Table of Contents

As filed with the Securities and Exchange Commission on October 7, 2014.

Registration No. 333-198777

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

Amendment No. 1
to

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**	**Amount of Registration Fee(3)**

	Price(1)(2)	
Common Stock, $0.001 par value per share	$75,670,000	$9,664

(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(a) under the Securities Act of 1933, as amended.

(3) Of this amount, $8,888 was previously paid in connection with the initial filing of the Registration Statement on September 16, 2014.

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.

Table of Contents

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 OCTOBER 7, 2014

PRELIMINARY PROSPECTUS

PROTEON Therapeutics

4,700,000 Shares

Common Stock

$ per share

This is the initial public offering of Proteon Therapeutics, Inc. We are offering 4,700,000 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 $12.00 and $14.00 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 705,000 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.

Certain of our existing stockholders and their affiliated entities, including holders of more than 5% of our common stock, have indicated an interest in purchasing an aggregate of approximately $30.4 million in shares of our common stock in this offering at the initial public offering price. However, because indications of interest are not binding agreements or commitments to purchase, the underwriters could determine to sell more, less or no shares to any of these existing stockholders and any of these existing stockholders could determine to purchase more, less or no shares in this offering.

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

TABLE OF CONTENTS

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 investme decision. 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 No Regarding Forward-Looking Statements" and "Management's Discussion and Analysis of Financial Condition and Results of Operations" before deciding whether to purchase share of our 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 vascul 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 undergoin 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-20 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, 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 AVFs.

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 initiated the first of two Phase 3 trials for PRT-20 in radiocephalic AVFs, our initial indication, in the third quarter of 2014 and expect to 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 Foo and 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 inclu claims covering formulations, methods of manufacturing and uses of elastases, providing protection in the United States through mid 2029 and the European Union through 2028, ar with 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 communit endorses 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.

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 great than 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-20 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 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 f an 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 f 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 risk of primary unassisted patency loss was reduced by 31% for the 10 microgram dose group and by 33% for the 30 microgram dos group versus placebo.

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. In that analysis, the risk of primary unassisted patency loss was reduced by 31% for the 10 microgram dose group and by 48% for th 30 microgram dose group versus placebo. The comparison of the 30 microgram dose versus placebo was significant from a statistical point of view.

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 risk of primary unassisted patency loss was reduced by 41% for the 10 microgram dose group ar by 63% for the 30 microgram dose group versus placebo. Median patency was 125 days in the placebo group and 377 days in the 30 microgram group (in some cases the 12 mon follow up occured after day 365 due to patient schedules), indicating an improvement in primary unassisted patency that was significant from a statistical point of view.

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 pla to 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 showe the 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, th FDA 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 the first quarter of 2017. Th Phase 3 clinical trial includes two groups, one receiving PRT-201 (n=200) and the other receiving placebo (n=100). We expect to initiate the second, substantially similar, Phase clinical 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 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.

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 angioplast

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 a unacceptably 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 end stag renal disease, or ESRD, bundle, the single bundled payment from Medicare for a number of the costs of hemodialysis treatments, medications, labs and supplies for patients with er stage renal disease. We believe that PRT-201 adoption will be supported by key stakeholders, including referring nephrologists, patient advocacy groups, large dialysis organizatio and payors. 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 believ 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 surgic placements performed in 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 are conducting our first Phase 3 clinical trial and plan to conduct our second Phase 3 clinical trial i radiocephalic AVFs 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 trials, primary unassisted patency, will be the same as that used 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. 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.* 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 the 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.
- *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 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.
- *Experienced team.* Both 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 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 summary. 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 foreseeable 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 us 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 advers effect 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 a 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 f 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 achievi 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 June 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) th 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 $1.0 billion, or (c) in whic 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 the prior June 30th, a (2) the date 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 A of 2012 in this 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 compani that 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 an Analysis 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 grow 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	4,700,000 shares
Common stock outstanding after giving effect to this offering	14,045,374 shares
Option to purchase additional shares	The underwriters have a 30-day option to purchase a total of 705,000 additional shares of common stock.
Use of proceeds	We estimate that our net proceeds from this offering will be approximately $54.2 million, or approximately $62.7 million if the underwriters exercise their option to purchase additional shares in full, at an assumed initial public offering price of $13.00 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. 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 deciding to invest in our common stock.
Proposed NASDAQ Global Market Symbol	"PRTO"

Certain of our existing stockholders and their affiliated entities, including holders of more than 5% of our common stock, have indicated an interest in purchasing an aggregate o approximately $30.4 million in shares of our common stock in this offering at the initial public offering price. Assuming an initial public offering price of $13.00 per share, which the midpoint of the price range set forth on the cover page of this prospectus, these entities would purchase an aggregate of up to approximately 2,341,215 of the 4,700,000 shares this offering based on these indications of interest. However, because indications of interest are not binding agreements or commitments to purchase, the underwriters could determi to sell more, less or no shares to any of these existing stockholders and any of these existing stockholders could determine to purchase, more, less or no shares in this offering.

In this prospectus, unless otherwise indicated, the number of shares of common stock outstanding and the other information based thereon is based on 9,345,374 shares o common stock outstanding as of September 30, 2014 and does not reflect:

- 1,133,052 shares of common stock issuable upon exercise of stock options outstanding as of September 30, 2014 at a weighted-average exercise price of $3.45 p share;
- 659,806 shares of our common stock issuable upon exercise of warrants with a weighted-average exercise price of $4.60 per share that we expect to be exercised pri to the closing of this offering;
- 1,156 shares of common stock reserved for issuance pursuant to future equity awards under our 2006 Equity Incentive Plan;
- 704,000 shares of common stock reserved for future issuance under our 2014 Equity Incentive Plan, which will become effective immediately prior to effectiveness o this offering; and

- 140,500 shares of common stock reserved for future issuance under 2014 Employee Stock Purchase Plan, which will become effective upon the closing of th offering.

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 9,103,815 shares of common stock, including the conversion of our Series D convertib preferred stock, assuming the full issuance of incremental shares upon its conversion based on the midpoint of the price range set forth on the cover page of th prospectus, which will occur automatically upon the closing of this offering. See "Capitalization—Series D Convertible Preferred Stock" for applicable conversio price adjustments;
- a one-for-15.87 reverse stock split of our common stock that we effected on October 6, 2014 prior to completion of this offering;
- no exercise of stock options on or after September 30, 2014; and
- no exercise by the underwriters of their option to purchase up to a total of 705,000 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 statemen 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 da together with our audited financial statements and related notes included elsewhere in this prospectus and the information under the captions "Selected Financial Data" an "Management's Discussion and Analysis of Financial Condition and Results of Operations." Our historical results are not necessarily indicative of our future results, and our operatin results for the 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 oth interim periods or any 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) gain 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	$ (61.16)	$ (59.66)	$ (27.97)	$ (36.64)
Weighted-average number of common shares used in net loss per share attributable to common stockholders—basic and diluted	230,607	235,184	230,607	240,254
Pro forma net loss per share attributable to common stockholders—basic and diluted (unaudited)		$ (1.54)		$ (0.66)
Pro forma weighted-average number of common shares used in net loss per share attributable to common stockholders—basic and diluted (unaudited)		4,565,620		6,763,218

	As of June 30, 2014		
	Actual	Pro Forma(2)	Pro Forma As Adjusted(3)(4)(5)
	(unaudited) (in thousands)		
Balance Sheet Data:			
Cash, cash equivalents and available-for-sale investments	$ 25,416	$ 25,416	$ 79,914
Working capital	19,915	19,915	75,325
Total assets	27,142	27,142	80,446
Preferred stock	123,904	—	—
Common stock and additional paid in capital	0	123,904	178,121
Total stockholders' (deficit) equity	(109,290)	21,194	75,411

(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 and the extinguishment of the liability related to t Series D investors' purchase rights.

(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 $13.00 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 $13.00 per share, the midpoint of the price range set forth on the cover of this prospectus, would increase (decrease) the p forma 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 approximate $4.4 million, 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 estimat offering expenses 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 $13.00 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 $17.4 million, af 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 the end of 2017, 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 ongoing and 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 we 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 in our ongoing and planned 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 trials;
- 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 may 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 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, which are proteins that cut other proteins to activate, inactivate or degrade these other proteins, 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 ACA, 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 warning letters, 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 26 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 September 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 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 and may 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 the prior June 30th, 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.

Certain of our existing stockholders and their affiliated entities, including holders of more than 5% of our common stock, have indicated an interest in purchasing an aggregate of approximately $30.4 million in shares of our common stock in this offering at the initial public offering price. To the extent these existing stockholders are allocated and purchase shares in this offering, such purchases would reduce the available public float for our shares because these stockholders will be restricted from selling the shares by restrictions under applicable securities laws described in the "Shares Eligible for Future Sale" section of this prospectus. As a result, the liquidity of our common stock could be significantly reduced from what it would have been if these shares had not been purchased by investors that were not affiliated with us.

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, directors, current 5% or greater stockholders, and their respective affiliates will together beneficially own or control, in aggregate, approximately 65.9% of the shares of our outstanding common stock, after giving effect to the conversion of all outstanding preferred stock and assuming the exercise of outstanding options and warrants following the closing of this offering (assuming no exercise of the underwriters' option to purchase additional shares). Assuming an initial offering price of $13.00 per share, if our 5% or greater stockholders and their respective affiliates purchase all they have indicated an interest in purchasing in this offering, the number of shares of our common stock beneficially owned by our executive officers, directors, current 5% or greater stockholders, and their respective affiliates will, in the aggregate, increase to 70.6% of our capital stock. 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. Upon the closing of this offering, we will have 14,045,374 shares of common stock outstanding, assuming no exercise of the underwriters' option to purchase additional shares. Of these, only the shares of our common stock sold in this offering, plus any shares sold upon exercise of the underwriters' option to purchase additional shares, 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 underwriters for this offering. After the lock-up agreements expire, up to an additional 9,345,374 shares of common stock will be eligible for sale in the public market, of which 8,027,984 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 $13.00 per share (the midpoint of the price range set forth on the cover page of this prospectus). In addition, 1,977,552 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 $13.00 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 $7.63 per share. Further, investors purchasing common stock in this offering will contribute approximately 37% of the total amount invested by stockholders since our inception, but will own only approximately 33% of the shares of common stock outstanding after giving effect to this offering. If the underwriters

exercise their option to purchase additional shares, 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 amended and 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 amended and 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 amended and 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 amended and 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 amended and 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 amended and 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 amended and 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 amended and 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 amended and 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 amended and 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 $54.2 million, assuming an initial public offering price of $13.00 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 $62.7 million.

Each $1.00 increase or decrease in the assumed initial public offering price of $13.00 per share, which is the midpoint of the price range set forth on the cover page of this prospectus, would result in an approximately $4.4 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 $12.1 million, assuming that the public offering price is $13.00 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 $9.4 million to accelerate the commencement of the second of our Phase 3 trials for PRT-201 in its lead indication;
- approximately $28.4 million to accelerate our chemistry and manufacturing controls, or CMC, activities;
- approximately $1.6 million to fund additional research and development activities; and
- the remainder for working capital and general corporate purposes and the costs associated with being a public company.

We believe that the net proceeds from the offering, together with our existing cash and cash equivalents and investments, will be sufficient to fund our projected operating expenses and capital expenditure requirements through the end of 2017, allowing us to obtain results from our first Phase 3 clinical trial of PRT-201 in radiocephalic AVFs and complete our anticipated chemistry, manufacturing and controls activities required for a BLA submission. However, this may change 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 the proceeds to be sufficient to obtain the results from our second Phase 3 trial.

