by you, is received by the Company, subject to Section 3(d) hereof.

(b) By the Company for Cause. The Company may terminate your employment hereunder for Cause, as defined below, provided that the Company has given written notice to you setting forth in reasonable detail the nature of such Cause. The following, as determined by the Board in its reasonable judgment, shall constitute Cause for Termination:

(i) Your conviction of any crime involving a felony or any crime involving moral turpitude;

(ii) Your willful failure to perform, or gross negligence in the performance of, your duties and responsibilities to the Company which, if capable of being cured, is not cured within 30 days after written notice by the Company specifying in reasonable detail the nature of such failure or negligence;

(iii) Your material breach of this Agreement which, if capable of being cured, is not cured within 30 days after written notice by the Company specifying in reasonable detail the nature of such breach;

(iv) Your material breach of any agreements between you and the Company relating to confidentiality or inventions, including, without limitation, the Employee Confidentiality and Inventions Assignment Agreement between you and the Company that you are executing concurrently with this Agreement, which, if capable of being cured, is not cured within 30 days after written notice by the Company specifying in reasonable detail the nature of such breach;

Upon giving written notice to you that your employment with the Company has been terminated for Cause, the Company shall have no further obligation to you, other than for Final Compensation, as defined below.

(c) If any payment or benefit you would receive under this Agreement, when combined with any other payment or benefit you receive pursuant to the termination of your employment with the Company ("Payment") would (i) constitute a "parachute payment" within the meaning of Section 280G of the Internal Revenue Code of 1986, as amended (the "Code"), and (ii) but for this sentence, be subject to the excise tax imposed by Section 4999 of the Code (the "Excise Tax"), then such Payment shall be either (x) the full amount of such Payment or (y) such lesser amount (with your choice of whether to reduce cash payments or stock option compensation or both) as would result in no portion of the Payment being subject to the Excise Tax, whichever of the foregoing amounts, taking into account the applicable federal, state and local employment taxes, income taxes and the Excise Taxes results in your receipt, on an after-tax basis, of the greater amount of the Payment notwithstanding that all or some portion of the Payment may be subject to the Excise Tax.

2. **Definitions**. Words or phrases which are initially capitalized or are within quotation marks shall have the meanings provided in this Section and as provided elsewhere herein. For purposes of this Agreement, the following definitions apply:

(a) "Affiliates" means all persons and entities directly or indirectly controlling, controlled by or under common control with the Company, where control may be by either management authority, contract or equity interest.

(b) "Corporate Transaction" as used herein shall mean any (i) consolidation or merger of the Company with or into any other corporation or other entity or person, or any other corporate reorganization in which the stockholders of the Company prior to such consolidation, merger or reorganization shall own less than fifty percent (50%) of the voting stock of the continuing or surviving entity after such consolidation, merger or reorganization, (ii) any transaction or series of related transactions to which the Company is a party, in which in excess of fifty percent (50%) of the Company's voting stock is transferred, except for bona fide sales of the Company's equity securities to venture investors for primarily fundraising purposes, or (iii) a sale of substantially all of the assets of the Company.

(c) "Final Compensation" means (1) any Base Salary earned but not paid through the date of termination; (2) pay for any vacation time earned but not used through the date of termination, and (3) any business expenses incurred by you but un-reimbursed on the date of termination, provided that such expenses and required substantiation and documentation are submitted within thirty (30) days of termination and that such expenses are reimbursable under Company policy.

(d) "Person" means an individual, a corporation, a limited liability company, an association, a partnership, an estate, a trust and any other entity or organization, other than the Company or any of its Affiliates.

3. **Tax Matters**.

(a) Subsections (a) through (e) of this section are intended to help ensure that compensation paid or delivered to you pursuant to this Agreement either is paid in compliance with, or is exempt from, Section 409A of the Internal Revenue Code of 1986, as amended and the rules and regulations promulgated thereunder (collectively, "Section 409A"). However, the Company does not warrant to you that all compensation paid or delivered to you for your services will be exempt from, or paid in compliance with, Section 409A. You bear the entire risk of any adverse federal, state or local tax consequences and penalty taxes which may result from payment of compensation for your services on a basis contrary to the provisions of Section 409A or comparable provisions of any applicable state or local income tax laws.

(b) For the purposes determining when amounts of otherwise payable on account of your termination of employment will be paid, "termination of employment" or words of similar import, as used in this Agreement, shall mean the date as of which the Company and you reasonably anticipate that no further services will be performed by you and shall be construed as the date that you first incur a "separation from service" for purposes of Section 409A on or following termination of employment. Furthermore, if you are a "specified employee" of a public company as determined pursuant to Section 409A as of your termination of employment, any amounts payable on account of your termination of employment which constitute deferred compensation within the meaning of Section 409A and which are otherwise payable during the first six months following your termination of employment shall be paid or provided to you in a lump sum on the earlier of (1) the date of your death and (2) the first business day of the seventh calendar month immediately following the month in which your termination of employment occurs.

(c) Any taxable reimbursement of business or other expenses, or any provision of taxable in-kind benefits to you, as specified under this Agreement, shall be subject to the following conditions: (1)

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the expenses eligible for reimbursement or the amount of in-kind benefits provided in one taxable year shall not affect the expenses eligible for reimbursement or the amount of in-kind benefits provided in any other taxable year, except for any medical reimbursement arrangement providing for the reimbursement of expenses referred to in Section 105(b) of the Code (and, as a result, if there is a maximum dollar amount of expense reimbursement specified in this Agreement, only expenses in the first taxable year in which you could incur eligible expenses shall be eligible for reimbursement, to the limitation specified); (2) the reimbursement of an eligible expense shall be made no later than the end of the year after the year in which such expense was incurred; and (3) the right to reimbursement or in-kind benefits shall not be subject to liquidation or exchange for another benefit.

(d) Any amounts otherwise payable on account of your termination of employment under this Agreement which (i) are conditioned in any part on a release of claims and (ii) would otherwise be paid (assuming the release is given) prior to the last day on which the release could become irrevocable assuming your latest possible execution and delivery of the release (such last day, the "Release Deadline") shall be paid, if ever, only on the Release Deadline, even if your release becomes irrevocable before that date. The Employer may elect to make such payment up to thirty (30) days prior to the Release Deadline, however. If no such last day is specified in this Agreement, then, such last day will be the sixtieth (60th) day after your termination of employment.

(e) In applying Section 409A to compensation paid pursuant to this Agreement, any right to a series of installment payments under this Agreement shall be treated as a right to a series of separate payments.

(f) The Company makes no representation or warranty as to the tax treatment to you of your receipt or exercise of any options granted to you in connection with this Agreement or upon your sale or other disposition of the shares underlying any such options. You should rely on your own tax advisors for such advice. In particular, you acknowledge that in any event an option will not be treated as an ISO as to any shares acquired under any such option.

(i) more than twelve months after your employment ends, if your employment ends on account of your death or total and permanent disability, or,

(ii) more than three months after your employment ends, if your employment ends in any other circumstance.

4. **Withholding**. All payments made by the Company under this Agreement shall be reduced by any tax or other amounts required to be withheld by the Company under applicable law.

5. **Assignment and Successors**. The Company may assign this Agreement and its rights and obligations hereunder in whole, but not in part, to any Company or other entity with or into which the Company may hereafter merge or consolidate, or to which the Company may transfer all or substantially all of its assets, if in any such case said Company or other entity shall by operation of law or expressly in writing assume all obligations of the Company hereunder as fully as if it had been originally made a party hereto, and may not otherwise assign this Agreement or its rights and obligations hereunder. You may not assign or transfer this Agreement or any rights or obligations hereunder.

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6. **Severability**. If any portion or provision of this Agreement shall to any extent be declared illegal or unenforceable by a court of competent jurisdiction, then the remainder of this Agreement, or the application of such portion or provision in circumstances other than those as to which it is so declared illegal or unenforceable, shall not be affected thereby, and each portion and provision of this Agreement shall be valid and enforceable to the fullest extent permitted by law.

7. **Waiver**. No waiver of any provision hereof shall be effective unless made in writing and signed by the waiving party. The failure of either party to require the performance of any term or obligation of this Agreement, or the waiver by either party of any breach of this Agreement, shall not prevent any subsequent enforcement of such term or obligation or be deemed a waiver of any subsequent breach.

8. **Notices**. Any and all notices, requests, demands and other communications provided for by this Agreement shall be in writing and shall be effective when delivered in person, consigned to a reputable national courier service or deposited in the United States mail, postage prepaid, registered or certified, and addressed to you at your last known address on the books of the Company or, in the case of the Company, at its principal place of business, attention of the Chair of the Board, or to such other address as either party may specify by notice to the other actually received.

9. **Entire Agreement**. This letter, the Employee Confidentiality and Inventions Assignment Agreement that you are executing with the Company on the date hereof and the Stock Agreement constitute the entire agreement between the parties and amend and supersede all prior communications, agreements and understandings, written or oral, with respect to the terms and conditions of your employment.

10. **Miscellaneous**. This Agreement may not be modified or amended, and no breach shall be deemed to be waived, unless agreed to in writing by you and the Company. This is a Massachusetts contract and shall be governed and construed in accordance with the laws of the Commonwealth of Massachusetts, without regard to the conflict of laws principles thereof.

Best Regards,

/s/ Timothy Noyes
Timothy P. Noyes
President and Chief Executive Officer

I have read, understand and accept the enclosed severance benefits from Proteon Therapeutics, Inc.

/s/ Daniel Gottlieb	10-2-13
Daniel Gottlieb	Date

Exhibit A

Form of Release of Claims

[AGE 40 and OVER FORM — Put final signatory version on Proteon Letterhead]

[Date]

[name and address]

Dear :

Your last day of employment with Proteon Therapeutics, Inc. (the "Company") will be ("Separation Date"). Information concerning various aspects of your benefit programs and severance arrangements are described below.

Effect of Separation

As of the Separation Date, you will be paid for all work performed through the Separation Date. Your eligibility to participate in any of the Company's benefit plans will end as of the Separation Date.

You will be provided under separate cover an election form allowing you and your eligible dependents to participate in Company's health and dental plans under the federal law known as COBRA. If you sign and return the election form in a timely manner, the Company will process enrollment so that you can receive health and dental insurance under COBRA. Even if you do not execute this Agreement, you have the right to continue your insurance under COBRA in accordance with the provisions of COBRA, which will be explained in the election form.

Severance Benefits

The Company is offering you the following severance consideration in exchange for a release by you of all claims against the Company, whether or not you actually have any such claims:

Subject to your execution of this Agreement as provided below, Company will provide you with the severance benefits set forth in that certain Severance Agreement, dated as of [**DATE**], 2013, by and between you and the Company.

Your Undertakings

You agree that the Company's undertakings in this Agreement shall be in full and complete satisfaction of any and all sums which are now or might hereafter have become owing to you for services rendered by you to the Company during your employment, or otherwise in connection with your employment or the termination of your employment with the Company. You agree that the Company's undertakings herein include consideration to which you would not be entitled absent entering into this Agreement.

Confidentiality and Nondisclosure

You agree that this Agreement is confidential and that you will not discuss the fact that it exists or its terms with anyone else except your immediate family members, attorney, tax accountant, or as required by law, and that disclosure under this paragraph will only be made after the individuals agree to maintain the confidential nature of this Agreement.

Protection of Confidential Information

You are reminded that, notwithstanding any provisions of this Agreement, you are subject to the terms of the Confidentiality, Developments, and Non-Competition Agreement executed by you on [**DATE**]. You acknowledge you have had access to information concerning the Company, its clients, and its affiliates, which is confidential or proprietary in nature (the "Confidential Information"). You agree that you will continue to protect the Confidential Information and that you will not use for your benefit or that of anyone else or disclose to anyone the Confidential Information in any manner. You acknowledge you have had access to information concerning the Company and its products and processes, which is confidential or proprietary in nature (the "Confidential Information"). You agree that you will continue to protect the Confidential Information and that you will not use for your benefit or that of anyone else or disclose to anyone the Confidential Information in any manner.

Return of Property

In signing this Agreement, you state that you have returned to the Company any and all documents, materials and information related to the business, whether present or otherwise, of the Company and its affiliates, and all copies, and all keys, credit cards, computers, phone, and other tangible property of the Company and its affiliates, in your possession or control.

Non-Disparagement

The Company and you mutually agree not to make any statement or otherwise take any other action that would or might reasonably be interpreted as disparaging to the other. Notwithstanding the foregoing, nothing in this Agreement shall be construed to prevent either you or the Company from providing truthful testimony in any legal proceeding.

Release of Claims

The Company wants to be certain that this Agreement will resolve any and all concerns that you might have and therefore requests that you carefully consider the terms of this Agreement, including the release of claims set forth below. This is an important legal document, and, accordingly, the Company encourages you to seek the advice of an attorney before you sign this Agreement.

Except as specifically described in this Agreement, this Agreement constitutes the entire agreement between you and the Company and replaces all prior and contemporaneous agreements, communications and understandings, whether written or oral, with respect to your employment and its termination and all related matters.

In exchange for the consideration provided you under this Agreement, including the severance benefits described above, which you acknowledge you would not otherwise be entitled to receive, you hereby release, waive and discharge his right to assert any legal claim or right, known or unknown, that arose on or before the Effective Date (as defined below), against the Company and its affiliates, and all of their respective past and present directors, trustees, officers, shareholders, employees, agents, successors and assigns, both individually and in their official capacities arising from any conduct by the Company or any of the Company's affiliates, parents, subsidiaries, directors, officers, shareholders, creditors, insurers, representatives, agents, or employees.

The claims you are releasing include, without limitation, any and all claims arising out of or related to your employment with the Company and your separation from employment with the Company. Such claims include, without limitation, any claims under the Massachusetts Fair Employment Practices Act,

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M. GL c. 151B, the Massachusetts Wage Act, M GL c. 149 §148 et seq., Title VII of the Civil Rights Act of 1964, 42 U.S.C. § 2000e et seq., the Americans With Disabilities Act, 42 U.S.C. § 12101 et seq., the Employee Retirement Income Security Act of 1974 ("ERISA"), the Family and Medical Leave Act of 1993, 29 U.S.C. § 2601 et seq., and any federal, state and local statutes, common law, orders, and regulations prohibiting discrimination or harassment on the basis of age, sex, sexual orientation, race, color, disability, religion, national origin, and any other protected characteristic, as well as any common law claims, including without limitation claims arising out of agreements, representations or policies related to your employment, and claims for wrongful termination, misrepresentation, personal injury, emotional distress, breach of contract, interference with contractual or advantageous relations, and violation of the covenant of good faith and fair dealing. Notwithstanding the foregoing, nothing in this Agreement shall be construed to waive claims which cannot be waived under applicable law.

You acknowledge that you are waiving and releasing any rights you may have under the Age Discrimination in Employment Act ("ADEA") and the Older Workers Benefit Protection Act ("OWBPA"). You are advised that this is an important legal document, and are further advised to consult with an attorney before entering into it. You affirm that you understands the terms of this Agreement and that you knowingly and voluntarily are entering into this Agreement.

Nothing in this Agreement shall be construed to affect the Equal Employment Opportunity Commission's or any state Commission's independent right and responsibility to enforce the law. You recognize, however, that this Agreement bars any claim you might have to receive monetary damages in connection with any Commission proceeding concerning matters covered by this Agreement.

You acknowledge that you have been paid all compensation owed for services performed for Company, and that in executing this release of claims, you are releasing all claims under the Massachusetts Wage Act. You acknowledge that you have not been denied any leave under the FMLA, and that you have not been retaliated against for taking such leave. You agree that these terms represent a full and final settlement of any and all claims you may have arising out of your employment with the Company, except that this Agreement shall not release or affect any vested rights you may have (1) under the Company's 401 (k) plan, (2) under the terms of this Agreement, (3) to continue health insurance coverage under COBRA, and (4) which by law cannot be released in this manner.

Acknowledgments; Return and Effective Date

In signing this Agreement, you give assurance that you have had a full and reasonable opportunity to consider its terms; that you have read and understood all of those terms; and that your acceptance of this Agreement is freely and voluntarily given.

If the terms of this Agreement are acceptable to you, please sign and return this Agreement to me no later than twenty-one (21) days from the date you receive it. You may revoke this Agreement at any time during the seven (7) day period immediately following the date of your signing by either delivering a signed revocation notice or mailing such notice to me, at the Company's offices so that it is postmarked no later than 7 days after you sign this Agreement. If you do not revoke this Agreement, then, at the expiration of that seven-day period, this Agreement shall take effect as a legally binding agreement between you and the Company on the basis set forth above (the "Effective Date").

The enclosed copy of this Agreement, which you should also sign and date, is for your records.

I want to take this opportunity on behalf of Company to wish you well in your future endeavors. If you should have any questions, please call me.

Sincerely,

Proteon Therapeutics, Inc.

By: _____
Name: Timothy P. Noyes
Title: President and Chief Executive Officer

I, the undersigned, having had the time to reflect, freely accept the above Agreement.

_____ _____
[employee name] Date

_____

[employee name]
(PRINT)

200 WEST STREET
WALTHAM, MASSACHUSETTS

Lease dated July 13, 2009

THIS INSTRUMENT IS AN INDENTURE OF LEASE in which the Landlord and the Tenant are the parties hereinafter named, and which relates to space in a certain building (the "Building") known as, and with an address at, 200 West Street, Waltham, Massachusetts 02451. The parties to this Indenture of Lease hereby agree with each other as follows:

ARTICLE I

Reference Data

1.1 Subjects Referred To

Each reference in this Lease to any of the following subjects shall be construed to incorporate the data stated for that subject in this Article:

Landlord:	Boston Properties Limited Partnership, a Delaware limited partnership.
Landlord's Original Address:	c/o Boston Properties Limited Partnership Prudential Center 800 Boylston Street, Suite 1900 Boston, MA 02199-8103
Landlord's Construction Representative:	Mike Bowers
Tenant:	Proteon Therapeutics, Inc., a Delaware corporation.
Tenant's North American Industry Classification System (NAICS) Code:	541711
Tenant's Original Address:	200 West Street Waltham, MA 02451
Tenant's Construction Representative	Mark Fitzpatrick

Commencement Date:	The later of (i) October 1, 2009 or (ii) the date upon which the Premises are "Substantially Complete" (as defined in Exhibit B-1 attached hereto).
Outside Completion Date:	January 1, 2010.
Term (Sometimes called the "Original Term"):	That period of time commencing on the Commencement Date and ending at 11:59 p.m., Boston Time, on June 30, 2013, unless sooner terminated as provided in this Lease.
The Site:	That certain parcel of land known as and numbered 200 West Street, Waltham, Middlesex County, Massachusetts, being more particularly described in Exhibit A attached hereto.
The Building:	The Building known as and numbered 200 West Street, Waltham, Massachusetts.
The Complex:	The Building together with all common areas, surface and parking areas, the Site and all improvements (including landscaping) thereon and thereto.
Tenant's Premises:	A portion of the first floor of the Building in accordance with the floor plan attached hereto as Exhibit E and incorporated herein by reference.
Number of Parking Spaces:	Twenty (20); five (5) of which shall be located in the garage on the Site and fifteen (15) of which shall be located on the surface parking area on the Site.
Annual Fixed Rent:	(a) From the first (1st) calendar month through the eighth (8th) calendar month of the Original Term of this Lease at the annual rate of $153,233.00, being the product of (i) $31.00 and (ii) the "Rentable Floor Area of the Premises" (hereinafter defined in this Section 1.1). (b) From the ninth (9th) calendar month

through the twentieth (20th) calendar month of the Original Term of this Lease at the annual rate of $158,176.00, being the product of (i) $32.00 and (ii) the Rentable Floor Area of the Premises.

(c) From the twenty first (21st) calendar month through the thirty second (32nd) calendar month of the Original Term of this Lease at the annual rate of $163,119.00, being the product of (i) $33.00 and (ii) the Rentable Floor Area of the Premises.

	(d) From the thirty third (33rd) calendar month through the remainder of the Original Term of this Lease at the annual rate of $168,062.00, being the product of (i) $34.00 and (ii) the Rentable Floor Area of the Premises.
Operating Expenses:	As provided in Section 2.6 hereof.
Real Estate Taxes:	As provided in Section 2.7 hereof.
Tenant Electricity:	Initially as provided in Section 2.5 subject to adjustment as provided in Section 2.8 hereof.
Additional Rent:	All charges and other sums payable by Tenant as set forth in this Lease, in addition to Annual Fixed Rent.
Rentable Floor Area of the Premises:	4,943 square feet.
Total Rentable Floor Area of the Building:	248,341 square feet.
Permitted Use:	General office purposes.
Broker:	Newmark Knight Frank One Federal Street 21st Floor Boston, MA 02110
Security Deposit:	$38,308.25

1.2 Exhibits

There are incorporated as part of this Lease:

Exhibit A	—	Description of Site
Exhibit B-1	—	Work Agreement
Exhibit B-2	—	Plans
Exhibit C	—	Intentionally Omitted
Exhibit D	—	Landlord's Services
Exhibit E	—	Floor Plan
Exhibit F	—	Form of Declaration Affixing the Commencement Date of Lease
Exhibit G	—	Intentionally Omitted
Exhibit H	—	Form of Letter of Credit
Exhibit I	—	Form of Certificate of Insurance

1.3 Table of Articles and Sections.

ARTICLE II

Building, Premises, Term and Rent

2.1 The Premises

Landlord hereby demises and leases to Tenant, and Tenant hereby hires and accepts from Landlord, Tenant's Premises in the Building excluding exterior faces of exterior walls, the common stairways and stairwells, elevators and elevator wells, fan rooms, electric and telephone closets, janitor closets, and pipes, ducts, conduits, wires and

appurtenant fixtures serving exclusively, or in common, other parts of the Building, and if Tenant's Premises includes less than the entire rentable area of any floor, excluding the common corridors, elevator lobbies and toilets located on such floor.

Tenant's Premises with such exclusions is hereinafter referred to as the "Premises." The term "Building" means the Building identified on the first page, and which is the subject of this Lease; the term "Site" means all, and also any part of the Land described in Exhibit A, plus any additions or reductions thereto resulting from the change of any abutting street line and all parking areas and structures. The term "Property" means the Building and the Site.

2.1.1 Relocation of Tenant's Premises

Tenant hereby agrees with Landlord that, upon at least sixty (60) days prior notice from Landlord to Tenant given not more than once during the Original Term, Tenant shall relocate from the Premises then demised to Tenant under this Lease (the "Original Premises") to other premises which are comparable to the Original Premises in terms of size and general layout and contain at least the same number of comparably sized offices and conference rooms as the Original Premises (the "Relocated Premises") within the Building and upon such relocation the Relocated Premises shall become the premises demised under this Lease and wherever the term "Premises" is used herein the same thereafter shall mean and refer to the Relocated Premises. Landlord, at its sole cost and expense, shall perform the partitioning of the Relocated Premises and shall place the same into substantially equivalent condition to that in which the Original Premises were in prior to such relocation, and Landlord shall also reimburse Tenant for Tenant's reasonable out-of-pocket moving expenses in so relocating to the Relocated Premises upon billing therefor from Tenant, which billing shall include reasonable evidence thereof in the form of paid invoices, receipts and the like. Landlord shall use reasonable efforts to coordinate such relocation so as to minimize disruption with Tenant's business. Tenant shall not be required to vacate the Original Premises and to relocate to the Relocated Premises until the Relocated Premises shall be substantially complete subject to punch list items. In connection with the foregoing, it is understood and agreed that in the event of any such relocation, Tenant's payments on account of Annual Fixed Rent, operating expenses and real estate taxes for the Relocated Premises during the Original Term shall not exceed the amounts that would have been payable for the same by Tenant for the Original Premises for the same time period had the relocation not occurred. Upon any such relocation the Tenant shall enter into an amendment to this Lease confirming such relocation, but the Tenant's failure to enter into such amendment shall not affect in any manner the relocation of the Premises demised under this Lease from the Original Premises to the Relocated Premises.

2.2 Rights to Use Common Facilities

Subject to Landlord's right to change or alter any of the following in Landlord's discretion as herein provided, Tenant shall have, as appurtenant to the Premises, the non-exclusive right to use in common with others, subject to reasonable rules of general applicability to tenants of the Building from time to time made by Landlord of which Tenant is given notice (a) the common lobbies, corridors, stairways, elevators and

loading area of the Building, and the pipes, ducts, conduits, wires and appurtenant meters and equipment serving the Premises in common with others, (b) common walkways and driveways necessary for access to the Building, and (c) if the Premises include less than the entire rentable floor area of any floor, the common toilets, corridors and elevator lobby of such floor. No such change to the common areas shall materially and adversely affect Tenant's use of or access to the Premises, and such changes shall be consistent with the operation and maintenance of the Building as a first class building in the Boston West Suburban Market. Notwithstanding anything to the contrary herein, Landlord has no obligation to allow any particular telecommunication service provider to have access to the Building or to the Premises except as may be required by applicable law. If Landlord permits such access, Landlord may condition such access upon the payment to Landlord by the service provider of commercially reasonable fees assessed by Landlord in its sole discretion. Notwithstanding the foregoing, in the event such service provider is able to tie into the existing infrastructure in the Building, no such service fee shall be assessed.

2.2.1 Tenant's Parking

In addition, Tenant shall have the right to use in the parking area the Number of Parking Spaces (referred to in Section 1.1) for the parking of automobiles, in common with use by other tenants from time to time of the Complex, provided, however, Landlord shall not be obligated to furnish stalls or spaces in any parking area specifically designated for Tenant's use. In the event that the Rentable Floor Area of the Premises decreases at any time during the Lease Term, the Number of Parking Spaces provided to Tenant hereunder shall be reduced proportionately. Tenant covenants and agrees that it and all persons claiming by, through and under it, shall at all times abide by all reasonable rules and regulations promulgated by Landlord with respect to the use of the parking areas on the Site. The parking privileges granted herein are non- transferable except to a permitted assignee or subtenant as provided in Section 5.6. Further, Landlord assumes no responsibility whatsoever for loss or damage due to fire, theft or otherwise to any automobile(s) parked on the Site or to any personal property therein, however caused, and Tenant covenants and agrees, upon request from Landlord from time to time, to notify its officers, employees, agents and invitees of such limitation of liability. Tenant acknowledges and agrees that a license only is hereby granted, and no bailment is intended or shall be created.

2.3 Landlord's Reservations

Landlord reserves the right from time to time, without unreasonable interference with Tenant's use: (a) to install, use, maintain, repair, replace and relocate for service to the Premises and other parts of the Building, or either, pipes, ducts, conduits, wires and appurtenant fixtures, wherever located in the Premises or Building, and (b) subject to Section 2.2 above to alter or relocate any other common facility, provided that substitutions are substantially equivalent or better. Installations, replacements and relocations referred to in clause (a) above shall be located so far as practicable in the central core area of the Building, above ceiling surfaces, below floor surfaces or within

perimeter walls of the Premises. In the event Landlord makes any changes within the Premises, Landlord will, if necessary, appropriately paint or decorate any affected areas so that it is consistent with the adjacent area.

2.4 Habendum.

Tenant shall have and hold the Premises for a period commencing on the Commencement Date and continuing for the Term unless sooner terminated as provided in Article VI or Article VII.

As soon as may be convenient after the date has been determined on which the Term commences, Landlord and Tenant agree to join with each other in the execution of a written Declaration, in the form of Exhibit F, in which the date on which the Term commences as aforesaid and the Term of this Lease shall be stated.

2.5 Fixed Rent Payments

Tenant agrees to pay to Landlord, (a) on the Commencement Date (defined in Section 1.1 hereof) and thereafter monthly, in advance, on the first day of each and every calendar month during the Original Term, a sum equal to one twelfth (1/12th) of the Annual Fixed Rent (sometimes hereinafter referred to as "fixed rent") and (b) on the

Commencement Date and thereafter monthly, in advance, on the first day of each and every calendar month during the Original Term, an amount reasonably estimated by Landlord from time to time to cover Tenant's monthly payments for electricity under Section 2.8 hereinbelow, Until notice of some other designation is given, fixed rent and all other charges for which provision is herein made shall be paid by remittance to or for the order of Boston Properties Limited Partnership either (i) by mail to P.O. Box 3557, Boston, Massachusetts 02241-3557, (ii) by wire transfer to Bank of America in Dallas, Texas, Bank Routing Number 0260-0959-3 or (iii) by ACH transfer to Bank of America in Dallas, Texas, Bank Routing Number 111 000 012, and in the case of (ii) or (iii) referencing Account Number 3756454460, Account Name of Boston Properties, LP, Tenant's name and the Property address. All remittances received by Boston Properties Limited Partnership as aforesaid, or by any subsequently designated recipient, shall be treated as payment to Landlord.

Annual Fixed Rent for any partial month shall be paid by Tenant to Landlord at such rate on a pro rata basis, and, if the Commencement Date is a day other than the first day of a calendar month, the first payment of Annual Fixed Rent which Tenant shall make to Landlord shall be a payment equal to a proportionate part of such monthly Annual Fixed Rent for the partial month from the Commencement Date to the first day of the succeeding calendar month.

Additional Rent payable by Tenant on a monthly basis, as hereinafter provided, likewise shall be prorated, and the first payment on account thereof shall be determined in similar fashion but shall commence on the Commencement Date; and other provisions of this Lease calling for monthly payments shall be read as incorporating this undertaking by Tenant.

The Annual Fixed Rent and all other charges for which provision is herein made shall be paid by Tenant to Landlord, without offset, deduction or abatement except as otherwise specifically set forth in this Lease.

2.6 Operating Expenses

"Landlord's Operating Expenses" means the cost of operation of the Building and the Site which shall include, without limitation, the following: premiums for insurance carried with respect to the Building and the Site (including, without limitation, liability insurance, insurance against loss in case of fire or casualty and insurance of monthly installments of fixed rent and any Additional Rent which may be due under this Lease and other leases of space in the Building for not more than 12 months in the case of both fixed rent and Additional Rent and if there be any first mortgage of the Property, including such insurance as may be required by the unaffiliated, institutional holder of such first mortgage); compensation and all fringe benefits, worker's compensation insurance premiums and payroll taxes paid to, for or with respect to all persons engaged in the operating, maintaining or cleaning of the Building or Site, water, sewer, electric (excluding any electric payable by Tenant pursuant to Section 2.8), gas, oil and telephone charges (excluding utility charges separately chargeable to tenants for additional or special services); cost of building and cleaning supplies and equipment; cost of maintenance, cleaning and repairs (other than repairs not properly chargeable against income or reimbursed from contractors under guarantees); cost of operating and maintaining a food service facility in the Building, less any rent or other amounts received by Landlord from any third-party operator of such facility; cost of snow removal and care of landscaping; payments under service contracts with independent contractors; management fees at reasonable rates for self managed buildings consistent with the type of occupancy and the service rendered not to exceed 3.5% of the base rents for the Building; costs of maintaining a regional property management office in connection with the operation, management and maintenance of the Building; and all other actual, reasonable and necessary expenses paid in connection with the operation, cleaning and maintenance of the Building and the Site and properly chargeable against income. There may be included in Operating Expenses (a) the annual depreciation for capital expenditures made by Landlord during the Lease Term and which particular expenditure has not been excluded from Base Operating Expenses (i) to reduce Landlord's Operating Expenses if Landlord shall have reasonably determined that the annual reduction in Landlord's Operating Expenses shall exceed depreciation therefor or (ii) to comply with applicable laws, rules, regulations, requirements, statutes, ordinances, by-laws and court decisions of all public authorities which are first in effect after the Commencement Date (the capital expenditures described in subsections (i) and (ii) being hereinafter referred to as "Permitted Capital Expenditures"); plus (b) in the case of both (i) and (ii) an interest factor, reasonably determined by Landlord, as being the interest rate then charged for long term mortgages by institutional lenders on like properties within the locality in which the Building is located; depreciation in the case of both (i) and (ii) shall be determined by dividing the original cost of such capital expenditure, less a reasonable salvage value, by the number of years of useful life of the capital item acquired and the useful life shall be reasonably determined by Landlord in accordance with generally

accepted accounting principles and practices in effect at the time of acquisition of the capital item.

Notwithstanding the foregoing, the following shall be excluded from Landlord's Operating Expenses for the Property:

(i) All capital expenditures and depreciation, except Permitted Capital Expenditures;

(ii) Leasing fees or commissions, advertising and promotional expenses, legal fees, the cost of tenant improvements, build out allowances, moving expenses, assumption of rent under existing leases and other concessions incurred in connection with leasing space in the Building;

(iii) Interest on indebtedness, debt amortization, ground rent, and refinancing costs for any mortgage or ground lease of the Building or the Site;

(iv) Costs incurred in performing work or furnishing services for any tenant (including Tenant), whether at such tenant's or Landlord's expense, to the extent that such work or services is in excess of any work or service that Landlord is obligated to furnish to Tenant at Landlord's expense (e.g., if Landlord agrees to provide extra cleaning to another tenant, the cost thereof would be excluded since Landlord is not obligated to furnish extra cleaning to Tenant);

(v) The cost of any item or service to the extent to which Landlord is actually reimbursed or compensated by insurance, any tenant, or any third party;

(vi) Insurance premiums to the extent any tenant causes Landlord's existing insurance premiums to increase or requires Landlord to purchase additional insurance because of such tenant's use of the Building for other than office purposes or as a result of Landlord's negligent failure to comply with the terms of the Lease;

(vii) The cost of any service or materials provided by any party related to Landlord, to the extent such costs exceed the reasonable cost for such service or materials absent such relationship in self managed buildings similar to the Building in the vicinity of the Building;

(viii) Salaries or other compensation paid to employees above the grade of Building manager;

(ix) The costs of correcting defects in the construction of tenant spaces that Landlord has agreed to make under this Lease or other leases affecting the Building; and

(x) damage and repairs necessitated by the negligence or willful misconduct of Landlord, Landlord's employees, contractors or agents.

"Operating Expenses Allocable to the Premises" shall mean the same proportion of Landlord's Operating Expenses for and pertaining to the Building and the Site as the

Rentable Floor Area of the Premises bears to 95% of the Total Rentable Floor Area of the Building.