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 9,103,815 shares of common stock upon the closing of this offering, the extinguishment of the liability related to the Series D investors' purchase rights 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 4,700,000 shares of our common stock offered in this offering, assuming an initial public offering price of $13.00 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, cash equivalents and available-for-sale investments	$ 25,416	$ 25,416	$ 79,914
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	130,484	—	—
Stockholders' deficit:			
Preferred stock, par value $0.001 per share; no shares authorized, issued and outstanding, actual, 10,000,000 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, 241,559 shares issued and outstanding, actual; 205,926,290 shares authorized, 9,345,374 shares issued and outstanding, pro forma and 100,000,000 shares authorized, 14,045,374 shares issued and outstanding, pro forma as adjusted	0	9	14
Additional paid-in capital	—	123,895	178,107
Accumulated deficit	(109,267)	(102,687)	(102,687)
Accumulated other comprehensive income	(23)	(23)	(23)
Total stockholders' (deficit) equity	(109,290)	21,194	75,411
Total capitalization	$ 21,194	$ 21,194	$ 75,411

Each $1.00 increase or decrease in the assumed initial public offering price of $13.00 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 $4.4 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 $12.1 million, assuming no change in the assumed initial public offering price of $13.00 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:

- 1,133,052 shares of our common stock issuable upon the exercise of stock options outstanding at a weighted-average exercise price of $3.45 per share;
- 659,806 shares of our common stock issuable upon the exercise of outstanding warrants at a weighted average exercise price of $4.60 per share that we expect to be exercised in full prior to the closing of this offering;
- 1,156 shares of common stock reserved for issuance pursuant to future equity awards under our 2006 Equity Incentive Plan;
- 704,000 shares of common stock reserved for future issuance under our 2014 Equity Incentive Plan, which will become effective immediately prior to effectiveness of this offering; and
- 140,500 shares of common stock reserved for future issuance under our 2014 Employee Stock Purchase Plan, which will become effective upon the closing of this offering.

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 2,140,876 shares of our common stock, assuming an initial public offering price greater than $9.34, the Series D conversion price immediately prior to this offering, 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) $9.34, 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 2,140,876 shares of our common stock, and if we or our underwriters offer to such investors the opportunity to purchase an aggregate of 1,538,452 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 1,538,452 shares of our common stock, and if we or our underwriters offer to such investors the opportunity to purchase an aggregate of only 1,038,452 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 1,038,452 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 500,000 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) 3,327,894 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 $9.34, 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 1,538,452 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 $9.34, 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 $13.00 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 52,813,827 shares of our Series D convertible preferred stock outstanding as of September 30, 2014 automatically will convert into 3,327,894 shares of our common stock.

Upon the closing of this offering, assuming an initial public offering price of $13.00 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 1,538,452 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 52,813,827 shares of our Series D convertible preferred stock outstanding as of September 30, 2014 automatically will convert into 3,930,306 shares of

our common stock. A $1.00 decrease in the assumed initial public offering price (until the assumed initial public offering price is equal to $9.34) would decrease by an additional 128,201 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 $9.34, the 52,813,827 shares of our Series D convertible preferred stock outstanding as of September 30, 2014 automatically will convert into 3,327,894 shares of our common stock upon the closing of this offering. Each $1.00 increase in the assumed initial public offering price above $13.00 would increase by an additional 109,894 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 $9.34, each decrease of 500,000 shares in the number of shares purchased in this offering by holders of our Series D convertible preferred stock would decrease by an additional 195,796 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 issued upon the conversion of our Series D convertible preferred stock, assuming the full issuance of incremental shares upon its conversion based on the midpoint of the price range set forth on the cover page of this prospectus and assuming the initial public offering prices for our common stock shown below:

	Assumed Initial Public Offering Price				
	$11.00	$12.00	$13.00	$14.00	$15.00
Shares Outstanding	3,650,588	3,802,103	3,930,306	4,040,198	4,135,437

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 $(452.44) per share of common stock, based on 241,559 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 $2.27 per share of common stock, based on 9,345,374 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 9,103,815 shares of common stock upon the listing of our common stock on the NASDAQ Global Market. These shares include an additional 919,928 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." Our pro forma net tangible book gain also includes the extinguishment of the liability related to the Series D investors' purchase rights.

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 4,700,000 shares of our common stock in this offering at an assumed initial public offering price of $13.00 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 $75.4 million, or $5.37 per share. This represents an immediate increase in pro forma net tangible book value per share of $3.10 to existing stockholders and immediate dilution of $7.63 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		$ 13.00
Historical net tangible book value per share as of June 30, 2014	$ (452.44)	
Pro forma increase per share as of June 30, 2014 attributable to conversion of convertible preferred stock	$ 454.71	
Pro forma net tangible book value per share as of June 30, 2014 before giving effect to this offering	$ 2.27	
Increase per share attributable to this offering	$ 3.10	
Pro forma net tangible book value per share, as adjusted to give effect to this offering		$ 5.37
Dilution in pro forma net tangible book value per share to new investors in this offering		$ 7.63

Each $1.00 increase or decrease in the assumed initial public offering price of $13.00 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 $4.4 million, our pro forma net tangible book value per share by approximately $0.31 and dilution per share to new investors by approximately $0.69, 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 $12.1 million, or $0.45 per share, and would decrease the dilution per share to new investors in this offering by $0.45 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 $12.1 million, or $0.52 per share, and would increase the dilution per share to new investors in this offering by $0.52 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 option to purchase additional shares in full, the following will occur:

- the percentage of shares of our common stock held by existing stockholders will decrease to approximately 63% 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 37% 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
(in thousands, except share and per share amounts)	Number	Percent	Amount	Percent	Per Share
Existing stockholders	9,345,374	66.6%	$ 105,813	63.4%	$ 11.32
Investors participating in this offering	4,700,000	33.4	61,100	36.6	13.00
Total	14,045,374	100.0%	$ 166,913	100.0%	$ 11.88

Each $1.00 increase or decrease in the assumed public offering price of $13.00 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 $4,700,000 million and increase or decrease the percentage of total consideration paid by new investors by approximately 7.7%, 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 9,345,374 shares of common stock outstanding as of June 30, 2014, including 9,103,815 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 exclude:

- 1,133,052 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 $3.45 per share;

- 659,806 shares of our common stock issuable upon the exercise of outstanding warrants at a weighted average exercise price of $4.60 per share;
- 1,156 shares of common stock reserved for issuance pursuant to future equity awards under our 2006 Equity Incentive Plan;
- 704,000 shares of common stock reserved for future issuance under our 2014 Equity Incentive Plan, which will become effective immediately prior to the effectiveness of this offering; and
- 140,500 shares of common stock reserved for future issuance under our 2014 Employee Stock Purchase Plan, which will become effective upon the closing of this offering.

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.

Certain of our existing stockholders and their affiliated entities, including holders of more than 5% of our common stock, have indicated an interest in purchasing an aggregate of approximately $30.4 million in shares of our common stock in this offering at the initial public offering price. Assuming an initial public offering price of $13.00 per share, which is the midpoint of the price range set forth on the cover page of this prospectus, these entities would purchase an aggregate of up to approximately 2,341,215 of the 4,700,000 shares in this offering based on these indications of interest. However, because indications of interest are not binding agreements or commitments to purchase, the underwriters could determine to sell more, less or no shares to any of these existing stockholders and any of these existing stockholders could determine to purchase more, less or no shares in this offering. The foregoing discussion and tables do not reflect any potential purchases by these existing stockholders or their affiliated entities.

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 at 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
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) gain 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(1)(2)	$ (61.66)	$ (59.66)	$ (27.97)	$ (36.64)
Weighted-average number of common shares used in net loss per share attributable to common stockholders—basic and diluted	230,607	235,184	230,607	240,254
Pro forma net loss per share attributable to common stockholders—basic and diluted (unaudited)(1)(2)		$ (1.54)		$ (0.66)
Pro forma weighted-average number of common shares used in net loss per share attributable to common stockholders—basic and diluted (unaudited)		4,565,620		6,763,218

	December 31, 2012	December 31, 2013	June 30, 2014 (unaudited)
		(in thousands)	
Balance Sheet Data:			
Cash, cash equivalents and available-for-sale investments	$ 7,471	$ 5,152	$ 25,416
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	0	0	0
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 and the extinguishment of the liability related to the Series D investors' purchase rights.

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 expect to 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 the end of 2017, 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) 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	3,150	$ 22.22	$ 22.22
6/24/2014	527,718	$ 4.92	$ 4.92

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 trials. 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 convertible 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 convertible 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 and investments, will be sufficient to fund our operations through the end of 2017. 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 convertible 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 and 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 initiated the first of two Phase 3 trials for PRT-201 in radiocephalic AVFs, our initial indication, in the third quarter of 2014 and expect to 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 the first quarter of 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 are conducting our first Phase 3 clinical trial and plan to conduct our second Phase 3 clinical trial 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 trials, 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 trials 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 commenced 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.

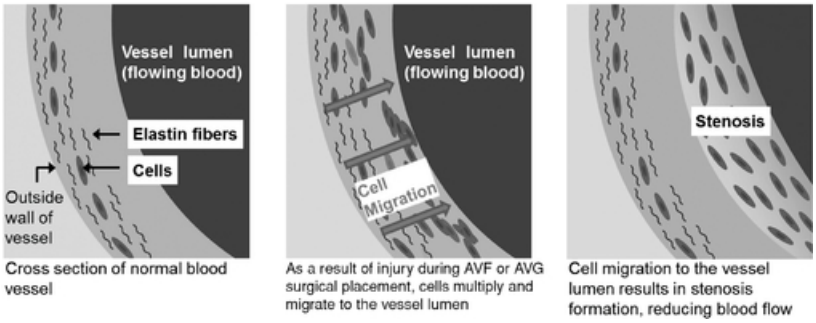
PRT-201

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.

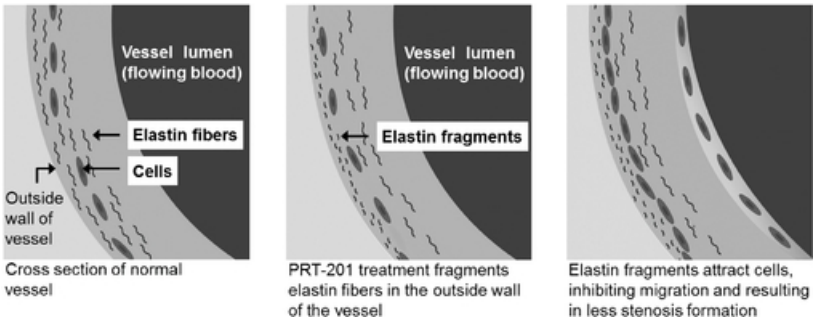
Vessel Injury During AVF and AVG Surgical Placement Results in Stenosis Formation



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

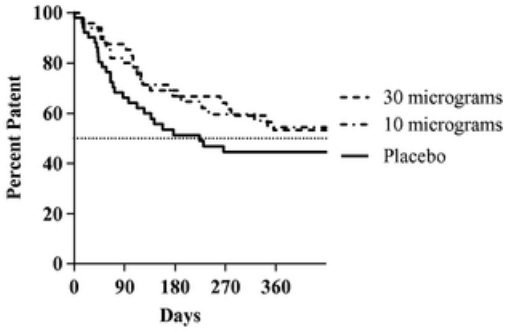
We completed a multicenter, randomized, double-blind, placebo-controlled Phase 2 trial of PRT-201 in AVF that treated 151 patients with CKD undergoing creation of a radiocephalic AVF (n=67) or brachiocephalic AVF (n=84). Patients were treated with PRT-201 at doses of 10 or 30 micrograms or placebo at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

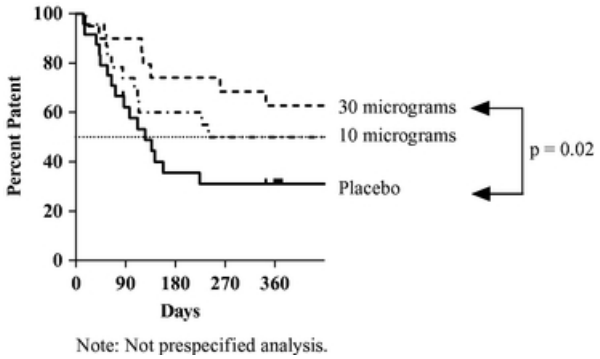
Note: Prespecified analysis.

(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 more 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.

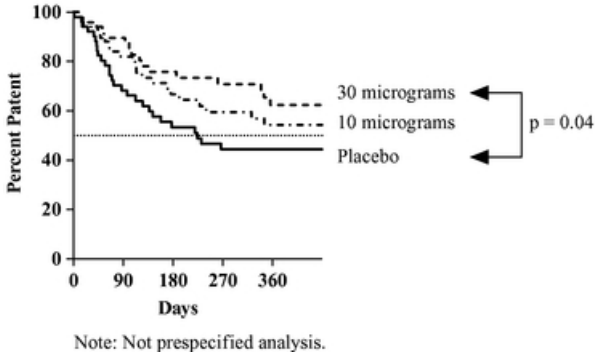
Reduction in Risk of Primary Unassisted Patency Loss vs. Placebo—Brachiocephalic AVFs

	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 ongoing Phase 3 clinical trial and the planned Phase 3 clinical trial, 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)

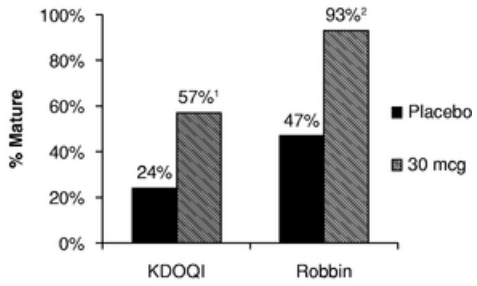
	Placebo	PRT-201 10 micrograms	PRT-201 30 micrograms
All AVFs			
Number of Patients	N=39	N=39	N=37
Percentage Mature NKF-KDOQI(1)	46%	64% (p=0.11)	70% (p=0.03)
Percentage Mature Robbin(2)	67%	87% (p=0.03)	92% (p<0.01)
Radiocephalic AVFs			
Number of Patients	N=17	N=19	N=14
Percentage Mature NKF-KDOQI(1)	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)

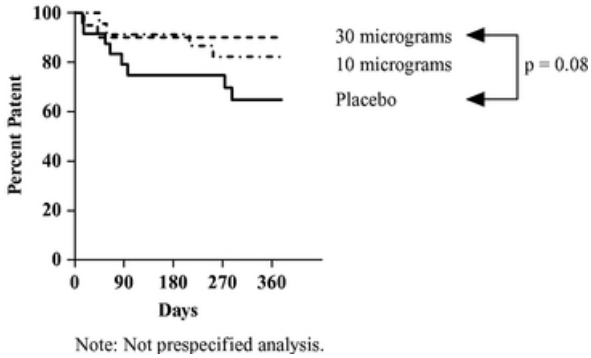
Patients completing 12 months of follow-up in the initial trial were followed in a registry to obtain additional data related to the efficacy endpoints. In this follow up, the PRT-201 benefit on procedure rates persisted out to 900 days as set out in the following table.

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 initiated 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 the first quarter of 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 in which the single Phase 3 trial would form the primary basis of the demonstration of safety and efficacy, and the Phase 2 trial, including non-prespecified analyses, would provide supportive information. We 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 a correlation 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 26 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 Federal Food, Drug, and Cosmetic Act, or 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 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 reviewing an NDA or a BLA, the FDA will consider all information submitted in the NDA or BLA, including the results of all clinical trials conducted. 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 such as supportive results from Phase 1 and Phase 2 trials, including non-prespecified analyses, 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 trials and preclinical testing, 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 $2,335,200, and the manufacturer and/or sponsor under an approved new drug application are also subject to annual product and establishment user fees, currently $110,370 per product and $569,200 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 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, 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 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 September 30, 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 September 30, 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
Garen Bohlin(2)	67	Director
Todd Foley*	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.

* We expect that, effective immediately prior to the effectiveness of this offering, Mr. Foley and Dr. Franano will resign from our board of directors and we will reduce the size of our board of directors by two from 10 to eight.

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.

Garen Bohlin has served as a member of our board of directors since September 2014. Since May 2012, Mr. Bohlin has served as a consultant to various life sciences and healthcare companies. From January 2010 until April 2012, he served as Executive Vice President of Constellation Pharmaceuticals, a biopharmaceutical company. Prior to joining Constellation Pharmaceuticals, Mr. Bohlin served as Chief Operating Officer of Sirtris Pharmaceuticals, a biopharmaceutical company, from 2006 to December 2009. Mr. Bohlin was the founding Chief Executive Officer of Syntonix Pharmaceuticals, Inc., a biopharmaceutical company, from 1999 through December 2008. Earlier in his career, he held multiple executive positions at Genetics Institute, a biopharmaceutical company, and was a partner at Arthur Andersen & Co., a public accounting and consulting organization. Mr. Bohlin currently serves on the board of directors of Tetraphase Pharmaceuticals and Karyopharm Therapeutics, both NASDAQ listed, and Acusphere, Inc. He also served on the board of directors for Targanta Therapeutics from 2007 to 2009, SpringLeaf Therapeutics from 2010 to 2013 and Precision Dermatology from 2012 to July 2014. Mr. Bohlin

received his B.S. in accounting and finance from The University of Illinois. We believe that Mr. Bohlin is qualified to serve on 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 Director 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 Alacer Biomedical Inc. (acquired by Allergan), Atritech (acquired by Boston Scientific), Serica Technologies (acquired by Allergan), and Trius Therapeutics (acquired by Cubist). 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 10 members. However, we expect that, effective immediately prior to the effectiveness of this offering, Mr. Foley and Dr. Franano will resign from our board of directors and we will reduce the size of our board from 10 to eight. 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.

In connection with this offering, our amended and restated certificate of incorporation provides for a classified board. At each annual meeting of the stockholders, a class of directors will be elected for a three-year term to succeed the directors of the same class whose terms are then expiring. As a result approximately one-third of our directors will be elected each year. The initial term of office of the directors of Class I shall expire as of the first annual meeting of the Company's stockholders following the closing of this offering; the initial term of office of the directors of Class II shall expire as of the second annual meeting of the Company's stockholders following the closing of this offering; and the initial term of office of the directors of Class III shall expire as of the third annual meeting of the Company's stockholders following the closing of this offering.

- Our Class I directors will be Timothy Noyes, Garen Bohlin and John Freund;
- Our Class II directors will be Hubert Birner, Dmitry Kobyzev and Gregory Phelps; and
- Our Class III directors will be Brendan O'Leary and Tim Haines.

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 Hubert Birner, Garen Bohlin, Dmitry Kobyzev and Brendan O'Leary, with Garen Bohlin serving as chairman of the committee. Our board of directors has determined that each of Hubert Birner, Garen Bohlin, Dmitry Kobyzev and Brendan O'Leary satisfies the NASDAQ Stock Market independence standards and the independence standards of Rule 10A-3(b)(1) of the Exchange Act. In the case of Mr. Birner, the board of directors specifically determined that he is independent under Rule 10A-3 of the Exchange Act, notwithstanding Mr. Birner's affiliation with TVM Capital and its related funds, which will beneficially own more than 10% of our outstanding common stock following the IPO, and thus falls outside the safe harbor of such rule. Our board of directors has determined that Garen Bohlin 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 Hubert Birner, Tim Haines, Brendan O'Leary and Gregory Phelps 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 and Tim Haines with Hubert Birner serving as chair of the committee. Our board of directors has determined that each of Hubert Birner, Dmitry Kobyzev and Tim Haines 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.

In connection with this offering, Messrs. Noyes and Gottlieb and Dr. Burke will receive an increase in base salary. See "—Employment Agreements" for additional information.

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

We have entered into an amended and restated employment agreement, effective upon the completion of this offering, with Mr. Noyes to serve as our President and Chief Executive Officer. 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 $437,280 in 2014, and that he is eligible for an annual incentive bonus, with his target bonus being 50% 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 or, in the event constructive termination (as defined in the agreement) occurs within 30 days prior to or 365 days following a corporate transaction, 18 months plus, only following a corporation transaction (as defined in the agreement), an amount equal to his bonus pro rated to reflect the number of days worked during that fiscal year; reimbursement of his COBRA premiums for up to 12 months or, in the event constructive termination occurs within 30 days prior to or 365 days following a corporate transaction (as defined in the agreement), 18 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 365 days after a corporate transaction (as defined in the agreement). 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 or, in the event constructive termination (as defined in the agreement) occurs within 30 days prior to or 365 days following a corporate transaction (as defined in the agreement), 18 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.

Upon the effectiveness of this offering, we expect to make an option grant to purchase 35,391 shares of common stock to Mr. Noyes, which option grant will be at an exercise price equal to the price of our common stock in connection with the offering. This option grant will vest 25% annually over four years, generally subject to Mr. Noyes's continued employment.

Steven K. Burke, M.D.

We have entered into an amended and restated employment agreement effective upon completion of this offering with Dr. Burke to serve as our Senior Vice President and Chief Medical Officer. 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 $378,100 in 2014, and that he is eligible for an annual incentive bonus, with his target bonus being 35% 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 or, in the event constructive termination (as defined in the agreement) occurs within 30 days prior to or 365 days following a corporate transaction (as defined in the agreement), 12 months plus an amount equal to his bonus pro rated to reflect the number of days worked during that fiscal year; reimbursement of his COBRA premiums for up to twelve months; and any unvested stock options or unvested restricted shares (excluding certain grants) shall vest in full if the termination

occurs 30 days prior to or 365 days after a corporate transaction (as defined in the agreement). 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

We have entered into an amended and restated employment agreement effective upon completion of this offering with Mr. Gottlieb to serve as our Vice President of Marketing and 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 $221,230 in 2014, and that he is eligible for an annual incentive bonus, with his target bonus being 30% 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 Mr. Gottlieb's 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 nine months of his base salary or, in the event constructive termination (as defined in the agreement) occurs within 30 days prior to or 365 days following a corporate transaction (as defined in the agreement), 12 months plus an amount equal to his bonus pro rated to reflect the number of days worked during that fiscal year; reimbursement of his COBRA premiums for up to nine months; and any unvested stock options or unvested restricted shares (excluding certain grants) shall vest in full if termination occurs 30 days prior to or 365 days after a corporate transaction (as defined in the agreement).

The agreement includes a noncompetition covenant during Mr. Gottlieb's employment under the agreement and for 9 months or, in the event constructive termination (as defined in the agreement) occurs within 30 days prior to or 365 days following a corporate transaction (as defined in the agreement), 12 months thereafter. The agreement provides that we shall indemnify Mr. Gottlieb 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.

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)	83,742	—	$ 1.91	8/1/2016
	(3)	31,505	—	$ 2.39	9/10/2017
	(3)	55,829	—	$ 3.18	6/18/2019
	(3)	3,479	—	$ 3.18	12/15/2019
	(4)	85,388	—	$ 1.27	10/26/2021
Steven K. Burke, M.D.	(3)	30,411	—	$ 1.91	8/1/2016
	(3)	12,287	—	$ 2.39	9/10/2017
	(3)	14,898	—	$ 3.18	6/18/2019
	(4)	57,934	—	$ 1.27	10/26/2021
Daniel P. Gottlieb	(3)	5,316	—	$ 2.39	9/10/2017
	(3)	1,855	—	$ 3.18	6/18/2019
	(4)	3,780	—	$ 1.27	10/26/2021
	(5)	630	—	$ 22.22	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. Under the 2006 Plan, we granted 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. On August 21, 2014, our board of directors resolved to amend and restate the 2006 Plan, effective upon completion of this offering. No new awards will be granted under the 2006 Plan after the consummation of this initial public offering.