"Base Operating Expenses" shall mean Landlord's Operating Expenses for calendar year 2010 (that is, the period beginning January 1, 2010 and ending December 31, 2010). Base Operating Expenses shall not include (i) market-wide cost increases in ordinarily included costs due to extraordinary circumstances, included but not limited to Force Majeure (as defined in Section 6.1), conservation surcharges, boycotts, strikes, embargoes or shortages ("Extraordinary Expense") and (ii) the cost of any Permitted Capital Expenditures. However, if a particular Extraordinary Expense continues for more than twenty-four (24) consecutive months, then during each year after the calendar year 2010 ("Base Year") in which it continues (and on a pro rata basis if it continues for part, but not all, of a subsequent year), Base Operating Expenses shall include such Extraordinary Expense. By way of example only, if there is a conservation surcharge that constitutes an Extraordinary Expense, and if such surcharge continues for more than twenty-four (24) consecutive months, then for every year after the Base Year in which surcharge exists, Base Operating Expenses shall be increased (in a pro rata basis for partial years after the Base Year) by amount of such surcharge in the Base Year.

"Base Operating Expenses Allocable to the Premises" shall mean the same proportion of Base Operating Expenses as the Rentable Floor Area of the Premises bears to 95% of the Total Rentable Floor Area of the Building.

If with respect to any calendar year falling within the Term, or fraction of a calendar year falling within the Term at the beginning or end thereof, the Operating Expenses Allocable to the Premises for a full calendar year exceed Base Operating Expenses Allocable to the Premises, or for any such fraction of a calendar year exceed the corresponding fraction of Base Operating Expenses Allocable to the Premises; then, Tenant shall pay to Landlord, as Additional Rent, the amount of such excess. Such payments shall be made at the times and in the manner hereinafter provided in this Section 2.6. (Base Operating Expenses Allocable to the Premises do not include the tenant electricity to be paid by Tenant together with Annual Fixed Rent and for which provision is made in Section 2.5 hereof, separate provision being made in Section 2.8 of this Lease for Tenant's share of increases in electricity costs.) The Base Operating Expenses referred to above shall not include (i) market-wide cost increases due to extraordinary circumstances, included but not limited to Force Majeure (as defined in Section 6.1), conservation, surcharges, boycotts, strikes, embargoes or shortages and (ii) the cost of any Permitted Capital Expenditures.

Not later than one hundred and twenty (120) days after the end of the first calendar year or fraction thereof ending December 31 and of each succeeding calendar year during the Term or fraction thereof at the end of the Term, Landlord shall render Tenant a statement in reasonable detail and according to usual accounting practices certified by a representative of Landlord, showing for the preceding calendar year or fraction thereof, as the case may be, Landlord's Operating Expenses and Operating Expenses Allocable to the Premises. Said statement to be rendered to Tenant shall also show for the preceding year or fraction thereof as the case may be the amounts of operating expenses already paid by Tenant as Additional Rent, and the amount of operating expenses remaining due

from, or overpaid by, Tenant for the year or other period covered by the statement. Within thirty (30) days after the date of delivery of such statement, Tenant shall pay to Landlord the balance of the amounts, if any, required to be paid pursuant to the above provisions of this Section 2.6 with respect to the preceding year or fraction thereof, or Landlord shall credit any amounts due from it to Tenant pursuant to the above provisions of this Section 2.6 against (i) monthly installments of fixed rent next thereafter coming due or (ii) any sums then due from Tenant to Landlord under this Lease (or refund such portion of the overpayment as aforesaid if the Term has ended and Tenant has no further obligation to Landlord).

In addition, Tenant shall make payments monthly on account of Tenant's share of increases in Landlord's Operating Expenses anticipated for the then current year at the time and in the fashion herein provided for the payment of fixed rent. The amount to be paid to Landlord shall be an amount reasonably estimated annually by Landlord to be sufficient to cover, in the aggregate, a sum equal to Tenant's share of such increases in operating expenses for each calendar year during the Term.

Notwithstanding the foregoing, in determining the amount of Landlord's Operating Expenses for any calendar year or portion thereof falling within the Lease Term (including, without limitation, calendar year 2010 for purposes of calculating Base Operation Expenses), if less than ninety-five percent (95%) of the Total Rentable Floor Area of the Building shall have been occupied by tenants at any time during the period in question, then, at Landlord's election, those components of Landlord's Operating Expenses that vary based on occupancy for such period shall be equitably adjusted, on a line item by line item basis, to equal the amount such components of Landlord's Operating Expenses would have been for such period had occupancy been ninety-five percent (95%) throughout such period.

Within a reasonable period of time after Tenant's written, reasonable request therefor, which request may be made only as to the calendar year immediately preceding the calendar year in which Tenant shall make such request and only within ninety (90) days of Tenant's receipt of the aforesaid annual statement for such preceding calendar year, as a limited audit right, and so long as no Event of Default exists Landlord shall provide Tenant with back-up information relating to a specific item of common area costs and expenses, but in no event shall Tenant withhold payment of all or any portion of its share of the common area costs and expenses or other amounts due under this Lease on account of such request. Tenant agrees that any such information obtained from Landlord shall remain absolutely confidential, except for such information Tenant is required to furnish to Tenant's tax auditors, accountants, attorneys or others in accordance with any court or administrative order or proceedings. Without limiting the generality of the foregoing, under no circumstances shall Tenant provide any such information to any examiner of Tenant who is being paid by Tenant on a contingent fee basis. The provisions of the two immediately preceding sentences shall survive the expiration or earlier termination of this Lease.

2.7 Real Estate Taxes

If with respect to any full Tax Year or fraction of a Tax Year falling within the Term, Landlord's Tax Expenses Allocable to the Premises as hereinafter defined for a full Tax Year exceed Base Taxes Allocable to the Premises, or for any such fraction of a Tax Year exceed the corresponding fraction of Base Taxes Allocable to the Premises; then, on or before the thirtieth (30th) day following receipt by Tenant of the certified statement referred to below in this Section 2.7, then Tenant shall pay to Landlord, as Additional Rent, the amount of such excess. Not later than ninety (90) days after Landlord's Tax Expenses Allocable to the Premises are determined for the first such Tax Year or fraction thereof and for each succeeding Tax Year or fraction thereof during the Term, Landlord shall render Tenant a statement in reasonable detail certified by a representative of Landlord showing for the preceding year or fraction thereof, as the case may be, real estate taxes on the Building and the Site and any abatements and refunds of any taxes and assessments. Upon request by Tenant, Landlord shall provide to Tenant a copy of the tax bill it used to prepare such statement. Expenditures for legal fees and for other expenses incurred in seeking the tax refund or abatement may be charged against the tax refund or abatement before the adjustments are made for the Tax Year. Said statement to be rendered to Tenant shall also show for the preceding Tax Year or fraction thereof as the case may be the amounts of real estate taxes already paid by Tenant as Additional Rent, and the amount of real estate taxes remaining due from, or overpaid by, Tenant for the year or other period covered by the statement. Within thirty (30) days after the date of delivery of the foregoing statement, Tenant shall pay to Landlord the balance of the amounts, if any, required to be paid pursuant to the above provisions of this Section 2.7 with respect to the preceding Tax Year or fraction thereof, or Landlord shall credit any amounts due from it to Tenant pursuant to the provisions of this Section 2.7 against (i) monthly installments of fixed rent next thereafter coming due or (ii) any sums then due from Tenant to Landlord under this Lease (or refund such portion of the overpayment as aforesaid if the Term has ended and Tenant has no further obligation to Landlord).

In addition, payments by Tenant on account of increases in real estate taxes anticipated for the then current year shall be made monthly at the time and in the fashion herein provided for the payment of fixed rent. The amount so to be paid to Landlord shall be an amount reasonably estimated by Landlord to be sufficient to provide Landlord, in the aggregate, a sum equal to Tenant's share of such increases, at least ten (10) days before the day on which such payments by Landlord would become delinquent.

To the extent that real estate taxes shall be payable to the taxing authority in installments with respect to periods less than a Tax Year, the foregoing statement shall be rendered and payments made on account of such installments.

Terms used herein are defined as follows:

(i) "Tax Year" means the twelve-month period beginning July 1 each year during the Term or if the appropriate governmental tax fiscal period shall begin on any date other than July 1, such other date.

(ii) "Landlord's Tax Expenses Allocable to the Premises" shall mean the same proportion of Landlord's Tax Expenses for and pertaining to the Building and the Site as the Rentable Floor Area of the Premises bears to 95% of the Total Rentable Floor Area of the Building.

(iii) "Landlord's Tax Expenses" with respect to any Tax Year means the aggregate real estate taxes on the Building and Site with respect to that Tax Year, reduced by any abatement receipts with respect to that Tax Year.

(iv) "Base Taxes" means Landlord's Tax Expenses (hereinbefore defined) for fiscal tax year 2010 (that is, the period beginning July 1, 2009 and ending June 30, 2010).

(v) "Base Taxes Allocable to the Premises" means the same proportion of Base Taxes as the Rentable Floor Area of the Premises bears to 95% of the Total Rentable Floor Area of the Building.

(vi) "Real estate taxes" means all taxes and special assessments of every kind and nature and user fees and other like fees assessed by any governmental authority on the Building or Site which the Landlord shall become obligated to pay because of or in connection with the ownership, leasing and operation of the Site, the Building and the Property (including without limitation, if applicable, the excise prescribed by Mass Gen Laws (Ter Ed) Chapter 121A, Section 10 and amounts in excess thereof paid to the City of Waltham pursuant to agreement between Landlord and the City) and reasonable expenses of and fees for any formal or informal proceedings for negotiation or abatement of taxes {collectively, "Abatement Expenses"), which Abatement Expenses shall be excluded from Base Taxes. The amount of special taxes or special assessments to be included shall be limited to the amount of the installment (plus any interest, other than penalty interest, payable thereon) of such special tax or special assessment required to be paid during the year in respect of which such taxes are being determined. There shall be excluded from such taxes all income, estate, succession, inheritance, corporate, franchise and transfer taxes; provided, however, that if at any time during the Term the present system of ad valorem taxation of real property shall be changed so that in lieu of the whole or any part of the ad valorem tax on real property there shall be assessed on Landlord a capital levy or other tax on the gross rents received with respect to the Site or Building or Property, or a federal, state, county, municipal, or other local income, franchise, excise or similar tax, assessment, levy or charge (distinct from any now in effect in the jurisdiction in which the Property is located) measured by or based, in whole or in part, upon any such gross rents, then any and all of such taxes, assessments, levies or charges, to the extent so measured or based, shall be deemed to be included within the term "real estate taxes" but only to the

extent that the same would be payable if the Site and Building were the only property of Landlord,

(vii) If during the Lease Term the Tax Year is changed by applicable law to less than a full 12-month period, the Base Taxes and Base Taxes Allocable to the Premises shall each be proportionately reduced.

2.8 Tenant Electricity

(A) If with respect to any calendar year falling within the Term or fraction of a calendar year falling within the Term at the beginning or end thereof, the actual cost of furnishing electricity to the Building and the Site, including common areas and facilities and space occupied by tenants, (but expressly excluding utility charges separately chargeable to tenants for additional or special services) for a full calendar year exceeds the estimated payments for tenant electricity (payable pursuant to Section 2.5 hereof), or for any such fraction of a calendar year exceeds the corresponding fraction of such estimated payments, then Tenant shall pay to Landlord, as Additional Rent, on or before the thirtieth (301h) day following receipt by Tenant of the statement referred to below in this Section 2.8, its proportionate share of the amount of such excess (i.e. the same proportion of such excess as the Rentable Floor Area of the Premises bears to the total rentable floor area of the Building from time to time under lease to tenants); provided, however, that if at any time during the Term more than 49,668 square feet of the Total Rentable Floor Area of the Building are not under lease to tenants, then for the purposes of determining Tenant's proportionate share of and with respect to electricity under this Section 2.8 (A), the denominator shall be deemed to be 235,924 square feet irrespective of the total rentable floor area of the Building then under lease to tenants. Payments by Tenant on account of such excess shall be made monthly at the time and in the fashion herein provided for the payment of Annual Fixed Rent. If the Landlord shall reasonably determine that the cost of the electricity furnished to the Tenant at the Premises exceeds the amount being paid under Sections 2.5 and 2.8, then the Landlord may charge the Tenant for such excess and the Tenant shall promptly pay the same upon billing therefor.

Not later than ninety (90) days after the end of the first calendar year or fraction thereof ending December 31 and of each succeeding calendar year during the Term or fraction thereof at the end of the Term, Landlord shall render Tenant a reasonably detailed accounting certified by a representative of Landlord showing for the preceding calendar year, or fraction thereof, as the case may be, the costs of furnishing electricity to the Building. Said statement to be rendered to Tenant also shall show for the preceding year or fraction thereof, as the case may be, the amount already paid by Tenant on account of electricity, and the amount remaining due from, or overpaid by, Tenant for the year or other period covered by the statement.

(B) Upon election by either Landlord or Tenant, Landlord shall install, at the expense of the requesting party, one or more direct meters or check meters (so-called) for the Premises in locations and in a manner as determined by Landlord in order to measure Tenant's consumption of electricity. In the event of installation of a direct meter or check

meter, in lieu of the payments for electricity referred to in Section 2.8(A) hereinabove, Tenant shall pay to Landlord, as Additional Rent, the cost of furnishing electricity to the Premises including lights, plugs and electricity for Tenant's supplemental or additional heating, ventilating, air-conditioning and cooling equipment, if any, as monitored by such cheek meter or direct meter ("Tenant Electricity"), but excluding (i) electricity for common areas, facilities and systems of the Building and Site and electricity for base building heating, ventilating and air-conditioning, all of which should be covered by and included in Landlord's Operating Expenses under Section 2.6 and (ii) utility charges separately chargeable to tenants for additional or special services. Landlord shall bill Tenant for Tenant Electricity on a monthly basis and Tenant shall pay such monthly Tenant Electricity charges to Landlord within ten (10) days after receipt of Landlord's billing therefore.

ARTICLE III

Condition of Premises; Alterations

3.1 Preparation of Premises

The condition of the Premises upon Landlord's delivery along with any work to be performed by either Landlord or Tenant shall be as set forth in the Work Agreement attached hereto as Exhibit B-1 and made a part hereof.

ARTICLE IV

Landlord's Covenants; Interruptions and Delays

4.1 Landlord Covenants

4.1.1 Services Furnished by Landlord

To furnish services, utilities, facilities and supplies set forth in Exhibit D equal to those customarily provided by landlords in high quality buildings in the Boston West Suburban Market subject to escalation reimbursement in accordance with Section 2.6.

4.1.2 Additional Services Available to Tenant

To furnish, at Tenant's expense, reasonable additional Building operation services which are usual and customary in similar office buildings in the Boston West Suburban Market upon reasonable advance request of Tenant at reasonable and equitable rates from time to time established by Landlord. Tenant agrees to pay to Landlord, as Additional Rent, the cost of any such additional Building services requested by Tenant and for the cost of any additions, alterations, improvements or other work performed by Landlord in the Premises following the

Commencement Date (and not part of Landlord's Work) at the request of Tenant within thirty (30) days after being billed therefor.

4.1.3 Roof, Exterior Wall, Floor Slab and Common Facility Repairs

Except to (a) normal and reasonable wear and use and (b) damage caused by fire and casualty and eminent domain, and except as otherwise provided in Article VI and subject to the escalation provisions of Section 2.6, (1) to make such repairs to the roof, exterior walls, floor slabs and common areas and facilities as may be necessary to keep them in the condition referred to below and (ii) to maintain the Building and the Property (exclusive of Tenant's responsibilities under this Lease) in a first class manner comparable to the maintenance of similar properties in the Boston West Suburban Market.

4.1.4 Door Signs

To provide and install, at Landlord's expense, letters or numerals on the exterior doors to the Premises to identify Tenant's official name and Building address; all such letters and numerals shall be in the building standard graphics and no others shall be used or permitted on the Premises.

4.2 Interruptions and Delays in Services and Repairs, etc

Landlord shall not be liable to Tenant for any compensation or reduction of rent by reason of inconvenience or annoyance or for loss of business arising from the necessity of Landlord or its agents entering the Premises for any of the purposes in this Lease authorized, or for repairing the Premises or any portion of the Building however the necessity may occur. In case Landlord is prevented or delayed from making any repairs, alterations or improvements, or furnishing any services or performing any other covenant or duty to be performed on Landlord's part, by reason of any cause reasonably beyond Landlord's control, including without limitation by reason of Force Majeure (as defined in Section 6.1 hereof), Landlord shall not be liable to Tenant therefor, nor, except as expressly otherwise provided in Article VI, shall Tenant be entitled to any abatement or reduction of rent by reason thereof, or right to terminate this Lease, nor shall the same give rise to a claim in Tenant's favor that such failure constitutes actual or constructive, total or partial, eviction from the Premises.

In the event that the electrical, heating, ventilating, air conditioning, water, sewer or all elevator service to the Premises shall be shut down for more than five (5) full and consecutive business days, but only as a result of causes which are covered by Landlord's loss of rentals insurance, then, Tenant shall be entitled to an abatement of Annual Fixed Rent equal to the "Insurance Amount" (hereinafter defined). The "Insurance Amount" shall be an amount equal to the payment actually received by Landlord (but only allocable to and on account of the Premises) for such shut down of electricity service to the Premises from Landlord's insurance carrier providing such loss of rents insurance less the amount of any deductible contained in such loss of rents insurance coverage. Notwithstanding anything herein contained to the contrary, in no event shall any of the

events referred to in this Section give rise to a claim in Tenant's favor that such failure constitutes actual or constructive, total or partial, eviction from the Premises.

Landlord reserves the right to stop any service or utility system, when necessary by reason of accident or emergency, or until necessary repairs have been completed; provided, however, that in each instance of stoppage, Landlord shall exercise reasonable diligence to eliminate the cause thereof. Except in case of emergency repairs, Landlord will give Tenant reasonable advance notice of any contemplated stoppage and will use reasonable efforts to avoid unnecessary inconvenience to Tenant by reason thereof.

ARTICLE V

Tenant's Covenants

Tenant covenants and agrees to the following during the Term and such further time as Tenant occupies any part of the Premises:

5.1 Payments

To pay when due all fixed rent and Additional Rent and all charges for utility services rendered to the Premises (except as otherwise provided in Exhibit D) and, further, as Additional Rent, all charges for additional services rendered pursuant to Section 4.1.2.

5.2 Repair and Yield Up

Except as otherwise provided in Article VI and Section 4.1.3, to keep the Premises in good order, repair and condition, excepting reasonable wear and tear, damage by fire or other casualty and damage caused by the gross negligence or willful misconduct of Landlord or its agents, employees or contractors, and all glass in windows (except glass in exterior walls unless the damage thereto is attributable to Tenant's negligence or misuse) and doors of the Premises whole and in good condition with glass of the same type and quality as that injured or broken, damage by fire or taking under the power of eminent domain only excepted, and at the expiration or termination of this Lease peaceably to yield up the Premises all construction, work, improvements, and all alterations and additions thereto in good order, repair and condition, subject to the foregoing exceptions, first removing all goods and effects of Tenant and, to the extent specified by Landlord by notice to Tenant given at least ten (10) days before such

expiration or termination (unless otherwise specified by Landlord as set forth in Section 5.12), the wiring installed by or for Tenant's computer, telephone and other communication systems and equipment whether located in the Premises or in any other portion of the Building, including all risers and all alterations and additions made by Tenant and all partitions, and repairing any damage caused by such removal and restoring the Premises and leaving them clean and neat. Tenant shall not permit or commit any waste, and (subject to applicable waivers of claims and rights of subrogation under this Lease) Tenant shall be responsible for the cost of repairs which may be made necessary by reason of damage to common areas in the Building or to the Site caused by Tenant,

Tenant's agents, contractors, employees, sublessees, licensees, concessionaires or invitees.

5.3 Use

To use and occupy the Premises for the Permitted Use only, and not to injure or deface the Premises, Building, the Site or any other part of the Complex nor to permit in the Premises or on the Site any auction sale, vending machine, or inflammable fluids or chemicals, or nuisance, or the emission from the Premises of any objectionable noise or odor nor to permit in the Premises anything which would in any way result in the leakage of fluid or the growth of mold, and not to use or devote the Premises or any part thereof for any purpose other than the Permitted Uses, nor for any use thereof which is inconsistent with maintaining the Building as a first class office building in the quality of its maintenance, use and occupancy, or which is improper, offensive, contrary to law or ordinance or liable to render necessary any alteration or addition to the Building. Nothing herein shall ever be construed to require Tenant to continuously use or occupy all or any portion of the Premises, however, Tenant shall always be required to maintain the Premises as set forth in this Lease. Further, (i) Tenant shall not, nor shall Tenant permit its employees, invitees, agents, independent contractors, contractors, assignees or subtenants to, keep, maintain, store or dispose of (into the sewage or waste disposal system or otherwise) or engage in any activity which might produce or generate any substance which is at the time in question classified as a hazardous material, waste or substance (collectively "Hazardous Materials"), under federal, state or local laws, rules and regulations, including, without limitation, 42 U.S.C. Section 6901 et seq., 42 U.S.C. Section 9601 et seq., 42 U.S.C. Section 2601 et seq., 49 U.S.C. Section 1802 et seq. and Massachusetts General Laws, Chapter 21E and the rules and regulations promulgated under any of the foregoing, as such laws, rules and regulations may be amended from time to time (collectively "Hazardous Materials Laws"), (ii) Tenant shall promptly upon its actual knowledge thereof, notify Landlord of any incident in, on or about the Premises, the Building or the Site that would require the filing of a notice under any Hazardous Materials Laws, (iii) Tenant shall comply and shall cause its employees, invitees, agents, independent contractors, contractors, assignees and subtenants to comply with each of the foregoing and (iv) Landlord shall have the right (at reasonable intervals and upon reasonable advance notice, except in the event of an emergency when no notice is required) to make such inspections (including testing) as Landlord shall elect from time to time to determine that Tenant is complying with the foregoing. Notwithstanding the foregoing, Tenant may use normal amounts and types of substances typically used for office uses, provided that Tenant uses such substances in the manner which they are normally used, and in compliance with all Hazardous Materials Laws and other applicable laws, ordinances, bylaws, rules and regulations, and Tenant obtains and complies with all permits required by Hazardous Materials Laws or any other laws, ordinances, bylaws, rules or regulations prior to the use or presence of any such substances in the Premises.

5.4 Obstructions; Items Visible from Exterior; Rules and Regulations

Not to obstruct in any manner any portion of the Building not hereby leased or any portion thereof or of the Site used by Tenant in common with others; not without prior consent of Landlord to permit the painting or placing of any signs, curtains, blinds, shades, awnings, aerials or flagpoles, or the like, visible from outside the Premises; and to comply with all reasonable Rules and Regulations now or hereafter made by Landlord, of which Tenant has been given notice and which are of general applicability to all tenants of the Building, for the care and use of the Building and Site and their facilities and approaches; Landlord shall not be liable to Tenant for the failure of other occupants of the Building to conform to such Rules and Regulations. In the event there shall be a conflict between such rules and regulations and this Lease, the provisions of this Lease shall prevail.

5.5 Safety Appliances

To keep the Premises equipped with all safety appliances required by any public authority because of any use made by Tenant other than normal office use, and to procure all licenses and permits so required because of such use and, if requested by Landlord, to do any work so required because of such use, it being understood that the foregoing provisions shall not be construed to broaden in any way Tenant's Permitted Use.

5.6 Assignment; Sublease

Except as otherwise expressly provided herein, Tenant covenants and agrees that it shall not assign, mortgage, pledge, hypothecate or otherwise transfer this Lease and/or Tenant's interest in this Lease or sublet (which term, without limitation, shall include granting of concessions, licenses or the like) the whole or any part of the Premises. Any assignment, mortgage, pledge, hypothecation, transfer or subletting not expressly permitted in or consented to by Landlord under Sections 5.6.1-5.6.6 shall be void, ab initio; shall be of no force and effect; and shall confer no rights on or in favor of third parties. In addition, Landlord shall be entitled to seek specific performance of or other equitable relief with respect to the provisions hereof.

5.6.1 Notwithstanding the provisions of Section 5.6 above, in the event Tenant desires to assign this Lease or to sublet the whole (but not part) of the Premises (no partial subletting being permitted other than as provided in Section 5.6.4 below), Tenant shall give Landlord notice (the "Proposed Transfer Notice") of any proposed sublease or assignment, and said notice shall specify the provisions of the proposed assignment or subletting, including (a) the name and address of the proposed assignee or subtenant, (b) in the case of a proposed assignment or subletting pursuant to Section 5.6.3 below, such information as to the proposed assignee's or proposed subtenant's net worth and financial capability and standing as may reasonably be required for Landlord to make the determination referred to in said Section 5.6.3 (provided, however, that Landlord shall hold such information confidential having the right to release same to its officers, accountants, attorneys and mortgage lenders on a confidential basis), (c) all of the

material terms and provisions upon which the proposed assignment or subletting is to be made, (d) in the case of a proposed assignment or subletting pursuant to Section 5.6.3 below, all other information reasonably necessary to make the determination referred to in said Section 5.6.3 and (e) in the case of a proposed assignment or subletting pursuant to Section 5.6.4 below, such information as may be reasonably required by Landlord to determine that such proposed assignment or subletting complies with the requirements of said Section 5.6.4.

5.6.2 Landlord shall have the right at its sole option, to be exercised within twenty (20) days after receipt of Tenant's Proposed Transfer Notice (the "Acceptance Period"), to terminate this Lease as of a date specified in a notice to Tenant, which date shall not be earlier than sixty (60) days nor later than one hundred and twenty (120) days after Landlord's notice to Tenant; provided, however, that upon the termination date as set forth in Landlord's notice, all obligations relating to the period after such termination date (but not those relating to the period before such termination date) shall cease and promptly upon being billed therefor by Landlord, Tenant shall make final payment of all Annual Fixed Rent and Additional Rent due from Tenant through the termination date. In the event that Landlord shall not exercise its termination rights as aforesaid, or shall fail to give any or timely notice pursuant to this Section the provisions of Sections 5.6.3, 5.6.5 and 5.6.6 shall be applicable. This Section 5.6.2 shall not be applicable to an assignment or sublease pursuant to Section 5.6.4.

5.6.3 Notwithstanding the provisions of Section 5.6 above, but subject to the provisions of this Section 5.6.3 and the provisions of Sections 5.6.5 and 5.6.6 below, in the event that Landlord shall not have exercised the termination right as set forth in Section 5.6.2, or shall have failed to give any or timely notice under Section 5.6.2, then for a period of one hundred and twenty (120) days (i) after the receipt of Landlord's notice stating that Landlord does not elect the termination right, or (ii) after the expiration of the Acceptance Period, in the event Landlord shall not give any or timely notice under Section 5.6.2 as the case may be, Tenant shall have the right to assign this Lease or sublet the whole (but not part) of the Premises in accordance with the Proposed Transfer Notice provided that, in each instance, Tenant first obtains the express prior written consent of Landlord, which consent shall not be unreasonably withheld or delayed.

Without limiting the foregoing standard, Landlord shall not be deemed to be unreasonably withholding its consent to such a proposed assignment or subleasing if:

(a) the proposed assignee or subtenant is a tenant in the Building or elsewhere on the Site or is in active negotiation with Landlord or an affiliate of Landlord for premises in the Building or elsewhere on the Site (as evidenced by the receipt by Landlord of a request for proposal to lease from such party and/or the exchange by Landlord and such party of a proposed draft lease no more than ninety (90) days prior to Tenant's request for consent) or is not of a

character consistent with the operation of a first class office building (by way of example Landlord shall not be deemed to be unreasonably withholding its consent to an assignment or subleasing to any governmental or quasi-governmental agency), or

(b) the proposed assignee or subtenant does not possess adequate financial capability to perform the Tenant obligations as and when due or required, or

(c) the assignee or subtenant proposes to use the Premises (or part thereof) for a purpose other than the purpose for which the Premises may be used as stated in Section 1.1 hereof, or

(d) the character of the business to be conducted or the proposed use of the Premises by the proposed subtenant or assignee shall (i) be likely to increase Landlord's Operating Expenses beyond that which Landlord now incurs for use by Tenant; (ii) be likely to increase the burden on elevators or other Building systems or equipment over the burden prior to such proposed subletting or assignment; or (iii) violate or be likely to violate any provisions or restrictions contained herein relating to the use or occupancy of the Premises, or

(e) there shall be existing an uncured Event of Default (defined in Section 7.1) or there have been three (3) or more Event of Default occurrences during the prior eighteen (18) months, or

(f) the proposed rent and other charges to be payable by the proposed assignee or subtenant are less than the market rent and other charges for first class office sublease space for properties of a similar character in the Boston West Suburban market, or

(g) any part of the rent payable under the proposed assignment or sublease shall be based in whole or in part on the income or profits derived from the Premises or if any proposed assignment or sublease shall potentially have any adverse effect on the real estate investment trust qualification requirements applicable to Landlord and its affiliates, or

(h) the holder of any mortgage or ground lease on property which includes the Premises does not approve of the proposed assignment or sublease pursuant to written documentation between Landlord and such holder, or

(i) due to the identity or business of a proposed assignee or subtenant, such approval would cause Landlord to be in violation of any covenant or restriction contained in another lease or other

agreement affecting space in the Building or elsewhere in the Property.

If Landlord shall consent to the proposed assignment or subletting, as the case may be, then, in such event, Tenant may thereafter sublease (the whole but not part of the Premises) or assign pursuant to Tenant's notice, as given hereunder; provided, however, that if such assignment or sublease shall not be executed and delivered to Landlord within one hundred twenty (120) days after the date of Landlord's consent, the consent shall be deemed null and void and the provisions of Section 5.6.1 shall be applicable.

5.6.4 Notwithstanding the foregoing provisions of Sections 5.6.2, 5.6.3 and 5.6.5, but subject to the provisions of Sections 5.6.1, 5.6.5 and 5.6.6, Tenant shall have the right without the prior consent of Landlord but upon notice to Landlord as set forth in Section 5.6.1 to assign this Lease or to sublet the Premises (in whole or in part) to any other entity (the "Successor Entity") (i) which controls or is controlled by Tenant or Tenant's parent corporation, or (ii) which is under common control with Tenant, or (iii) which purchases all or substantially all of the assets of Tenant, or (iv) which purchases all or substantially all of the stock of (or other membership interests in) Tenant or (v) which merges or combines with Tenant, provided that the entity to which this Lease is so assigned or which so sublets the Premises has a credit worthiness (e.g. assets on a pro forma basis using generally accepted accounting principles consistently applied and using the most recent financial statements) which is the same or better than the Tenant as of the date of this Lease (the foregoing transferees referred to, individually or collectively, as a "Permitted Transferee"). Except in cases of statutory merger, in which case the surviving entity in the merger shall be liable as the Tenant under this Lease, Tenant shall continue to remain fully liable under this Lease, on a joint and several basis with the Permitted Transferee. If any parent or subsidiary of Tenant to which this Lease is assigned or the Premises sublet (in whole or in part) shall cease to be such a parent or subsidiary, such cessation shall be considered an assignment or subletting requiring Landlord's consent.

5.6.5 In the case of any assignment or subleasing as to which Landlord may consent (other than an assignment or subletting permitted under Section 5.6.4 above) such consent shall be upon the express and further condition, covenant and agreement, and Tenant hereby covenants and agrees that, in addition to the Annual Fixed Rent, Additional Rent and other charges to be paid pursuant to this Lease, fifty percent (50%) of the "Assignment/Sublease Profits" (hereinafter defined), if any, shall be paid to Landlord. The "Assignment/Sublease Profits" shall be the excess, if any, of (a) the "Assignment/Sublease Net Revenues" as hereinafter defined over (b) the Annual Fixed Rent and Additional Rent and other charges provided in this Lease (provided, however, that for the purpose of calculating the Assignment/Sublease Profits in the case of a sublease, appropriate proportions in the applicable Annual Fixed Rent, Additional Rent and other charges under this Lease shall be made based on the percentage of the Premises subleased and on the terms of the sublease). The "Assignment/Sublease Net Revenues" shall be the

fixed rent, Additional Rent and all other charges and sums payable either initially or over the term of the sublease or assignment plus all other profits and increases to be derived by Tenant as a result of such subletting or assignment, less the reasonable costs of Tenant incurred in such subleasing or assignment (the

definition of which shall be limited to brokerage commissions, legal fees and alteration allowances, in each case actually paid), as set forth in a statement certified by an appropriate officer of Tenant and delivered to Landlord within thirty (30) days of the full execution of the sublease or assignment document, amortized over the term of the sublease or assignment.

All payments of the Assignment/Sublease Profits due Landlord shall be made within ten (10) days of receipt of same by Tenant.

5.6.6 (A) It shall be a condition of the validity of any assignment or subletting consented to under Section 5.6.3 above, or any assignment or subletting of right under Section 5.6.4 above, that both Tenant and the assignee or sublessee enter into a separate written instrument directly with Landlord in a form and containing terms and provisions reasonably required by Landlord, including, without limitation, the agreement of the assignee or sublessee to be bound directly to Landlord for all the obligations of the Tenant hereunder, including, without limitation, the obligation (a) to pay the rent and other amounts provided for under this Lease (but in the case of a partial subletting pursuant to Section 5.6.4, such subtenant shall agree on a pro rata basis to be so bound), (b) to comply with the provisions of Sections 5.6 through 5.6.6 hereof and (c) to indemnify the "Landlord Parties" (as defined in Section 8.13) as provided in Section 8.1 hereof. Such assignment or subletting shall not relieve the Tenant named herein of any of the obligations of the Tenant hereunder and Tenant shall remain fully and primarily liable therefor and the liability of Tenant and such assignee (or subtenant, as the case may be) shall be joint and several. Further, and notwithstanding the foregoing, the provisions hereof shall not constitute a recognition of the sublease or the subtenant thereunder, as the case may be, and at Landlord's option, upon the termination or expiration of the Lease (whether such termination is based upon a cause beyond Tenant's control, a default of Tenant, the agreement of Tenant and Landlord or any other reason), the sublease shall be terminated.

(B) As Additional Rent, Tenant shall pay to Landlord as a fee for Landlord's review of any proposed assignment or sublease requested by Tenant and the preparation of any associated documentation in connection therewith, within thirty (30) days after receipt of an invoice from Landlord, an amount equal to the sum of (i) $1,000,00 and/or (ii) reasonable out of pocket legal fees or other expenses incurred by Landlord in connection with such request, not to exceed $2,500.00 for each request.

(C) If this Lease be assigned, or if the Premises or any part thereof be sublet or occupied by anyone other than Tenant, Landlord may after an Event of Default upon prior notice to Tenant, at any time and from time to time, collect rent and

other charges from the assignee, sublessee or occupant and apply the net amount collected to the rent and other charges herein reserved, but no such assignment, subletting, occupancy or collection shall be deemed a waiver of this covenant, or a waiver of the provisions of Sections 5.6 through 5.6.6 hereof, or the acceptance of the assignee, sublessee or occupant as a tenant or a release of Tenant from the further performance by Tenant of covenants on the part of Tenant herein contained, the Tenant herein named to remain primarily liable under this Lease.

(D) The consent by Landlord to an assignment or subletting under Section 5.6.3 above, or the consummation of an assignment or subletting of right under Section 5.6.4 above, shall in no way be construed to relieve Tenant from obtaining the express consent in writing of Landlord to any further assignment or subletting.

(E) On or after the occurrence of an "Event of Default" (defined in Section 7.1), Landlord shall be entitled to one hundred percent (100%) of any Assignment/Sublease Profits.

(F) Without limiting Tenant's obligations under Section 5.12, Tenant shall be responsible, at Tenant's sole cost and expense, for performing all work necessary to comply with Legal Requirements and Insurance Requirements in connection with any assignment or subletting hereunder including, without limitation, any work in connection with such assignment or subletting.

5.7 Right of Entry

To permit Landlord and its agents to examine the Premises at reasonable times and upon reasonable advance written or electronic notice (which notice shall not be required in the event of an emergency), if Landlord shall so elect, to make any repairs or replacements Landlord may deem necessary; to remove, at Tenant's expense, any alterations, addition, signs, curtains, blinds, shades, awnings, aerials, flagpoles, or the like not consented to in writing; and to show the Premises to prospective tenants during the nine (9) months preceding expiration of the Term and to prospective purchasers and mortgagees at all reasonable times. Landlord shall take reasonable efforts not to unreasonably interfere with Tenant's use of the Premises during any such entry.

5.8 Floor Load, Prevention of Vibration and Noise

Not to place a load upon the Premises exceeding an average rate of 100 pounds of live load per square foot of floor area (partitions shall be considered as part of the live load); and not to move any safe, vault or other heavy equipment in, about or out of the Premises except in such manner and at such time as Landlord shall in each instance reasonably authorize; Tenant's business machines and mechanical equipment which cause vibration or noise that may be transmitted to the Building structure or to any other space in the Building shall be so installed, maintained and used by Tenant so as to eliminate such vibration or noise.

5.9 Personal Property Taxes

To pay promptly when due all taxes which may be imposed upon "Tenant's Property" (as defined in Section 8.4 hereof) in the Premises to whomever assessed.

5.10 Compliance with Laws

To comply with all applicable Legal Requirements now or hereafter in force which shall impose a duty on Landlord or Tenant relating to or as a result of the use or occupancy of the Premises; provided that Tenant shall not be required to make any alterations or additions to the structure, roof, exterior and load bearing walls, foundation, structural floor slabs and other structural elements of the Building unless the same are required by such Legal Requirements as a result of or in connection with Tenant's particular use or occupancy of the Premises beyond normal use of space of this kind. Tenant shall promptly pay all fines, penalties and damages that may arise out of or be imposed because of its failure to comply with the provisions of this Section 5.10.

5.11 Payment of Litigation Expenses

To pay, as Additional Rent, all reasonable costs, counsel and other fees incurred by Landlord in connection with the successful enforcement by Landlord of any obligations of Tenant under this Lease or in connection with any bankruptcy case involving Tenant or any guarantor. Landlord hereby similarly agrees to pay all reasonable costs, counsel and other fees incurred by Tenant in connection with the successful enforcement by Tenant of any obligations of Landlord under this Lease or in connection with any bankruptcy case involving Landlord.

5.12 Alterations

Tenant shall not make alterations and additions to Tenant's Premises except in accordance with plans and specifications therefor first approved by Landlord, which approval shall not be unreasonably withheld, delayed or conditioned. However, Landlord's determination of matters relating to aesthetic issues relating to alterations,

additions or improvements which are visible outside the Premises shall be in Landlord's sole discretion. Without limiting such standard Landlord shall not be deemed unreasonable for withholding approval of any alterations or additions (including, without limitation, any alterations or additions to be performed by Tenant under Article III) which (a) in Landlord's opinion are reasonably likely to adversely affect any structural or exterior element of the Building, any area or element outside of the Premises, or any facility or base building mechanical system serving any area of the Building outside of the Premises, or (b) involve or affect the exterior design, size, height, or other exterior dimensions of the Building or (c) will require unusual expense to readapt the Premises to normal office use on Lease termination or expiration or increase the cost of construction or of insurance or taxes on the Building or of the services called for by Section 4.1 unless Tenant first gives assurance acceptable to Landlord for payment of such increased cost

and that such readaptation will be made prior to such termination or expiration without expense to Landlord, (d) enlarge the Rentable Floor Area of the Premises, or (e) are inconsistent, in Landlord's judgment, with alterations satisfying Landlord's standards for new alterations in the Building. Landlord's review and approval of any such plans and specifications and consent to perform work described therein shall not be deemed an agreement by Landlord that such plans, specifications and work conform with applicable Legal Requirements and requirements of insurers of the Building and the other requirements of this Lease with respect to Tenant's insurance obligations (herein called "Insurance Requirements") nor deemed a waiver of Tenant's obligations under this Lease with respect to applicable Legal Requirements and Insurance Requirements nor impose any liability or obligation upon Landlord with respect to the completeness, design sufficiency or compliance of such plans, specifications and work with applicable Legal Requirements and Insurance Requirements nor give right to any other parties. Further, Tenant acknowledges that Tenant is acting for its own benefit and account, and that Tenant shall not be acting as Landlord's agent in performing any work in the Premises, accordingly, no contractor, subcontractor or supplier shall have a right to lien Landlord's interest in the Property in connection with any such work. Within thirty (30) days after receipt of an invoice from Landlord, Tenant shall pay to Landlord as a fee for Landlord's review of any work or plans (excluding any review respecting initial improvements performed pursuant to Article III hereof for which a fee has previously been paid but including any review of plans or work relating to any assignment or subletting), as Additional Rent, an amount equal to the sum of: (i) $150.00 per hour, plus (ii) third party expenses incurred by Landlord to review Tenant's plans and Tenant's work. Except for any additions or alterations which Tenant requests to remain in the Premises in Tenant's notice seeking Landlord's consent for the installation thereof (which notice shall specifically refer to this Section 5.12) and for which Landlord specifically agrees in writing may remain, all alterations and additions shall be part of the Building unless and until Landlord shall specify the same for removal pursuant to Section 5.2. All of Tenant's alterations and additions and installation of furnishings shall be coordinated with any work being performed by Landlord and in such manner as to maintain harmonious labor relations and not to damage the Buildings or Site or interfere with construction or operation of the Buildings and other improvements to the Site and, except for installation of furnishings, cabling and wiring shall be performed by Landlord's general contractor (whose prices shall be competitive and reasonable taking into consideration the quality and nature of the work) or by contractors or workers first reasonably approved by Landlord. Except for work by Landlord's general contractor, Tenant, before its work is started, shall secure all licenses and permits necessary therefor; deliver to Landlord a statement of the names of all its contractors and subcontractors and the estimated cost of all labor and material to be furnished by them and security reasonably satisfactory to Landlord protecting Landlord against liens arising out of the furnishing of such labor and material; and cause each contractor to carry insurance in accordance with Section 8.14 herein and to deliver to Landlord certificates of all such insurance. To the extent usual and customary in light of the nature of the work being performed, Tenant shall also prepare and submit to Landlord a set of as-built plans, in both print and electronic forms, showing such work performed by Tenant to the Premises promptly after any such alterations, improvements or installations are substantially complete and promptly after any wiring or cabling for Tenant's computer, telephone and

other communications systems is installed by Tenant or Tenant's contractor. Without limiting any of Tenant's obligations hereunder, Tenant shall be responsible, as Additional Rent, for the costs of any alterations, additions or improvements in or to the Building that are required in order to comply with Legal Requirements as a result of any work performed by Tenant. Landlord shall have the right to provide such rules and regulations relative to the performance of any alterations, additions, improvements and installations by Tenant hereunder and Tenant shall abide by all such reasonable rules and regulations and shall cause all of its contractors to so abide including, without limitation, payment for the costs of using Building services. Tenant agrees to pay promptly when due the entire cost of any work done on the Premises by Tenant, its agents, employees, or independent contractors, and not to cause or permit any liens for labor or materials performed or furnished in connection therewith to attach to the Premises or the Buildings or the Site and immediately to discharge any such liens which may so attach. Tenant shall pay, as Additional Rent, 100% of any real estate taxes on the Complex which shall, at any time after commencement of the Term, result from any alteration, addition or improvement to the Premises made by Tenant. Tenant acknowledges and agrees that Landlord shall be the owner of any additions, alterations and improvements in the Premises or the Building to the extent paid for by Landlord.

5.13 Vendors

Any vendors engaged by Tenant to perform services in or to the Premises including, without limitation, janitorial contractors and moving contractors shall be coordinated with any work being performed by or for Landlord and in such manner as to maintain harmonious labor relations and not to damage the Building or the Property or interfere with Building construction or operation and shall be performed by vendors first approved by Landlord.

5.14 Patriot Act

As an inducement to Landlord to enter into this Lease, Tenant hereby represents and warrants that: (i) Tenant is not, nor is it owned or controlled directly or indirectly by, any person, group, entity or nation named on any list issued by the Office of Foreign Assets Control of the United States Department of the Treasury ("OFAC") pursuant to Executive Order 13224 or any similar list or any law, order, rule or regulation or any Executive Order of the President of the United States as a terrorist, "Specially Designated National and Blocked Person" or other banned or blocked person (any such person, group, entity or nation being hereinafter referred to as a "Prohibited Person"); (ii) Tenant is not (nor is it owned, controlled, directly or indirectly, by any person, group, entity or nation which is) acting directly or indirectly for or on behalf of any Prohibited Person; and (iii) from and after the effective date of the above-referenced Executive Order, Tenant (and any person, group, or entity which Tenant controls, directly or indirectly) has not conducted nor will conduct business nor has engaged nor will engage in any transaction or dealing with any Prohibited Person in violation of the U.S. Patriot Act or any OFAC rule or regulation, including without limitation any assignment of this Lease or any subletting of all or any portion of the Premises or the making or receiving of any contribution of funds, goods or services to or for the benefit of a Prohibited Person in violation of the U.S.

Patriot Act or any OFAC rule or regulation. In connection with the foregoing, it is expressly understood and agreed that (x) any breach by Tenant of the foregoing representations and warranties shall be deemed an immediate Event of Default by Tenant under Section 7.1 of this Lease (without the benefit of notice or grace) and shall be covered by the indemnity provisions of Section 8.1 below, and (y) the representations and warranties contained in this subsection shall be continuing in nature and shall survive the expiration or earlier termination of this Lease.

ARTICLE VI

Casualty and Taking

6.1 Damage Resulting from Casualty

In case during the Lease Term the Building or the Site are damaged by fire or casualty and such fire or casualty damage cannot, in the ordinary course, reasonably be expected to be repaired within one hundred fifty (150) days from the time that repair work would commence, Landlord may, at its election, terminate this Lease by notice given to Tenant within sixty (60) days after the date of such fire or other casualty, specifying the effective date of termination. The effective date of termination specified by Landlord shall not be less than thirty (30) days nor more than forty-five (45) days after the date of notice of such termination.

In case during the last year of the Lease Term, the Premises are damaged by fire or casualty (or common areas essential for Tenant's use of or access to the Premises) and such fire or casualty damage cannot, in the ordinary course, reasonably be expected to be repaired within one hundred fifty (150) days (and/or as to special work or work which requires long lead time then if such work cannot reasonably be expected to be repaired within such additional time as is reasonable under the circumstances given the nature of the work) from the time that repair work would commence, Tenant may, at its election, terminate this Lease by notice given to Landlord within sixty (60) days after the date of such fire or other casualty, specifying the effective date of termination. The effective date of termination specified by Tenant shall be not less than thirty (30) days nor more than forty-five (45) days after the date of notice of such termination.

Unless terminated pursuant to the foregoing provisions, this Lease shall remain in full force and effect following any such damage subject, however, to the following provisions:

If the Building or the Site or any part thereof are damaged by fire or other casualty and this Lease is not so terminated, or Landlord or Tenant have no right to terminate this Lease, and in any such case the holder of any mortgage which includes the Building as a part of the mortgaged premises or any ground lessor of any ground lease which includes the Site as part of the demised premises allows the net insurance proceeds to be applied to the restoration of the Building (and/or the Site), Landlord shall, promptly after such damage and the determination of the net amount of insurance proceeds available, use due

diligence to restore the Premises and the Building in the event of damage thereto (excluding "Tenant's Property" (as defined in Section 8.4 hereof)) into proper condition for use and occupation and a just proportion of the Annual Fixed Rent, Tenant's share of Operating Costs, Tenant's share of real estate taxes and Tenant's payments for electricity shall be abated from the date of the casualty according to the nature and extent of the injury to the Premises, until the Premises (and the common areas essential for Tenant's use of the Premises, i.e. parking) shall have been restored by Landlord substantially into such condition except for punch list items. Notwithstanding anything herein contained to the contrary, so long as Landlord carries the property insurance required under this Lease, Landlord shall not be obligated to expend for such repair and restoration any amount in excess of the net insurance proceeds.

If such restoration is not completed within ten (10) months from the date of the fire or casualty, such period to be subject, however, to extension where the delay in completion of such work is due Force Majeure, as defined hereinbelow (but in no event beyond fourteen (14) months from the date of the fire or casualty), Tenant, as its sole and exclusive remedy, shall have the right to terminate this Lease at any time after the expiration of such ten (10) month period (as extended), which right shall continue until the restoration is substantially completed. Such termination shall be effective as of the thirtieth (30th) day after the date of receipt by Landlord of Tenant's notice, with the same force and effect as if such date were the date originally established as the expiration date hereof unless, within thirty (30) days after Landlord's receipt of Tenant's notice, such restoration is substantially completed, in which case Tenant's notice of termination shall be of no force and effect and this Lease and the Lease Term shall continue in full force and effect. When used herein, "Force Majeure" shall mean any prevention, delay or stoppage due to governmental regulation, strikes, lockouts, acts of God, acts of war, terrorists acts, civil commotions, unusual scarcity of or inability to obtain labor or materials, labor difficulties, casualty or other causes reasonably beyond Landlord's control or attributable to Tenant's action or inaction.

6.2 Uninsured Casualty

Notwithstanding anything to the contrary contained in this Lease, if the Building or the Premises shall be substantially damaged by fire or casualty as the result of a risk not covered by the forms of casualty insurance at the time actually maintained or required to be maintained (whichever is greater) by Landlord and such fire or casualty damage cannot, in the ordinary course, reasonably be expected to be repaired within ninety (90) days from the time that repair work would commence, Landlord may, at its election, terminate the Term of this Lease by notice to the Tenant given within sixty (60) days after such loss. If Landlord shall give such notice, then this Lease shall terminate as of the date of such notice with the same force and effect as if such date were the date originally established as the expiration date hereof.

6.3 Rights of Termination for Taking

If the entire Building, or such portion of the Premises as to render the balance (if reconstructed to the maximum extent practicable in the circumstances) unsuitable for

Tenant's purposes, shall be taken by condemnation or right of eminent domain, Landlord or Tenant shall have the right to terminate this Lease by notice to the other of its desire to do so, provided that such notice is given not later than thirty (30) days after Tenant has been deprived of possession, If either party shall give such notice, then this Lease shall terminate as of the date of such notice with the same force and effect as if such date were the date originally established as the expiration date hereof.

Further, if so much of the Building shall be so taken that continued operation of the Building would be uneconomic as a result of the taking, Landlord shall have the right to terminate this Lease by giving notice to Tenant of Landlord's desire to do so not later than thirty (30) days after Tenant has been deprived of possession of the Premises (or such portion thereof as may be taken) provided that the leases of all other tenants in the Building similarly affected by the taking at issue are concurrently terminated (to the extent permitted under the terms of Landlord's leases with such tenants). If Landlord shall give such notice, then this Lease shall terminate as of the date of such notice with the same force and effect as if such date were the date originally established as the expiration date hereof.

Should any part of the Premises be so taken or condemned during the Lease Term hereof, and should this Lease not be terminated in accordance with the foregoing provisions, and the holder of any mortgage which includes the Premises as part of the mortgaged premises or any ground lessor of any ground lease which includes the Site as part of the demised premises allows the net condemnation proceeds to be applied to the restoration of the Building, Landlord agrees, after the determination of the net amount of condemnation proceeds available to Landlord, to use due diligence to put what may remain of the Premises into proper condition for use and occupation as nearly like the condition of the Premises prior to such taking as shall be practicable (excluding Tenant's Property). Notwithstanding the foregoing, Landlord shall not be obligated to expend for such repair and restoration any amount in excess of the net condemnation proceeds made available to it.

If the Premises shall be affected by any exercise of the power of eminent domain, then the Annual Fixed Rent, Tenant's share of operating costs and Tenant's share of real estate taxes shall be justly and equitably abated and reduced according to the nature and extent of the loss of use thereof suffered by Tenant; and in case of a taking which permanently reduces the Rentable Floor Area of the Premises, a just proportion of the Annual Fixed Rent, Tenant's share of operating costs and Tenant's share of real estate taxes shall be abated for the remainder of the Lease Term.

6.4 Award

Landlord shall have and hereby reserves to itself any and all rights to receive awards made for damages to the Premises, the Building, the Complex and the Site and the leasehold hereby created, or any one or more of them, accruing by reason of exercise of eminent domain or by reason of anything lawfully done in pursuance of public or other authority. Tenant hereby grants, releases and assigns to Landlord all Tenant's rights to

such awards, and covenants to execute and deliver such further assignments and assurances thereof as Landlord may from time to time reasonably request.

Nothing contained herein shall be construed to prevent Tenant from prosecuting in any condemnation proceeding a claim for the value of any of Tenant's usual trade fixtures installed in the Premises by Tenant at Tenant's expense and for relocation and moving expenses, provided that such action and any resulting award shall not affect or diminish the amount of compensation otherwise recoverable by Landlord from the taking authority.

ARTICLE VII

Default

7.1 Tenant's Default

(a) If at any time subsequent to the date of this Lease any one or more of the following events (herein sometimes called an "Event of Default") shall occur:

(i) Tenant shall fail to pay the fixed rent, Additional Rent or other charges for which provision is made herein on or before the date on which the same become due and payable, and the same continues for seven (7) days after notice from Landlord thereof; or

(ii) Landlord having rightfully given the notice specified in subdivision (i) above twice in any calendar year, Tenant shall thereafter in the same calendar year fail to pay the fixed rent, Additional Rent or other charges on or before the date on which the same become due and payable; or

(iii) Tenant shall assign its interest in this Lease or sublet any portion of the Premises in violation of the requirements of Section 5.6 through 5.6.5 of this Lease; or

(iv) Tenant shall neglect or fail to perform or observe any other covenant herein contained on Tenant's part to be performed or observed and Tenant shall fail to remedy the same within thirty (30) days after notice to Tenant specifying such neglect or failure, or if such failure is of such a nature that Tenant cannot reasonably remedy the same within such thirty (30) day period, Tenant shall fail to commence promptly to remedy the same and to prosecute such remedy to completion with diligence and continuity; or

(v) Tenant's leasehold interest in the Premises shall be taken on execution or by other process of law directed against Tenant; or

(vi) Tenant shall make an assignment for the benefit of creditors or shall file a voluntary petition in bankruptcy or shall be adjudicated bankrupt or insolvent, or shall file any petition or answer seeking any reorganization, arrangement, composition, readjustment, liquidation, dissolution or similar relief for itself under any present or future federal, state or other statute, law or regulation for the relief of debtors, or shall seek or consent to or acquiesce in the appointment of any trustee, receiver or liquidator of Tenant or of all or any substantial part of its properties, or shall admit in writing its inability to pay its debts generally as they become due; or

(vii) A petition shall be filed against Tenant in bankruptcy or under any other law seeking any reorganization, arrangement, composition, readjustment, liquidation, dissolution, or similar relief under any present or future Federal, State or other statute, law or regulation and shall remain undismissed or unstayed for an aggregate of sixty (60) days (whether or not consecutive), or if any debtor in possession (whether or not Tenant) trustee, receiver or liquidator of Tenant or of all or any substantial part of its properties or of the Premises shall be appointed without the consent or acquiescence of Tenant and such appointment shall remain unvacated or unstayed for an aggregate of sixty (60) days (whether or not consecutive) then, and in any of said cases (notwithstanding any license of a former breach of covenant or waiver of the benefit hereof or consent in a former instance).

Landlord lawfully may, immediately or at any time thereafter, and without demand or further notice terminate this Lease by notice to Tenant, specifying a date not less than ten (10) days after the giving of such notice on which this Lease shall terminate, and this Lease shall come to an end on the date specified therein as fully and completely as if such date were the date herein originally fixed for the expiration of the Lease Term (Tenant hereby waiving any rights of redemption), and Tenant will then quit and surrender the Premises to Landlord, but Tenant shall remain liable as hereinafter provided.

(b) If this Lease shall have been terminated as provided in this Article, then Landlord may, without notice, re- enter the Premises, either by summary proceedings, ejectment or legal means, and remove and dispossess Tenant and all other persons and any and all property from the same, as if this Lease had not been made, and Tenant hereby waives the service of notice of intention to re-enter or to institute legal proceedings to that end.

(c) In the event that this Lease is terminated under any of the provisions contained in Section 7.1 (a) or shall be otherwise terminated by breach of any obligation of Tenant, Tenant covenants and agrees forthwith to pay and be liable for, on the days originally fixed herein for the payment thereof, amounts equal to the several installments of rent and other charges reserved as they would, under the terms of

this Lease, become due if this Lease had not been terminated or if Landlord had not entered or re-entered, as aforesaid, and whether the Premises be relet or remain vacant, in whole or in part, or relet for a period less than the remainder of the Term, and for the whole thereof, but in the event the Premises be relet by Landlord, Tenant shall be entitled to a credit in the net amount of rent and other charges received by Landlord in reletting, after deduction of all actual and reasonable out-of-pocket expenses incurred in reletting the Premises (including, without limitation, remodeling costs, brokerage fees and the like), and in collecting the rent in connection therewith, in the following manner:

Amounts received by Landlord after reletting shall first be applied against such Landlord's expenses, until the same are recovered, and until such recovery, Tenant shall pay, as of each day when a payment would fall due under this Lease, the amount which Tenant is obligated to pay under the terms of this Lease (Tenant's liability prior to any such reletting and such recovery not in any way to be diminished as a result of the fact that such reletting might be for a rent higher than the rent provided for in this Lease); when and if such expenses have been completely recovered, the amounts received from reletting by Landlord as have not previously been applied shall be credited against Tenant's obligations as of each day when a payment would fall due under this Lease, and only the net amount thereof shall be payable by Tenant. Further, amounts received by Landlord from such reletting for any period shall be credited only against obligations of Tenant allocable to such period, and shall not be credited against obligations of Tenant hereunder accruing subsequent or prior to such period; nor shall any credit of any kind be due for any period after the date when the term of this Lease is scheduled to expire according to its terms.

Landlord agrees to use reasonable efforts to relet the Premises after Tenant vacates the same in the event this Lease is terminated based upon an Event of Default by Tenant hereunder. The marketing of the Premises in a manner similar to the manner in which Landlord markets other premises within Landlord's control within the Building shall be deemed to have satisfied Landlord's obligation to use "reasonable efforts" hereunder. In no event shall Landlord be required to (i) solicit or entertain negotiations with any other prospective tenant for the Premises until Landlord obtains full and complete possession of the Premises

(including, without limitation, the final and unappealable legal right to relet the Premises free of any claim of Tenant), (ii) relet the Premises before leasing other vacant space in the Building, or (iii) lease the Premises for a rental less than the current fair market rent then prevailing for similar office space in the Building.

(d) (i) Landlord may elect, as an alternative, to have Tenant pay liquidated damages, which election may be made by notice given to Tenant at any time after such termination and whether or not Landlord shall have collected any damages as aforesaid, as liquidated final damages and in lieu of all other damages beyond

the date of such notice. Upon such notice, Tenant shall promptly pay to Landlord, as liquidated damages, in addition to any damages collected or due from Tenant for any period prior to such notice and all expenses which Landlord may have incurred with respect to the collection of such damages, such a sum as at the time of the giving of such notice represents the amount of the excess, if any, of the total rent and other benefits which would have accrued to Landlord under this Lease from the date of such notice for what would be the then unexpired Lease Term if the Lease terms had been fully complied with by Tenant over and above the then cash rental value (in advance) of the Premises for the balance of the Lease Term discounted to present value at a discount rate equal to the then-prevailing prime rate in Boston as set by Bank of America, NA. (or its successor).

(ii) For the purposes of this Article, if Landlord elects to require Tenant to pay damages in accordance with the immediately preceding paragraph, the total rent shall be computed by assuming that Tenant's share of excess taxes and Tenant's share of excess operating costs would be, for the balance of the unexpired Term from the date of such notice, the amount thereof (if any) for the immediately preceding annual period payable by Tenant to Landlord.

(e) In case of any Event of Default, re-entry, dispossession by summary proceedings or otherwise, Landlord may (i) re-let the Premises or any part or parts thereof, either in the name of Landlord or otherwise, for a term or terms which may at Landlord's option be equal to or less than or exceed the period which would otherwise have constituted the balance of the Term of this Lease and may grant concessions or free rent to the extent that Landlord considers advisable or necessary to re-let the same and (ii) may make such alterations, repairs and decorations in the Premises as Landlord in its sole judgment considers advisable or necessary for the purpose of reletting the Premises; and the making of such alterations, repairs and decorations shall not operate or be construed to release Tenant from liability hereunder as aforesaid. Landlord shall in no event be liable in any way whatsoever for failure to re-let the Premises, or, in the event that the Premises are re-let, for failure to collect the rent under re-letting. Tenant hereby expressly waives any and all rights of redemption granted by or under any present or future laws in the event of Tenant being evicted or dispossessed, or in the event of Landlord obtaining possession of the Premises, by reason of the violation by Tenant of any of the covenants and conditions of this Lease.

(f) The specified remedies to which Landlord may resort hereunder are not intended to be exclusive of any remedies or means of redress to which Landlord may at any time be entitled lawfully, and Landlord may invoke any remedy (including the remedy of specific performance) allowed at law or in equity as if specific remedies were not herein provided for. Further, nothing contained in this Lease shall limit or prejudice the right of Landlord to prove and obtain in proceedings for bankruptcy or insolvency by reason of the termination of this Lease, an amount equal to the maximum allowed by any statute or rule of law in effect at the time when, and governing the proceedings in which, the damages are to be

proved, whether or not the amount be greater, equal to, or less than the amount of the loss or damages referred to above.

(g) In lieu of any other damages or indemnity and in lieu of the recovery by Landlord of all sums payable under all the foregoing provisions of this Section 7.1, Landlord may elect to collect from Tenant, by notice to Tenant, at any time after this Lease is terminated under any of the provisions contained in this Article VII or otherwise terminated by breach of any obligation of Tenant and before full recovery under such foregoing provisions, and Tenant shall thereupon pay, as liquidated damages, an amount equal to the sum of the Annual Fixed Rent and all Additional Rent payable for the twelve (12) months ended next prior to the such termination plus the amount of Annual Fixed Rent and Additional Rent of any kind accrued and unpaid at the time of such election plus any and all expenses which the Landlord may have incurred for and with respect of the collection of any of such rent.

7.2 Landlord's Default

Landlord shall in no event be in default in the performance of any of Landlord's obligations hereunder unless and until Landlord shall have failed to perform such obligations within thirty (30) days, or such additional time as is reasonably required to correct any such default, after notice by Tenant to Landlord properly specifying wherein Landlord has failed to perform any such obligation. The Tenant shall not assert any right to deduct the cost of repairs or any monetary claim against the Landlord from rent thereafter due and payable, but shall look solely to the Landlord for satisfaction of such claim.

ARTICLE VIII

Insurance and Indemnity

8.1 Tenant's Indemnity

(a) Indemnity. To the maximum extent permitted by law, and subject to applicable waivers of claim and rights of subrogation under this Lease, Tenant waives any right to contribution against the Landlord Parties (as hereinafter defined) and agrees to indemnify and save harmless the Landlord Parties from and against all claims of whatever nature arising from or claimed to have arisen from (i) any act, omission or negligence of the Tenant Parties (as hereinafter defined); (ii) any accident, injury or damage whatsoever caused to any person, or to the property of any person, occurring in or about the Premises from the earlier of (A) the date on which any Tenant Party first enters the Premises for any reason or (B) the Commencement Date, and thereafter throughout and until the end of the Lease Term, and after the end of the Lease Term for so long after the end of the Lease Term as Tenant or anyone acting by, through or under Tenant is in occupancy of the Premises or any portion thereof; (iii) any accident, injury or damage whatsoever occurring outside the Premises but within the Building or on common areas or the Complex, where such accident, injury or damage results, or is claimed to have resulted,

from any act, omission or negligence on the part of any of the Tenant Parties; or (iv) any breach of this Lease by Tenant. Tenant shall pay such indemnified amounts as they are incurred by the Landlord Parties. Notwithstanding anything contained herein to the contrary, Tenant shall not be obligated to indemnify a Landlord Party for any claims to the extent that such Landlord Party's damages in fact result from such Landlord Party negligence or willful misconduct. This indemnification shall not be construed to deny or reduce any other rights or obligations of indemnity that any of the Landlord Parties may have under this Lease or the common law.

(b) Breach. In the event that Tenant breaches any of its indemnity obligations hereunder or under any other contractual or common law indemnity: (i) Tenant shall pay to the Landlord Parties all liabilities, loss, cost, or expense (including attorney's fees) incurred as a result of said breach; and (ii) the Landlord Parties may deduct and offset from any amounts due to Tenant under this Lease any amounts owed by Tenant pursuant to this Section 8.1(b).

(c) No limitation. The indemnification obligations under this Section 8.1 shall not be limited in any way by any limitation on the amount or type of damages, compensation or benefits payable by or for Tenant or any subtenant or other occupant of the Premises under workers' compensation acts, disability benefit acts, or other employee benefit acts. Tenant waives any immunity from or limitation on its indemnity or contribution liability to the Landlord Parties based upon such acts.

(d) Subtenants and other occupants. Tenant shall require its subtenants and other occupants of the Premises to provide similar indemnities to the Landlord Parties in a form acceptable to Landlord.

(e) Survival. The terms of this Section 8.1 shall survive any termination or expiration of this Lease.

(f) Costs. The foregoing indemnity and hold harmless agreement shall include indemnity for all costs, expenses and liabilities (including, without limitation, attorneys' fees and disbursements) incurred by the Landlord Parties in connection with any such claim or any action or proceeding brought thereon, and the defense thereof, In addition, in the event that any action or proceeding shall be brought against one or more Landlord Parties by reason of any such claim, Tenant, upon request from the Landlord Party, shall resist and defend such action or proceeding on behalf of the Landlord Party by counsel appointed by Tenant's insurer (if such claim is covered by insurance without reservation) or otherwise by counsel reasonably satisfactory to the Landlord Party. The Landlord Parties shall not be bound by any compromise or settlement of any such claim, action or proceeding without the prior written consent of such Landlord Parties.

8.2 Tenant's Risk

Tenant agrees to use and occupy the Premises, and to use such other portions of the Building and the Complex as Tenant is given the right to use by this Lease at Tenant's own risk, The Landlord Parties shall not be liable to the Tenant Parties for any damage,

injury, loss, compensation, or claim (including, but not limited to, claims for the interruption of or loss to a Tenant Party's business) based on, arising out of or resulting from any cause whatsoever, including, but not limited to, repairs to any portion of the Premises or the Building or the Complex, any fire, robbery, theft, mysterious disappearance, or any other crime or casualty, the actions of any other tenants of the Building or of any other person or persons, or any leakage in any part or portion of the Premises or the Building or the Complex, or from water, rain or snow that may leak into, or flow from any part of the Premises or the Building or the Complex, or from drains, pipes or plumbing fixtures in the Building or the Complex, Any goods, property or personal effects stored or placed in or about the Premises shall be at the sole risk of the Tenant Party, and neither the Landlord Parties nor their insurers shall in any manner be held responsible therefor. The Landlord Parties shall not be responsible or liable to a Tenant Party, or to those claiming by, through or under a Tenant Party, for any loss or damage that may be occasioned by or through the acts or omissions of persons occupying adjoining premises or any part of the premises adjacent to or connecting with the Premises or any part of the Building or otherwise.

Notwithstanding the foregoing, the Landlord Parties shall not be released from liability for any injury, loss, damages or liability to the extent arising from any negligence or willful misconduct of the Landlord Parties on or about the Premises; provided, however, in no event shall the Landlord Parties have any liability to a Tenant Party based on any loss with respect to or interruption in the operation of Tenant's business.

8.3 Tenant's Commercial General Liability Insurance

Tenant agrees to maintain in full force on or before the earlier of (i) the date on which any Tenant Party first enters the Premises for any reason or (ii) the Commencement Date, and thereafter throughout and until the end of the Lease Term, and after the end of the Lease Term for so long as Tenant or anyone acting by, through or under Tenant is in occupancy of the Premises or any portion thereafter, a policy of commercial general liability insurance, on an occurrence basis, issued on a form at least as broad as Insurance Services Office ("ISO") Commercial General Liability Coverage "occurrence" form CG 00 01 10 01 or another Commercial General Liability "occurrence" form providing equivalent coverage. Such insurance shall include broad form contractual liability coverage, specifically covering but not limited to the indemnification obligations undertaken by Tenant in this Lease. The minimum limits of liability of such insurance shall be Three Million Dollars ($3,000,000) per occurrence. In addition, in the event Tenant hosts a function in the Premises, Tenant agrees to obtain, and cause any persons or parties providing services for such function to obtain, the appropriate insurance coverages as determined by Landlord (including liquor liability coverage, if applicable) and provide Landlord with evidence of the same.