Administration

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.

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 that are not terminated prior or upon the transaction, 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, to the extent the surviving entity declines to continue, convert, assume or replace outstanding awards, then 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 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 immediately prior to effectiveness 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 under Section 162(m) of the Code, 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, which is made up of independent outside non employee directors for the purposes of applicable securities and tax laws. 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 made in good faith 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 704,000 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) four percent (4%) of our outstanding common stock on a fully diluted basis as of the end of our immediately preceding fiscal year, and (ii) any lower amount determined by our board prior to each such January 1. In no event shall the number of shares of our common stock available for issuance pursuant to incentive options exceed 14,080,000 shares of common stock.

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.

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 a specified exercise 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 will be the same as 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 but any stock dividends or other distributions payable in shares of stock or other securities of ours will be subject to the same vesting conditions that apply to the shares of restricted stock in respect of which the dividend was made. The receipt of cash dividends may also be deferred or required to be invested in additional shares of restricted stock. 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 over an initial value for such number of shares (which may be zero) established by the compensation committee at the time of grant if certain performance goals or other business objectives are met within the specified performance period. 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 compensation committee may, in its discretion, pay earned performance shares in cash, or stock, or a combination of both.

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.

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 stock grants, may be granted as a qualified performance-based award, but in the case of awards other than stock options or SARs will be subject to satisfaction of performance goals. 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, other than stock grants, 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 that are not terminated prior to or upon the transaction, 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, to the extent that the surviving entity declines to continue, convert, assume or replace outstanding awards, then 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 compensation committee of board of directors is expressly authorized to amend any or all outstanding options at any time and from time to time to effect a repricing thereof by lowering the exercise price applicable to the shares of stock subject to such option(s) without the consent or approval of the stockholders of the Company or the holder or holders of such option(s), and, in connection with such repricing, to amend or modify any of the other terms of the option(s) so repriced, including, without limitation, for purposes of reducing the number of shares subject to such option(s) or for purposes of adversely affecting the provisions applicable to such option(s) that relate to the vesting or exercisability thereof, in each case without the approval or consent of stockholders of the Company or the holder(s) of such option(s). 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.

2014 Employee Stock Purchase Plan

The following is a summary of the material terms of the 2014 employee stock purchase plan, the ESPP, which will be in effect upon completion of this offering. It does not purport to be complete and is qualified by reference to the full text of the ESPP, which we will file as an exhibit to our registration statement of which this prospectus is a part. The ESPP provides an incentive to, and encourages stock ownership by, all of our eligible employees and those of our participating subsidiaries so that they may share in our growth by acquiring or increasing their share ownership in the Company. It is intended that the ESPP constitute an "employee stock purchase plan" within the meaning of Section 423 of the Code. Under the ESPP, eligible employees may purchase shares of our common stock through payroll deductions.

Administration

The ESPP is administered by the compensation committee of our board of directors. The board of directors itself may exercise any of the powers and responsibilities under the ESPP. The compensation committee may delegate its duties in order to facilitate the purchase and transfer of shares of our common stock and for the day-to-day administration of the ESPP. The compensation committee, has the discretion, subject to the provisions of the ESPP, to make or to select the manner of making all determinations with respect to options granted under the ESPP. Further, the compensation committee has complete authority to interpret the ESPP, to prescribe, amend and rescind rules and regulations relating to it, and to make all other determinations necessary or advisable for the administration of the ESPP. All decisions, determinations and interpretations made in good faith by the compensation committee with respect to the ESPP are final an binding on all persons having or claiming any interest in the ESPP or any option granted under the ESPP.

Shares Subject to the Plan

The shares issued or to be issued under the ESPP are authorized but unissued shares of our common stock. The ESPP authorizes the issuance of up to 140,500 shares of common stock. The number of shares authorized under the ESPP will be increased each January 1, commencing on January 1, 2015 and ending on (and including) January 1, 2024, by an amount equal to the lesser of (i) one percent (1%) of outstanding shares as of the end of the immediately preceding fiscal year and (ii) 281,000. Notwithstanding the foregoing, our board of directors may act prior to January 1 of a given year to provide that there will be no such January 1 increase in the number of shares authorized under the ESPP for such year, or that the increase in the number of shares authorized under the ESPP for such year will be a lesser number than would otherwise occur pursuant to the preceding sentence.

Terms of Participation

The ESPP will be implemented through a series of purchase periods called "plan periods." The initial plan period shall commence on such date following the closing of our initial public offering as the compensation committee may determine in its sole discretion and continue until December 31, 2014. After the initial plan period, each calendar year shall be divided into two plan periods, the first beginning on January 1 and ending on the immediately following June 30, and the second beginning on July 1 and ending on the immediately following December 31. An eligible employee will be granted an option at the beginning of the plan period, and can accumulate money to pay the exercise price for the option by electing to have payroll deductions taken from each payroll during a plan period of an amount, in whole

percentages, between 1% and 15% of his or her compensation, but will not exceed $25,000 on an annual basis. At the end of each plan period, unless the participating employee has withdrawn from the ESPP, the option will be exercised by applying the employee's accumulated payroll deductions to the purchase of Common Stock. The exercise price paid by the employee will be the lower of 85% of the fair market value of our common stock at (i) the commencement of the plan period and (ii) the end of the plan period.

Withdrawal

An employee may withdraw from participation in an offering up to two weeks prior to the plan period termination date and permanently draw out the balance accumulated in his or her account. In such case, the employee's option for the plan period he or she is withdrawing from will be automatically terminated. A participant's withdrawal from a plan period will not have any effect upon his or her eligibility to participate in a succeeding plan period or in any similar plan which we may adopt. If a participant's employment ends prior to a plan period termination date for any reason, including retirement or death, the contributions credited to his or her account will be returned to him or her or, in the case of his or her death, to his or her designated beneficiaries, and his or her option will be automatically terminated.

Eligibility

Our employees and those of a participating subsidiary are eligible to participate in the ESPP if we employ them for at least 20 hours per week and more than five months per year. However, no employee shall be granted an option under the ESPP if, immediately after the grant, the employee would own stock, including any outstanding options to purchase stock, equaling 5% or more of the total voting power or value of all classes of our stock. In addition, the ESPP provides that no employee may be granted an option if the option would permit the employee to purchase stock under all of our employee stock purchase plans in an amount that exceeds $25,000 of the fair market value of such stock for each calendar year in which the option is outstanding.

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 ESPP, (ii) the numbers and kinds of shares or other securities subject to the then outstanding options, and (iii) the exercise price for each share or other unit of any other securities subject to then outstanding options.

Corporate Transactions

In the event of our dissolution or liquidation, the plan period then in progress will terminate unless otherwise provided by the compensation committee. In the event of another significant corporate transaction such as a merger or consolidation of us with and into another person or entity or the sale or transfer of all or substantially all of our assets, each right to purchase stock under the ESPP may be assumed, or an equivalent right substituted by, the successor corporation or a parent or subsidiary of the successor corporation. In the event that the successor corporation refuses to assume each purchase right or to substitute an equivalent right, any ongoing offering period will be shortened so that employees' rights to purchase stock under the ESPP are exercised prior to the transaction, unless the employee has withdrawn.

Amendment and Termination

Our board of directors has the power to amend or terminate the ESPP and to change or terminate plan periods as long as any such action does not adversely affect any outstanding rights to purchase stock; provided, however, that the board of directors may amend or terminate the ESPP or a plan period even if it would adversely affect outstanding options in order to avoid our incurring adverseaccounting charges or if the board of directors determines that termination of the ESPP and/or plan period is in our best interest

and the best interest of our stockholders. The ESPP will continue in effect until the tenth anniversary of the closing of the offering described in this prospectus, unless earlier terminated by the board of directors.

Amount of Benefits

The dollar value of benefits that will be received by any employee or group of employees in the ESPP is not determinable due to the voluntary nature of the ESPP and the variables involved in the calculation of any such benefits (including our stock price).

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.

Name	Fees Earned or Paid in Cash	Stock Options	All Other Compensation
Hubert Birner, Ph.D.	—	—	—
Garen Bohlin	—	—	—
Todd Foley	—	—	—
F. Nicholas Franano, M.D.(1)	—	—	$ 43,000
John G. Freund, M.D.	—	—	—
Tim Haines	—	—	—
Dmitry Kobyzev	—	—	—
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.

We will adopt a new compensation program for our non-employee directors concurrent with the consummation of this offering. We retained an independent compensation consultant to help us determine the terms of the non-employee director compensation program. Under the program, effective upon the closing of this offering, each non-employee director shall be paid an annual fee of $35,000 and such additional fees as set out in the following table. All payments are to be made semi-annually, in arrears.

Non-Employee Director	Annual Fee
Chairman of the Company	$ 25,000
Chairman of the audit committee	$ 15,000
Member of the audit committee (other than chairman)	$ 7,500
Chairman of the compensation committee	$ 10,000
Member of the compensation committee (other than chairman)	$ 5,000
Chairman of the governance and nominating committee	$ 7,500
Member of the governance and nominating committee (other than chairman)	$ 3,750

Upon the effectiveness of this offering, we will be making an initial option grant to purchase 12,100 shares of common stock to Mr. Bohlin, which option grant will be at an exercise price equal to the price of our common stock in connection with the offering. Excluding Mr. Bohlin, each current non-employee director on the Board, upon the effectiveness of this offering, will receive an option grant being exercisable for such number of shares of common stock equal to 6,050, which option grant will be at an exercise price equal to the price of our common stock in connection with the offering. Mr. Bohlin's initial option grant will vest annually over three years. The option grants received by the current non-employee directors, upon the effectiveness of this offering, will vest 100% on the earlier of the one-year anniversary of such grant and the next annual meeting of the stockholders.

In addition, upon completion of this offering, we intend to provide our non-employee directors with equity compensation for service on our board of directors and committees on annual basis. We expect to make these grants around the time of the Company's annual meeting of stockholders. This equity compensation will consist of a grant of options to purchase 6,050 shares of common stock at an exercise price equal to the fair market value of the Company's common stock on the date of grant and will vest at the Company's next annual meeting of the stockholders. Additionally, after completion of this offering, we intend to provide any new non-employee director appointed to the board of directors an initial grant to purchase 12,100 shares of common stock at an exercise price equal to the fair market value of the Company's common stock on the date of such director's appointment which shall vest annually over three years. These annual grants and new director grants will be subject to approval by the Company's board of directors at the time.

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 659,806 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 659,806 shares of our common stock issuable upon exercise of outstanding warrants at a weighted average exercise price of $4.60 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	156,443	$ 3,599,999
Skyline Venture Partners Qualified Purchaser Fund IV, L.P.	2,436,437	121,760	$ 2,801,903
Prism Venture Partners and related funds	2,478,183	123,846	$ 2,849,910
Intersouth Partners VI, L.P.	1,729,523	86,432	$ 1,988,951
MPM Bio IV NVS Strategic Fund, LP	1,645,073	82,212	$ 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

Participation in this Offering

Certain holders of more than 5% of our voting securities have indicated an interest in purchasing shares of our common stock in this offering at the initial public offering price. However, because indications of interest are not binding agreements or commitments to purchase, the underwriters could determine to sell more, less or no shares to any of these existing stockholders and any of these existing stockholders could determine to purchase more, less or no shares in this offering.

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 September 30, 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 September 30, 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 9,345,374 shares of our common stock outstanding as of September 30, 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 assuming the full issuance of incremental shares upon its conversion based on the midpoint of the price range set forth on the cover page of this prospectus. 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 September 30, 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.