8.4 Tenant's Property Insurance

Tenant shall maintain at all times during the Term of the Lease, and during such earlier time as Tenant may be performing work in or to the Premises or have property, fixtures, furniture, equipment, machinery, goods, supplies, wares or merchandise on the Premises,

and containing thereafter so long as Tenant is in occupancy of any part of the Premises, business interruption insurance and insurance against loss or damage covered by the so-called "all risk" type insurance coverage with respect to Tenant's property, fixtures, furniture, equipment, machinery, goods, supplies, wares and merchandise, and all alterations, improvements and other modifications made by or on behalf of the Tenant in the Premises, and other property of Tenant located at the Premises, which are permitted to be removed by Tenant at the expiration or earlier termination of the Lease Term except to the extent paid for by Landlord or which are part of Landlord's Work (collectively "Tenant's Property"). The business interruption insurance, required by this Section 8.4 shall be in minimum amounts typically carried by prudent tenants engaged in similar operations, but in no event shall be in an amount less than the Annual Fixed Rent then in effect during any year during the Term, plus any Additional Rent due and payable for the immediately preceding year during the Term. The "all risk" insurance required by this section shall be in an amount at least equal to the full insurable replacement cost of Tenant's Property. In addition, during such time as Tenant is performing work in or to the Premises, Tenant, at Tenant's expense, shall also maintain, or shall cause its contractor(s) to maintain, builder's risk insurance for the full insurable value of such work. Landlord and such additional persons or entities as Landlord may reasonably request shall be named as loss payees, as their interests may appear, on the policy or policies required by this Lease. In the event of loss or damage covered by the "all risk" insurance required by this Lease, the responsibilities for repairing or restoring the loss or damage shall be determined in accordance with Article VI. To the extent that Landlord is obligated to pay for the repair or restoration of the loss or damage covered by the policy, Landlord shall be paid the proceeds of the "all risk" insurance covering the loss or damage. To the extent Tenant is obligated to pay for the repair or restoration of the loss or damage, covered by the policy, Tenant shall be paid the proceeds of the "all risk" insurance covering the loss or damage. If both Landlord and Tenant are obligated to pay for the repair or restoration of the loss or damage covered by the policy, the insurance proceeds shall be paid to each of them in the pro rata proportion of their obligations to repair or restore the loss or damage. If the loss or damage is not repaired or restored (for example, if the Lease is terminated pursuant to Article VI), the insurance proceeds shall be paid to Landlord and Tenant in the pro rata proportion of their relative contributions to the cost of the leasehold improvements covered by the policy.

8.5 Tenant's Other Insurance

Tenant agrees to maintain in full force on or before the earlier of (i) the date on which any Tenant Party first enters the Premises for any reason or (ii) the Commencement Date, and thereafter throughout the end of the Term, and after the end of the Term for so long after the end of the Term as Tenant or anyone acting by, through or under Tenant is in occupancy of the Premises or any portion thereafter, (1) comprehensive automobile liability insurance (covering any automobiles owned or operated by Tenant) issued on a form at least as broad as ISO Business Auto Coverage form CA 00 01 07 97 or other form providing equivalent coverage; (2) worker's compensation insurance; and (3) employer's liability insurance. Such automobile liability insurance shall be in an amount not less than One Million Dollars ($1,000,000) for each accident. Such worker's compensation insurance shall carry minimum limits as defined by the law of the

jurisdiction in which the Premises are located (as the same may be amended from time to time). Such employer's liability insurance shall be in an amount not less than One Million Dollars ($1,000,000) for each accident, One Million Dollars ($1,000,000) disease-policy limit, and One Million Dollars ($1,000,000) disease-each employee.

8.6 Requirements for Tenant's Insurance

All insurance required to be maintained by Tenant pursuant to this Lease shall be maintained with responsible companies that are admitted to do business, and are in good standing in the Commonwealth of Massachusetts and that have a rating of at least "A-" and are within a financial size category of not less than "Class VII" in the most current Best's Key Rating Guide or such similar rating as may be reasonably selected by Landlord. All such insurance shall: (1) be reasonably acceptable in form and content to Landlord; (2) be primary and noncontributory; and (3) contain an endorsement prohibiting cancellation, failure to renew, reduction of amount of insurance, or change in coverage without thirty (30) days' prior written notice to Landlord (by certified or registered mail, return receipt requested, or by fax or email) of such proposed action. No such policy shall contain any deductible or self-insured retention greater than Twenty Five Thousand Dollars ($25,000). Any deductibles and self-insured retentions shall be deemed to be "insurance" for purposes of the waiver in Section 8.13 below. Landlord reserves the right from time to time, after the first twenty four (24) months of the Lease Term, to require Tenant to obtain higher minimum amounts of insurance based on such limits as are customarily carried with respect to similar properties in the area in which the Premises are located, The minimum amounts of insurance required by this Lease shall not be reduced by the payment of claims or for any other reason. In the event Tenant shall fail to obtain or maintain any insurance meeting the requirements of this Article, or to deliver such policies or certificates as required by this Article, Landlord may, at its option, on seven (7) days notice to Tenant, procure such policies for the account of Tenant, and the cost thereof shall be paid to Landlord within five (5) days after delivery to Tenant of bills therefor.

8.7 Additional Insureds

The commercial general liability and auto insurance carried by Tenant pursuant to this Lease, and any additional liability insurance carried by Tenant pursuant to Section 8.3 of this Lease, shall name Landlord, Landlord's managing agent, and such other Persons as Landlord may reasonably request from time to time as additional insureds with respect to liability arising out of or related to this Lease or the operations of Tenant (collectively "Additional Insureds"). Such insurance shall provide primary coverage without contribution from any other insurance carried by or for the benefit of Landlord, Landlord's managing agent, or other Additional Insureds. Such insurance shall also waive any right of subrogation against each Additional Insured.

8.8 Certificates of Insurance

On or before the earlier of (i) the date on which any Tenant Party first enters the Premises for any reason or (ii) the Commencement Date, Tenant shall furnish Landlord with

certificates evidencing the insurance coverage required by this Lease, and renewal certificates shall be furnished to Landlord at least annually thereafter, and at least fifteen (15) days prior to the expiration date of each policy for which a certificate was furnished (acceptable forms of such certificates for liability and property insurance, respectively, are attached as Exhibit I). Failure by the Tenant to provide the certificates or letters required by this Section 8.8 shall not be deemed to be a waiver of the requirements in this Section 8.8. Upon request by Landlord at reasonable intervals, a true and complete copy of any insurance policy required by this Lease shall be delivered to Landlord within ten (10) days following Landlord's request.

8.9 Subtenants and Other Occupants

Tenant shall require its subtenants and other occupants of the Premises to provide written documentation evidencing the obligation of such subtenant or other occupant to indemnify the Landlord Parties to the same extent that Tenant is required to indemnify the Landlord Parties pursuant to Section 8.1 above, and to maintain insurance that meets the requirements of this Article, and otherwise to comply with the requirements of this Article. Tenant shall require all such subtenants and occupants to supply certificates of insurance evidencing that the insurance requirements of this Article have been met and shall forward such certificates to Landlord on or before the earlier of (i) the date on which the subtenant or other occupant or any of their respective direct or indirect partners, officers, shareholders, directors, members, trustees, beneficiaries, servants, employees, principals, contractors, licensees, agents, invitees or representatives first enters the Premises or (ii) the commencement of the sublease. Tenant shall be responsible for identifying and remedying any deficiencies in such certificates or policy provisions.

8.10 No Violation of Building Policies

Tenant shall not commit or permit any violation of the policies of fire, boiler, sprinkler, water damage or other insurance covering the Complex and/or the fixtures, equipment and property therein carried by Landlord, or do or permit anything to be done, or keep or permit anything to be kept, in the Premises, which in case of any of the foregoing (i) would result in termination of any such policies, (ii) would adversely affect Landlord's right of recovery under any of such policies, or (iii) would result in reputable and independent insurance companies refusing to insure the Complex or the property of Landlord in amounts reasonably satisfactory to Landlord.

8.11 Tenant to Pay Premium Increases

If, because of anything done, caused or permitted to be done, or omitted by Tenant (or its subtenant or other occupants of the Premises), the rates for liability, fire, boiler, sprinkler, water damage or other insurance on the Complex and equipment of Landlord or any other tenant or subtenant in the Building shall be higher than they otherwise would be, Tenant shall reimburse Landlord and/or the other tenants and subtenants in the Building for the additional insurance premiums thereafter paid by Landlord or by any of the other tenants and subtenants in the Building which shall have been charged because of the aforesaid reasons, such reimbursement to be made from time to time on Landlord's demand.

8.12 Landlord's Insurance

(a) Required insurance. Landlord shall maintain (i) insurance against loss or damage with respect to the Building on an "all risk" type insurance form, with customary exceptions, subject to such commercially reasonable deductibles as Landlord may determine, in an amount equal to at least the full insurable replacement value of the Building from time to time; (ii) insurance with respect to any improvements, alterations, and fixtures of Tenant located at the Premises to the extent paid for by Landlord; (iii) commercial general liability insurance with respect to the Building in an amount not less than Five Million ($5,000,000.00) per occurrence, with deductibles as determined by Landlord; and (iv) insurance covering loss of rents in the amounts payable under this Lease. The cost of such insurance shall be treated as a part of Operating Expenses. Such insurance shall be maintained with a reputable and licensed insurance company or companies selected by Landlord. Payment for losses thereunder shall be made solely to Landlord and used for the purposes intended.

(b) Optional insurance. Landlord may maintain such additional insurance with respect to the Building and the Complex, including, without limitation, earthquake insurance, terrorism insurance, flood insurance, and/o· rent insurance, as may from time to time be reasonable and customary for similar office buildings in the Boston west suburban market. Landlord may also maintain such other insurance as may from time to time be required by the holder of any mortgage for the Property. Such

insurance shall be maintained with an insurance company or companies selected by Landlord. Payment for losses thereunder shall be made solely to Landlord. The cost of all such additional insurance shall also be part of the Operating Expenses.

(c) Blanket and self-insurance. Any or all of Landlord's insurance may be provided by blanket coverage maintained by Landlord or any affiliate of Landlord under its insurance program for its portfolio of properties, or by Landlord or any affiliate of Landlord under a program of self-insurance, and in such event Landlord's Operating Expenses shall include the portion of the reasonable cost of blanket insurance or self-insurance that is allocated to the Building.

(d) No obligation. Landlord shall not be obligated to insure, and shall not assume any liability of risk of loss for, Tenant's Property, including any such property or work of Tenant's subtenants or occupants. Landlord will also have no obligation to carry insurance against, nor be responsible for, any loss suffered by Tenant, subtenants or other occupants due to interruption of Tenant's or any subtenant's or occupant's business.

8.13 Waiver of Subrogation

The parties hereto waive and release any and all rights of recovery against the other, and agree not to seek to recover from the other or to make any claim against the other, and in the case of Landlord, against all "Tenant Parties" (hereinafter defined), and in the case of Tenant, against all "Landlord Parties" (hereinafter defined), for any loss or damage incurred or suffered by the waiving/releasing party to the extent such loss or damage is

insured under any insurance policy required by this Lease or which would have been so insured had the party carried the insurance it was required to carry hereunder, Tenant shall obtain from its subtenants and other occupants of the Premises a similar waiver and release of claims against any or all of Tenant or Landlord. In addition, the parties hereto (and in the case of Tenant, its subtenants and other occupants of the Premises) shall procure an appropriate clause in, or endorsement on, any insurance policy required by this Lease pursuant to which the insurance company waives subrogation. The insurance policies required by this Lease shall contain no provision that would invalidate or restrict the parties' waiver and release of the rights of recovery in this section. The parties hereto covenant that no insurer shall hold any right of subrogation against the parties hereto by virtue of such insurance policy.

The term "Landlord Party" or "Landlord Parties" shall mean Landlord, any affiliate of Landlord, Landlord's managing agents for the Building, each mortgagee (if any), each ground lessor (if any), and each of their respective direct or indirect partners, officers, shareholders, directors, members, trustees, beneficiaries, servants, employees, principals, contractors, licensees, agents or representatives, For the purposes of this Lease, the term "Tenant Party" or "Tenant Parties" shall mean Tenant, any affiliate of Tenant, any permitted subtenant or any other permitted occupant of the Premises, and each of their respective direct or indirect partners, officers, shareholders, directors, members, trustees, beneficiaries, servants, employees, principals, contractors, licensees, agents, invitees or representatives.

8.14 Tenant's Work

During such times as Tenant is performing work or having work or services performed in or to the Premises, Tenant shall require its contractors, and their subcontractors of all tiers, to obtain and maintain commercial general liability, automobile, workers compensation, employer's liability, builder's risk, and equipment/property insurance in such amounts and on such terms as are customarily required of such contractors and subcontractors on similar projects. The amounts and terms of all such insurance are subject to Landlord's written approval, which approval shall not be unreasonably withheld. The commercial general liability and auto insurance carried by Tenant's contractors and their subcontractors of all tiers pursuant to this section shall name Landlord, Landlord's managing agent, and such other persons as Landlord may reasonably request from time to time as additional insureds with respect to liability arising out of or related to their work or services (collectively "Additional Insureds"). Such insurance shall provide primary coverage without contribution from any other insurance carried by or for the benefit of Landlord, Landlord's managing agent, or other Additional Insureds. Such insurance shall also waive any right of subrogation against each Additional Insured. Tenant shall obtain and submit to Landlord, prior to the earlier of (i) the entry onto the Premises by such contractors or subcontractors or (ii) commencement of the work or services, certificates of insurance evidencing compliance with the requirements of this section.

ARTICLE IX

Miscellaneous Provisions

9.1 Waiver

Failure on the part of Landlord or Tenant to complain of any action or non-action on the part of the other, no matter how long the same may continue, shall never be a waiver by Tenant or Landlord, respectively, of any of its rights hereunder. Further, no waiver at any time of any of the provisions hereof by Landlord or Tenant shall be construed as a waiver of any of the other provisions hereof, and a waiver at any time of any of the provisions hereof shall not be construed as a waiver at any subsequent time of the same provisions. The consent or approval of Landlord or Tenant to or of any action by the other requiring such consent or approval shall not be construed to waive or render unnecessary Landlord's or Tenant's consent or approval to or of subsequent similar act by the other.

No payment by Tenant, or acceptance by Landlord, of a lesser amount than shall be due from Tenant to Landlord shall be treated otherwise than as a payment on account. The acceptance by Landlord of a check for a lesser amount with an endorsement or statement thereon, or upon any letter accompanying such check, that such lesser amount is payment in full, shall be given no effect, and Landlord may accept such check without prejudice to any other rights or remedies which Landlord may have against Tenant.

9.2 Cumulative Remedies

Except as expressly provided in this Lease, the specific remedies to which Landlord may resort under the terms of this Lease are cumulative and are not intended to be exclusive of any other remedies or means of redress to which such party may be lawfully entitled in case of any breach or threatened breach by Tenant of any provisions of this Lease. In addition to the other remedies provided in this Lease, Landlord shall be entitled to the restraint by injunction of the violation or attempted or threatened violation of any of the covenants, conditions or provisions of this Lease or to a decree compelling specific performance of any such covenants, conditions or provisions.

9.3 Quiet Enjoyment

This Lease is subject and subordinate to all matters of record, which Landlord represents as of the date hereof do not interfere with the use of the Premises for the Permitted Use. Tenant, subject to the terms and provisions of this Lease on payment of the rent and observing, keeping and performing all of the terms and provisions of this Lease on Tenant's part to be observed (within any applicable notice and cure periods), kept and performed, shall lawfully, peaceably and quietly have, hold, occupy and enjoy the Premises during the Term (exclusive of any period during which Tenant is holding over after the termination or expiration of this Lease without the consent of Landlord), without hindrance or ejection by any persons lawfully claiming under Landlord to have title to the Premises superior to Tenant; the foregoing covenant of quiet enjoyment is in lieu of any other covenant, express or implied; and it is understood and agreed that this covenant and

any and all other covenants of Landlord contained in this Lease shall be binding upon Landlord and Landlord's successors, including ground or master lessees, only with respect to breaches occurring during Landlord's or Landlord's successors' respective ownership of Landlord's interest hereunder, as the case may be.

Further, Tenant specifically agrees to look solely to Landlord's then equity interest in the Building (together with the rents, profits, issues, and proceeds therefrom) at the time owned, or in which Landlord holds an interest as ground lessee, for recovery of any judgment from Landlord; it being specifically agreed that neither Landlord (original or successor), nor any partner in or of Landlord, nor any beneficiary of any trust of which any person holding Landlord's interest is trustee, nor any member, manager, partner, director or stockholder, nor Landlord's managing agent, shall ever be personally liable for any such judgment, or for the payment of any monetary obligation to Tenant. The provision contained in the foregoing sentence is not intended to, and shall not, limit any right that Tenant might otherwise have to obtain injunctive relief against Landlord or Landlord's successors in interest, or any action not involving the personal liability of Landlord (original or successor), any partner in or of Landlord, any successor trustee to the persons named herein as Landlord, or any beneficiary of any trust of which any person holding Landlord's interest is trustee, or of any manager, member, partner, director or stockholder of Landlord or of Landlord's managing agent to respond in monetary damages from Landlord's assets other than Landlord's equity interest aforesaid in the Building, but (subject to abatement rights specifically provided for in this Lease) in no event shall Tenant have the right to terminate or cancel this Lease or to withhold rent or to set-off any claim or damages against rent as a result of any default by Landlord or breach by Landlord of its covenants or any warranties or promises hereunder, except in the case of a wrongful eviction of Tenant from the demised premises (constructive or actual) by Landlord continuing after notice to Landlord thereof and a reasonable opportunity for Landlord to cure the same. In the event that Landlord shall be determined to have acted unreasonably in withholding any consent or approval under this Lease, the sole recourse and remedy of the Tenant in respect thereof shall be to specifically enforce Landlord's obligation to grant such consent or approval, and in no event shall the Landlord be responsible for any damages of whatever nature in respect of its failure to give such consent or approval nor shall the same otherwise affect the obligations of the Tenant under this Lease or act as any termination of this Lease. In no event shall Landlord or Tenant ever be liable to the other party for any indirect or consequential damages suffered from whatever cause; provided that the foregoing shall not limit or alter any procedural right or remedy of Landlord under this Lease nor shall the same apply to the obligations of Tenant with respect to any hold over by Tenant after the expiration or earlier termination of this Lease.

9.4 Notice to Mortgagee and Ground Lessor

After receiving notice from any person, firm or other entity that it holds a mortgage which includes the Premises as part of the mortgaged premises, or that it is the ground lessor under a lease with Landlord, as ground lessee, which includes the Premises as a part of the demised premises, no notice from Tenant to Landlord shall be effective unless and until a copy of the same is given to such holder or ground lessor, and the curing of

any of Landlord's defaults by such holder or ground lessor within the time period provided for in this Lease (including a reasonable time to obtain possession of the premises if the mortgagee or ground lessor elects to do so) shall be treated as performance by Landlord. For the purposes of this Section 9.4 or Section 9.14, the term "mortgage" includes a mortgage on a leasehold interest of Landlord (but not one on Tenant's leasehold interest).

9.5 Assignment of Rents

With reference to any assignment by Landlord or Landlord's interest in this Lease, or the rents payable hereunder, conditional in nature or otherwise, which assignment is made to the holder of a mortgage or ground lease on property which includes the Premises, Tenant agrees:

(a) That the execution thereof by Landlord, and the acceptance thereof by the holder of such mortgage or the ground lessor, shall never be treated as an assumption by such holder or ground lessor of any of the obligations of Landlord hereunder, unless such holder, or ground lessor, shall, by notice sent to Tenant, specifically otherwise elect; and

(b) That, except as aforesaid, such holder or ground lessor shall be treated as having assumed Landlord's obligations hereunder only upon foreclosure of such holder's mortgage and the taking of possession of the Premises, or, in the case of a ground lessor, the assumption of Landlord's position hereunder by such ground lessor.

In no event shall the acquisition of title to the Building and the land on which the same is located by a purchaser which, simultaneously therewith, leases the entire Building or such land back to the seller thereof be treated as an assumption by such purchaser-lessor, by operation of law or otherwise, of Landlord's obligations hereunder, but Tenant shall look solely to such seller-lessee, and its successors from time to time in title, for performance of Landlord's obligations hereunder subject to the provisions of Section 8.4 hereof. In any such event, this Lease shall be subject and subordinate to the lease to such purchaser provided that such purchaser agrees to recognize the right of Tenant to use and occupy the Premises upon the payment of rent and other charges payable by Tenant under this Lease and the performance by Tenant of Tenant's obligations under this Lease and provided that Tenant agrees to attorn to such purchaser. For all purposes, such seller-lessee, and its successors in title, shall be the landlord hereunder unless and until Landlord's position shall have been assumed by such purchaser-lessor.

9.6 Surrender

No act or thing done by Landlord during the Lease Term shall be deemed an acceptance of a surrender of the Premises, and no agreement to accept such surrender shall be valid,

unless in writing signed by Landlord. No employee of Landlord or of Landlord's agents shall have any power to accept the keys of the Premises prior to the termination of this Lease. The delivery of keys to any employee of Landlord or of Landlord's agents shall not operate as a termination of the Lease or a surrender of the Premises.

9.7 Brokerage

(A) Tenant warrants and represents that Tenant has not dealt with any broker in connection with the consummation of this Lease other than the broker, person or firm, if any, designated in Section 1.1 hereof; and in the event any claim is made against the Landlord relative to dealings by Tenant with brokers other than the Brokers, if any, designated in Section 1.1 hereof, Tenant shall defend the claim against Landlord with counsel of Tenant's selection first approved by Landlord (which approval will not be unreasonably withheld) and save harmless and indemnify Landlord on account of loss, cost or damage which may arise by reason of such claim.

(B) Landlord warrants and represents that Landlord has not dealt with any broker in connection with the consummation of this Lease other than the broker, person or firm, if any, designated in Section 1.1 hereof; and in the event any claim is made against the Tenant relative to dealings by Landlord with brokers other than the Brokers, if any, designated in Section 1.1 hereof, Landlord shall defend the claim against Tenant with counsel of Landlord's selection and save harmless and indemnify Tenant on account of loss, cost or damage which may arise by reason of such claim. Landlord agrees that it shall be solely responsible for the payment of brokerage commissions to the Broker for the Original Term of this Lease, if any, designated in Section 1.1 hereof.

9.8 Invalidity of Particular Provisions

If any term or provision of this Lease, or the application thereof to any person or circumstance shall, to any extent, be invalid or unenforceable, the remainder of this Lease, or the application of such term or provision to persons or circumstances other than those as to which it is held invalid or unenforceable, shall not be affected thereby, and each term and provision of this Lease shall be valid and be enforced to the fullest extent permitted by law.

9.9 Provisions Binding, etc

The obligations of this Lease shall run with the land, and except as herein otherwise provided, the terms hereof shall be binding upon and shall inure to the benefit of the successors and assigns, respectively, of Landlord and Tenant and, if Tenant shall be an individual, upon and to his heirs, executors, administrators, successors and assigns. Each term and each provision of this Lease to be performed by Tenant shall be construed to be both a covenant and a condition. The reference contained to successors and assigns of Tenant is not intended to constitute a consent to subletting or assignment by Tenant.

9.10 Recording; Confidentiality

Tenant agrees not to record the within Lease, but each party hereto agrees, on the request of the other, to execute a so-called Notice of Lease or short form lease in form recordable and complying with applicable law and reasonably satisfactory to both Landlord's and Tenant's attorneys. In no event shall such document set forth rent or other charges payable by Tenant under this Lease; and any such document shall expressly state that it is executed pursuant to the provisions contained in this Lease, and is not intended to vary the terms and conditions of this Lease.

Tenant agrees that this Lease and the terms contained herein will be treated as strictly confidential and except as required by law Tenant shall not disclose the same to any third party except for Tenant's existing and potential partners, lenders and their respective, accountants, consultants, advisors and attorneys who have been advised of the confidentiality provisions contained herein and agree to be bound by the same. In the event Tenant is required by law to provide this Lease or disclose any of the economic or other material terms, Tenant shall give Landlord prompt notice of such requirement prior to making disclosure so that Landlord may seek an appropriate protective order. If failing the entry of a protective order Tenant is compelled to make disclosure, Tenant shall only disclose portions of the Lease which Tenant is required to disclose and will exercise reasonable efforts to obtain assurance that confidential treatment will be accorded to the information so disclosed. Notwithstanding the foregoing, the provisions of this paragraph shall not be construed so as to prevent Tenant from (x) disclosing the fact that Tenant has a lease with Landlord or (y) including the rent and other amounts payable under this Lease as part of any consolidated reporting of Tenant's financial liabilities, so long as the economic terms of this Lease are not specifically identified with or attributed to this Lease, Landlord or any of Landlord's affiliates.

9.11 Notices

Whenever, by the terms of this Lease, notice shall or may be given either to Landlord or to Tenant, such notice shall be in writing and shall be sent by overnight commercial courier or by registered or certified mail postage or delivery charges prepaid, as the case may be:

If intended for Landlord, addressed to Landlord at the address set forth in Article of this Lease (or to such other address or addresses as may from time to time hereafter be designated by Landlord by like notice) with a copy to Landlord, Attention: General Counsel.

If intended for Tenant, addressed to Tenant at the address set forth in Article I of this Lease except that from and after the Commencement Date the address of Tenant shall be the Premises (or to such other address or addresses as may from time to time hereafter be designated by Tenant by like notice). Copies of any notices to Tenant (other than routine notices of an operational nature) shall simultaneously be sent to Stephen T. Langer, Esq., Langer & McLaughlin, LLP, 855 Boylston Street, 6th Floor, Boston, Massachusetts 02116.

Except as otherwise provided herein, all such notices shall be effective when received; provided, that (i) if receipt is refused, notice shall be effective upon the first occasion that such receipt is refused, (ii) if the notice is unable to be delivered due to a change of address of which no notice was given, notice shall be effective upon the date such delivery was attempted, (iii) if the notice address is a post office box number, notice shall be effective the day after such notice is sent as provided hereinabove or (iv) if the notice is to a foreign address, notice shall be effective two (2) days after such notice is sent as provided hereinabove.

Where provision is made for the attention of an individual or department, the notice shall be effective only if the wrapper in which such notice is sent is addressed to the attention of such individual or department.

Any notice given by an attorney on behalf of Landlord or by Landlord's managing agent shall be considered as given by Landlord and shall be fully effective.

Time is of the essence with respect to any and all notices and periods for giving notice or taking any action thereto under this Lease.

9.12 When Lease Becomes Binding and Authority

Employees or agents of Landlord have no authority to make or agree to make a lease or any other agreement or undertaking in connection herewith. The submission of this document for examination and negotiation does not constitute an offer to lease, or a reservation of, or option for, the Premises, and this document shall become effective and binding only upon the execution and delivery hereof by both Landlord and Tenant. All negotiations, considerations, representations and understandings between Landlord and Tenant are incorporated herein and may be modified or altered only by written agreement between Landlord and Tenant, and no act or omission of any employee or agent of Landlord shall alter, change or modify any of the provisions hereof. Landlord and Tenant hereby represents and warrants to the other that all necessary action has been taken to enter this Lease and that the person signing this Lease on behalf of Landlord and Tenant has been duly authorized to do so.

9.13 Section Headings

The titles of the Articles throughout this Lease are for convenience and reference only, and the words contained therein shall in no way be held to explain, modify, amplify or aid in the interpretation, construction or meaning of the provisions of this Lease.

9.14 Rights of Mortgagee

This Lease shall be subject and subordinate to the lien of any mortgage now or hereafter on the Site or the Building, or both, and to each advance made or hereafter to be made under any mortgage, and to all renewals, modifications, consolidations, replacements and extensions thereof and all substitutions therefor provided that the holder of such mortgage

agrees to recognize the rights of Tenant under this Lease (including the right to use and occupy the Premises) upon the payment of rent and other charges payable by Tenant under this Lease and the performance by Tenant of Tenant's obligations hereunder. In confirmation of such subordination and recognition, Tenant shall execute and deliver promptly such commercially reasonable instruments of subordination and recognition as such mortgagee may reasonably request subject to receipt of such instruments of recognition from such mortgagee as Tenant may reasonably request (Tenant hereby agreeing to pay any legal or other fees charged by the mortgagee in connection with providing the same). In the event that any mortgagee or its respective successor in title shall succeed to the interest of Landlord, then, this Lease shall nevertheless continue in full force and effect and Tenant shall and does hereby agree to attorn to such mortgagee or successor and to recognize such mortgagee or successor as its landlord. If any holder of a mortgage which includes the Premises, executed and recorded prior to the date of this Lease, shall so elect, this Lease and the rights of Tenant hereunder, shall be superior in right to the rights of such holder, with the same force and effect as if this Lease had been executed, delivered and recorded, or a statutory notice hereof recorded, prior to the execution, delivery and recording of any such mortgage. The election of any such holder shall become effective upon either notice from such holder to Tenant in the same fashion as notices from Landlord to Tenant are to be given hereunder or by the recording in the appropriate registry or recorder's office of an instrument in which such holder subordinates its rights under such mortgage to this Lease.

If in connection with obtaining financing a bank, insurance company, pension trust or other institutional lender shall request reasonable modifications in this Lease as a condition to such financing, Tenant will not unreasonably withhold, delay or condition its consent thereto, provided that such modifications do not increase the monetary obligations of Tenant hereunder or materially adversely affect the leasehold interest hereby created.

9.15 Status Reports and Financial Statements

Recognizing that Landlord and Tenant may find it necessary to establish to third parties, such as accountants, banks, potential or existing mortgagees, potential purchasers or the like, the then current status of performance hereunder, each party, on the request of the other made from time to time (but not more often than once annually), will promptly furnish to the other, or any existing or potential holder of any mortgage encumbering the Premises, the Building, the Site and/or the Complex or any potential purchaser of the Premises, the Building, the Site and/or the Complex, (each an "Interested Party"), a statement of the status of any matter pertaining to this Lease, including, without limitation, acknowledgments that (or the extent to which) each party is in compliance with its obligations under the terms of this Lease. In addition, Tenant shall deliver to Landlord, or any Interested Party designated by Landlord, financial statements of Tenant and any guarantor of Tenant's obligations under this Lease, as reasonably requested by Landlord (but not more often than once annually), including, but not limited to financial statements for the past three (3) years. Landlord shall keep any non-public information provided by Tenant pursuant to this Section 9.15 confidential, and shall not disclose the same other than (i) to Landlord's officers, employees and consultants (or to any of the

Interested Parties) or (ii) to the extent required by applicable law or by any administrative, governmental or judicial proceeding. Any such status statement or financial statement delivered by Landlord or Tenant pursuant to this Section 9,15 may be relied upon by any Interested Party.

9.16 Self-Help

If an Event of Default of Tenant shall exist, Landlord shall have the right, but shall not be obligated, to enter upon the Premises and to perform such obligation notwithstanding the fact that no specific provision for such substituted performance by Landlord is made in this Lease with respect to such default. In performing such obligation, Landlord may make any payment of money or perform any other act. All sums so paid by Landlord (together with interest at the rate of one and one-half percentage points over the then prevailing prime rate in Boston as set by Bank of America, N.A. or its successor (but in no event greater than the maximum rate permitted by applicable law) and all costs and expenses in connection with the performance of any such act by Landlord, shall be deemed to be Additional Rent under this Lease and shall be payable to Landlord immediately on demand, Landlord may exercise the foregoing rights without waiving any other of its rights or releasing Tenant from any of its obligations under this Lease.

9.17 Holding Over

Any holding over by Tenant after the expiration of the term of this Lease shall be treated as a tenancy at sufferance and shall be on the terms and conditions as set forth in this Lease, as far as applicable except that Tenant shall pay as a use and occupancy charge an amount equal to the greater of (x) for the first thirty days in which the Tenant holds over an amount equal to one hundred and fifty (150%) of the Annual Fixed Rent and Additional Rent calculated (on a daily basis) at the highest rate payable under the terms of this Lease and after the first thirty days in which the Tenant holds over and thereafter an amount equal to two hundred percent (200%) of the Annual Fixed Rent and Additional Rent calculated (on a daily basis) at the highest rate payable under the terms of this Lease, or (y) the fair market rental value of the Premises, in each case for the period measured from the day on which Tenant's hold-over commences and terminating on the day on which Tenant vacates the Premises. In addition, Tenant shall save Landlord, its agents and employees harmless and will exonerate, defend and indemnify Landlord, its agents and employees from and against any and all damages which Landlord may suffer on account of Tenant's hold-over in the Premises after the expiration or prior termination of the term of this Lease. Nothing in the foregoing nor any other term or provision of this Lease shall be deemed to permit Tenant to retain possession of the Premises or hold over in the Premises after the expiration or earlier termination of the Lease Term. All property which remains in the Building or the Premises after the expiration or termination of this Lease shall be conclusively deemed to be abandoned and may either be retained by Landlord as its property or sold or otherwise disposed of in such manner as Landlord may see fit. If any part thereof shall be sold, then Landlord may receive the proceeds of such sale and apply the same, at its option against the expenses of the sale, the cost of moving and storage, any arrears of rent or other charges payable hereunder by Tenant to Landlord and any damages to which Landlord may be entitled under this Lease and at law and in

equity.

9.18 Security Deposit

Concurrently with the execution of this Lease, Tenant shall pay to Landlord a security deposit in the amount of Thirty Eight Thousand Three Hundred Eight and 25/100 ($38,308.25) and Landlord shall hold the same, throughout the Term of this Lease (including the Extended Term, if applicable), unless sooner returned to Tenant as provided in this Section 9.18, as security for the performance by Tenant of all obligations on the part of Tenant to be performed under this Lease. Such deposit shall be in the form of an irrevocable, unconditional, negotiable letter of credit (the "Letter of Credit"). The Letter of Credit shall (i) be issued by and drawn on a bank reasonably approved by Landlord and at a minimum having a long term issuer credit rating from Standard and Poor's Professional Rating Service of A or a comparable rating from Moody's Professional Rating Service, (ii) be substantially in the form attached hereto as Exhibit H, (iii) permit one or more draws thereunder to be made accompanied only by certification by Landlord or Landlord's managing agent that pursuant to the terms of this Lease, Landlord is entitled to draw upon such Letter of Credit, (iv) permit transfers at any time without charge, (v) permit presentment in Boston, Massachusetts and (vi) provide that any notices to Landlord be sent to the notice address provided for Landlord in this Lease. If the credit rating for the issuer of such Letter of Credit falls below the standard set forth in (i) above or if the financial condition of such issuer changes in any other material adverse way, Landlord shall have the right to require that Tenant provide a substitute letter of credit that complies in all respects with the requirements of this Section, and Tenant's failure to provide the same within thirty (30) days following Landlord's written demand therefor shall entitle Landlord to immediately draw upon the Letter of Credit. Any such Letter of Credit shall be for a term of two (2) years (or for one (1) year if the issuer thereof regularly and customarily only issues letters of credit for a maximum term of one (1) year) and shall in either case provide for automatic renewals through the date which is sixty (60) days subsequent to the scheduled expiration of this Lease (as the same may be extended) or if the issuer will not grant automatic renewals, the Letter of Credit shall be renewed by Tenant each year and each such renewal shall be delivered to and received by Landlord not later than thirty (30) days before the expiration of the then current Letter of Credit (herein called a "Renewal Presentation Date"). In the event of a failure to so deliver any such renewal Letter of Credit on or before the applicable Renewal

Presentation Date, Landlord shall be entitled to present the then existing Letter of Credit for payment and to receive the proceeds thereof, which proceeds shall be held as Tenant's security deposit, subject to the terms of this Section 9.18. Any failure or refusal of the issuer to honor the Letter of Credit shall be at Tenant's sole risk and shall not relieve Tenant of its obligations hereunder with regard to the security deposit. Upon the occurrence and during the existence of any Event of Default, Landlord shall have the right from time to time without prejudice to any other remedy Landlord may have on account thereof, to draw on all or any portion of such deposit held as a Letter of Credit and to apply the proceeds of such Letter of Credit or any cash held as such deposit, or any part thereof, to Landlord's damages arising from such Event of Default on the part of Tenant under the terms of this Lease. If Landlord so applies all or any portion of such deposit, Tenant shall within ten (10) days after notice from Landlord deposit cash with

Landlord in an amount sufficient to restore such deposit to the full amount stated in this Section 9.18. While Landlord holds any cash deposit Landlord shall have no obligation to pay interest on the same and shall have the right to commingle the same with Landlord's other funds. Neither the holder of a mortgage nor the Landlord in a ground lease on property which includes the Premises shall ever be responsible to Tenant for the return or application of any such deposit, whether or not it succeeds to the position of Landlord hereunder, unless such deposit shall have been received in hand by such holder or ground Landlord.

Landlord shall return the deposit to Tenant, or so much thereof as shall not have theretofore been applied in accordance with the terms of this Section 9.18 or applied to any remaining obligations of Tenant under this Lease of which Tenant has been notified, within sixty (60) days subsequent to the expiration or earlier termination of the term of this Lease (as the same may have been extended) and surrender possession of the Premises by Tenant to Landlord in the condition required in the Lease at such time.

9.19 Late Payment

If Landlord shall not have received any payment or installment of Annual Fixed Rent or Additional Rent (the "Outstanding Amount") on or before the date on which the same first becomes payable under this Lease (the "Due Date"), the amount of such payment or installment shall incur a late charge equal to the sum of: (a) five percent (5%) of the Outstanding Amount for administration and bookkeeping costs associated with the late payment and (b) interest on the Outstanding Amount from the Due Date through and including the date such payment or installment is received by Landlord, at a rate equal to the lesser of (i) the rate announced by Bank of America, N.A. (or its successor) from time to time as its prime or base rate (or if such rate is no longer available, a comparable rate reasonably selected by Landlord), plus two percent (2%), or (ii) the maximum applicable legal rate, if any. Such interest shall be deemed Additional Rent and shall be paid by Tenant to Landlord upon demand.

9.20 Tenant's Payments

Each and every payment and expenditure, other than Annual Fixed Rent, shall be deemed to be Additional Rent or additional rent hereunder, whether or not the provisions requiring payment of such amounts specifically so state, and shall be payable, unless otherwise provided in this Lease, within thirty (30) days after written demand by Landlord, and in the case of the non-payment of any such amount, Landlord shall have, in addition to all of its other rights and remedies, all the rights and remedies available to Landlord hereunder or by law in the case of non-payment of Annual Fixed Rent. Unless expressly otherwise provided in this Lease, the performance and observance by Tenant of all the terms, covenants and conditions of this Lease to be performed and observed by Tenant shall be at Tenant's sole cost and expense. In the event that Tenant shall seek Landlord's consent or approval under this Lease, then Tenant shall reimburse Landlord, upon demand, as Additional Rent, for all reasonable costs and expenses, including legal and architectural costs and expenses, incurred by Landlord in processing such request, whether or not such consent or approval shall be given.

9.21 Waiver of Trial by Jury

Landlord and Tenant hereby waive any right to trial by jury in any action, proceeding or counterclaim brought by either Landlord or Tenant on any matters whatsoever arising out of or any way connected with this Lease, the relationship of the Landlord and the Tenant, the Tenant's use or occupancy of the Premises and/or any claim of injury or damage, including but not limited to, any summary process eviction action.

9.22 Governing Law

This Lease shall be governed exclusively by the provisions hereof and by the law of the Commonwealth of Massachusetts, as the same may from time to time exist.

9.23 Tenant's Force Majeure

Except for Tenant's obligations to make payments, maintain insurance, give notices or maintain harmonious labor relations as set forth in this Lease, if Tenant is delayed in performing its obligations hereunder, by reason of delay or stoppage due to governmental regulation, strikes, lockouts, acts of God, acts of war, terrorist acts, civil commotions, unusual scarcity of or inability to obtain labor or materials, labor difficulties, casualty or other causes beyond the reasonable control of Tenant, the time for Tenant's performance shall be extended for the period of any such delay.

(PAGE ENDS HERE)

EXECUTED as a sealed instrument in two or more counterparts, each of which shall be deemed to be an original.

LANDLORD:

BOSTON PROPERTIES LIMITED PARTNERSHIP,
a Delaware limited partnership

By: BOSTON PROPERTIES, INC.,
its general partner

By: /s/ David C. Provost
Name: David C. Provost
Title: Senior Vice President
Boston Properties

TENANT:

PROTEON THERAPEUTICS, INC.

By: /s/ Timothy P. Noyes
Name: Timothy P. Noyes
Title: President and CEO
Hereto duly authorized

WITNESS:

By: /s/ Steven Burke
Name: Steven Burke
Title: CMO

By: /s/ Mark J. Fitzpatrick
Name: Mark J. Fitzpatrick
Title: Vice President and CFO
Hereto duly authorized

EXHIBIT A

DESCRIPTION OF SITE

A certain parcel of land of West Street, Waltham, Middlesex County, as shown on a plan entitled "Atwater Lane, A Subdivision in Waltham, MA, Middlesex County, Lot Layout Plan," dated July 22, 1988, recorded with Middlesex South Registry of Deeds as Plan #6 of 1989 in Book 19575, Page 351, and shown thereon as Lot A, containing 142,769± square feet, according to said plan, and Lot B, containing 501,550± square feet, according to said plan, and the parcel of land shown on said plan as Atwater Lane.

Said Lots A and B consist of the following:

PARCEL I:

A certain parcel of land situate on First Avenue and West Street, Waltham, Middlesex County, Massachusetts, and shown as Lots 13 and 14 on Plan entitled "Plan of Land in Waltham, Mass.," dated August 31, 1962, revised October 26, 1962 and October 30, 1962, by Raymond C. Pressey, Inc., Registered Land Surveyors, recorded as Plan No. 10 of 1963 in Book 10196, Page 40, bounded and described as follows:

NORTHEASTERLY	by the End of First Avenue by two lines measuring respectively forty-seven and 50/100 feet and seven and 53/100 feet;
NORTHWESTERLY	by other land of the Grantors herein three hundred eighty-seven and 17/100 feet;
WESTERLY	by land now or formerly of United Electric Controls Company by two lines measuring respectively one hundred seventy and 51/100 feet and five hundred and twenty-one and 92/100 feet;
NORTHEASTERLY	by the same by a curved line measuring seventy-six and 05/100 feet;
NORTHEASTERLY	by the same by two lines measuring respectively one hundred forty-one and 17/100 feet and one hundred seventy feet;
WESTERLY	by West Street by two lines measuring respectively forty-five and 26/100 feet and eleven and 16/100 feet;

SOUTHWESTERLY	by the line between Weston and Waltham and land believed to be now or formerly of Ralph P. Hussey three hundred twenty-eight and 28/100 feet;
SOUTHERLY	by land of owners unknown one hundred four and 77/100 feet;
WESTERLY	by the same forty-eight and 80/100 feet;
SOUTHWESTERLY	by said line between Weston and Waltham, and land believed to be now or formerly of said Hussey one hundred eighty-one and 61/100 feet;
SOUTHERLY	by land believed to be now of formerly of Frederick C. Dumaine Jr. and another one hundred seventeen and 30/100 feet;
NORTHWESTERLY	by the same forty-four and 80/100 feet;
SOUTHWESTERLY	by said line between Weston and Waltham and other land of the Grantors herein one hundred fifty four feet;
SOUTHEASTERLY and EASTERLY	by other land of the Grantors herein by two lines measuring respectively four hundred ten and 53/100 feet and seventy-three feet;
NORTHERLY	by land now or formerly of David Burstein et al., Trustees, one hundred sixteen and 14/100 feet;
SOUTHEASTERLY	by the same two hundred ninety-one and 99/100 feet;
NORTHEASTERLY	by the same three hundred fifty-five and 99/100 feet;
SOUTHEASTERLY	by the same five hundred forty-eight and 31/100 feet.

Containing 397,490 square feet of land, according to said plan.

PARCEL II:

The parcel of land on West Street, Waltham, Middlesex County, Massachusetts, shown as Lot E containing 2.37 acres on a plan by Raymond C. Pressey, Inc., Registered Land Surveyors, dated 1 October 1965 recorded as Plan No. 1339 of 1965 in Book 10961, Page 438, and bounded and described according to said plan as follows:

WESTERLY	in a curved line by West Street two hundred twenty-one and 05/100 (221.05) feet;
NORTHERLY	by land of Leland L. Crowell and of Clifford Griggs, two hundred four and 98/100 (204.98) feet, and by Lot "A" on Plan No. 1530 of 1960 (being the second parcel herein described) two hundred seventy-five and 40/100ths (275.40) feet;
EASTERLY	by Lot 13 on Plan 10 of 1963, Book 10196, Page 40, two hundred twenty-three (223) feet; and
SOUTHERLY	by Lot D, being remaining land of the Grantor, four hundred forty-eight and 35/100ths (448.35) feet.

Also, the parcel of land situated in Waltham, Middlesex County, Massachusetts, and shown as Lot A on plan entitled "Plan of Land in Waltham, Mass." dated June 29, 1960, by Raymond C. Pressey, Inc. recorded with said Deeds as Plan No. 1530 of 1960, Book 9693, Page 417, bounded and described as follows:

SOUTHERLY	by Lot B on said Plan, two hundred seventy-five and 40/100 feet;
WESTERLY	by land now or formerly, of Clifford Griggs, two hundred ten and no/100 feet;
NORTHERLY	by land of Trustees of Waltham Properties Trust two hundred fifty-two and no/100 feet; and
EASTERLY	by the same, one hundred seventy and 51/100 feet.

Containing 49,400 square feet of land, according to said plan.

PARCEL III:

The parcel of land on West Street, Waltham, Middlesex County, Massachusetts, shown as Lot D containing 3 acres on a plan by Raymond C. Pressey, Inc., Registered Land Surveyors, dated 1 October 1965, recorded in Middlesex South District Deeds in Book 10961, Page 438, and bounded and described according to said plan as follows:

WESTERLY	in a curved line by West Street, three hundred fifty-one and 70/100ths (351.70) feet;

NORTHERLY	by Lot E, being land owned now or formerly by Little, Brown and Company (Inc), four hundred forty eight and 35/100ths (448.35) feet;
EASTERLY	by Lot 13 on Plan 10 of 1963, Book 10196, Page 40, two hundred ninety-eight and 92/100ths (298.92) feet;
EASTERLY	by the same in a curved line, seventy-six and 5/100ths (76.05) feet;
SOUTHERLY	by Lot 14 on Plan 10 of 1963, Book 10196, Page 40, three hundred eleven and 17/100ths (311.17) feet.

TOGETHER WITH THE FOLLOWING APPURTENANT RIGHTS:

Right to use twenty-foot wide utility easement as recited in deed dated August 12, 1960, recorded in Book 9693, Page 417.

Right to use twenty-foot wide utility easement as recited in deed dated August 12, 1960, recorded in Book 9693, Page 420.

Easement reserved in Grant of Right and Easement for ten-foot wide water main dated September 8, 1980, recorded in Book 14118, Page 227.

Right to tie-in to water line as recited in Easement Agreement dated June 12, 1996, recorded in Book 26436, Page 15.

EXHIBIT B-1

WORK AGREEMENT

1.1 Substantial Completion

(A) Plans and Construction Process.

(1) *Landlord's Work*. Landlord shall perform the work shown on the plans (the "Plans") listed on Exhibit B-2 attached to the Lease ("Landlord's Work"); provided, however, that Landlord shall have no responsibility for the installation or connection of Tenant's computer, telephone, other communication equipment, systems or wiring. Any items of work requested by Tenant and not shown or referred to on the Plans shall be deemed to be Change Proposal(s) (as defined below) and shall be subject to the terms and provisions of subsection (2) below.

(2) *Charge Orders*. Tenant shall have the right, in accordance herewith, to submit for Landlord's approval change proposals with respect to items of work not shown on the Plans (each, a "Change Proposal"). Landlord agrees to respond to any such Change Proposal within such time as is reasonably necessary (taking into consideration the information contained in such Change Proposal) after the submission thereof by Tenant, advising Tenant of any anticipated increase in costs which costs shall include a construction management fee equal to 6% of the Change Proposal ("Change Order Costs") associated with such Change Proposal, as well as an estimate of any delay which would likely result in the completion of the Landlord's Work if a Change Proposal is made pursuant thereto ("Landlord's Change Order Response"). Tenant shall have the right to then approve or withdraw such Change Proposal within five (5) days after receipt of Landlord's Change Order Response. If Tenant fails to respond to Landlord's Change Order Response within such five (5) day period, such Change Proposal shall be deemed withdrawn. If Tenant approves Landlord's Change Order Response, then such Change Proposal shall be deemed a "Change Order" hereunder and if the Change Order is made, then the Change Order Costs associated with the Change Order shall be deemed additions to the Tenant Plan Excess Costs and shall be paid in the same manner as Tenant Plan Excess Costs are paid as set forth in Section 1.5 of this Work Agreement.

(3) *Tenant Response to Requests for Information and Approvals*. Except to the extent that another time period is expressly herein set forth, Tenant shall respond to any request from Landlord, Landlord's architect, Landlord's contractor and/or Landlord's Construction Representative for approvals or information in connection with Landlord's Work, within five, (5) business days of Tenant's receipt of such request. In addition, Tenant shall, within five (5) business days after receipt thereof from Landlord, execute and deliver to Landlord any affidavits and documentation required in order to obtain all permits and approvals necessary for Landlord to commence and complete Landlord's Work on a timely basis ("Permit Documentation").

(4) *Time of the Essence*. Time is of the essence in connection with Tenant's obligations under this Section 1.1.

(B) Substantial Completion; Tenant Delay.

(1) *Landlord's Obligations*. Subject to delays due to Tenant Delays (as hereinafter defined) and delays due to Force Majeure, as defined in Section 6.1 of the Lease, Landlord shall use reasonable speed and diligence to have the Landlord's Work substantially completed on or before the October 1, 2009, but Tenant shall have no claim against Landlord for failure so to complete construction of Landlord's Work in the Premises, except for the right to terminate the Lease, without further liability to either party, in accordance with the provisions hereinafter specified in Section 1.2 of this Work Agreement.

(2) *Definition of Substantial Completion*. The Premises shall be "Substantially Complete" and be deemed ready for Tenant's occupancy on the later of:

(a) The date on which Landlord's Work, together with common facilities for access and services to the Premises, has been completed (or would have been completed except for Tenant Delay) except for items of work and adjustment of equipment and fixtures which can be completed without causing substantial interference with Tenant's use of the Premises (i.e. so-called "punch list" items), or

(b) The date when a certificate of occupancy, has been approved for issuance by the City of Waltham for occupancy by Tenant of the Premises for the Permitted Use (to the extent necessary), unless the failure to obtain such approval is due solely to a Tenant Delay.

In the event of any dispute as to the date on which Landlord's Work has been completed, the reasonable determination of Landlord's architect as to such date shall be deemed conclusive and binding on both Landlord and Tenant.

(3) *Incomplete Work*. Landlord shall complete as soon as conditions practically permit any punch-list items of Landlord's Work, and Tenant shall cooperate with Landlord in providing access as may be required to complete such work in a normal manner.

(4) *Early Access by Tenant*. To the extent possible, Landlord shall permit Tenant access for installing Tenant's trade fixtures, cabling and wiring in portions of the Premises prior to substantial completion when it can be done without material interference with remaining work or with the maintenance of harmonious labor relations. Any such access by Tenant

shall be upon all of the terms and conditions of the Lease (other than the payment of Annual Fixed Rent) and shall be at Tenant's sole risk, and Landlord shall not be responsible for any injury to persons or damage to property resulting from such early access by Tenant unless caused by the gross negligence or willful misconduct of Landlord.

(5) *Prohibition on Access by Tenant Prior to Actual Substantial Completion*. If, prior to the date that the Premises are in fact actually substantially complete, the Premises are deemed to be substantially complete pursuant to the provisions of this Section 1.1 (i.e. and the Commencement Date has therefore occurred), Tenant shall not (except with Landlord's consent) be entitled to take possession of the Premises for the Permitted Use until the Premises are in fact actually substantially complete.

(C) Tenant Delay.

(1) A "*Tenant Delay*" shall be defined as the following:

(a) Tenant's failure timely to respond to any request from Landlord, Landlord's architect, Landlord's contractor and/or Landlord's Construction Representative or to timely provide all required Permit Documentation, if any, to Landlord within the applicable time periods set forth in this Work Agreement;

(b) Tenant's failure to pay the Tenant Plan Excess Costs in accordance with Section 1.5 hereinbelow;

(c) Any delay due to items of work for which there is long lead time in obtaining the materials therefor or which are specially or specifically manufactured, produced or milled for the work in or to the Premises and require additional time for receipt or installation (Landlord represents that there are no long lead items included in the work described on Exhibit B-2);

(d) Any delay due to changes, alterations or additions required or made by Tenant with respect to items not shown on the Plans including, without limitation, Change Orders; or

(e) Any other delays caused by Tenant, Tenant's contractors, architects, engineers, or anyone else engaged by Tenant in connection with the preparation of the Premises for Tenant's occupancy, including, without limitation, utility companies and other entities furnishing communications, data processing or other service, equipment, or furniture.

The Tenant Delays described above shall only be deemed a Tenant Delay if Landlord has first given Tenant notice (which notice may be verbal, written or given electronically by email) that a situation exists which constitutes a Tenant Delay, provided that, if notice has been given pursuant to another section of this Lease for such event or failure no further notice shall be required hereunder.

(2) *Tenant Obligations with Respect to Tenant Delays*.

(a) Tenant covenants that no Tenant Delay shall delay commencement of the Term or the obligation to pay Annual Fixed Rent or Additional Rent, regardless of the reason for such Tenant Delay or whether or not it is within the control of Tenant or any such employee. Landlord's Work shall be deemed substantially completed as of the date when Landlord's Work would have been substantially completed but for any Tenant Delays, as determined by Landlord in the exercise of its good faith business judgment.

(b) Tenant shall reimburse Landlord the amount, if any, by which the cost of Landlord's Work is actually increased as the result of any Tenant Delay.

(c) Any amounts due from Tenant to Landlord under this Section 1.1(C)(2) shall be due and payable within thirty (30) days of billing therefore (except that amounts due in connection with Change Orders shall be paid as provided in Section 1.5), and shall be considered to be Additional Rent. Nothing contained in this Section 1.1(C)(2) shall limit or qualify or prejudice any other covenants, agreements, terms, provisions and conditions contained in the Lease.

1.2 Outside Completion Date

If Landlord shall have failed substantially to complete Landlord's Work in the Premises described in the Plans on or before the Outside Completion Date as defined in Section 1.1 of the Lease (which date shall be extended automatically for such periods of time as Landlord is prevented from proceeding with or completing the same by reason of Landlord's Force Majeure as defined in Section 6.1 of the Lease or any Tenant Delay, Tenant shall have the right to terminate the Lease by giving notice to Landlord of Tenant's desire to do so before such completion and within the time period from the Outside Completion Date (as so extended) until the date which is thirty (30) days subsequent to the Outside Completion Date (as so extended); and, upon the giving of such notice, the term of the Lease shall cease and come to an end without further liability or obligation on the part of either party (and if Tenant is then in occupancy, Tenant shall yield up the Premises as required by this Lease at the expiration or earlier termination of the Term) unless, within thirty (30) days after receipt of such notice, Landlord substantially completes Landlord's Work; and such right of termination shall be Tenant's

sole and exclusive remedy for Landlord's failure so to complete Landlord's Work within such time. Each day of Tenant Delay shall be deemed conclusively to cause an equivalent day of delay by Landlord in substantially completing Landlord's Work pursuant to Section 1.1 of this Work Agreement, and thereby automatically extend for each such equivalent day of delay the date of the Outside Completion Date.

1.3 Quality and Performance of Work

All construction work required or permitted by the Lease shall be done in a good and workmanlike manner using new and first quality materials and in compliance with all applicable laws, ordinances, rules, regulations, statutes, by-laws, court decisions, and orders and requirements of all public authorities ("Legal Requirements") and all Insurance Requirements (as defined in Section 5.12 of the Lease). All of Tenant's work shall be coordinated with any work being performed by or for Landlord and in such manner as to maintain harmonious labor relations. Each party may inspect the work of the other at reasonable times and shall promptly give notice of observed defects, but the foregoing shall not release Landlord of its obligation to properly perform Landlord's Work. Each party authorizes the other to rely in connection with design and construction upon approval and other actions on the party's behalf by any Construction Representative of the party named in Section 1.1 of the Lease or any person hereafter designated in substitution or addition by notice to the party relying. Except to the extent to which Tenant shall have given Landlord notice of respects in which Landlord has not performed Landlord's construction obligations under this Work Agreement (if any) (i) not later than the end of the twelfth (12th) full calendar month next beginning after the Commencement Date with respect to the heating, ventilating and air conditioning systems servicing the Premises and other items which could not readily have been discovered in the exercise of reasonable diligence shortly after Substantial Completion, and (ii) not later than the third (3rd) full calendar month next beginning after the Commencement Date with respect to Landlord's construction obligations under this Work Agreement not referenced in (i) above, Tenant shall be deemed conclusively to have approved Landlord's construction and shall have no claim that Landlord has failed to perform any of Landlord's obligations under this Work Agreement (if any). Landlord agrees to correct or repair at its expense items which are then incomplete or do not conform to the work contemplated under the Plans and as to which, in either case, Tenant shall have given notice to Landlord, as aforesaid.

1.4 Intentionally Omitted

1.5 Tenant Plan Excess Costs

Notwithstanding anything contained in this Work Agreement to the contrary, it is understood and agreed that Tenant shall be fully responsible for the costs of any items of work not shown on Exhibit B-2 attached to the Lease as being paid for by Landlord (the "Tenant Plan Excess Costs"). To the extent, if any, that there are Tenant Plan Excess Costs, Tenant shall pay Landlord, as Additional Rent, the Tenant Plan Excess Costs prior to the commencement of the Landlord's Work.

EXHIBIT B-2

Plans

Boston Properties Proteon Therapeutics Tenant Work Letter 200 West Street

DELINEATION OF Proteon Therapeutics TURN-KEY MATRIX
May 21, 2009

Element	Description	Turn-Key Scope	Tenant Cost
Demo			
Finish Carpentry			
Doors & Frames	Existing Office Doors to Remain As-Is	X	
	Install New Wood Doors PM Frames And Sidelight In New Offices (4) To Match Existing	X	
	Install New Passage Sets On New Offices	X	
Drywall	Build (4) New Offices Along Perimeter Wall (Fl To ACT Ceiling)	X	
Acoustic Ceilings	Kerf Existing Ceiling Tile Around New Walls To Accommodate New Layout.	X	
Flooring	Install New Vinyl Wall Base In 4 New Offices	X	
Wall Finishes	Paint Wall In 4 New Offices (2 Coats)	X	

Element	Description	Turn-Key Scope	Tenant Cost
Equipment/Specialties			
Equipment/Specialties cont.	Fire Extinguishers As Required by Code	X	
	Signage Building Directory	X	
Fire Protection	Relocate/Add Fire Sprinkler Heads To Accommodate New Layout	X	
	New Fire Horn/Strobe Units To Accommodate New Layout	X	
Plumbing			
HVAC	Relocate/Add New Ductwork And Diffuser To Accommodate New Layout	X	
Electrical	Existing Light Fixtures/Wall Switches And Outlets Will Remain As-is In Existing Offices	X	
	Install New Or Relocate Existing 2'X4' Parabolic Light Fixtures To Accommodate New Layout	X	
	Install (1) New Wall Switch Per New Office	X	
	Exist Signs/Fire Alarm Devices as Required by Code	X	

Element	Description	Turn-Key Scope	Tenant Cost
	Install (2) New Outlets In 4 New Offices	X	
Telecom/Security	Design of Tel/Data/Furniture		X
	Tel/Data Cabling And Final Connections		X
Telecom/Security cont.	Tel/Data Equipment And Permit		X
Design Services	Design for Turnkey Scope	X	
	Life/Safety Engineering for Fire Protection & Fire Alarm Modification if Required by Code	X	

EXHIBIT C

Intentionally Omitted

EXHIBIT D

LANDLORD SERVICES

I. CLEANING

Cleaning and janitorial services shall be provided as needed Monday through Friday, exclusive of holidays observed by the cleaning company and Saturdays and Sundays.

A. OFFICE AREAS

Cleaning and janitorial services to be provided in the office areas shall include:

1. Vacuuming, damp mopping of resilient floors and trash removal.

2. Dusting of horizontal surfaces within normal reach (tenant equipment to remain in place).

3. High dusting and dusting of vertical blinds to be rendered as needed.

B. LAVATORIES

Cleaning and janitorial services to be provided in the common area lavatories of the building shall include:

1. Dusting, damp mopping of resilient floors, trash removal, sanitizing of basins, bowls and urinals as well as cleaning of mirrors and bright work.

2. Refilling of soap, towel, tissue and sanitary dispensers to be rendered as necessary.

3. High dusting to be rendered as needed.

C. MAIN LOBBIES, ELEVATORS, STAIRWELLS AND COMMON CORRIDORS

Cleaning and janitorial services to be provided in the common areas of the building shall include:

1. Trash removal, vacuuming, dusting and damp mopping of resilient floors and cleaning and sanitizing of water fountains.

2. High dusting to be rendered as needed.

D. WINDOW CLEANING

All exterior windows shall be washed on the inside and outside surfaces at frequency necessary to maintain a first class appearance.

II. HVAC

A. Heating, ventilating and air conditioning equipment will be provided with sufficient capacity to accommodate a maximum population density of one (1) person per one hundred fifty (150) square feet of useable floor area served, and a combined lighting and standard electrical load of 3.0 watts per square foot of useable floor area. In the event Tenant introduces into the Premises personnel or equipment which overloads the system's ability to adequately perform its proper functions, Landlord shall so notify Tenant in writing and supplementary system(s) may be required and installed by Landlord at Tenant's expense, if within fifteen (15) days Tenant has not modified its use so as not to cause such overload.

Operating criteria of the basic system are in accordance with the Massachusetts Energy Code and shall not be less than the following:

(i) Cooling season indoor temperatures of not in excess of 73 -79 degrees Fahrenheit when outdoor temperatures are 91 degrees Fahrenheit ambient.

(ii) Heating season minimum room temperature of 68 - 75 degrees Fahrenheit when outdoor temperatures are 6 degrees Fahrenheit ambient.

B. Landlord shall provide heating, ventilating and air conditioning as normal seasonal changes may require during the hours of 8:00 a.m. to 6:00 p.m., Monday through Friday (legal holidays in all cases excepted).

If Tenant shall require air conditioning (during the air conditioning season) or heating or ventilating during any other time period, Landlord shall use landlord's best efforts to furnish such services for the area or areas specified by written request of Tenant delivered to the Building Superintendent or the Landlord before 3:00 p.m. of the business day preceding the extra usage. Landlord shall charge Tenant for such extra-hours usage at reasonable rates customary for first-class office buildings in the Boston Suburban market, and Tenant shall pay Landlord, as additional rent, upon receipt of billing therefor.

III. ELECTRICAL SERVICES

A. Landlord shall provide electric power for a combined load of 3.0 watts per square foot of useable area for lighting and for office machines through standard receptacles for the typical office space.

B. In the event that Tenant has special equipment (such as computers and reproduction equipment) that requires either 3-phase electric power or any voltage other than 120 volts, or for any other usage in excess of 3.0 watts per square foot, Landlord may at its option require the installation of separate metering (Tenant being solely responsible for the costs of any such separate meter and the installation thereof) and direct billing to Tenant for the electric power required for any such special equipment.

C. Landlord will furnish and install, at Tenant's expense, all replacement lighting tubes, lamps and ballasts required by Tenant. Landlord will clean lighting fixtures on a regularly scheduled basis at Tenant's expense.

IV. ELEVATORS

Provide passenger elevator service.

V. WATER

Provide hot water for lavatory purposes and cold water for drinking, lavatory and toilet purposes.

VI. CARD ACCESS SYSTEM

Landlord will provide a card access system at one entry door of the building.

EXHIBIT E

FLOOR PLAN

[Floor Plan Drawing]

EXHIBIT F

DECLARATION AFFIXING THE COMMENCEMENT DATE OF LEASE

THIS AGREEMENT made this day of , 200 , by and between ***[LANDLORD]*** (hereinafter "Landlord") and ***[TENANT]*** (hereinafter "Tenant").

WITNESSETH THAT:

1. This Agreement is made pursuant to Section ***[2.4]*** of that certain Lease dated ***[date]***, between Landlord and Tenant (the "Lease").

2. It is hereby stipulated that the Lease Term commenced on ***[commencement date]***, (being the "Commencement Date" under the Lease), and shall end and expire on ***[expiration date]***, unless sooner terminated or extended, as provided for in the Lease.

WITNESS the execution hereof under seal by persons hereunto duly authorized, the date first above written.

LANDLORD:

[INSERT LL SIGNATURE BLOCK]

By: _____
Name: _____
Title: _____

TENANT:

ATTEST:

[TENANT]

By: _____
Name: _____
Title: _____

By: _____
Name: _____
Title: _____
Hereunto duly authorized

EXHIBIT G

Intentionally Omitted

EXHIBIT H

FORM OF LETTER OF CREDIT

[Letterhead of a money center bank acceptable to the Owner]

[Please note the tenant on this Letter of Credit must match the exact tenant entity in the Lease]

[date]

[Landlord]

c/o Boston Properties LP
800 Boylston Street, Suite 1900
Boston, Massachusetts 02199-8103
Attn: Lease Administration, Legal Dept.

Gentlemen:

We hereby establish our Irrevocable Letter of Credit and authorize you to draw on us at sight for the account of ***[Tenant]*** ("Applicant"), the aggregate amount of ***[spell out dollar amount]*** and ***[ ]***/100 Dollars ***[($)]***. You shall have the right to make partial draws against this Letter of Credit from time to time.

Funds under this Letter of Credit are available to the beneficiary hereof as follows:

Any or all of the sums hereunder may be drawn down at any time and from time to time from and after the date hereof by ***[Landlord]*** ("Beneficiary") when accompanied by this Letter of Credit and a written statement signed by an individual purporting to be an authorized agent of Beneficiary, certifying that such moneys are due and owing to Beneficiary, and a sight draft executed and endorsed by such individual.

This Letter of Credit is transferable in its entirety to any successor in interest to Beneficiary as owner of ***[Property, Address, City/Town, State]***. Should a transfer be desired, such transfer will be subject to the return to us of this advice, together with written instructions. Any fees related to such transfer shall be for the account of the Applicant.

The amount of each draft must be endorsed on the reverse hereof by the negotiating bank. We hereby agree that this Letter of Credit shall be duly honored upon presentation and delivery of the certification specified above.

This Letter of Credit shall expire on ***[Final Expiration Date]***.

Notwithstanding the above expiration date of this Letter of Credit, the term of this Letter of Credit shall be automatically renewed for successive, additional one (1) year periods unless, at

least sixty (60) days prior to any such date of expiration, the undersigned shall give written notice to Beneficiary, by certified mail, return receipt requested and at the address set forth above or at such other address as may be given to the undersigned by Beneficiary, that this Letter of Credit will not be renewed.

This Letter of Credit is governed by the Uniform Customs and Practice for Documentary Credits (1993 Revision), International Chamber of Commerce Publication 500.

Very truly yours,

[Name of Issuing Bank]

By: _____
Name: _____
Title: _____

EXHIBIT I

FORM OF CERTIFICATE OF INSURANCE

[Form of Certificate of Insurance]

[Form of Certificate of Insurance]

FIRST AMENDMENT TO LEASE

FIRST AMENDMENT TO LEASE dated as of this 14 day of Sep, 2012 by and between BOSTON PROPERTIES LIMITED PARTNERSHIP, a Delaware limited partnership ("Landlord") and PROTEON THERAPEUTICS, INC., a Delaware corporation ("Tenant").