Certain holders of more than 5% of our common stock and their affiliated entities have indicated an interest in purchasing an aggregate of approximately $30.4 million in shares of our common stock in this offering at the initial public offering price. Assuming an initial public offering price of $13.00 per share, which is the midpoint of the price range set forth on the cover page of this prospectus, these entities would purchase an aggregate of up to approximately 2,341,215 of the 4,700,000 shares in this offering based on these indications of interest. However, because indications of interest are not binding agreements or commitments to purchase, the underwriters could determine to sell more, less or no shares to any of these existing stockholders and any of these existing stockholders could determine to purchase more, less or no shares in this offering. The following table does not reflect any such potential purchases by these existing principal stockholders or their affiliated entities. However, if any shares are purchased by these stockholders, the number of shares of common stock beneficially owned after this offering and the

percentage of common stock beneficially owned after this offering will differ from that set forth in the table below.

Beneficial Owner	Number of Shares Beneficially Owned	Percentage of Shares Beneficially Owned	
		Before Offering	After Offering
5% Stockholders:			
Abingworth Bioventures VI, LP.(1)	1,819,743	18.3%	12.4%
TVM Capital and related funds(2)	1,746,617	18.2	12.2
Prism Venture Partners and related funds(3)	1,394,048	14.6	9.8
Skyline Venture Partners Qualified Purchaser Fund IV, L.P.(4)	1,370,334	14.4	9.6
Pharmstandard International S.A.(6)	963,392	10.0	6.7
Deerfield and related funds(5)	963,389	10.0	6.7
Intersouth Partners VI, L.P.(7)	920,055	9.7	6.5
MPM Bio IV NVS Strategic Fund, L.P.(8)	916,097	9.7	6.5
Directors and Named Executive Officers:			
Timothy P. Noyes(9)	385,970	4.0	2.7
Gregory D. Phelps(10)	31,672	*	*
Hubert Birner, Ph.D.(1)	1,746,617	18.2	12.2
Brendan M. O'Leary, Ph.D.(3)	1,394,048	14.6	9.8
John G. Freund, M.D.(4)	1,370,334	14.4	9.6
Timothy Haines(2)	1,819,743	18.3	12.4
F. Nicholas Franano, M.D.(11)	310,253	3.3	2.2
Todd Foley(8)	916,097	9.7	6.5
Dmitry Kobyzev(6)	963,392	10.0	6.7
Garen Bohlin	—	*	*
Steven K. Burke(12)	197,447	2.1	1.4
Daniel P. Gottlieb(13)	61,992	*	*
All executive officers and directors as a group (13 persons)(14)	9,323,588	78.5%	56.2%

* *Indicates ownership of less than one percent.*

(1) Includes 1,238,547 shares of common stock issuable upon conversion of convertible preferred stock. Includes 581,196 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.

(2) Includes (a) 1,124,660 shares of common stock issuable upon conversion of convertible preferred stock and warrants to purchase 116,511 shares of common stock held by TVM Life Science Ventures VI GmbH & Co. KG and (b) 385,461 shares of common stock issuable upon conversion of convertible preferred stock and warrants to purchase 39,932 shares of common stock held by TVM Life Science Ventures VI L.P. Includes 59,620 shares of common stock issuable upon conversion of convertible preferred stock and 20,433 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.

(3) Includes (a) 828,801 shares of common stock issuable upon conversion of convertible preferred stock and warrants to purchase 85,095 shares of common stock held by Prism Venture Partners V, L.P., and (b) 377,427 shares of common stock and warrants to purchase 38,751 shares of common stock held by Prism Venture Partners V-A, L.P. Includes 43,957 shares of common stock issuable upon conversion of convertible preferred stock and 20,017 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.

(4) Includes 1,185,676 shares of common stock issuable upon conversion of convertible preferred stock and warrants to purchase 121,760 shares of common stock. Includes 62,898 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.

(5) Includes (a) 473,562 shares of common stock issuable upon conversion of convertible preferred stock held by Deerfield Private Design Fund III, L.P., (b) 101,268 shares of common stock issuable upon conversion of convertible preferred stock held by Deerfield Special Situations Fund, L.P., and (c) 80,869 shares of common stock issuable upon conversion of convertible preferred stock held by Deerfield Special Situations International Master Fund, L.P. Includes 222,221 shares of common stock issuable upon conversion of convertible preferred stock, 47,521 shares of common stock issuable upon conversion of convertible preferred stock and 37,948 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.

(6) Includes 655,700 shares of common stock issuable upon conversion of convertible preferred stock. Includes 307,692 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.

(7) Includes 806,069 shares of common stock issuable upon conversion of convertible preferred stock and warrants to purchase 86,432 shares of common stock. Includes 27,554 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.

(8) Includes 769,944 shares of common stock issuable upon conversion of convertible preferred stock and warrants to purchase 82,212 shares of common stock. Includes 63,941 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.

(9) Includes 385,970 shares of common stock which Mr. Noyes has the right to acquire upon the exercise of stock options that were exercisable as of September 30, 2014, or that will become exercisable within 60 days after that date.

(10) Includes 31,672 shares of common stock which Mr. Phelps has the right to acquire upon the exercise of stock options that were exercisable as of September 30, or that will become exercisable within 60 days after that date.

(11) Includes (a) 217,860 shares of common stock and 6,741 shares of common stock issuable upon conversion of convertible preferred stock held directly by Dr. Franano, (b) 413 shares of common stock issuable upon conversion of convertible preferred stock held by Mr. Franano and Lorie Beth Whitaker, and (c) 85,239 shares of common stock which Dr. Franano has the right to acquire upon the exercise of stock options that were exercisable as of September 30, 2014, or that will become exercisable within 60 days after that date.

(12) Includes 197,447 shares of common stock which Dr. Burke has the right to acquire upon the exercise of stock options that were exercisable as of September 30, 2014, or that will become exercisable within 60 days after that date.

(13) Includes 61,992 shares of common stock which Mr. Gottlieb has the right to acquire upon the exercise of stock options that were exercisable as of September 30, 2014, or that will become exercisable within 60 days after that date.

(14) Includes 888,343 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 September 30, 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 September 30, 2014, we had issued and outstanding:

- 241,559 shares of our common stock;
- 120,318,776 shares of our convertible preferred stock that will automatically convert into 9,103,815 shares of our common stock upon the closing of this offering;
- warrants to purchase a total of 659,806 shares of our common stock with a weighted-average exercise price of $4.60 per share that we expect to be exercised immediately prior to the closing of this offering; and
- options to purchase a total of 1,133,052 shares of our common stock with a weighted-average exercise price of $3.45 per share.

As of September 30, 2014, we had outstanding 9,345,374 shares of common stock held of record by 86 shareholders, assuming the conversion of 120,318,776 shares of preferred stock outstanding as of September 30, 2014 into shares of our common stock, and excluding the exercise of warrants to purchase an aggregate of 659,806 shares outstanding as of September 30, 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. An election of directors by our stockholders shall be determined by a plurality of votes cast by the stockholders entitled to vote on the election.

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 September 30, 2014, we had outstanding an aggregate of 120,318,776 shares of preferred stock held of record by 78 stockholders.

Upon closing of this offering, all outstanding shares of preferred stock will be automatically converted into 9,103,815 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 10,000,000 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 September 30, 2014, we had outstanding warrants to purchase an aggregate of 659,806 shares of common stock at a weighted average exercise price of $4.60, 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. At each annual meeting of the stockholders, a class of directors will be elected for a three-year term to succeed the directors of the same class whose terms are then expiring. As a result approximately one-third of our directors will be elected each year. The initial term of office of the directors of Class I shall expire as of the first annual meeting of the Company's stockholders following the closing of this offering; the initial term of office of the directors of Class II shall expire as of the second annual meeting of the Company's stockholders following the closing of this offering; and the initial term of office of the directors of Class III shall expire as of the third annual meeting of the Company's stockholders following the closing of this offering. The classification of directors will have the effect of making it more difficult for stockholders to change the composition of our board.

- Our Class I directors will be Timothy Noyes, Garen Bohlin and John Freund;
- Our Class II directors will be Hubert Birner, Dmitry Kobyzev and Gregory Phelps; and
- Our Class III directors will be Brendan O'Leary and Tim Haines.

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. Any additional directorships resulting from an increase in the number of directors will be distributed among the three classes so that, as nearly as possible, each class shall consist of one third of the board of directors. Upon completion of this offering, we expect that our board of directors will have eight 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 and entitled to vote in the election of directors. 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 outstanding shares of capital stock, voting together as a single class and entitled to vote in the election of directors will be required to amend, alter, change or repeal the amended and restated bylaws and the amended and restated certificate of incorporation. 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 Computershare.

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 September 30, 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 14,045,374 shares of common stock. Of these shares, all of the 4,700,000 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
9,313,859	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 more than 99% of our shares of common stock outstanding as of September 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 Stifel, Nicolaus & Company, Incorporated and JMP Securities LLC, 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 140,500 shares immediately after the completion of this offering based on the number of shares outstanding as of September 30, 2014; 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 8,501,403 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	4,700,000

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 705,000 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 $30,000.

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 $2,607,000.

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' option to purchase additional shares from us in this offering. The underwriters may close out any covered short position by either exercising their 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 option to purchase additional shares. Naked short sales are any short sales in excess of such option to purchase additional shares. 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,

except for Note 15,
as to which the date is October 6, 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); 230,607, 239,905 and 240,378 issued and outstanding at December 31, 2012, December 31, 2013, and June 30, 2014, respectively, and 8,741,816 shares issued and outstanding pro forma (unaudited)	0	0	0	9
Additional paid-in capital	—	—	—	123,895
Accumulated deficit	(86,657)	(100,514)	(109,267)	(102,687)
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	$ (61.16)	$ (59.66)	$ (27.97)	$ (36.64)
Weighted-average number of common shares used in net loss per share attributable to common stockholders—basic and diluted	230,607	235,184	230,607	240,254
Pro forma net loss per share attributable to common stockholders—basic and diluted (unaudited)		$ (1.54)		$ (0.66)
Pro forma weighted-average number of common shares used in net loss per share attributable to common stockholders—basic and diluted (unaudited)		4,565,620		6,763,218

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 Stockholder (Deficit) Equity
	Shares	Amount	Shares	Amount	Shares	Amount	Shares	Amount	Shares	Amount	Shares	$0.001 Par Value				
Balance at December 31, 2011	22,638,465	$ 31,031	10,909,091	$ 15,677	20,754,461	$ 22,446	13,202,932	$ 14,999			230,607	$ 0	$ —	$ (72,664)	$ 5	$ (72,65
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)	—	(6,13
Stock-based compensation expense	—	—	—	—	—	—	—	—			—	—	110	—	—	11
Unrealized gain (loss) on short term investments	—	—	—	—	—	—	—	—			—	—	—	—	(4)	
Net loss	—	—	—	—	—	—	—	—			—	—	—	(7,970)	—	(7,97
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	—	$ —	230,607	$ 0	$ —	$ (86,657)	$ 1	$ (86,65
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)	—	(6,11
Exercise of common stock options	—	—	—	—	—	—	—	—			9,298	0	19	—	—	1
Stock-based compensation expense	—	—	—	—	—	—	—	—			—	—	155	—	—	15
Unrealized gain (loss) on short term investments	—	—	—	—	—	—	—	—			—	—	—	—	(1)	
Net loss	—	—	—	—	—	—	—	—			—	—	—	(7,912)	—	(7,91
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	—	$ —	239,905	$ 0	$ —	$ (100,514)	$ —	$ (100,51
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)	—	(3,40
Exercise of common stock options	—	—	—	—	—	—	—	—	—	—	473	0	1	—	—	
Stock-based compensation expense	—	—	—	—	—	—	—	—	—	—	—	—	49	—	—	4
Unrealized gain (loss) on short term investments	—	—	—	—	—	—	—	—	—	—	—	—	—	—	(23)	(2
Net loss	—	—	—	—	—	—	—	—	—	—	—	—	—	(5,394)	—	(5,39
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	240,378	$ 0	$ —	$ (109,267)	$ (23)	$ (109,29
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)	8,501,438	9	123,895	—	—	123,90
Extinguishment of investors rights and obligations (unaudited)	—	—	—	—	—	—	—	—	—	—	—	—	—	6,580	—	6,58
Pro forma balance at June 30, 2014 (unaudited)	—	$ —	—	$ —	—	$ —	—	$ —	—	$ —	8,741,816	$ 9	$ 123,895	$ (102,687)	$ (23)	$ 21,19

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 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

2. Summary of Significant Accounting Policies (Continued)

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.