RECITALS

By Lease dated July 13, 2009 (the "Lease"), Landlord did lease to Tenant and Tenant did hire and lease from Landlord 4,943 square feet of rentable floor area (the "Rentable Floor Area of the Premises") on the first (1st) floor of the building (the "Building") known as and numbered 200 West Street, Waltham, Massachusetts (referred to in the Lease as the "Premises").

Landlord and Tenant have agreed to extend the Term of the Lease for one (1) period of six (6) months upon all of the same terms and conditions set forth in the Lease except as set forth in this First Amendment to Lease (the "First Amendment").

Landlord and Tenant are entering into this instrument to set forth said extension of the Term of the Lease and to amend the Lease.

NOW THEREFORE, in consideration of One Dollar ($1.00) and other good and valuable consideration in hand this date paid by each of the parties to the other, the receipt and sufficiency of which are hereby severally acknowledged, and in further consideration of the mutual promises herein contained, Landlord and Tenant hereby agree to and with each other as follows:

1. The Term of the Lease, which but for this First Amendment is scheduled to expire on June 30, 2013, is hereby extended for one (1) period of six (6) months commencing on July 1, 2013 and expiring on December 31, 2013 (the "Extended Term"), unless sooner terminated in accordance with the provisions of the Lease, upon all the same terms and conditions contained in the Lease as herein amended.

2. Annual Fixed Rent shall continue to be payable by Tenant during the Extended Term at the annual rate of $168,062.00 (being the product of (i) $34.00 and (ii) the Rentable Floor Area of the Premises (being 4,943 square feet)).

3. Tenant shall accept the Premises in its "as is" condition during the Extended Term, without any obligation on the Landlord's part to perform any additions, alterations, improvements, demolition or other work therein or pertaining thereto (provided that the foregoing shall not be construed so as to relieve Landlord of any of its maintenance or repair obligations under the Lease).

4. (A) Tenant warrants and represents that Tenant has not dealt with any broker in connection with the consummation of this First Amendment; and in the event any claim is

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made against Landlord relative to dealings by Tenant with brokers, Tenant shall defend the claim against Landlord with counsel of Tenant's selection first approved by Landlord (which approval will not be unreasonably withheld) and save harmless and indemnify Landlord on account of loss, cost or damage which may arise by reason of such claim.

(B) Landlord warrants and represents that Landlord has not dealt with any broker in connection with the consummation of this First Amendment; and in the event any claim is made against Tenant relative to dealings by Landlord with brokers, Landlord shall defend the claim against Tenant with counsel of Landlord's selection first approved by Tenant (which approval will not be unreasonably withheld) and save harmless and indemnify Tenant on account of loss, cost or damage which may arise by reason of such claim.

5. Except as otherwise expressly provided herein, all capitalized terms used herein without definition shall have the same meanings as are set forth in the Lease.

6. Except as herein amended the Lease shall remain unchanged and in full force and effect. All references to the "Lease" shall be deemed to be references to the Lease as herein amended.

7. Each of Landlord and Tenant hereby represents and warrants to the other that all necessary action has been taken to enter this First Amendment and that the person signing this First Amendment on its behalf has been duly authorized to do so.

PAGE ENDS HERE

EXECUTED as a sealed instrument as of the date and year first above written.

WITNESS:

/s/illegible

LANDLORD:

BOSTON PROPERTIES LIMITED PARTNERSHIP

By: Boston Properties, Inc., its general partner

By: /s/ David C. Provost
Name: David C. Provost
Title: SVP
Hereunto duly authorized

WITNESS:

TENANT:

PROTEON THERAPEUTICS, INC.

By: /s/ Timothy Noyes
Name: Timothy Noyes
Title: President + CEO
Hereunto duly authorized

SECOND AMENDMENT TO LEASE

SECOND AMENDMENT TO LEASE dated as of this 17th day of October 2013 by and between BOSTON PROPERTIES LIMITED PARTNERSHIP, a Delaware limited partnership ("Landlord") and PROTEON THERAPEUTICS, INC., a Delaware corporation ("Tenant").

RECITALS

By Lease dated July 13, 2009 (as amended by the instrument described below, the "Lease"), Landlord did lease to Tenant and Tenant did hire and lease from Landlord 4,943 square feet of rentable floor area (the "Rentable Floor Area of the Premises") on the first (lst) floor of the building (the "Building") known as and numbered 200 West Street, Waltham, Massachusetts (referred to in the Lease as the "Premises").

By First Amendment to Lease dated as of September 14, 2012 (the "First Amendment"), Landlord and Tenant extended the Term of the Lease for one (1) period of six (6) months upon all of the same terms and conditions set forth in the Lease except as set forth in the First Amendment.

Landlord and Tenant have agreed to extend the Term of the Lease for one (1) period of one (1) year upon all of the same terms and conditions set forth in the Lease except as set forth in this Second Amendment to Lease (the "Second Amendment").

Landlord and Tenant are entering into this instrument to set forth said extension of the Term of the Lease and to amend the Lease.

NOW THEREFORE, in consideration of One Dollar ($1.00) and other good and valuable consideration in hand this date paid by each of the parties to the other, the receipt and sufficiency of which are hereby severally acknowledged, and in further consideration of the mutual promises herein contained, Landlord and Tenant hereby agree to and with each other as follows:

1. The Term of the Lease, which but for this Second Amendment is scheduled to expire on December 31, 2013, is hereby extended for one (1) period of one (1) year commencing on January 1, 2014 and expiring on December 31, 2014 (the "Second Extended Term"), unless sooner terminated in accordance with the provisions of the Lease, upon all the same terms and conditions contained in the Lease as herein amended.

2. Annual Fixed Rent shall continue to be payable by Tenant during the Second Extended Term at the annual rate of $168,062.00 (being the product of (i) $34.00 and (ii) the Rentable Floor Area of the Premises (being 4,943 square feet)).

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3. Tenant shall accept the Premises in its "as is" condition during the Second Extended Term, without any obligation on the Landlord's part to perform any additions, alterations, improvements, demolition or other work therein or pertaining thereto (provided that the foregoing shall not be construed so as to relieve Landlord of any of its maintenance or repair obligations under the Lease).

4. (A) Tenant warrants and represents that Tenant has not dealt with any broker in connection with the consummation of this Second Amendment; and in the event any claim is made against Landlord relative to dealings by Tenant with brokers, Tenant shall defend the claim against Landlord with counsel of Tenant's selection first approved by Landlord (which approval will not be unreasonably withheld) and save harmless and indemnify Landlord on account of loss, cost or damage which may arise by reason of such claim.

(B) Landlord warrants and represents that Landlord has not dealt with any broker in connection with the consummation of this Second Amendment; and in the event any claim is made against Tenant relative to dealings by Landlord with brokers, Landlord shall defend the claim against Tenant with counsel of Landlord's selection first approved by Tenant (which approval will not be unreasonably withheld) and save harmless and indemnify Tenant on account of loss, cost or damage which may arise by reason of such claim.

5. Except as otherwise expressly provided herein, all capitalized terms used herein without definition shall have the same meanings as are set forth in the Lease.

6. Except as herein amended the Lease shall remain unchanged and in full force and effect. All references to the "Lease" shall be deemed to be references to the Lease as amended and as herein amended.

7. Each of Landlord and Tenant hereby represents and warrants to the other that all necessary action has been taken to enter this Second Amendment and that the person signing this Second Amendment on its behalf has been duly authorized to do so.

PAGE ENDS HERE

EXECUTED as a sealed instrument as of the date and year first above written.

WITNESS:

/s/illegible

LANDLORD:

BOSTON PROPERTIES LIMITED PARTNERSHIP, a Delaware limited partnership

By: Boston Properties, Inc., a Delaware corporation, its general partner

By: /s/ David C. Provost
Name: David C. Provost
Title: Senior Vice President Boston Properties
Hereunto duly authorized

TENANT:

WITNESS:

PROTEON THERAPEUTICS, INC.

By: /s/ Timothy Noyes
Name: Timothy Noyes
Title: CEO
Hereunto duly authorized

THIRD AMENDMENT TO LEASE

THIRD AMENDMENT TO LEASE dated as of this Fourth day of August, 2014 by and between BOSTON PROPERTIES LIMITED PARTNERSHIP, a Delaware limited partnership ("Landlord"), and PROTEON THERAPEUTICS, INC., a Delaware corporation ("Tenant").

RECITALS

By Lease dated July 13, 2009 (as amended by the instruments described below, the "Lease"), Landlord did lease to Tenant and Tenant did hire and lease from Landlord 4,943 square feet of rentable floor area (the "Rentable Floor Area of the Premises") on the first (1st) floor of the building (the "Building") known as and numbered 200 West Street, Waltham, Massachusetts (referred to in the Lease as the "Premises").

By First Amendment to Lease dated as of September 14, 2012 (the "First Amendment"), Landlord and Tenant extended the Term of the Lease for one (1) period of six (6) months upon all of the same terms and conditions set forth in the Lease except as set forth in the First Amendment.

By Second Amendment to Lease dated as of October 17, 2013 (the "Second Amendment"), Landlord and Tenant extended the Term of the Lease for one (1) period of one (1) year upon all of the same terms and conditions set forth in the Lease except as set forth in the First Amendment.

Landlord and Tenant have agreed to (i) extend the Term of the Lease for a period of forty-two (42) months upon the terms and conditions contained in the Lease, except as otherwise set forth in this Third Amendment to Lease (the "Third Amendment"), (ii) provide Tenant with an option to further extend the Term of the Lease for one (1) additional period of one (1) year and (iii) make certain other modifications to the Lease, as further set forth in this Third Amendment.

Landlord and Tenant are entering into this instrument to set forth said agreements and to amend the Lease.

NOW THEREFORE, in consideration of One Dollar ($1.00) and other good and valuable consideration in hand this date paid by each of the parties to the other, the receipt and sufficiency of which are hereby severally acknowledged, and in further consideration of the mutual promises herein contained, Landlord and Tenant hereby agree to and with each other as follows:

1. The Term of the Lease, which but for this Third Amendment is scheduled to expire on December 31, 2014, is hereby extended for one (1) period of forty-two (42) months commencing on January 1, 2015 and expiring on June 30, 2018 (the "Third Extended Term"),

unless sooner terminated or extended in accordance with the provisions of the Lease, upon all the same terms and conditions contained in the Lease as herein amended.

2. Annual Fixed Rent shall continue to be payable by Tenant during the Third Extended Term at the annual rate of $168,062.00 (being the product of (i) $34.00 and (ii) the Rentable Floor Area of the Premises (being 4,943 square feet)).

3. (A) Commencing on January 1, 2015 and continuing through the Third Extended Term, the definition of "Base Operating Expenses" contained in Section 2.6 of the Lease shall be deleted in its entirety and the following substituted therefor:

> "Base Operating Expenses" shall mean Landlord's Operating Expenses for calendar year 2015 (that is, the period beginning January 1, 2015 and ending December 31, 2015). Base Operating Expenses shall not include (i) market-wide cost increases in ordinarily included costs due to extraordinary circumstances, included but not limited to Force Majeure (as defined in Section 6.1), conservation surcharges, boycotts, strikes, embargoes or shortages ("Extraordinary Expense") and (ii) the cost of any Permitted Capital Expenditures. However, if a particular Extraordinary Expense continues for more than twenty-four (24) consecutive months, then during each year after the calendar year 2015 ("Base Year") in which it continues (and on a pro rata basis if it continues for part, but not all, of a subsequent year), Base Operating Expenses shall include such Extraordinary Expense. By way of example only, if there is a conservation surcharge that constitutes an Extraordinary Expense, and if such surcharge continues for more than twenty-four (24) consecutive months, then for every year after the Base Year in which surcharge exists, Base Operating Expenses shall be increased (in a pro rata basis for partial years after the Base Year) by the amount of such surcharge in the Base Year.

For that portion of the Lease Term prior to January 1, 2015, such definition shall remain unchanged.

(B) Commencing on January 1, 2015, and continuing through the Third Extended Term, the definition of "Base Taxes" contained in Section 2.7, of the Original Lease shall be deleted in its entirety and the following substituted therefor:

> "Base Taxes" means Landlord's Tax Expenses (hereinbefore defined) for fiscal tax year 2015 (that is, the period beginning July 1, 2014 and ending June 30, 2015).

For that portion of the Lease Term prior to January 1, 2015, such definition shall remain unchanged.

4. Landlord and Tenant acknowledge and agree that Section 2.1.1 of the Lease is hereby deleted in its entirety and Landlord shall have no further relocation right thereunder.

5. Tenant shall accept the Premises in its "as is" condition during the Third Extended Term, without any obligation on the Landlord's part to perform any additions, alterations, improvements, demolition or other work therein or pertaining thereto (provided that the foregoing shall not be construed so as to relieve Landlord of any of its maintenance or repair obligations under the Lease). Notwithstanding the foregoing, Landlord agrees, at its expense, to perform the following work: (i) touch up paint on walls located within the Premises, as reasonably requested by Tenant, and (ii) steam clean the existing carpeting located within the Premises (collectively, the "Third Amendment Work"). Landlord shall use commercially reasonable efforts to complete the Third Amendment Work by October 1, 2014; provided, however, that Landlord shall have no liability to Tenant or any other person for the failure to complete the same by any particular date so long as Landlord has used commercially reasonable efforts as aforesaid. In addition, it is acknowledged and agreed that Landlord's Work will be performed while Tenant is in occupancy of the Premises, and accordingly, Landlord and Tenant hereby agree to cooperate with each other in good faith so that Landlord may complete the work in an efficient and economical manner while at the same time minimizing any unreasonable interference with Tenant's business operations in the Premises (consistent with the nature of the work being performed).

6. Section 9.18 of the Lease is hereby amended by inserting the following after the first paragraph thereof:

> Landlord shall return a Twenty-Four Thousand Three Hundred Three and 08/100 Dollar ($24,303.08) portion of the security deposit to Tenant so that the remainder of such deposit shall be Fourteen Thousand Five and 17/100 Dollars ($14,005.17) (or if such deposit is in the form of a Letter of Credit, Landlord shall exchange the Letter of Credit for a Letter of Credit delivered by Tenant which reduces the amount secured by the Letter of Credit by the amount stated hereinabove and otherwise in strict conformity with the requirements herein) on January 1, 2015 (the "Reduction Date"), if (i) Tenant is not then in default under the terms of this Lease without the benefit of notice or grace, (ii) Landlord has not applied such deposit or any portion thereof to Landlord's damages arising from any default on the part of Tenant, whether or not Tenant has restored the amount so applied by Landlord and (iii) there have been no more than two (2) Event of Default occurrences during the Term.
>
> If Tenant believes that it has satisfied all the conditions precedent to a reduction in the amount of the security deposit, then it shall request such reduction in writing to Landlord within sixty (60) days after the Reduction Date ("Tenant's Reduction Request Notice"), which request shall certify to Landlord that all such conditions have been satisfied and shall include any items required above. If Landlord reasonably determines that all of the aforesaid conditions are met, the security deposit shall be so reduced in accordance with this Section 6. No Letter of Credit shall automatically reduce, but any reduction in the amount thereof shall require Landlord's prior written notice to the issuer of the Letter of Credit of the reduced

amount. Promptly after Landlord's receipt of Tenant's request for a reduction as described above. Landlord shall determine whether such a reduction is permitted in accordance with this Section 6, and if it is, Landlord shall notify the issuer of the Letter of Credit of the amount to which the Letter of Credit shall be reduced.

7. The parties agree that during the Term, upon request of Tenant, to be made no more frequently than once per month, Landlord shall clean out the sink and drain located within the Premises at Landlord's sole cost and expense.

8. (A) On the conditions (which conditions Landlord may waive by written notice to Tenant) that at the time of exercise of the option to extend and at the commencement date of the extension option period (i) there exists no Event of Default (defined in Section 7.1) and there have been no more than two (2) Event of Default occurrences during the Term, (ii) this Lease is still in full force and effect, and (iii) Tenant has neither assigned this Lease nor sublet the Premises except for an assignment or subletting permitted without Landlord's consent under Section 5.6.4 hereof, Tenant shall have the right to extend the Term hereof upon all the same terms, conditions, covenants and agreements herein contained (except for the Annual Fixed Rent which shall be adjusted during the option periods as hereinbelow set forth) for one (1) period of one (1) year as hereinafter set forth. Notwithstanding any implication to the contrary Landlord has no obligation to make any additional payment to Tenant in respect of any construction allowance or the like or to perform any work to the Premises as a result of the exercise by Tenant of such option.

(B) If Tenant desires to exercise said option to extend the Term, then Tenant shall give notice to Landlord ("Exercise Notice"), not earlier than twelve (12) months nor later than nine (9) months prior to the expiration of the Term, as it may have been previously extended, hereunder of Tenant's request for Landlord's quotation ("Landlord's Rent Quotation") of the annual fair market rent for the Premises as of the commencement date of the extension period, such quotation to be based on the use of the Premises as first class office space utilizing properties of a similar character within the Boston West Suburban market and including consideration of all relevant factors (including, without limitation, premises within the Complex if at the time such quotation is requested such premises shall be available for rent) (hereinafter called the "Annual Market Rent"). Within thirty (30) days after Landlord's receipt of Tenant's notice requesting such a quotation, Landlord shall notify Tenant of Landlord's quotation of the Annual Market Rent. If at the expiration of fifteen (15) days after the date when Landlord provides Landlord's Rent Quotation to Tenant as aforesaid (the "Negotiation Period"), Landlord and Tenant have not reached agreement on a determination of an Annual Fixed Rent for such extension period and executed a written instrument extending the Term of this Lease pursuant to such agreement, then Tenant shall have the right, for fifteen (15) days following the expiration of the Negotiation Period, to make a request to Landlord for a broker determination (the "Broker Determination") of the Prevailing Market Rent (as defined in Exhibit A attached hereto) for such extension period, which Broker Determination shall be made in the manner set forth in Exhibit A. If Tenant timely shall have requested the Broker Determination, then the Annual Fixed Rent for such extension period shall be the Prevailing Market Rent as determined by the Broker Determination. If Tenant does not timely request the Broker Determination, then the Annual

Fixed Rent during such extension term shall be equal to the greater of (a) Landlord's Rent Quotation or (b) the Annual Fixed Rent in effect during the last twelve (12) month period of the Lease Term immediately prior to such extension term.

(C) Upon the giving of the Exercise Notice by Tenant to Landlord exercising Tenant's option to extend the Lease Term in accordance with the provisions of Section 8(B) above, then this Lease and the Term hereof automatically shall be deemed extended for the option period, without the necessity for the execution of any additional documents (except that Landlord and Tenant agree to enter into an instrument in writing setting forth the Annual Fixed Rent for the extension term as determined in the relevant manner set forth in this Section 8); and in such event all references herein to the Term or the term of this Lease shall be construed as referring to the Term, as so extended, unless the context clearly otherwise requires and except that there shall be no further option to extend the Lease Term.

9. (A) Tenant warrants and represents that Tenant has not dealt with any broker in connection with the consummation of this Third Amendment other than Jones Lang Lasalle (the "Broker"); and in the event any claim is made against Landlord relative to dealings by Tenant with brokers other than the Broker, Tenant shall defend the claim against Landlord with counsel of Tenant's selection first approved by Landlord (which approval will not be unreasonably withheld) and save harmless and indemnify Landlord on account of loss, cost or damage which may arise by reason of such claim.

(B) Landlord warrants and represents that Landlord has not dealt with any broker in connection with the consummation of this Third Amendment other than the Broker; and in the event any claim is made against Tenant relative to dealings by Landlord with brokers other than the Broker, Landlord shall defend the claim against Tenant with counsel of Landlord's selection first approved by Tenant (which approval will not be unreasonably withheld) and save harmless and indemnify Tenant on account of loss, cost or damage which may arise by reason of such claim. Landlord agrees that it shall be solely responsible for the payment of any brokerage commission to the Broker with respect to this Third Amendment pursuant to a separate agreement.

10. Except as otherwise expressly provided herein, all capitalized terms used herein without definition shall have the same meanings as are set forth in the Lease.

11. Except as herein amended the Lease shall remain unchanged and in full force and effect. All references to the "Lease" shall be deemed to be references to the Lease as amended and as herein amended.

12. Each of Landlord and Tenant hereby represents and warrants to the other that all necessary action has been taken to enter this Third Amendment and that the person signing this Third Amendment on its behalf has been duly authorized to do so.

PAGE ENDS HERE

EXECUTED as a sealed instrument as of the date and year first above written.

WITNESS:

[Illegible]

LANDLORD:

BOSTON PROPERTIES LIMITED PARTNERSHIP,
a Delaware limited partnership

BY: BOSTON PROPERTIES, INC.,
a Delaware corporation, its general partner

By: /s/ David C Provost
Name: David C Provost
Title: SVP
Hereunto duly authorized

WITNESS:

/s/ Dean Profis

TENANT:

PROTEON THERAPEUTICS, INC.

By: /s/ George Eldridge

Name: George Eldridge
Title: Senior Vice President and CFO
Hereunto duly authorized

EXHIBIT A

BROKER DETERMINATION OF PREVAILING MARKET RENT

The following procedures and requirements shall apply to the Broker Determination of Prevailing Market Rent called for pursuant to Section 8 of the Third Amendment to Lease to which this Exhibit is attached:

1. Tenant's Request. Tenant shall send a notice to Landlord by the time set for such notice in the applicable section of the Lease, requesting a Broker Determination of the Prevailing Market Rent, which notice to be effective must (i) make explicit reference to the Lease and to the specific section of the Lease pursuant to which said request is being made, (ii) include the name of a broker selected by Tenant to act for Tenant, which broker shall be affiliated with a major Boston commercial real estate brokerage firm selected by Tenant and which broker shall have at least ten (10) years experience dealing in properties of a nature and type generally similar to the Building located in the Boston West Suburban Market, and (iii) explicitly state that Landlord is required to notify Tenant within thirty (30) days of an additional broker selected by Landlord.

2. Landlord's Response. Within thirty (30) days after Landlord's receipt of Tenant's notice requesting the Broker Determination and stating the name of the broker selected by Tenant, Landlord shall give written notice to Tenant of Landlord's selection of a broker having at least the affiliation and experience referred to above.

3. Selection of Third Broker. Within ten (10) days thereafter the two (2) brokers so selected shall select a third such broker also having at least the affiliation and experience referred to above.

4. Rental Value Determination. Within thirty (30) days after the selection of the third broker, the three (3) brokers so selected, by majority opinion, shall make a determination of the annual fair market rental value of the Premises for the period referred to in the Lease. Such annual fair market rental value determination (x) may include provision for annual increases in rent during said term if so determined, (y) shall take into account the as-is condition of the Premises and (z) shall take account of, and be expressed in relation to, the tax and operating cost bases and provisions for paying for so-called tenant electricity as contained in the Lease. The brokers shall advise Landlord and Tenant in writing by the expiration of said thirty (30) day period of the annual fair market rental value which as so determined shall be referred to as the Prevailing Market Rent.

5. Resolution of Broker Deadlock. If the Brokers are unable to agree at least by majority on a determination of annual fair market rental value, then the brokers shall send a notice to Landlord and Tenant by the end of the thirty (30) day period for making said determination setting forth their individual determinations of annual fair market rental value, and the highest such determination and the lowest such determination shall be disregarded and the remaining determination shall be deemed to be the determination of annual fair market rental value and

shall be referred to as the Prevailing Market Rent.

6. Costs. Each party shall pay the costs and expenses of the broker selected by it and each shall pay one half (1/2) of the costs and expenses of the Third Broker.

7. Failure to Select Broker or Failure of Broker to Serve. If Tenant shall have requested a Broker Determination and Landlord shall not have designated a broker within the time period provided therefor above, then Tenant's Broker shall alone make the determination of Prevailing Market Rent in writing to Landlord and Tenant within thirty (30) days after the expiration of Landlord's right to designate a broker hereunder. If Tenant and Landlord have both designated brokers but the two brokers so designated do not, within a period of fifteen (15) days after the appointment of the second broker, agree upon and designate the Third Broker willing so to act, the Tenant, the Landlord or either broker previously designated may request the Boston Bar Association (or such organization as may succeed to the Boston Bar Association) to designate the Third Broker willing so to act and a broker so appointed shall, for all purposes, have the same standing and powers as though he had been seasonably appointed by the brokers first appointed. In case of the inability or refusal to serve of any person designated as a broker, or in case any broker for any reason ceases to be such, a broker to fill such vacancy shall be appointed by the Tenant, the Landlord, the brokers first appointed or the Boston Bar Association as the case may be, whichever made the original appointment, or if the person who made the original appointment fails to fill such vacancy, upon application of any broker who continues to act or by the Landlord or Tenant such vacancy may be filled by the Boston Bar Association and any broker so appointed to fill such vacancy shall have the same standing and powers as though originally appointed.

Exhibit 10.13

[Department of Health & Human Services Letterhead]

National Institutes of Health
Bethesda, Maryland 20892

October 1st, 2010

BY CERTIFIED MAIL

F. Nicholas Franano, M.D.
1010 W. 69th Terrace
Kansas City, MO 64113

Invention Title: Local, transcatheter delivery of proteases to reopen obstructed biological conduits
Inventor(s): F. Nicholas Franano
NIH Grant #: HL007712
NIH EIR #: 9999207-99-0001
Patents: 7,361,335; 7,632,494; 7,063,838; 7,153,505.
Patent publications: 12/229,372; 11/454,554, 12/229,428.
Reference: Third Party Waiver Request — F. Nicholas Franano to Proteon Therapeutics, Inc.

Dear Dr. Franano,

In reference to your request for approval to make an assignment of rights from F. Nicholas Franano to Proteon Therapeutics, Inc., the NIH has approved your request. Please note however, that the provisions of 37 CFR 401 continue to apply to any assignee(s) herein and its/their successor(s) once you have executed the transfer. In addition, terms applicable to the original funding agreement, including, but not limited to, rights in data and sharing of unique research resources, also flow down to the assignee(s), if applicable to the original recipient. In this case, the Invention ownership has already been assigned from Johns Hopkins University to you personally, and this letter gives approval for the title of the intellectual property to go now to Proteon Therapeutics, Inc. These terms need to be incorporated, at least by reference, in the assignment document.

It is your responsibility to notify the assignee(s)/recipient(s) of this transfer of the decision of our office for this Third Party Waiver to permit assignment to Proteon Therapeutics, Inc. Also, both parties involved are required to sign and send a copy of this letter back to our office at the address or fax number listed below.

Annual Utilization Reports detailing utilization-related activities related to the Subject Invention continue to be required. In addition the filing and maintenance of any Patents and/or Patent Applications claiming the Subject Invention is required, unless waived with proper notice and lead time so that the Government may Elect Title if it chooses to do so. These terms also need to be incorporated, at least by reference, in the assignment document.

Finally, the authorized representative of the Assignee, in this case Proteon Therapeutics, Inc., should go to the iEdison Invention and Patent Reporting web site, located at http://iEdison.gov, and register within 90 days from the date of this notification. This iEdison web site permits the Assignee to make the required reports on the assigned inventions. Once the Assignee registers at the iEdison web site, our office needs to be contacted at (301) 435-1986 to transfer the technology appropriately to the new iEdison account of the Assignee.

This determination is effective upon the signature & return from the Authorized Personal Representative of F. Nicholas Franano and the Authorized Organizational Representative of Proteon Therapeutics, Inc., within 90 days from the correspondence date of this letter.

If you have any additional questions, please contact the Waiver Coordinator at (301) 435-1986.

Sincerely,

/s/John Salzman
John Salzman
Assistant Extramural Invention Policy Officer
Division of Extramural Inventions and Technology Resource (DEITR)
Office of Policy for Extramural Research Administration (OPERA), OER, OD

Please direct all correspondence to:

Waiver Coordinator
6705 Rockledge Drive
Suite 310, MSC 7980
Bethesda, MD 20892-1910

Phone: (301) 435-1986
Fax: (301) 480-0272
Email: waiver@nih.gov

Accepted: /s/ F. Nicholas Franano M.D.
Authorized Official's Signature for F. Nicholas Franano

F. Nicholas Franano M.D. **Date**: 11/26/2010
Print Name and Title

Accepted:

Authorized Official's Signature for Proteon Therapeutics, Inc.

Date: _____

Print Name and Title

Invention Title: Local, transcatheter delivery of proteases to reopen obstructed biological conduits
NIH Grant #: HL007712
EIR #: 9999207-99-0001
Patents: 7,361,335; 7,632,494; 7,063,838; 7,153,505.
Patent publications: 12/229,372; 11/454,554, 12/229,428.
Individual's name requesting waiver: F. Nicholas Franano
Institution to which the technology is to be transferred: Proteon Therapeutics, Inc.
Current Date: October 1st, 2010

Exhibit 10.14

[Proteon Therapeutics Letterhead]

January 12, 2009

F. Nicholas Franano, M.D.
1010 W. 69th Terr.
Kansas City, Missouri 64113

Re: U.S. Provisional Patent Application No. 60/155,938
U.S. Patent Application No. 09/669,051
International Patent Application No. PCT/US00/26237

Dear Nick:

This letter confirms that by accepting your December 30, 2002 assignment of rights to the inventions disclosed in the above-referenced patent applications (the "Invention"), Proteon Therapeutics, LLC (i) agreed to comply with the terms of the Assignment of Rights/License Agreement between Nicholas Franano and the Johns Hopkins University dated March 25, 2002 (the "JHU Agreement") and (ii) assumed your obligations arising from the JHU Agreement (the "Franano Obligations"), including the obligation to honor the provisions imposed by the federal government sponsor of the research underlying the Invention (the "Bayh-Dole Obligations").

This letter further confirms that upon merger of Proteon Therapeutics, LLC into Proteon Therapeutics, Inc. on March 27, 2006, Proteon Therapeutics Inc. acquiesced to the terms of the JHU Agreement and assumed the Franano Obligations, including the Bayh-Dole Obligations.

Sincerely,

/s/Timothy P. Noyes
Timothy P. Noyes
President and Chief Executive Officer

Exhibit 10.15

QUITCLAIM DEED

WHEREAS **F. Nicholas Franano**, an individual residing at 1010 W. 69th Terrace, Kansas City, Missouri 64113 is the inventor of the invention described in an application for a Patent of the United States which was filed on September 24, 2000, Application No. 09/669,051; and

WHEREAS, by an instrument dated September 19, 2003, the said **F. Nicholas Franano** assigned and transferred the said invention and application to Proteon Therapeutics LLC, an entity established under Missouri law that was subsequently merged into **Proteon Therapeutics, Inc.**, a Delaware corporation presently having a principal place of business at 200 West Street, Waltham, MA 02451; and

WHEREAS, by letter dated October 1, 2010, the applicable terms of which are hereby incorporated by reference herein, the National Institutes of Health formally approved the assignment of the said invention and application from the said F. Nicholas Franano to Proteon Therapeutics, Inc.; and

WHEREAS the said **F. Nicholas Franano** (hereinafter referred to as "ASSIGNOR") and **Proteon Therapeutics, Inc.** (hereinafter referred to as "ASSIGNEE") desire to re-confirm that the said ASSIGNEE owns all right, title and interest in, to, and under the said invention and application:

NOW, THEREFORE, in consideration of good and valuable consideration, the receipt and sufficiency of which is hereby acknowledged, the said ASSIGNOR by these presents does hereby assign, transfer and set over, unto the said ASSIGNEE, its successors, legal representatives and assigns, any right, title and interest the said ASSIGNOR may have in, to and under the said invention, and the said United States application and all divisions, renewals and continuations thereof, and all Patents of the United States which may be granted or have been granted thereon and all reissues and extensions thereof; and all applications for industrial property protection, including, without limitation, all applications for patents, utility models, and designs which may be or have been pending or may hereafter be filed for said invention in any country or countries foreign to the United States, together with the right to file such applications and the right to claim for the same the priority rights derived from said United States application under the Patent Laws of the United States, the International Convention for the Protection of Industrial Property, or any other international agreement or the domestic laws of the country in which any such application is or has been filed, as may be applicable; and all forms of industrial property protection, including, without limitation, patents, utility models, inventors' certificates and designs which may be granted of have been granted for said invention in any country or countries foreign to the United States and all extensions, renewals and reissues thereof, and all right to recover for past, present or future infringement thereof;

AND THE SAID ASSIGNOR DOES HEREBY authorize and request the Director of the United States Patent and Trademark Office, and any Official of any country or countries foreign to the United States, whose duty it is to issue patents or other evidence or forms of industrial property protection on applications as aforesaid, to issue the same to the said ASSIGNEE, its successors, legal representatives and assigns, in accordance with the terms of this instrument;

AND THE SAID ASSIGNOR DOES HEREBY further covenant and agree that he will communicate to the said ASSIGNEE, its successors, legal representatives and assigns, any facts known to him respecting said invention, and testify in any legal proceeding, sign all lawful papers, execute all divisional, continuing, reissue and foreign applications, make all rightful oaths, and generally do everything possible to aid the said ASSIGNEE, its successors, legal representatives and assigns, to obtain and enforce proper protection for said invention in all countries;

AND THE SAID ASSIGNOR DOES HEREBY and irrevocably appoint the said ASSIGNEE his agent and attorney-in-fact for the purpose of executing any lawful papers that ASSIGNEE may file in support of intellectual property protection for said invention, which power shall survive any death or incapacity of ASSIGNOR and be appurtenant to the said invention and application.

IN TESTIMONY WHEREOF, I hereunto set my hand and seal this 17 day of January, 2011.

/s/ F. Nicholas Franano L.S.
F. Nicholas Franano

State of Kansas)
)ss.:
County of Johnson)

On January 17, 2011, before me, Sarah Hemann, Notary Public, personally appeared Nicholas Franano, personally known to me on the basis of satisfactory evidence to be the person whose name is subscribed to the within instrument and acknowledged to me that he/she executed the same in his/her authorized capacity, and that by his/her signature on the instrument the person, or the entity upon behalf of which the person acted, executed the instrument.