On October 1, 2014, the Board of Directors and, on October 3, 2014, the stockholders approved a 1-for-15.87 reverse stock split of the Company's Common Stock and a proportional adjustment to the existing conversion ratios for each series of Preferred Stock. The effective date of the reverse stock split is October 6, 2014. All share, share equivalent and per share amounts have been adjusted to reflect the reverse stock split. The ratios by which shares of Preferred Stock are convertible into shares of Common Stock have been adjusted to reflect the effects of the reverse stock split.

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.

2. Summary of Significant Accounting Policies (Continued)

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 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. The unaudited

2. Summary of Significant Accounting Policies (Continued)

pro forma information also assumes the extinguishment of the liability related to the Series D investors' purchase rights upon the closing of an IPO of the Company's Common Stock. 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.

As noted above, the unaudited pro forma information reflects the automatic conversion, upon the closing of this initial public offering of the Company's Common Stock, of all outstanding shares of Preferred Stock into shares of Common Stock. The conversion has been adjusted in connection with the 1-for-15.87 reverse stock split of the Company's Common Stock effected on October 6, 2014, for all series of Preferred Stock. For purposes of the unaudited pro forma information included within these financial statements, the conversion of the Preferred Stock has been reflected assuming the conversion ratio, adjusted for the 1-for-15.87 reverse stock split, in effect as of each balance sheet date or on the date of the assumed conversion (upon the closing of this initial public offering) for pro forma net loss per share considerations. 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.

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.

2. Summary of Significant Accounting Policies (Continued)

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.

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

2. Summary of Significant Accounting Policies (Continued)

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.

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

2. Summary of Significant Accounting Policies (Continued)

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 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

2. Summary of Significant Accounting Policies (Continued)

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 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.

2. Summary of Significant Accounting Policies (Continued)

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 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, and through October 6, 2014, the date the revised 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,		June 30,
	2012	2013	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. Both the Company and the tranche right holders have the right to exercise these tranche features. However, the Company's right is contingent upon the achievement of certain pre-defined milestones and terminates at the closing of an initial public offering. The holders of the tranche rights have the ability to exercise the second and third tranche rights to purchase additional shares of the Company's Series D Preferred Stock at any time prior to an initial public offering and excluding certain black-out dates. The Series D Purchase Agreement also provides to the Series D investors party to the agreement certain individual purchase rights, as further outlined below.

Individual Purchase Rights after the Closing of an Initial Public Offering. If, following the closing of an initial public offering, the second and third tranche features have not been exercised in full the Series D investors will have individual purchase rights under the Series D Purchase Agreement, until May 13, 2024. Up to $20 million of Common Stock could be subject to these individual purchase rights provided for under the Series D Purchase Agreement. The purchase price per share for the Common Stock purchasable pursuant to the individual purchase rights will be the lower of (i) $9.34, 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

9. Redeemable Convertible Preferred Stock (Continued)

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 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. Under certain circumstances, the Series D investor rights will terminate upon the closing of an IPO of the Company's Common Stock. For purposes of the unaudited pro forma financial information, the Company has assumed these circumstances have occurred and therefore, the associated liability has been reflected as extinguished.

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

9. Redeemable Convertible Preferred Stock (Continued)

Series D Preferred Stock. The remaining $77,000 of issuance costs have been allocated to the tranche right liability.

Conversion

In connection with the 1-for-15.87 reverse stock split of the Company's Common Stock effected on October 6, 2014, 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 0.06, 0.08, 0.08, 0.08 and 0.08, 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 aggregate proceeds are at least $40 million with an offering price of at least $54.75 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.

9. Redeemable Convertible Preferred Stock (Continued)

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 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.

9. Redeemable Convertible Preferred Stock (Continued)

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 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	1,426,482	1,426,482	1,700,622
Conversion of Series A-1 Preferred Stock	687,395	687,395	838,101
Conversion of Series B Preferred Stock	1,307,771	1,307,771	1,610,383
Conversion of Series C Preferred Stock	1,105,907	1,105,907	1,361,809
Conversion of Series D Preferred Stock	—	—	3,327,894
Stock-based compensation awards	632,409	623,111	1,135,415
Warrants to purchase Common Stock	659,806	659,806	659,806
Total	5,819,770	5,810,472	10,634,030

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 1,148,214 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	613,590	$ 2.06	6.2	$ 12,370
Granted	3,150	$ 22.22		
Exercised	(9,298)	$ 2.06		
Cancelled or forfeited	(425)	$ 2.54		
Outstanding at December 31, 2013	607,017	$ 2.22	5.2	$ 1,627
Granted (unaudited)	527,718	$ 4.92		
Exercised (unaudited)	(473)	$ 1.27		
Cancelled or forfeited (unaudited)	—	$ —		
Outstanding at June 30, 2014 (unaudited)	1,134,262	$ 3.49	7.2	$ 1,722
Exercisable at December 31, 2013	509,609	$ 2.22	4.7	$ 1,307
Vested or expected to vest at December 31, 2013(1)	583,625	$ 2.22	5.1	$ 1,561
Exercisable at June 30, 2014 (unaudited)	536,583	$ 2.22	4.4	$ 1,483
Vested or expected to vest at June 30, 2014 (unaudited)(1)	1,062,276	$ 3.33	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 3,150 shares of its Common Stock with a weighted-average grant date fair value of $16.50. During the six months ended June 30, 2014 (unaudited) the Company granted stock options to purchase an aggregate of 527,718 shares of its Common Stock with a weighted-average grant date fair value of $3.38.

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,	Six Months Ended June 30,	
	2013	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	4,254	4,254	4,254	7,581
Common stock warrants	660	660	660	660
Outstanding stock options	614	607	617	1,134
Convertible notes	—	243	—	—
	5,528	5,764	5,531	9,375

15. Subsequent Events

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.

In connection with preparing for its initial public offering, on October 1, 2014, the Board of Directors and, on October 3, 2014, the stockholders approved a 1-for-15.87 reverse stock split of the Company's Common Stock and a proportional adjustment to the existing conversion ratios for each series of Preferred Stock. The stock split became effective on October 6, 2014. The stockholders entitled to fractional shares as a result of the reverse stock split will receive a cash payment in lieu of receiving fractional shares. The Company's historical share and per share information presented in these consolidated financial statements and notes thereto has been retroactively adjusted to give effect to this reverse stock split. The shares of Common Stock underlying outstanding stock options were proportionately reduced and the respective exercise prices were proportionately increased. Shares of Common Stock reserved for future issuance were presented on an as converted basis and the financial statements disclose the adjusted conversion ratios.

On August 21, 2014, the Board of Directors adopted the Proteon Therapeutics, Inc. 2014 Incentive Plan, the 2014 Employee Stock Purchase Plan and the 2006 Equity Incentive Plan, as amended and restated, and on October 3, 2014, the stockholders approved such plans.

The 2014 Equity Incentive Plan, which will become effective immediately prior to effectiveness of the Company's initial public offering, 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

15. Subsequent Events (Continued)

and qualified performance-based awards. The number of shares initially reserved for issuance under the 2014 Equity Incentive Plan is 704,000 shares of Common Stock and will be increased each January 1 starting in 2015 by an amount equal to the lesser of (i) four percent (4%) of our outstanding Common Stock on a fully diluted basis as of the end of our immediately preceding fiscal year, and (ii) any lower amount determined by our Board of Directors prior to each such January 1.

The 2014 Employee Stock Purchase Plan, which will become effective upon the completion of the Company's initial public offering, authorizes the issuance of up to 140,500 shares of Common Stock. The number of shares will be increased each January 1, commencing on January 1, 2015 and ending on (and including) January 1, 2024, by an amount equal to the lesser of (i) one percent (1%) of outstanding shares as of the end of the immediately preceding fiscal year, (ii) 281,000, and (iii) any lower amount determined by our Board of Directors prior to each such January 1.

4,700,000 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	$ 9,664
FINRA filing fee	11,851
NASDAQ listing fee	125,000
Legal fees and expenses	1,279,000
Accounting fees and expenses	954,000
Printing expenses	150,000
Transfer agent fees and expenses	15,000
Miscellaneous	62,485
Total	$ 2,607,000

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 659,806 shares of its common stock, at a purchase price of $4.60 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 September 30, 2014, we have granted to employees, consultants and directors options to purchase 1,133,052 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 $1.27 to

$22.22. 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 September 30, 2014, an aggregate of 10,364 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 $1.27 to $3.17 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**	Fifth Amended and Restated Certificate of Incorporation of the Company, as currently in effect.
3.2	Form of Sixth Amended and Restated Certificate of Incorporation of the Company, to be in effect upon completion of the offering.
3.3**	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.
3.5	Amendment No. 1 to the Fifth Amended and Restated Certificate of Incorporation of the Company, as currently in effect.
3.6	Amendment No. 2 to the Fifth Amended and Restated Certificate of Incorporation of the Company, as currently in effect.
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†	2006 Equity Incentive Plan, as amended and restated August 21, 2014.

Exhibit No.	Description
10.2†	2014 Equity Incentive Plan, Form of Stock Option Agreement and Form of Option Exercise Notice under the Company's 2014 Equity Incentive Plan.
10.3†**	Offer Letter by and between the Company and Daniel Gottlieb, dated July 19, 2007.
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†**	Letter Agreement by and between the Company and F. Nicholas Franano, dated August 22, 2014.
10.9‡**	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**	Assignment of Rights/License Agreement, effective as of February 4, 2002, by and between Johns Hopkins University and F. Nicholas Franano.
10.12**	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†**	Form of Stock Option Agreement under the Company's 2006 Equity Incentive Plan, as amended.
10.17**	Indemnification Agreement, dated as of March 29, 2006, by and between the Company and Brendan O'Leary.
10.18**	Indemnification Agreement, dated as of June 26, 2007, by and between the Company and Hubert Birner.
10.19**	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.

Exhibit No.	Description
10.21**	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.
10.23**	Indemnification Agreement, dated as of May 13, 2014, by and between the Company and Tim Haines.
10.24**	Indemnification Agreement, dated as of May 13, 2014, by and between the Company and Dmitry Kobyzev.
10.25†	2014 Employee Stock Purchase Plan.
10.26†	Amended and Restated Employment Agreement by and between the Company and Timothy P. Noyes, dated October 1, 2014.
10.27†	Amended and Restated Employment Agreement by and between the Company and Steven K. Burke, dated October 1, 2014.
10.28†	Amended and Restated Employment Agreement by and between the Company and George A. Eldridge, dated October 1, 2014.
10.29†	Amended and Restated Employment Agreement by and between the Company and Daniel Gottlieb, dated October 1, 2014.
10.30	Form of Amended and Restated Indemnification Agreement.
21.1**	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).

** Previously filed with the Registration Statement on Form S-1 as filed with the Commission on September 16, 2014.

† 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.

(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 Amendment No.1 to the Registration Statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the city of Waltham, Commonwealth of Massachusetts on October 7, 2014.

PROTEON THERAPEUTICS, INC.

By: /s/ TIMOTHY P. NOYES

Timothy P. Noyes
President & Chief Executive Officer

Pursuant to the requirements of the Securities Act of 1933, as amended, this Amendment No.1 to the Registration Statement has been signed by the following persons in the capacities and on the dates indicated.

Name	Title	Date
/s/ TIMOTHY P. NOYES Timothy P. Noyes	President, Chief Executive Officer and Director (*Principal Executive Officer*)	October 7, 2014
/s/ GEORGE ELDRIDGE George Eldridge	Senior Vice President, Chief Financial Officer, Treasurer and Secretary (*Principal Financial Officer and Principal Accounting Officer*)	October 7, 2014
* Hubert Birner, Ph.D.	Director	October 7, 2014
* Todd Foley	Director	October 7, 2014
* F. Nicholas Franano, M.D.	Director	October 7, 2014
* John G. Freund, M.D.	Director	October 7, 2014
* Tim Haines	Director	October 7, 2014
* Dmitry Kobyzev, Ph.D.	Director	October 7, 2014
* Brendan M. O'Leary, Ph.D.	Director	October 7, 2014
* Gregory D. Phelps	Director	October 7, 2014

*By: /s/ TIMOTHY P. NOYES

Timothy P. Noyes
Attorney-in-fact

EXHIBIT INDEX

Exhibit No.	Description
1.1	Form of Underwriting Agreement.
3.1**	Fifth Amended and Restated Certificate of Incorporation of the Company, as currently in effect.
3.2	Form of Sixth Amended and Restated Certificate of Incorporation of the Company, to be in effect upon completion of the offering.
3.3**	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.
3.5	Amendment No. 1 to the Fifth Amended and Restated Certificate of Incorporation of the Company, as currently in effect.
3.6	Amendment No. 2 to the Fifth Amended and Restated Certificate of Incorporation of the Company, as currently in effect.
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†	2006 Equity Incentive Plan, as amended and restated August 21, 2014.
10.2†	2014 Equity Incentive Plan, Form of Stock Option Agreement and Form of Option Exercise Notice under the Company's 2014 Equity Incentive Plan.
10.3†**	Offer Letter by and between the Company and Daniel Gottlieb, dated July 19, 2007.
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†**	Letter Agreement by and between the Company and F. Nicholas Franano, dated August 22, 2014.
10.9‡**	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.

Exhibit No.	Description
10.11**	Assignment of Rights/License Agreement, effective as of February 4, 2002, by and between Johns Hopkins University and F. Nicholas Franano.
10.12**	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†**	Form of Stock Option Agreement under the Company's 2006 Equity Incentive Plan, as amended.
10.17**	Indemnification Agreement, dated as of March 29, 2006, by and between the Company and Brendan O'Leary.
10.18**	Indemnification Agreement, dated as of June 26, 2007, by and between the Company and Hubert Birner.
10.19**	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**	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.
10.23**	Indemnification Agreement, dated as of May 13, 2014, by and between the Company and Tim Haines.
10.24**	Indemnification Agreement, dated as of May 13, 2014, by and between the Company and Dmitry Kobyzev.
10.25†	2014 Employee Stock Purchase Plan.
10.26†	Amended and Restated Employment Agreement by and between the Company and Timothy P. Noyes, dated October 1, 2014.
10.27†	Amended and Restated Employment Agreement by and between the Company and Steven K. Burke, dated October 1, 2014.
10.28†	Amended and Restated Employment Agreement by and between the Company and George A. Eldridge, dated October 1, 2014.
10.29†	Amended and Restated Employment Agreement by and between the Company and Daniel Gottlieb, dated October 1, 2014.
10.30	Form of Amended and Restated Indemnification Agreement.
21.1**	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.

Exhibit No.	Description
24.1**	Power of Attorney (included on signature page).

** Previously filed with the Registration Statement on Form S-1 as filed with the Commission on September 16, 2014.

† 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.

UNDERWRITING AGREEMENT
[Number of Firm Shares] Shares
Proteon Therapeutics, Inc.
Common Stock

UNDERWRITING AGREEMENT

[·], 2014

STIFEL, NICOLAUS & COMPANY, INCORPORATED
JMP SECURITIES, LLC
As representatives of the several Underwriters
named in Schedule I hereto

c/o Stifel, Nicolaus & Company, Incorporated
One South Street, 15th Floor
Baltimore, Maryland 21202

c/o JMP Securities, LLC
600 Montgomery Street, Suite 1100
San Francisco, CA 94111

Ladies and Gentlemen:

Proteon Therapeutics, Inc., a Delaware corporation (the "Company"), proposes to issue and sell to the several underwriters named in Schedule I hereto (the "Underwriters") for whom you are acting as representatives (the "Representatives"), an aggregate of [·] shares (the "Firm Shares") of the common stock, par value $0.001 per share, of the Company ("Common Stock"). The Company also proposes to sell to the several Underwriters, for the sole purpose of covering over-allotments in connection with the sale of the Firm Shares, at the option of the Underwriters, up to an additional [·] shares of Common Stock (the "Option Shares"). The Firm Shares and the Option Shares are hereinafter referred to collectively as the "Shares".

The Company confirms as follows its agreements with the Representatives and the several other Underwriters.

1. (a) The Company represents and warrants to, and agrees with, each of the Underwriters that, as of the date hereof and as of the Closing Date (as hereinafter defined) and each Option Closing Date (as hereinafter defined), if any:

(i) A registration statement on Form S-1 (File No. [·]) in respect of the Shares and one or more pre-effective amendments thereto (together, the "Initial Registration Statement") have been filed with the Securities and Exchange Commission (the "Commission"); the Initial Registration Statement and any post-effective amendment thereto, each in the form heretofore delivered to you, have been declared effective by the Commission in such form; other than a registration statement, if any, increasing the size of the offering (a "Rule 462(b) Registration Statement"), filed pursuant to Rule 462(b) under the Securities Act of 1933, as amended (the "Securities Act"), which became effective upon filing, no other document with respect to the Initial Registration Statement has heretofore been filed with the Commission; no stop order suspending the effectiveness of the Initial Registration Statement, any post-effective amendment thereto or the Rule 462(b) Registration Statement, if any, has been issued, no proceeding for that purpose has been initiated or, to the Company's knowledge, threatened by the Commission and any request on the part of the Commission for additional information from the Company has been satisfied in all material respects; any preliminary prospectus included in the Initial Registration Statement, as originally filed or as part of any amendment thereto, or filed with the Commission pursuant to Rule 424(a) of the rules and regulations of the Commission under the Securities Act is hereinafter called a "Preliminary Prospectus"; the various parts of the Initial Registration Statement and the Rule 462(b) Registration Statement, if any, including all schedules and exhibits thereto and including the information contained in the form of final prospectus filed with the Commission pursuant to Rule 424(b) under the Securities Act and deemed by virtue of Rule 430A under the Securities Act to be part of the Initial Registration Statement at the time it was declared effective or such part of the Rule 462(b) Registration Statement, if any, became or hereafter becomes effective, each as amended at the time such part of the Initial Registration Statement became effective, are hereinafter collectively called the "Registration Statement"; the Preliminary Prospectus relating to the Shares that was included in the Registration Statement immediately prior to the Applicable Time (as defined in Section 1(a) (iii) hereof) is hereinafter called the "Pricing Prospectus"; such final prospectus, in the form first filed pursuant to Rule 424(b) under the Securities Act, is hereinafter called the "Prospectus"; and any "issuer free writing prospectus" as defined in Rule 433 under the Securities Act relating to the Shares is hereinafter called an "Issuer Free Writing Prospectus"; and all references to the Registration Statement, any Preliminary Prospectus, the Pricing Prospectus, the Prospectus, any Issuer Free Writing Prospectus or any amendment or supplement to any of the foregoing shall be deemed to include the copy filed with the Commission pursuant to its Electronic Data Gathering, Analysis and Retrieval system ("EDGAR"). From the time of the initial confidential submission of the Registration Statement to the Commission (or, if earlier, the first date on which the Company engaged directly or through any person authorized to act on its behalf in any Testing-the-Waters Communication) through the date hereof, the Company has been and is an "emerging growth company," as defined in Section 2(a) of the Securities Act (an "Emerging Growth Company"). "Testing-the-Waters Communication" means any oral or written communication with potential investors undertaken in reliance on Section 5(d) of the Securities Act;

(ii) (1) at the respective times the Initial Registration Statement, any Rule 462(b) Registration Statement and any post-effective amendments thereto became effective and at the Closing Date (as defined herein) (and, if any Option Shares are purchased, at each Option Closing Date) (as defined herein)), the Initial Registration Statement, any Rule 462(b)

Registration Statement and any amendments and supplements thereto complied and will comply in all material respects with the requirements of the Securities Act and the rules and regulations of the Commission thereunder (the "Rules and Regulations") and did not and will not contain an untrue statement of a material fact or omit to state a material fact required to be stated therein or necessary to make the statements therein not misleading, and (2) at the time the Prospectus or any amendments or supplements thereto were issued and at the Closing Date (and, if any Option Shares are purchased, at each Option Closing Date), neither the Prospectus nor any amendment or supplement thereto included or will include an untrue statement of a material fact or omitted or will omit to state a material fact necessary in order to make the statements therein, in the light of the circumstances under which they were made, not misleading; provided that the representations and warranties in clauses (1) and (2) above shall not apply to statements in or omissions from the Registration Statement or the Prospectus made in reliance upon and in strict conformity with information furnished to the Company in writing by any Underwriter through the Representatives expressly for use in the Registration Statement or the Prospectus, it being understood and agreed that the only such information provided by any Underwriter is that described as such in Section 9(b) hereof. No order preventing or suspending the use of any Preliminary Prospectus, the Pricing Prospectus or any Issuer Free Writing Prospectus has been issued by the Commission;

Each Preliminary Prospectus, Pricing Prospectus, Issuer Free Writing Prospectus and the Prospectus filed as part of the Initial Registration Statement as originally filed or as part of any amendment thereto, or filed pursuant to Rule 424 under the Securities Act, complied when so filed in all material respects with the requirements

of the Securities Act and the Rules and Regulations and each Preliminary Prospectus, Pricing Prospectus, Issuer Free Writing Prospectus and the Prospectus delivered to the Underwriters for use in connection with this offering was identical to the electronically transmitted copies thereof filed with the Commission pursuant to EDGAR, except to the extent permitted by Regulation S-T;

(iii) For the purposes of this Agreement, the "Applicable Time" is [·]:[·] [A][P].M. (New York time) on the date of this Agreement; the Pricing Prospectus as supplemented by the Issuer Free Writing Prospectuses and Written Testing-the-Waters Communications (as hereinafter defined) listed on Schedule [·] hereto, taken together (collectively, the "Pricing Disclosure Package") as of the Applicable Time, did not include any untrue statement of a material fact or omit to state any material fact necessary in order to make the statements therein, in the light of the circumstances under which they were made, not misleading; and each Issuer Free Writing Prospectus and Written Testing-the-Waters Communication listed on Schedule [·] hereto does not conflict with the information contained in the Registration Statement, the Pricing Prospectus or the Prospectus and each Issuer Free Writing Prospectus and Written Testing-the-Waters Communication listed on Schedule [·] hereto, as supplemented by and taken together with the Pricing Disclosure Package as of the Applicable Time, did not include any untrue statement of a material fact or omit to state any material fact necessary in order to make the statements therein, in the light of the circumstances under which they were made, not misleading; provided, however, that this representation and warranty shall not apply to statements or omissions made in an Issuer Free Writing Prospectus or Written Testing-the-Waters Communication in reliance upon and in strict conformity with information

furnished in writing to the Company by an Underwriter through the Representatives expressly for use therein;

(iv) The Company has filed a registration statement pursuant to the Securities Exchange Act of 1934, as amended (the "Exchange Act"), to register the Common Stock, and such registration statement has been declared effective; At the time of filing the Initial Registration Statement the Company was not and is not an "ineligible issuer," as defined under Rule 405 under the Securities Act;