WITNESS my hand and official seal

/s/ Sarah Hemann [Notary Public - State of Kansas - SARAH HEMANN - Appt. Expires 11/18/2013 Stamp]

INDEMNIFICATION AGREEMENT

THIS INDEMNIFICATION AGREEMENT (the "**Agreement**") is made and entered into as of February 6, 2013 between **PROTEON THERAPEUTICS, INC.**, a Delaware corporation (the "**Company**"), and F. Nicholas Franano, M.D. ("**Indemnitee**").

WITNESSETH THAT:

WHEREAS, highly competent persons have become more reluctant to serve corporations as directors or in other capacities unless they are provided with adequate protection through insurance or adequate indemnification against inordinate risks of claims and actions against them arising out of their service to and activities on behalf of the corporation;

WHEREAS, the Board of Directors of the Company (the "**Board**") has determined that, in order to attract and retain qualified individuals, the Company will attempt to maintain on an ongoing basis, at its sole expense, liability insurance to protect persons serving the Company and its subsidiaries from certain liabilities. Although the furnishing of such insurance has been a customary and widespread practice among United States-based corporations and other business enterprises, the Company believes that, given current market conditions and trends, such insurance may be available to it in the future only at higher premiums and with more exclusions. At the same time, directors, officers, and other persons in service to corporations or business enterprises are being increasingly subjected to expensive and time-consuming litigation relating to, among other things, matters that traditionally would have been brought only against the Company or business enterprise itself. The Certificate of Incorporation of the Company permits, and the By-laws of the Company require, indemnification of directors of the Company. Indemnitee may also be entitled to indemnification pursuant to the General Corporation Law of the State of Delaware ("**DGCL**"). The By-laws and the DGCL expressly provide that the indemnification provisions set forth therein are not exclusive, and thereby contemplate that contracts may be entered into between the Company and members of the board of directors with respect to indemnification;

WHEREAS, the uncertainties relating to such insurance and to indemnification have increased the difficulty of attracting and retaining such persons;

WHEREAS, the Board has determined that the increased difficulty in attracting and retaining such persons is detrimental to the best interests of the Company's stockholders and that the Company should act to assure such persons that there will be increased certainty of such protection in the future;

WHEREAS, it is reasonable, prudent and necessary for the Company contractually to obligate itself to indemnify, and to advance expenses on behalf of, such persons to the fullest extent permitted by applicable law so that they will serve or continue to serve the Company free from undue concern that they will not be so indemnified;

WHEREAS, this Agreement is a supplement to and in furtherance of the By-laws of the Company and any resolutions adopted pursuant thereto, and shall not be deemed a substitute therefor, nor to diminish or abrogate any rights of Indemnitee thereunder;

WHEREAS, Indemnitee does not regard the protection available under the Company's By-laws and insurance as adequate in the present circumstances, and may not be willing to serve as a director without adequate protection, and the Company desires Indemnitee to serve in such capacity. Indemnitee is willing to serve, continue to serve and to take on additional service for or on behalf of the Company on the condition that he be so indemnified; and

NOW, THEREFORE, in consideration of Indemnitee's agreement to serve as a director after the date hereof, the parties hereto agree as follows:

1. Indemnity of Indemnitee. The Company hereby agrees to hold harmless and indemnify Indemnitee to the fullest extent permitted by law, as such may be amended from time to time. In furtherance of the foregoing indemnification, and without limiting the generality thereof:

(a) Proceedings Other Than Proceedings by or in the Right of the Company. Indemnitee shall be entitled to the rights of indemnification provided in this Section 1(a) if, by reason of his Corporate Status (as hereinafter defined), the Indemnitee is, or is threatened to be made, a party to or participant in any Proceeding (as hereinafter defined) other than a Proceeding by or in the right of the Company. Pursuant to this Section 1(a), Indemnitee shall be indemnified against all Expenses (as hereinafter defined), judgments, penalties, fines and amounts paid in settlement actually and reasonably incurred by him, or on his behalf, in connection with such Proceeding or any claim, issue or matter therein, if the Indemnitee acted in good faith and in a manner the Indemnitee reasonably believed to be in or not opposed to the best interests of the Company, and with respect to any criminal Proceeding, had no reasonable cause to believe the Indemnitee's conduct was unlawful.

(b) Proceedings by or in the Right of the Company. Indemnitee shall be entitled to the rights of indemnification provided in this Section 1(b) if, by reason of his Corporate Status, the Indemnitee is, or is threatened to be made, a party to or participant in any Proceeding brought by or in the right of the Company. Pursuant to this Section 1(b), Indemnitee shall be indemnified against all Expenses actually and reasonably incurred by the Indemnitee, or on the Indemnitee's behalf, in connection with such Proceeding if the Indemnitee acted in good faith and in a manner the Indemnitee reasonably believed to be in or not opposed to the best interests of the Company; provided, however, if applicable law so provides, no indemnification against such Expenses shall be made in respect of any claim, issue or matter in such Proceeding as to which Indemnitee shall have been adjudged to be liable to the Company unless and to the extent that the Court of Chancery of the State of Delaware shall determine that such indemnification may be made.

(c) Indemnification for Expenses of a Party Who is Wholly or Partly Successful. Notwithstanding any other provision of this Agreement, to the extent that Indemnitee is, by reason of his Corporate Status, a party to and is successful, on the merits or otherwise, in any Proceeding, he shall be indemnified to the maximum extent permitted by law, as such may be amended from time to time, against all Expenses actually and reasonably incurred by him or on his behalf in connection therewith. If Indemnitee is not wholly successful in such Proceeding but is successful, on the merits or otherwise, as to one or more but less than all claims, issues or matters in such Proceeding, the Company shall indemnify Indemnitee against all Expenses actually and reasonably incurred by him or on his behalf in connection with each successfully resolved claim, issue or matter. For purposes of this Section and without

limitation, the termination of any claim, issue or matter in such a Proceeding by dismissal, with or without prejudice, shall be deemed to be a successful result as to such claim, issue or matter.

2. Additional Indemnity. In addition to, and without regard to any limitations on, the indemnification provided for in Section 1 of this Agreement, the Company shall and hereby does indemnify and hold harmless Indemnitee against all Expenses, judgments, penalties, fines and amounts paid in settlement actually and reasonably incurred by him or on his behalf if, by reason of his Corporate Status, he is, or is threatened to be made, a party to or participant in any Proceeding (including a Proceeding by or in the right of the Company), including, without limitation, all liability arising out of the negligence or active or passive wrongdoing of Indemnitee. The only limitation that shall exist upon the

Company's obligations pursuant to this Agreement shall be that the Company shall not be obligated to make any payment to Indemnitee that is finally determined (under the procedures, and subject to the presumptions, set forth in Sections 6 and 7 hereof) to be unlawful.

3. Contribution.

(a) Whether or not the indemnification provided in Sections 1 and 2 hereof is available, in respect of any threatened, pending or completed action, suit or proceeding in which the Company is jointly liable with Indemnitee (or would be if joined in such action, suit or proceeding), the Company shall pay, in the first instance, the entire amount of any judgment or settlement of such action, suit or proceeding without requiring Indemnitee to contribute to such payment and the Company hereby waives and relinquishes any right of contribution it may have against Indemnitee. The Company shall not enter into any settlement of any action, suit or proceeding in which the Company is jointly liable with Indemnitee (or would be if joined in such action, suit or proceeding) unless such settlement provides for a full and final release of all claims asserted against Indemnitee.

(b) Without diminishing or impairing the obligations of the Company set forth in the preceding subparagraph, if, for any reason, Indemnitee shall elect or be required to pay all or any portion of any judgment or settlement in any threatened, pending or completed action, suit or proceeding in which the Company is jointly liable with Indemnitee (or would be if joined in such action, suit or proceeding), the Company shall contribute to the amount of expenses (including attorneys' fees), judgments, fines and amounts paid in settlement actually and reasonably incurred and paid or payable by Indemnitee in proportion to the relative benefits received by the Company and all officers, directors or employees of the Company, other than Indemnitee, who are jointly liable with Indemnitee (or would be if joined in such action, suit or proceeding), on the one hand, and Indemnitee, on the other hand, from the transaction from which such action, suit or proceeding arose; provided, however, that the proportion determined on the basis of relative benefit may, to the extent necessary to conform to law, be further adjusted by reference to the relative fault of the Company and all officers, directors or employees of the Company other than Indemnitee who are jointly liable with Indemnitee (or would be if joined in such action, suit or proceeding), on the one hand, and Indemnitee, on the other hand, in connection with the events that resulted in such expenses, judgments, fines or settlement amounts, as well as any other equitable considerations which the Law may require to be considered. The relative fault of the Company and all officers, directors or employees of the Company, other than Indemnitee, who are jointly liable with Indemnitee (or would be if joined in such action, suit or proceeding), on the one hand, and Indemnitee, on the other hand, shall be determined by reference to, among other things, the degree to which their actions were motivated

by intent to gain personal profit or advantage, the degree to which their liability is primary or secondary and the degree to which their conduct is active or passive.

(c) The Company hereby agrees to fully indemnify and hold Indemnitee harmless from any claims of contribution which may be brought by officers, directors or employees of the Company, other than Indemnitee, who may be jointly liable with Indemnitee.

(d) To the fullest extent permissible under applicable law, if the indemnification provided for in this Agreement is unavailable to Indemnitee for any reason whatsoever, the Company, in lieu of indemnifying Indemnitee, shall contribute to the amount incurred by Indemnitee, whether for judgments, fines, penalties, excise taxes, amounts paid or to be paid in settlement and/or for Expenses, in connection with any claim relating to an indemnifiable event under this Agreement, in such proportion as is deemed fair and reasonable in light of all of the circumstances of such Proceeding in order to reflect (i) the relative benefits received by the Company and Indemnitee as a result of the event(s) and/or transaction(s) giving cause to such Proceeding; and/or (ii) the relative fault of the Company (and its directors, officers, employees and agents) and Indemnitee in connection with such event(s) and/or transaction(s).

4. Indemnification for Expenses of a Witness. Notwithstanding any other provision of this Agreement, to the extent that Indemnitee is, by reason of his Corporate Status, a witness in any Proceeding to which Indemnitee is not a party, he shall be indemnified against all Expenses actually and reasonably incurred by him or on his behalf in connection therewith.

5. Advancement of Expenses. Notwithstanding any other provision of this Agreement, the Company shall advance all Expenses incurred by or on behalf of Indemnitee in connection with any Proceeding by reason of Indemnitee's Corporate Status within thirty (30) days after the receipt by the Company of a statement or statements from Indemnitee requesting such advance or advances from time to time, whether prior to or after final disposition of such Proceeding. Such statement or statements shall reasonably evidence the Expenses incurred by Indemnitee and shall include or be preceded or accompanied by an undertaking by or on behalf of Indemnitee to repay any Expenses advanced if it shall ultimately be determined that Indemnitee is not entitled to be indemnified against such Expenses. Any advances and undertakings to repay pursuant to this Section 5 shall be unsecured and interest free.

6. Procedures and Presumptions for Determination of Entitlement to Indemnification. It is the intent of this Agreement to secure for Indemnitee rights of indemnity that are as favorable as may be permitted under the Delaware General Corporation Law and public policy of the State of Delaware. Accordingly, the parties agree that the following procedures and presumptions shall apply in the event of any question as to whether Indemnitee is entitled to indemnification under this Agreement:

(a) To obtain indemnification under this Agreement, Indemnitee shall submit to the Company a written request, including therein or therewith such documentation and information as is reasonably available to Indemnitee and is reasonably necessary to determine whether and to what extent Indemnitee is entitled to indemnification. The Secretary of the Company shall, promptly upon receipt of such a request for indemnification, advise the Board of Directors in writing that Indemnitee has requested indemnification.

(b) Upon written request by Indemnitee for indemnification pursuant to the first sentence of Section 6(a) hereof, a determination, if required by applicable law, with respect to Indemnitee's entitlement thereto shall be made in the specific case by one of the following three methods, which shall be at the election of the board: (1) by a majority vote of the disinterested directors, even though less than a quorum, by a committee of disinterested directors designated by a majority vote of the disinterested directors, even though less than a quorum, (2) if there are no disinterested directors or if the disinterested directors so direct, by independent legal counsel in a written opinion to the Board of Directors, a copy of which shall be delivered to the Indemnitee, or (3) if so directed by the Board of Directors, by the stockholders of the Company. For purposes hereof, disinterested directors are those members of the board of directors of the Company who are not parties to the action, suit or proceeding in respect of which indemnification is sought by Indemnitee.

(c) If the determination of entitlement to indemnification is to be made by Independent Counsel pursuant to Section 6(b) hereof, the Independent Counsel shall be selected as provided in this Section 6(c). The determination of whether Independent Counsel shall be engaged and the selection of such Independent Counsel shall be made by the Board of Directors. Indemnitee may, within 10 days after such written notice of selection shall have been given, deliver to the Company, as the case may be, a written objection to such selection; provided, however, that such objection may be asserted only on the ground that the Independent Counsel so selected does not meet the requirements of "**Independent Counsel**" as defined in Section 13 of this Agreement, and the objection shall set forth with particularity the factual basis of such assertion. Absent a proper and timely objection, the person so selected shall act as Independent Counsel. If a written objection is made and substantiated, the Independent Counsel selected may not serve as Independent Counsel unless and until such objection is withdrawn or a court has determined that such objection is without merit. If, within 20 days after submission by Indemnitee of a written request for indemnification pursuant to Section 6(a) hereof, no Independent Counsel shall have been selected and not objected to, either the Company or Indemnitee may petition the Court of Chancery of the State of Delaware or other court of competent jurisdiction for resolution of any objection which shall have been made by the Indemnitee to the Company's selection of Independent Counsel and/or for the appointment as Independent Counsel of a person selected by the court or by such other person as the court shall designate, and the person with respect to whom all objections are so resolved or the person so appointed shall act as Independent Counsel under Section 6(b) hereof. The Company shall pay any and all reasonable fees and expenses of Independent Counsel incurred by such Independent Counsel in connection with acting pursuant to

Section 6(b) hereof, and the Company shall pay all reasonable fees and expenses incident to the procedures of this Section 6(c), regardless of the manner in which such Independent Counsel was selected or appointed.

(d) In making a determination with respect to entitlement to indemnification hereunder, the person or persons or entity making such determination shall presume that Indemnitee is entitled to indemnification under this Agreement. Anyone seeking to overcome this presumption shall have the burden of proof and the burden of persuasion by clear and convincing evidence. Neither the failure of the Company (including by its directors or independent legal counsel) to have made a determination prior to the commencement of any action pursuant to this Agreement that indemnification is proper in the circumstances because Indemnitee has met the applicable standard of conduct, nor an actual determination by the Company (including by its directors or independent legal counsel) that Indemnitee has not met

such applicable standard of conduct, shall be a defense to the action or create a presumption that Indemnitee has not met the applicable standard of conduct.

(e) Indemnitee shall be deemed to have acted in good faith if Indemnitee's action is based on the records or books of account of the Enterprise (as hereinafter defined), including financial statements, or on information supplied to Indemnitee by the officers of the Enterprise in the course of their duties, or on the advice of legal counsel for the Enterprise or on information or records given or reports made to the Enterprise by an independent certified public accountant or by an appraiser or other expert selected with reasonable care by the Enterprise. In addition, the knowledge and/or actions, or failure to act, of any director, officer, agent or employee of the Enterprise shall not be imputed to Indemnitee for purposes of determining the right to indemnification under this Agreement. Whether or not the foregoing provisions of this Section 6(e) are satisfied, it shall in any event be presumed that Indemnitee has at all times acted in good faith and in a manner he reasonably believed to be in or not opposed to the best interests of the Company. Anyone seeking to overcome this presumption shall have the burden of proof and the burden of persuasion by clear and convincing evidence.

(f) If the person, persons or entity empowered or selected under Section 6 to determine whether Indemnitee is entitled to indemnification shall not have made a determination within sixty (60) days after receipt by the Company of the request therefor, the requisite determination of entitlement to indemnification shall be deemed to have been made and Indemnitee shall be entitled to such indemnification absent (i) a misstatement by Indemnitee of a material fact, or an omission of a material fact necessary to make Indemnitee's statement not materially misleading, in connection with the request for indemnification, or (ii) a prohibition of such indemnification under applicable law; provided, however, that such 60-day period may be extended for a reasonable time, not to exceed an additional thirty (30) days, if the person, persons or entity making such determination with respect to entitlement to indemnification in good faith requires such additional time to obtain or evaluate documentation and/or information relating thereto; and provided, further, that the foregoing provisions of this Section 6(f) shall not apply if the determination of entitlement to indemnification is to be made by the stockholders pursuant to Section 6(b) of this Agreement and if (A) within fifteen (15) days after receipt by the Company of the request for such determination, the Board of Directors or the Disinterested Directors, if appropriate, resolve to submit such determination to the stockholders for their consideration at an annual meeting thereof to be held within seventy-five (75) days after such receipt and such determination is made thereat, or (B) a special meeting of stockholders is called within fifteen (15) days after such receipt for the purpose of making such determination, such meeting is held for such purpose within sixty (60) days after having been so called and such determination is made thereat.

(g) Indemnitee shall cooperate with the person, persons or entity making such determination with respect to Indemnitee's entitlement to indemnification, including providing to such person, persons or entity upon reasonable advance request any documentation or information which is not privileged or otherwise protected from disclosure and which is reasonably available to Indemnitee and reasonably necessary to such determination. Any Independent Counsel, member of the Board of Directors or stockholder of the Company shall act reasonably and in good faith in making a determination regarding the Indemnitee's entitlement to indemnification under this Agreement. Any costs or expenses (including attorneys' fees and disbursements) incurred by Indemnitee in so cooperating with the person, persons or entity making such determination shall be borne by the Company (irrespective of the

determination as to Indemnitee's entitlement to indemnification) and the Company hereby indemnifies and agrees to hold Indemnitee harmless therefrom.

(h) The Company acknowledges that a settlement or other disposition short of final judgment may be successful if it permits a party to avoid expense, delay, distraction, disruption and uncertainty. In the event that any action, claim or proceeding to which Indemnitee is a party is resolved in any manner other than by adverse judgment against Indemnitee (including, without limitation, settlement of such action, claim or proceeding with or without payment of money or other consideration) it shall be presumed that Indemnitee has been successful on the merits or otherwise in such action, suit or proceeding. Anyone seeking to overcome this presumption shall have the burden of proof and the burden of persuasion by clear and convincing evidence.

(i) The termination of any Proceeding or of any claim, issue or matter therein, by judgment, order, settlement or conviction, or upon a plea of nolo contendere or its equivalent, shall not (except as otherwise expressly provided in this Agreement) of itself adversely affect the right of Indemnitee to indemnification or create a presumption that Indemnitee did not act in good faith and in a manner which he reasonably believed to be in or not opposed to the best interests of the Company or, with respect to any criminal Proceeding, that Indemnitee had reasonable cause to believe that his conduct was unlawful.

7. Remedies of Indemnitee.

(a) In the event that (i) a determination is made pursuant to Section 6 of this Agreement that Indemnitee is not entitled to indemnification under this Agreement, (ii) advancement of Expenses is not timely made pursuant to Section 5 of this Agreement, (iii) no determination of entitlement to indemnification is made pursuant to Section 6(b) of this Agreement within 90 days after receipt by the Company of the request for indemnification, (iv) payment of indemnification is not made pursuant to this Agreement within ten (10) days after receipt by the Company of a written request therefor or (v) payment of indemnification is not made within ten (10) days after a determination has been made that Indemnitee is entitled to indemnification or such determination is deemed to have been made pursuant to Section 6 of this Agreement, Indemnitee shall be entitled to an adjudication in an appropriate court of the State of Delaware, or in any other court of competent jurisdiction, of Indemnitee's entitlement to such indemnification. Indemnitee shall commence such proceeding seeking an adjudication within 180 days following the date on which Indemnitee first has the right to commence such proceeding pursuant to this Section 7(a). The Company shall not oppose Indemnitee's right to seek any such adjudication.

(b) In the event that a determination shall have been made pursuant to Section 6(b) of this Agreement that Indemnitee is not entitled to indemnification, any judicial proceeding commenced pursuant to this Section 7 shall be conducted in all respects as a de novo trial on the merits, and Indemnitee shall not be prejudiced by reason of the adverse determination under Section 6(b).

(c) If a determination shall have been made pursuant to Section 6(b) of this Agreement that Indemnitee is entitled to indemnification, the Company shall be bound by such determination in any judicial proceeding commenced pursuant to this Section 7, absent (i) a misstatement by Indemnitee of a material fact, or an omission of a material fact necessary to

make Indemnitee's statement not materially misleading in connection with the application for indemnification, or (ii) a prohibition of such indemnification under applicable law.

(d) In the event that Indemnitee, pursuant to this Section 7, seeks a judicial adjudication of his rights under, or to recover damages for breach of, this Agreement, or to recover under any directors' and officers' liability insurance policies maintained by the Company, the Company shall pay on his behalf, in advance, any and

all expenses (of the types described in the definition of Expenses in Section 13 of this Agreement) actually and reasonably incurred by him in such judicial adjudication, regardless of whether Indemnitee ultimately is determined to be entitled to such indemnification, advancement of expenses or insurance recovery.

(e) The Company shall be precluded from asserting in any judicial proceeding commenced pursuant to this Section 7 that the procedures and presumptions of this Agreement are not valid, binding and enforceable and shall stipulate in any such court that the Company is bound by all the provisions of this Agreement. The Company shall indemnify Indemnitee against any and all Expenses and, if requested by Indemnitee, shall (within ten (10) days after receipt by the Company of a written request therefore) advance, to the extent not prohibited by law, such expenses to Indemnitee, which are incurred by Indemnitee in connection with any action brought by Indemnitee for indemnification or advance of Expenses from the Company under this Agreement or under any directors' and officers' liability insurance policies maintained by the Company, regardless of whether Indemnitee ultimately is determined to be entitled to such indemnification, advancement of Expenses or insurance recovery, as the case may be.

(f) Notwithstanding anything in this Agreement to the contrary, no determination as to entitlement to indemnification under this Agreement shall be required to be made prior to the final disposition of the Proceeding.

8. Non-Exclusivity; Survival of Rights; Insurance; Subrogation.

(a) The rights of indemnification as provided by this Agreement shall not be deemed exclusive of any other rights to which Indemnitee may at any time be entitled under applicable law, the certificate of incorporation of the Company, the Bylaws, any agreement, a vote of stockholders, a resolution of directors or otherwise. No amendment, alteration or repeal of this Agreement or of any provision hereof shall limit or restrict any right of Indemnitee under this Agreement in respect of any action taken or omitted by such Indemnitee in his Corporate Status prior to such amendment, alteration or repeal. To the extent that a change in the Delaware General Corporation Law, whether by statute or judicial decision, permits greater indemnification than would be afforded currently under the Bylaws and this Agreement, it is the intent of the parties hereto that Indemnitee shall enjoy by this Agreement the greater benefits so afforded by such change. No right or remedy herein conferred is intended to be exclusive of any other right or remedy, and every other right and remedy shall be cumulative and in addition to every other right and remedy given hereunder or now or hereafter existing at law or in equity or otherwise. The assertion or employment of any right or remedy hereunder, or otherwise, shall not prevent the concurrent assertion or employment of any other right or remedy.

(b) To the extent that the Company maintains an insurance policy or policies providing liability insurance for directors, officers, employees, or agents or fiduciaries of

the Company or of any other corporation, partnership, joint venture, trust, employee benefit plan or other enterprise that such person serves at the request of the Company, Indemnitee shall be covered by such policy or policies in accordance with its or their terms to the maximum extent of the coverage available for any director, officer, employee, agent or fiduciary under such policy or policies. If, at the time of the receipt of a notice of a claim pursuant to the terms hereof, the Company has director and officer liability insurance in effect, the Company shall give prompt notice of the commencement of such proceeding to the insurers in accordance with the procedures set forth in the respective policies. The Company shall thereafter take all necessary or desirable action to cause such insurers to pay, on behalf of the Indemnitee, all amounts payable as a result of such proceeding in accordance with the terms of such policies.

(c) In the event of any payment under this Agreement, the Company shall be subrogated to the extent of such payment to all of the rights of recovery of Indemnitee, who shall execute all papers required and take all action necessary to secure such rights, including execution of such documents as are necessary to enable the Company to bring suit to enforce such rights.

(d) The Company shall not be liable under this Agreement to make any payment of amounts otherwise indemnifiable hereunder if and to the extent that Indemnitee has otherwise actually received such payment under any insurance policy, contract, agreement or otherwise.

(e) The Company's obligation to indemnify or advance Expenses hereunder to Indemnitee who is or was serving at the request of the Company as a director, officer, employee or agent of any other corporation, partnership, joint venture, trust, employee benefit plan or other enterprise shall be reduced by any amount Indemnitee has actually received as indemnification or advancement of expenses from such other corporation, partnership, joint venture, trust, employee benefit plan or other enterprise.

9. Exception to Right of Indemnification. Notwithstanding any provision in this Agreement, the Company shall not be obligated under this Agreement to make any indemnity in connection with any claim made against Indemnitee:

(a) for which payment has actually been made to or on behalf of Indemnitee under any insurance policy or other indemnity provision, except with respect to any excess beyond the amount paid under any insurance policy or other indemnity provision; or

(b) for an accounting of profits made from the purchase and sale (or sale and purchase) by Indemnitee of securities of the Company within the meaning of Section 16(b) of the Securities Exchange Act of 1934, as amended, or similar provisions of state statutory law or common law; or

(c) in connection with any Proceeding (or any part of any Proceeding) initiated by Indemnitee, including any Proceeding (or any part of any Proceeding) initiated by Indemnitee against the Company or its directors, officers, employees or other indemnitees, unless (i) the Board of Directors of the Company authorized the Proceeding (or any part of any Proceeding) prior to its initiation or (ii) the Company provides the indemnification, in its sole discretion, pursuant to the powers vested in the Company under applicable law.

10. Duration of Agreement. All agreements and obligations of the Company contained herein shall continue during the period Indemnitee is a director of the Company (or is or was serving at the request of the Company as a director, officer, employee or agent of another corporation, partnership, joint venture, trust or other enterprise) and for a period of five (5) years thereafter, and in addition shall continue thereafter so long as Indemnitee shall be subject to any Proceeding (or any proceeding commenced under Section 7 hereof) by reason of his Corporate Status, whether or not he is acting or serving in any such capacity at the time any liability or expense is incurred for which indemnification can be provided under this Agreement. This Agreement shall be binding upon and inure to the benefit of and be enforceable by the parties hereto and their respective successors (including any direct or indirect successor by purchase, merger, consolidation or otherwise to all or substantially all of the business or assets of the Company), assigns, spouses, heirs, executors and personal and legal representatives.

11. Security. To the extent requested by Indemnitee and approved by the Board of Directors of the Company, the Company may at any time and from time to time provide security to Indemnitee for the Company's obligations hereunder through an irrevocable bank line of credit, funded trust or other collateral. Any such security, once provided to Indemnitee, may not be revoked or released without the prior written consent of the Indemnitee.

12. Enforcement.

(a) The Company expressly confirms and agrees that it has entered into this Agreement and assumes the obligations imposed on it hereby in order to induce Indemnitee to serve as a director of the Company, and the Company acknowledges that Indemnitee is relying upon this Agreement in serving as a director of the Company.

(b) This Agreement constitutes the entire agreement between the parties hereto with respect to the subject matter hereof and supersedes all prior agreements and understandings, oral, written and implied, between the parties hereto with respect to the subject matter hereof.

13. Definitions. For purposes of this Agreement:

(a) "**Corporate Status**" describes the status of a person who is or was a director, officer, employee, agent or fiduciary of the Company or of any other corporation, partnership, joint venture, trust, employee benefit plan or other enterprise that such person is or was serving at the express written request of the Company.

(b) "**Disinterested Director**" means a director of the Company who is not and was not a party to the Proceeding in respect of which indemnification is sought by Indemnitee.

(c) "**Enterprise**" shall mean the Company and any other corporation, partnership, joint venture, trust, employee benefit plan or other enterprise that Indemnitee is or was serving at the express written request of the Company as a director, officer, employee, agent or fiduciary.

(d) "**Expenses**" shall include all reasonable attorneys' fees, retainers, court costs, transcript costs, fees of experts, witness fees, travel expenses, duplicating costs,

printing and binding costs, telephone charges, postage, delivery service fees and all other disbursements or expenses of the types customarily incurred in connection with prosecuting, defending, preparing to prosecute or defend, investigating, participating, or being or preparing to be a witness in a Proceeding. Expenses also shall include Expenses incurred in connection with any appeal resulting from any Proceeding, including without limitation the premium, security for, and other costs relating to any cost bond, supersedeas bond, or other appeal bond or its equivalent. Expenses, however, shall not include amounts paid in settlement by Indemnitee or the amount of judgments or fines against Indemnitee.

(e) "**Independent Counsel**" means a law firm, or a member of a law firm, that is experienced in matters of corporation law and neither presently is, nor in the past five years has been, retained to represent: (i) the Company or Indemnitee in any matter material to either such party (other than with respect to matters concerning Indemnitee under this Agreement, or of other indemnitees under similar indemnification agreements), or (ii) any other party to the Proceeding giving rise to a claim for indemnification hereunder. Notwithstanding the foregoing, the term "Independent Counsel" shall not include any person who, under the applicable standards of professional conduct then prevailing, would have a conflict of interest in representing either the Company or Indemnitee in an action to determine Indemnitee's rights under this Agreement. The Company agrees to pay the reasonable fees of the Independent Counsel referred to above and to fully indemnify such counsel against any and all Expenses, claims, liabilities and damages arising out of or relating to this Agreement or its engagement pursuant hereto.

(f) "**Proceeding**" includes any threatened, pending or completed action, suit, arbitration, alternate dispute resolution mechanism, investigation, inquiry, administrative hearing or any other actual, threatened or completed proceeding, whether brought by or in the right of the Company or otherwise and whether civil, criminal, administrative or investigative, in which Indemnitee was, is or will be involved as a party or otherwise, by reason of the fact that Indemnitee is or was a director of the Company, by reason of any action taken by him or of any inaction on his part while acting as a director of the Company, or by reason of the fact that he is or was serving at the request of the Company as a director, officer, employee, agent or fiduciary of another corporation, partnership, joint venture, trust or other Enterprise; in each case whether or not he is acting or serving in any such capacity at the time any liability or expense is incurred for which indemnification can be provided under this Agreement; including one pending on or before the date of this Agreement, but excluding one initiated by an Indemnitee pursuant to Section 7 of this Agreement to enforce his rights under this Agreement.

14. Severability. The invalidity of unenforceability of any provision hereof shall in no way affect the validity or enforceability of any other provision. Without limiting the generality of the foregoing, this Agreement is intended to confer upon Indemnitee indemnification rights to the fullest extent permitted by applicable laws. In the event any provision hereof conflicts with any applicable law, such provision shall be deemed modified, consistent with the aforementioned intent, to the extent necessary to resolve such conflict.

15. Modification and Waiver. No supplement, modification, termination or amendment of this Agreement shall be binding unless executed in writing by both of the parties hereto. No waiver of any of the provisions of this Agreement shall be deemed or shall constitute a waiver of any other provisions hereof (whether or not similar) nor shall such waiver constitute a continuing waiver.

16. Notice By Indemnitee. Indemnitee agrees promptly to notify the Company in writing upon being served with or otherwise receiving any summons, citation, subpoena, complaint, indictment, information or other document relating to any Proceeding or matter which may be subject to indemnification covered hereunder. The failure to so notify the Company shall not relieve the Company of any obligation which it may have to Indemnitee under this Agreement or otherwise unless and only to the extent that such failure or delay materially prejudices the Company.

17. Notices. All notices and other communications given or made pursuant to this Agreement shall be in writing and shall be deemed effectively given: (a) upon personal delivery to the party to be notified, (b) when sent by confirmed electronic mail or facsimile if sent during normal business hours of the recipient, and if not so confirmed, then on the next business day, (c) five (5) days after having been sent by registered or certified mail, return receipt requested, postage prepaid, or (d) one (1) day after deposit with a nationally recognized overnight courier, specifying next day delivery, with written verification of receipt. All communications shall be sent:

(a) To Indemnitee at the address set forth below Indemnitee's signature hereto.

(b) To the Company at:

200 West Street
Waltham, MA 02451
Attention: CEO

or to such other address as may have been furnished to Indemnitee by the Company or to the Company by Indemnitee, as the case may be.

18. Counterparts. This Agreement may be executed in two or more counterparts, each of which shall be deemed an original, but all of which together shall constitute one and the same Agreement. This Agreement may also be executed and delivered by facsimile signature and in two or more counterparts, each of which shall be deemed an original, but all of which together shall constitute one and the same instrument.

19. Headings. The headings of the paragraphs of this Agreement are inserted for convenience only and shall not be deemed to constitute part of this Agreement or to affect the construction thereof.

20. Governing Law and Consent to Jurisdiction. This Agreement and the legal relations among the parties shall be governed by, and construed and enforced in accordance with, the laws of the State of Delaware, without regard to its conflict of laws rules. The Company and Indemnitee hereby irrevocably and unconditionally (i) agree that any action or proceeding arising out of or in connection with this Agreement shall be brought only in the Chancery Court of the State of Delaware (the "**Delaware Court**"), and not in any other state or federal court in the United States of America or any court in any other country, (ii) consent to submit to the exclusive jurisdiction of the Delaware Court for

purposes of any action or proceeding arising out of or in connection with this Agreement, (iii) waive any objection to the laying of venue of any such action or proceeding in the Delaware Court, and (iv) waive, and agree not to plead or to

make, any claim that any such action or proceeding brought in the Delaware Court has been brought in an improper or inconvenient forum.

SIGNATURE PAGE TO FOLLOW

IN WITNESS WHEREOF, the parties hereto have executed this Indemnification Agreement on and as of the day and year first above written.

PROTEON THERAPEUTICS, INC.

By: /s/Timothy Noyes

Name: Timothy Noyes

Title: CEO

INDEMNITEE

/s/ F. Nicholas Franano, M.D.
Name: F. Nicholas Franano, M.D.

Address:
1010 W. 69th Terrace
Kansas City, MO 64113

SIGNATURE PAGE TO INDEMNIFICATION AGREEMENT - FRANANO

INDEMNIFICATION AGREEMENT

THIS INDEMNIFICATION AGREEMENT (the "**Agreement**") is made and entered into as of February 6, 2013 between **PROTEON THERAPEUTICS, INC**., a Delaware corporation (the "**Company**"), and Gregory D. Phelps ("**Indemnitee**").

WITNESSETH THAT:

WHEREAS, highly competent persons have become more reluctant to serve corporations as directors or in other capacities unless they are provided with adequate protection through insurance or adequate indemnification against inordinate risks of claims and actions against them arising out of their service to and activities on behalf of the corporation;

WHEREAS, the Board of Directors of the Company (the "**Board**") has determined that, in order to attract and retain qualified individuals, the Company will attempt to maintain on an ongoing basis, at its sole expense, liability insurance to protect persons serving the Company and its subsidiaries from certain liabilities. Although the furnishing of such insurance has been a customary and widespread practice among United States-based corporations and other business enterprises, the Company believes that, given current market conditions and trends, such insurance may be available to it in the future only at higher premiums and with more exclusions. At the same time, directors, officers, and other persons in service to corporations or business enterprises are being increasingly subjected to expensive and time-consuming litigation relating to, among other things, matters that traditionally would have been brought only against the Company or business enterprise itself. The Certificate of Incorporation of the Company permits, and the By-laws of the Company require, indemnification of directors of the Company. Indemnitee may also be entitled to indemnification pursuant to the General Corporation Law of the State of Delaware ("**DGCL**"). The By-laws and the DGCL expressly provide that the indemnification provisions set forth therein are not exclusive, and thereby contemplate that contracts may be entered into between the Company and members of the board of directors with respect to indemnification;

WHEREAS, the uncertainties relating to such insurance and to indemnification have increased the difficulty of attracting and retaining such persons;

WHEREAS, the Board has determined that the increased difficulty in attracting and retaining such persons is detrimental to the best interests of the Company's stockholders and that the Company should act to assure such persons that there will be increased certainty of such protection in the future;

WHEREAS, it is reasonable, prudent and necessary for the Company contractually to obligate itself to indemnify, and to advance expenses on behalf of, such persons to the fullest extent permitted by applicable law so that they will serve or continue to serve the Company free from undue concern that they will not be so indemnified;

WHEREAS, this Agreement is a supplement to and in furtherance of the By-laws of the Company and any resolutions adopted pursuant thereto, and shall not be deemed a substitute therefor, nor to diminish or abrogate any rights of Indemnitee thereunder;

WHEREAS, Indemnitee does not regard the protection available under the Company's By-laws and insurance as adequate in the present circumstances, and may not be willing to serve as a director without adequate protection, and the Company desires Indemnitee to serve in such capacity. Indemnitee is willing to serve, continue to serve and to take on additional service for or on behalf of the Company on the condition that he be so indemnified; and

NOW, THEREFORE, in consideration of Indemnitee's agreement to serve as a director after the date hereof, the parties hereto agree as follows:

1. Indemnity of Indemnitee. The Company hereby agrees to hold harmless and indemnify Indemnitee to the fullest extent permitted by law, as such may be amended from time to time. In furtherance of the foregoing indemnification, and without limiting the generality thereof:

(a) Proceedings Other Than Proceedings by or in the Right of the Company. Indemnitee shall be entitled to the rights of indemnification provided in this Section 1(a) if, by reason of his Corporate Status (as hereinafter defined), the Indemnitee is, or is threatened to be made, a party to or participant in any Proceeding (as hereinafter defined) other than a Proceeding by or in the right of the Company. Pursuant to this Section 1(a), Indemnitee shall be indemnified against all Expenses (as hereinafter defined), judgments, penalties, fines and amounts paid in settlement actually and reasonably incurred by him, or on his behalf, in connection with such Proceeding or any claim, issue or matter therein, if the Indemnitee acted in good faith and in a manner the Indemnitee reasonably believed to be in or not opposed to the best interests of the Company, and with respect to any criminal Proceeding, had no reasonable cause to believe the Indemnitee's conduct was unlawful.

(b) Proceedings by or in the Right of the Company. Indemnitee shall be entitled to the rights of indemnification provided in this Section 1(b) if, by reason of his Corporate Status, the Indemnitee is, or is threatened to be made, a party to or participant in any Proceeding brought by or in the right of the Company. Pursuant to this Section 1(b), Indemnitee shall be indemnified against all Expenses actually and reasonably incurred by the Indemnitee, or on the Indemnitee's behalf, in connection with such Proceeding if the Indemnitee acted in good faith and in a manner the Indemnitee reasonably believed to be in or not opposed to the best interests of the Company; provided, however, if applicable law so provides, no indemnification against such Expenses shall be made in respect of any claim, issue or matter in such Proceeding as to which Indemnitee shall have been adjudged to be liable to the Company unless and to the extent that the Court of Chancery of the State of Delaware shall determine that such indemnification may be made.

(c) Indemnification for Expenses of a Party Who is Wholly or Partly Successful. Notwithstanding any other provision of this Agreement, to the extent that Indemnitee is, by reason of his Corporate Status, a party to and is successful, on the merits or otherwise, in any Proceeding, he shall be indemnified to the maximum extent permitted by law, as such may be amended from time to time, against all Expenses actually and reasonably incurred by him or on his behalf in connection therewith. If Indemnitee is not wholly successful in such Proceeding but is successful, on the merits or otherwise, as to one or more but less than all claims, issues or matters in such Proceeding, the Company shall indemnify Indemnitee against all Expenses actually and reasonably incurred by him or on his behalf in connection with each successfully resolved claim, issue or matter. For purposes of this Section and without

limitation, the termination of any claim, issue or matter in such a Proceeding by dismissal, with or without prejudice, shall be deemed to be a successful result as to such claim, issue or matter.

2. Additional Indemnity. In addition to, and without regard to any limitations on, the indemnification provided for in Section 1 of this Agreement, the Company shall and hereby does indemnify and hold harmless Indemnitee against all Expenses, judgments, penalties, fines and amounts paid in settlement actually and reasonably incurred by him or on his behalf if, by reason of his Corporate Status, he is, or is threatened to be made, a party to or participant in any Proceeding (including a Proceeding by or in the right of the Company), including, without limitation, all liability arising out of the negligence or active or passive wrongdoing of Indemnitee. The only limitation that shall exist

upon the Company's obligations pursuant to this Agreement shall be that the Company shall not be obligated to make any payment to Indemnitee that is finally determined (under the procedures, and subject to the presumptions, set forth in Sections 6 and 7 hereof) to be unlawful.

3. Contribution.

(a) Whether or not the indemnification provided in Sections 1 and 2 hereof is available, in respect of any threatened, pending or completed action, suit or proceeding in which the Company is jointly liable with Indemnitee (or would be if joined in such action, suit or proceeding), the Company shall pay, in the first instance, the entire amount of any judgment or settlement of such action, suit or proceeding without requiring Indemnitee to contribute to such payment and the Company hereby waives and relinquishes any right of contribution it may have against Indemnitee. The Company shall not enter into any settlement of any action, suit or proceeding in which the Company is jointly liable with Indemnitee (or would be if joined in such action, suit or proceeding) unless such settlement provides for a full and final release of all claims asserted against Indemnitee.

(b) Without diminishing or impairing the obligations of the Company set forth in the preceding subparagraph, if, for any reason, Indemnitee shall elect or be required to pay all or any portion of any judgment or settlement in any threatened, pending or completed action, suit or proceeding in which the Company is jointly liable with Indemnitee (or would be if joined in such action, suit or proceeding), the Company shall contribute to the amount of expenses (including attorneys' fees), judgments, fines and amounts paid in settlement actually and reasonably incurred and paid or payable by Indemnitee in proportion to the relative benefits received by the Company and all officers, directors or employees of the Company, other than Indemnitee, who are jointly liable with Indemnitee (or would be if joined in such action, suit or proceeding), on the one hand, and Indemnitee, on the other hand, from the transaction from which such action, suit or proceeding arose; provided, however, that the proportion determined on the basis of relative benefit may, to the extent necessary to conform to law, be further adjusted by reference to the relative fault of the Company and all officers, directors or employees of the Company other than Indemnitee who are jointly liable with Indemnitee (or would be if joined in such action, suit or proceeding), on the one hand, and Indemnitee, on the other hand, in connection with the events that resulted in such expenses, judgments, fines or settlement amounts, as well as any other equitable considerations which the Law may require to be considered. The relative fault of the Company and all officers, directors or employees of the Company, other than Indemnitee, who are jointly liable with Indemnitee (or would be if joined in such action, suit or proceeding), on the one hand, and Indemnitee, on the other hand, shall be determined by reference to, among other things, the degree to which their actions were motivated

by intent to gain personal profit or advantage, the degree to which their liability is primary or secondary and the degree to which their conduct is active or passive.

(c) The Company hereby agrees to fully indemnify and hold Indemnitee harmless from any claims of contribution which may be brought by officers, directors or employees of the Company, other than Indemnitee, who may be jointly liable with Indemnitee.

(d) To the fullest extent permissible under applicable law, if the indemnification provided for in this Agreement is unavailable to Indemnitee for any reason whatsoever, the Company, in lieu of indemnifying Indemnitee, shall contribute to the amount incurred by Indemnitee, whether for judgments, fines, penalties, excise taxes, amounts paid or to be paid in settlement and/or for Expenses, in connection with any claim relating to an indemnifiable event under this Agreement, in such proportion as is deemed fair and reasonable in light of all of the circumstances of such Proceeding in order to reflect (i) the relative benefits received by the Company and Indemnitee as a result of the event(s) and/or transaction(s) giving cause to such Proceeding; and/or (ii) the relative fault of the Company (and its directors, officers, employees and agents) and Indemnitee in connection with such event(s) and/or transaction(s).

4. Indemnification for Expenses of a Witness. Notwithstanding any other provision of this Agreement, to the extent that Indemnitee is, by reason of his Corporate Status, a witness in any Proceeding to which Indemnitee is not a party, he shall be indemnified against all Expenses actually and reasonably incurred by him or on his behalf in connection therewith.

5. Advancement of Expenses. Notwithstanding any other provision of this Agreement, the Company shall advance all Expenses incurred by or on behalf of Indemnitee in connection with any Proceeding by reason of Indemnitee's Corporate Status within thirty (30) days after the receipt by the Company of a statement or statements from Indemnitee requesting such advance or advances from time to time, whether prior to or after final disposition of such Proceeding. Such statement or statements shall reasonably evidence the Expenses incurred by Indemnitee and shall include or be preceded or accompanied by an undertaking by or on behalf of Indemnitee to repay any Expenses advanced if it shall ultimately be determined that Indemnitee is not entitled to be indemnified against such Expenses. Any advances and undertakings to repay pursuant to this Section 5 shall be unsecured and interest free.

6. Procedures and Presumptions for Determination of Entitlement to Indemnification. It is the intent of this Agreement to secure for Indemnitee rights of indemnity that are as favorable as may be permitted under the Delaware General Corporation Law and public policy of the State of Delaware. Accordingly, the parties agree that the following procedures and presumptions shall apply in the event of any question as to whether Indemnitee is entitled to indemnification under this Agreement:

(a) To obtain indemnification under this Agreement, Indemnitee shall submit to the Company a written request, including therein or therewith such documentation and information as is reasonably available to Indemnitee and is reasonably necessary to determine whether and to what extent Indemnitee is entitled to indemnification. The Secretary of the Company shall, promptly upon receipt of such a request for indemnification, advise the Board of Directors in writing that Indemnitee has requested indemnification.

(b) Upon written request by Indemnitee for indemnification pursuant to the first sentence of Section 6(a) hereof, a determination, if required by applicable law, with respect to Indemnitee's entitlement thereto shall be made in the specific case by one of the following three methods, which shall be at the election of the board: (1) by a majority vote of the disinterested directors, even though less than a quorum, by a committee of disinterested directors designated by a majority vote of the disinterested directors, even though less than a quorum, (2) if there are no disinterested directors or if the disinterested directors so direct, by independent legal counsel in a written opinion to the Board of Directors, a copy of which shall be delivered to the Indemnitee, or (3) if so directed by the Board of Directors, by the stockholders of the Company. For purposes hereof, disinterested directors are those members of the board of directors of the Company who are not parties to the action, suit or proceeding in respect of which indemnification is sought by Indemnitee.

(c) If the determination of entitlement to indemnification is to be made by Independent Counsel pursuant to Section 6(b) hereof, the Independent Counsel shall be selected as provided in this Section 6(c). The determination of whether Independent Counsel shall be engaged and the selection of such Independent Counsel shall be made by the Board of Directors. Indemnitee may, within 10 days after such written notice of selection shall have been given, deliver to the Company, as the case may be, a written objection to such selection; provided, however, that such objection may be asserted only on the ground that the Independent Counsel so selected does not meet the requirements of "**Independent Counsel**" as defined in Section 13 of this Agreement, and the objection shall set forth with particularity the factual basis of such assertion. Absent a proper and timely objection, the person so selected shall act as Independent Counsel. If a written objection is made and substantiated, the Independent Counsel selected may not serve as Independent Counsel unless and until such objection is withdrawn or a court has determined that such objection is without merit. If, within 20 days after submission by Indemnitee of a written request for indemnification pursuant to Section 6(a) hereof, no Independent Counsel shall have been selected and not objected to, either the Company or Indemnitee may petition the Court of Chancery of the State of Delaware or other court of competent jurisdiction for resolution of any objection which shall have been made by the Indemnitee to the Company's selection of Independent Counsel and/or for the appointment as Independent Counsel of a person selected by the court or by such other person as the court shall designate, and the person with respect to whom all objections are so resolved or the person so appointed shall act as Independent Counsel under Section 6(b) hereof. The Company shall pay any and all reasonable fees and expenses of Independent Counsel incurred by such Independent Counsel in connection with acting pursuant to

Section 6(b) hereof, and the Company shall pay all reasonable fees and expenses incident to the procedures of this Section 6(c), regardless of the manner in which such Independent Counsel was selected or appointed.

(d) In making a determination with respect to entitlement to indemnification hereunder, the person or persons or entity making such determination shall presume that Indemnitee is entitled to indemnification under this Agreement. Anyone seeking to overcome this presumption shall have the burden of proof and the burden of persuasion by clear and convincing evidence. Neither the failure of the Company (including by its directors or independent legal counsel) to have made a determination prior to the commencement of any action pursuant to this Agreement that indemnification is proper in the circumstances because Indemnitee has met the applicable standard of conduct, nor an actual determination by the Company (including by its directors or independent legal counsel) that Indemnitee has not met

such applicable standard of conduct, shall be a defense to the action or create a presumption that Indemnitee has not met the applicable standard of conduct.

(e) Indemnitee shall be deemed to have acted in good faith if Indemnitee's action is based on the records or books of account of the Enterprise (as hereinafter defined), including financial statements, or on information supplied to Indemnitee by the officers of the Enterprise in the course of their duties, or on the advice of legal counsel for the Enterprise or on information or records given or reports made to the Enterprise by an independent certified public accountant or by an appraiser or other expert selected with reasonable care by the Enterprise. In addition, the knowledge and/or actions, or failure to act, of any director, officer, agent or employee of the Enterprise shall not be imputed to Indemnitee for purposes of determining the right to indemnification under this Agreement. Whether or not the foregoing provisions of this Section 6(e) are satisfied, it shall in any event be presumed that Indemnitee has at all times acted in good faith and in a manner he reasonably believed to be in or not opposed to the best interests of the Company. Anyone seeking to overcome this presumption shall have the burden of proof and the burden of persuasion by clear and convincing evidence.

(f) If the person, persons or entity empowered or selected under Section 6 to determine whether Indemnitee is entitled to indemnification shall not have made a determination within sixty (60) days after receipt by the Company of the request therefor, the requisite determination of entitlement to indemnification shall be deemed to have been made and Indemnitee shall be entitled to such indemnification absent (i) a misstatement by Indemnitee of a material fact, or an omission of a material fact necessary to make Indemnitee's statement not materially misleading, in connection with the request for indemnification, or (ii) a prohibition of such indemnification under applicable law; provided, however, that such 60-day period may be extended for a reasonable time, not to exceed an additional thirty (30) days, if the person, persons or entity making such determination with respect to entitlement to indemnification in good faith requires such additional time to obtain or evaluate documentation and/or information relating thereto; and provided, further, that the foregoing provisions of this Section 6(f) shall not apply if the determination of entitlement to indemnification is to be made by the stockholders pursuant to Section 6(b) of this Agreement and if (A) within fifteen (15) days after receipt by the Company of the request for such determination, the Board of Directors or the Disinterested Directors, if appropriate, resolve to submit such determination to the stockholders for their consideration at an annual meeting thereof to be held within seventy-five (75) days after such receipt and such determination is made thereat, or (B) a special meeting of stockholders is called within fifteen (15) days after such receipt for the purpose of making such determination, such meeting is held for such purpose within sixty (60) days after having been so called and such determination is made thereat.

(g) Indemnitee shall cooperate with the person, persons or entity making such determination with respect to Indemnitee's entitlement to indemnification, including providing to such person, persons or entity upon reasonable advance request any documentation or information which is not privileged or otherwise protected from disclosure and which is reasonably available to Indemnitee and reasonably necessary to such determination. Any Independent Counsel, member of the Board of Directors or stockholder of the Company shall act reasonably and in good faith in making a determination regarding the Indemnitee's entitlement to indemnification under this Agreement. Any costs or expenses (including attorneys' fees and disbursements) incurred by Indemnitee in so cooperating with the person, persons or entity making such determination shall be borne by the Company (irrespective of the

determination as to Indemnitee's entitlement to indemnification) and the Company hereby indemnifies and agrees to hold Indemnitee harmless therefrom.

(h) The Company acknowledges that a settlement or other disposition short of final judgment may be successful if it permits a party to avoid expense, delay, distraction, disruption and uncertainty. In the event that any action, claim or proceeding to which Indemnitee is a party is resolved in any manner other than by adverse judgment against Indemnitee (including, without limitation, settlement of such action, claim or proceeding with or without payment of money or other consideration) it shall be presumed that Indemnitee has been successful on the merits or otherwise in such action, suit or proceeding. Anyone seeking to overcome this presumption shall have the burden of proof and the burden of persuasion by clear and convincing evidence.

(i) The termination of any Proceeding or of any claim, issue or matter therein, by judgment, order, settlement or conviction, or upon a plea of nolo contendere or its equivalent, shall not (except as otherwise expressly provided in this Agreement) of itself adversely affect the right of Indemnitee to indemnification or create a presumption that Indemnitee did not act in good faith and in a manner which he reasonably believed to be in or not opposed to the best interests of the Company or, with respect to any criminal Proceeding, that Indemnitee had reasonable cause to believe that his conduct was unlawful.

7. Remedies of Indemnitee.

(a) In the event that (i) a determination is made pursuant to Section 6 of this Agreement that Indemnitee is not entitled to indemnification under this Agreement, (ii) advancement of Expenses is not timely made pursuant to Section 5 of this Agreement, (iii) no determination of entitlement to indemnification is made pursuant to Section 6(b) of this Agreement within 90 days after receipt by the Company of the request for indemnification, (iv) payment of indemnification is not made pursuant to this Agreement within ten (10) days after receipt by the Company of a written request therefor or (v) payment of indemnification is not made within ten (10) days after a determination has been made that Indemnitee is entitled to indemnification or such determination is deemed to have been made pursuant to Section 6 of this Agreement, Indemnitee shall be entitled to an adjudication in an appropriate court of the State of Delaware, or in any other court of competent jurisdiction, of Indemnitee's entitlement to such indemnification. Indemnitee shall commence such proceeding seeking an adjudication within 180 days following the date on which Indemnitee first has the right to commence such proceeding pursuant to this Section 7(a). The Company shall not oppose Indemnitee's right to seek any such adjudication.

(b) In the event that a determination shall have been made pursuant to Section 6(b) of this Agreement that Indemnitee is not entitled to indemnification, any judicial proceeding commenced pursuant to this Section 7 shall be conducted in all respects as a de novo trial on the merits, and Indemnitee shall not be prejudiced by reason of the adverse determination under Section 6(b).

(c) If a determination shall have been made pursuant to Section 6(b) of this Agreement that Indemnitee is entitled to indemnification, the Company shall be bound by such determination in any judicial proceeding commenced pursuant to this Section 7, absent (i) a misstatement by Indemnitee of a material fact, or an omission of a material fact necessary to

make Indemnitee's statement not materially misleading in connection with the application for indemnification, or (ii) a prohibition of such indemnification under applicable law.

(d) In the event that Indemnitee, pursuant to this Section 7, seeks a judicial adjudication of his rights under, or to recover damages for breach of, this Agreement, or to recover under any directors' and officers' liability insurance policies maintained by the Company, the Company shall pay on his behalf, in advance, any and

all expenses (of the types described in the definition of Expenses in Section 13 of this Agreement) actually and reasonably incurred by him in such judicial adjudication, regardless of whether Indemnitee ultimately is determined to be entitled to such indemnification, advancement of expenses or insurance recovery.

(e) The Company shall be precluded from asserting in any judicial proceeding commenced pursuant to this Section 7 that the procedures and presumptions of this Agreement are not valid, binding and enforceable and shall stipulate in any such court that the Company is bound by all the provisions of this Agreement. The Company shall indemnify Indemnitee against any and all Expenses and, if requested by Indemnitee, shall (within ten (10) days after receipt by the Company of a written request therefore) advance, to the extent not prohibited by law, such expenses to Indemnitee, which are incurred by Indemnitee in connection with any action brought by Indemnitee for indemnification or advance of Expenses from the Company under this Agreement or under any directors' and officers' liability insurance policies maintained by the Company, regardless of whether Indemnitee ultimately is determined to be entitled to such indemnification, advancement of Expenses or insurance recovery, as the case may be.

(f) Notwithstanding anything in this Agreement to the contrary, no determination as to entitlement to indemnification under this Agreement shall be required to be made prior to the final disposition of the Proceeding.

8. Non-Exclusivity; Survival of Rights; Insurance; Subrogation.

(a) The rights of indemnification as provided by this Agreement shall not be deemed exclusive of any other rights to which Indemnitee may at any time be entitled under applicable law, the certificate of incorporation of the Company, the Bylaws, any agreement, a vote of stockholders, a resolution of directors or otherwise. No amendment, alteration or repeal of this Agreement or of any provision hereof shall limit or restrict any right of Indemnitee under this Agreement in respect of any action taken or omitted by such Indemnitee in his Corporate Status prior to such amendment, alteration or repeal. To the extent that a change in the Delaware General Corporation Law, whether by statute or judicial decision, permits greater indemnification than would be afforded currently under the Bylaws and this Agreement, it is the intent of the parties hereto that Indemnitee shall enjoy by this Agreement the greater benefits so afforded by such change. No right or remedy herein conferred is intended to be exclusive of any other right or remedy, and every other right and remedy shall be cumulative and in addition to every other right and remedy given hereunder or now or hereafter existing at law or in equity or otherwise. The assertion or employment of any right or remedy hereunder, or otherwise, shall not prevent the concurrent assertion or employment of any other right or remedy.

(b) To the extent that the Company maintains an insurance policy or policies providing liability insurance for directors, officers, employees, or agents or fiduciaries of

the Company or of any other corporation, partnership, joint venture, trust, employee benefit plan or other enterprise that such person serves at the request of the Company, Indemnitee shall be covered by such policy or policies in accordance with its or their terms to the maximum extent of the coverage available for any director, officer, employee, agent or fiduciary under such policy or policies. If, at the time of the receipt of a notice of a claim pursuant to the terms hereof, the Company has director and officer liability insurance in effect, the Company shall give prompt notice of the commencement of such proceeding to the insurers in accordance with the procedures set forth in the respective policies. The Company shall thereafter take all necessary or desirable action to cause such insurers to pay, on behalf of the Indemnitee, all amounts payable as a result of such proceeding in accordance with the terms of such policies.

(c) In the event of any payment under this Agreement, the Company shall be subrogated to the extent of such payment to all of the rights of recovery of Indemnitee, who shall execute all papers required and take all action necessary to secure such rights, including execution of such documents as are necessary to enable the Company to bring suit to enforce such rights.

(d) The Company shall not be liable under this Agreement to make any payment of amounts otherwise indemnifiable hereunder if and to the extent that Indemnitee has otherwise actually received such payment under any insurance policy, contract, agreement or otherwise.

(e) The Company's obligation to indemnify or advance Expenses hereunder to Indemnitee who is or was serving at the request of the Company as a director, officer, employee or agent of any other corporation, partnership, joint venture, trust, employee benefit plan or other enterprise shall be reduced by any amount Indemnitee has actually received as indemnification or advancement of expenses from such other corporation, partnership, joint venture, trust, employee benefit plan or other enterprise.

9. Exception to Right of Indemnification. Notwithstanding any provision in this Agreement, the Company shall not be obligated under this Agreement to make any indemnity in connection with any claim made against Indemnitee:

(a) for which payment has actually been made to or on behalf of Indemnitee under any insurance policy or other indemnity provision, except with respect to any excess beyond the amount paid under any insurance policy or other indemnity provision; or

(b) for an accounting of profits made from the purchase and sale (or sale and purchase) by Indemnitee of securities of the Company within the meaning of Section 16(b) of the Securities Exchange Act of 1934, as amended, or similar provisions of state statutory law or common law; or

(c) in connection with any Proceeding (or any part of any Proceeding) initiated by Indemnitee, including any Proceeding (or any part of any Proceeding) initiated by Indemnitee against the Company or its directors, officers, employees or other indemnitees, unless (i) the Board of Directors of the Company authorized the Proceeding (or any part of any Proceeding) prior to its initiation or (ii) the Company provides the indemnification, in its sole discretion, pursuant to the powers vested in the Company under applicable law.

10. Duration of Agreement. All agreements and obligations of the Company contained herein shall continue during the period Indemnitee is a director of the Company (or is or was serving at the request of the Company as a director, officer, employee or agent of another corporation, partnership, joint venture, trust or other enterprise) and for a period of five (5) years thereafter, and in addition shall continue thereafter so long as Indemnitee shall be subject to any Proceeding (or any proceeding commenced under Section 7 hereof) by reason of his Corporate Status, whether or not he is acting or serving in any such capacity at the time any liability or expense is incurred for which indemnification can be provided under this Agreement. This Agreement shall be binding upon and inure to the benefit of and be enforceable by the parties hereto and their respective successors (including any direct or indirect successor by purchase, merger, consolidation or otherwise to all or substantially all of the business or assets of the Company), assigns, spouses, heirs, executors and personal and legal representatives.

11. Security. To the extent requested by Indemnitee and approved by the Board of Directors of the Company, the Company may at any time and from time to time provide security to Indemnitee for the Company's obligations hereunder through an irrevocable bank line of credit, funded trust or other collateral. Any such security, once provided to Indemnitee, may not be revoked or released without the prior written consent of the Indemnitee.

12. Enforcement.

(a) The Company expressly confirms and agrees that it has entered into this Agreement and assumes the obligations imposed on it hereby in order to induce Indemnitee to serve as a director of the Company, and the Company acknowledges that Indemnitee is relying upon this Agreement in serving as a director of the Company.

(b) This Agreement constitutes the entire agreement between the parties hereto with respect to the subject matter hereof and supersedes all prior agreements and understandings, oral, written and implied, between the parties hereto with respect to the subject matter hereof.

13. Definitions. For purposes of this Agreement:

(a) "**Corporate Status**" describes the status of a person who is or was a director, officer, employee, agent or fiduciary of the Company or of any other corporation, partnership, joint venture, trust, employee benefit plan or other enterprise that such person is or was serving at the express written request of the Company.

(b) "**Disinterested Director**" means a director of the Company who is not and was not a party to the Proceeding in respect of which indemnification is sought by Indemnitee.

(c) "**Enterprise**" shall mean the Company and any other corporation, partnership, joint venture, trust, employee benefit plan or other enterprise that Indemnitee is or was serving at the express written request of the Company as a director, officer, employee, agent or fiduciary.

(d) "**Expenses**" shall include all reasonable attorneys' fees, retainers, court costs, transcript costs, fees of experts, witness fees, travel expenses, duplicating costs,

printing and binding costs, telephone charges, postage, delivery service fees and all other disbursements or expenses of the types customarily incurred in connection with prosecuting, defending, preparing to prosecute or defend, investigating, participating, or being or preparing to be a witness in a Proceeding. Expenses also shall include Expenses incurred in connection with any appeal resulting from any Proceeding, including without limitation the premium, security for, and other costs relating to any cost bond, supersedeas bond, or other appeal bond or its equivalent. Expenses, however, shall not include amounts paid in settlement by Indemnitee or the amount of judgments or fines against Indemnitee.

(e) "**Independent Counsel**" means a law firm, or a member of a law firm, that is experienced in matters of corporation law and neither presently is, nor in the past five years has been, retained to represent: (i) the Company or Indemnitee in any matter material to either such party (other than with respect to matters concerning Indemnitee under this Agreement, or of other indemnitees under similar indemnification agreements), or (ii) any other party to the Proceeding giving rise to a claim for indemnification hereunder. Notwithstanding the foregoing, the term "Independent Counsel" shall not include any person who, under the applicable standards of professional conduct then prevailing, would have a conflict of interest in representing either the Company or Indemnitee in an action to determine Indemnitee's rights under this Agreement. The Company agrees to pay the reasonable fees of the Independent Counsel referred to above and to fully indemnify such counsel against any and all Expenses, claims, liabilities and damages arising out of or relating to this Agreement or its engagement pursuant hereto.

(f) "**Proceeding**" includes any threatened, pending or completed action, suit, arbitration, alternate dispute resolution mechanism, investigation, inquiry, administrative hearing or any other actual, threatened or completed proceeding, whether brought by or in the right of the Company or otherwise and whether civil, criminal, administrative or investigative, in which Indemnitee was, is or will be involved as a party or otherwise, by reason of the fact that Indemnitee is or was a director of the Company, by reason of any action taken by him or of any inaction on his part while acting as a director of the Company, or by reason of the fact that he is or was serving at the request of the Company as a director, officer, employee, agent or fiduciary of another corporation, partnership, joint venture, trust or other Enterprise; in each case whether or not he is acting or serving in any such capacity at the time any liability or expense is incurred for which indemnification can be provided under this Agreement; including one pending on or before the date of this Agreement, but excluding one initiated by an Indemnitee pursuant to Section 7 of this Agreement to enforce his rights under this Agreement.

14. Severability. The invalidity of unenforceability of any provision hereof shall in no way affect the validity or enforceability of any other provision. Without limiting the generality of the foregoing, this Agreement is intended to confer upon Indemnitee indemnification rights to the fullest extent permitted by applicable laws. In the event any provision hereof conflicts with any applicable law, such provision shall be deemed modified, consistent with the aforementioned intent, to the extent necessary to resolve such conflict.

15. Modification and Waiver. No supplement, modification, termination or amendment of this Agreement shall be binding unless executed in writing by both of the parties hereto. No waiver of any of the provisions of this Agreement shall be deemed or shall constitute a waiver of any other provisions hereof (whether or not similar) nor shall such waiver constitute a continuing waiver.

16. Notice By Indemnitee. Indemnitee agrees promptly to notify the Company in writing upon being served with or otherwise receiving any summons, citation, subpoena, complaint, indictment, information or other document relating to any Proceeding or matter which may be subject to indemnification covered hereunder. The failure to so notify the Company shall not relieve the Company of any obligation which it may have to Indemnitee under this Agreement or otherwise unless and only to the extent that such failure or delay materially prejudices the Company.

17. Notices. All notices and other communications given or made pursuant to this Agreement shall be in writing and shall be deemed effectively given: (a) upon personal delivery to the party to be notified, (b) when sent by confirmed electronic mail or facsimile if sent during normal business hours of the recipient, and if not so confirmed, then on the next business day, (c) five (5) days after having been sent by registered or certified mail, return receipt requested, postage prepaid, or (d) one (1) day after deposit with a nationally recognized overnight courier, specifying next day delivery, with written verification of receipt. All communications shall be sent:

(a) To Indemnitee at the address set forth below Indemnitee's signature hereto.

(b) To the Company at:

200 West Street
Waltham, MA 02451
Attention: CEO

or to such other address as may have been furnished to Indemnitee by the Company or to the Company by Indemnitee, as the case may be.

18. Counterparts. This Agreement may be executed in two or more counterparts, each of which shall be deemed an original, but all of which together shall constitute one and the same Agreement. This Agreement may also be executed and delivered by facsimile signature and in two or more counterparts, each of which shall be deemed an original, but all of which together shall constitute one and the same instrument.

19. Headings. The headings of the paragraphs of this Agreement are inserted for convenience only and shall not be deemed to constitute part of this Agreement or to affect the construction thereof.

20. Governing Law and Consent to Jurisdiction. This Agreement and the legal relations among the parties shall be governed by, and construed and enforced in accordance with, the laws of the State of Delaware, without regard to its conflict of laws rules. The Company and Indemnitee hereby irrevocably and unconditionally (i) agree that any action or proceeding arising out of or in connection with this Agreement shall be brought only in the Chancery Court of the State of Delaware (the "**Delaware Court**"), and not in any other state or federal court in the United States of America or any court in any other country, (ii) consent to submit to the exclusive jurisdiction of the Delaware Court

for purposes of any action or proceeding arising out of or in connection with this Agreement, (iii) waive any objection to the laying of venue of any such action or proceeding in the Delaware Court, and (iv) waive, and agree not to plead or to

make, any claim that any such action or proceeding brought in the Delaware Court has been brought in an improper or inconvenient forum.

SIGNATURE PAGE TO FOLLOW

IN WITNESS WHEREOF, the parties hereto have executed this Indemnification Agreement on and as of the day and year first above written.

PROTEON THERAPEUTICS, INC.

By: /s/ Timothy Noyes
Name: Timothy Noyes
Title: CEO

INDEMNITEE

/s/ Gregory D. Phelps
Name: Gregory D. Phelps

Address:
75 Farley Pond Road
Needham, MA 02492

SIGNATURE PAGE TO INDEMNIFICATION AGREEMENT - PHELPS