(v) The Company has been duly incorporated and is validly existing as a corporation in good standing under the laws of the State of Delaware, with power and authority (corporate and other) to own, lease and operate its properties and conduct its business as described in the Pricing Prospectus and to enter into and perform its obligations under this Agreement, and has been duly qualified as a foreign corporation for the transaction of business and is in good standing under the laws of each other jurisdiction in which it owns or leases properties or conducts any business so as to require such qualification, except where the failure so to qualify or be in good standing would not reasonably be expected to have a material adverse effect on the general affairs, business, prospects, management, financial position, shareholders' equity or results of operations of the Company and the Subsidiaries (as hereinafter defined), considered as one enterprise (a "Material Adverse Effect");

(vi) Each subsidiary of the Company (each a "Subsidiary") has been duly incorporated (or organized) and is validly existing as a corporation (or other organization) in good standing under the laws of the jurisdiction of its incorporation (or organization), with power and authority to own, lease and operate its properties and conduct its business as described in the Pricing Prospectus, and has been duly qualified as a foreign corporation (or other organization) for the transaction of business and is in good standing under the laws of each other jurisdiction in which its owns or leases properties or conducts any business so as to require such qualification, except where the failure so to qualify or be in good standing would not reasonably be expected to have a Material Adverse Effect; all of the issued and outstanding capital stock (or other ownership interests) of each Subsidiary has been duly and validly authorized and issued, is fully paid and non-assessable and is owned by the Company, directly or through Subsidiaries, free and clear of any security interest, mortgage, pledge, lien, encumbrance, claim or equity;

(vii) The Company has an authorized capitalization as set forth in the Pricing Prospectus, and all of the issued and outstanding shares of capital stock of the Company have been duly and validly authorized and issued, are fully paid and non-assessable and conform to the descriptions thereof contained in the Pricing Prospectus; and none of the issued and outstanding shares of capital stock of the Company are subject to any preemptive or similar rights;

(viii) The Shares to be issued and sold by the Company to the Underwriters hereunder have been duly and validly authorized and, when issued and delivered to and paid for by the Underwriters in accordance with the terms of this Agreement, will be duly and validly issued and fully paid and non-assessable and will conform to the descriptions thereof

contained in the Prospectus; and the issuance of such Shares is not subject to any preemptive or similar rights that have not been duly waived;

(ix) This Agreement has been duly authorized, executed and delivered by the Company;

(x) The issue and sale of the Shares to be sold by the Company hereunder, the execution of this Agreement by the Company and the compliance by the Company with all of the provisions of this Agreement and the consummation of the transactions herein contemplated will not conflict with or result in a breach or violation of any of the terms or provisions of, or constitute a default under, any indenture, mortgage, deed of trust, loan agreement or other agreement or instrument to which the Company or any of the Subsidiaries is a party or by which the Company or any of the Subsidiaries is bound or to which any of the property or assets of the Company or any of the Subsidiaries is subject, nor will such action result in any violation of the provisions of the certificate or articles of incorporation or by-laws (or other organization documents) of the Company or any of the Subsidiaries or any statute or any order, rule or regulation of any court or governmental agency or body having jurisdiction over the Company or any of the Subsidiaries or any of their properties; and no consent, approval, authorization, order, registration or qualification of or with any such court or governmental agency or body is required for the issue and sale of the Shares to be sold by the Company hereunder or the consummation by the Company of the transactions contemplated by this Agreement, except the registration under the Securities Act of the Shares and such consents, approvals, authorizations, registrations or qualifications as may be required under state securities or Blue Sky laws in connection with the purchase and distribution of the Shares by the Underwriters;

(xi) No holders of securities of the Company have rights to the registration of such securities under the Registration Statement, except for any such rights as have been effectively waived;

(xii) Ernst & Young LLP, who have certified certain financial statements of the Company and the Subsidiaries, are independent public accountants as required by the Securities Act and the Rules and Regulations. The financial statements, together with related schedules and notes, included in the Registration Statement and the Pricing Prospectus comply in all material respects with the requirements of the Securities Act and present fairly the consolidated financial position, results of operations and changes in financial position of the Company and the Subsidiaries on the basis stated in the Registration Statement at the respective dates or for the respective periods to which they apply; such financial statements and related schedules and notes have been prepared in accordance with generally accepted accounting principles consistently applied throughout the periods involved, except as disclosed therein; and the selected financial data and the summary financial data included in the Pricing Prospectus present fairly the information shown therein and have been compiled on a basis consistent with that of the financial statements included in the Registration Statement. The interactive data in eXtensible Business Reporting Language included or incorporated by reference in the Registration Statement fairly presents the information called for in all material respects and has been prepared in accordance with the Commission's rules and guidelines applicable thereto;

(xiii) Neither the Company nor any Subsidiary has sustained since the date of the latest audited financial statements included in the Pricing Prospectus any material loss or interference with its business from fire, explosion, flood or other calamity, whether or not covered by insurance, or from any labor dispute or court

or governmental action, order or decree, otherwise than as set forth or contemplated in the Pricing Prospectus; and, since the respective dates as of which information is given in the Registration Statement and the Pricing Prospectus, (1) there has not been any change in the capital stock or long-term debt of the Company or any of the Subsidiaries, (2) there has not been any material adverse change, or any development involving a prospective material adverse change, in or affecting the general affairs, business, prospects, management, financial position, shareholders' equity or results of operations of the Company and the Subsidiaries, considered as one enterprise, (3) there have been no transactions entered into by, and no obligations or liabilities, contingent or otherwise, incurred by the Company or any of the Subsidiaries, whether or not in the ordinary course of business, which are material to the Company and the Subsidiaries, considered as one enterprise or (4) there has been no dividend or distribution of any kind declared, paid or made by the Company on any class of its capital stock, in each case, otherwise than as set forth or contemplated in the Pricing Prospectus;

(xiv) Neither the Company nor any of the Subsidiaries is (1) in violation of its certificate or articles of incorporation or bylaws (or other organization documents) or (2) in violation of any law, ordinance, administrative or governmental rule or regulation applicable to the Company or any of the Subsidiaries, or (3) in violation of any decree of any court or governmental agency or body having jurisdiction over the Company or any of the Subsidiaries, or (4) in default in the performance of any obligation, agreement or condition contained in any bond, debenture, note or any other evidence of indebtedness or in any agreement, indenture, lease or other instrument to which the Company or any of the Subsidiaries is a party or by which any of them or any of their respective properties may be bound, except, in the case of clauses (2), (3) and (4), where any such violation or default, individually or in the aggregate, would not have a Material Adverse Effect;

(xv) Each of the Company and each Subsidiary has good and marketable title to all real and personal property owned by it, in each case free and clear of all liens, encumbrances and defects except such as are described in the Pricing Prospectus or such as do not materially affect the value of such property and do not interfere with the use made and proposed to be made of such property by the Company or any Subsidiary; and any real property and buildings held under lease by the Company or any Subsidiary are held under valid, subsisting and enforceable leases with such exceptions as are not material and do not interfere with the use made and proposed to be made of such property and buildings by the Company or any Subsidiary;

(xvi) Other than as set forth in the Pricing Prospectus, there are no legal or governmental proceedings pending to which the Company or any of the Subsidiaries is a party or of which any property of the Company or any of the Subsidiaries is the subject which, if determined adversely to the Company or the Subsidiary, individually or in the aggregate, would have or may reasonably be expected to have a Material Adverse Effect, or would prevent or

impair the consummation of the transactions contemplated by this Agreement, or which are required to be described in the Registration Statement or the Pricing Prospectus; and, to the best of the Company's knowledge, no such proceedings are threatened or contemplated by governmental authorities or other third parties;

(xvii) The Company and the Subsidiaries possess all necessary permits, licenses, approvals, consents and other authorizations (collectively, "Permits") issued by the appropriate federal, state, local or foreign regulatory agencies or bodies necessary to conduct the businesses now operated by them; the Company and the Subsidiaries are in compliance with the terms and conditions of all such Permits and all of the Permits are valid and in full force and effect, except, in each case, where the failure so to comply or where the invalidity of such Permits or the failure of such Permits to be in full force and effect, individually or in the aggregate, would not reasonably be expected to have a Material Adverse Effect; and neither the Company nor any Subsidiary has received any notice of proceedings relating to the revocation or material modification of any such Permits;

(xviii) Except as described in the Registration Statement, the Pricing Disclosure Package and the Prospectus, or except as would not, individually or in the aggregate, result in a Material Adverse Effect: (i) the Company and the Subsidiaries are and have been in compliance with statutes, laws, ordinances, rules and regulations applicable to the Company and the Subsidiaries for the testing, development, manufacture, packaging, processing, use, labeling, storage, or disposal of any product manufactured by or on behalf of the Company or out-licensed by the Company, including without limitation, the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 301, et seq., the Public Health Service Act, 42 U.S.C. § 262, similar laws of other Governmental Entities and the regulations promulgated pursuant to such laws (collectively, "Applicable Laws"); (ii) the Company has not received any written notice of adverse finding, warning letter or other written correspondence or notice from the U.S. Food and Drug Administration ("FDA") or any other Governmental Entity alleging or asserting noncompliance with any Applicable Laws or Permits; (iii) the Company has not received written notice of any ongoing claim, action, suit, proceeding, hearing, enforcement, investigation, arbitration or other action from any Governmental Entity or third party alleging that any product, operation or activity is in violation of any Applicable Laws or Permits or has any knowledge that any such Governmental Entity or third party is considering any such claim, litigation, arbitration, action, suit, investigation or proceeding, nor, to the best of the Company's knowledge, has there been any noncompliance with or violation of any Applicable Laws by the Company that could reasonably be expected to require the issuance of any such written notice or result in an investigation, corrective action, or enforcement action by FDA or similar Governmental Entity; (iv) the Company has not received written notice that any Governmental Entity has taken, is taking or intends to take action to limit, suspend, modify or revoke any Permits or has any knowledge that any such Governmental Entity has threatened or is considering such action; and (v) the Company has filed, obtained, maintained or submitted all reports, documents, forms, notices, applications, records, claims, submissions and supplements or amendments as required by any Applicable Laws or Permits and that all such reports, documents, forms, notices, applications, records, claims, submissions and supplements or amendments were materially complete, correct and not misleading on the date filed (or were corrected or supplemented by a subsequent submission). To the Company's knowledge, for the past five years, neither the

Company, nor any of its directors, officers, employees or agents, has made, or caused the making of, any false statements on, or material omissions from, any other records or documentation prepared or maintained to comply with the requirements of the FDA or any other Governmental Entity;

(xix) The pre-clinical and clinical studies conducted by the Company have been and, if still pending, are being conducted in all material respects pursuant to all Applicable Laws and Permits; the descriptions of the results of such clinical studies and tests contained in the Registration Statement, the Pricing Disclosure Package and the Prospectus are accurate and complete in all material respects and fairly present the data derived from such pre-clinical and clinical studies; except to the extent disclosed in the Registration Statement, the Pricing Disclosure Package and the Prospectus, the Company is not aware of any pre-clinical or clinical studies, the results of which the Company believes reasonably call into question the pre-clinical or clinical study results described or referred to in the Registration Statement, the Pricing Disclosure Package and the Prospectus when viewed in the context in which such results are described; and the Company has not received any written notices or correspondence from any Governmental Entity requiring the termination, suspension or material modification of any pre-clinical or clinical study conducted by or on behalf of the Company, except for such termination, suspension, or material modification as would not reasonably be expected to have a Material Adverse Effect;

(xx) There is no franchise, contract or other document of a character required to be described in the Registration Statement or Prospectus, or to be filed as an exhibit thereto, which is not described or filed as required (and the Preliminary Prospectus contains in all material respects the same description of the foregoing matters contained in the Prospectus); and the statements set forth in the Pricing Prospectus and the Prospectus under the caption "Description of Capital Stock", insofar as they purport to constitute a summary of the terms of the Common Stock, under the captions "Material United States Federal Income Consequences to Non-U.S. Holders of Our Common Stock," "Underwriting" and "Shares Eligible for Future Sale", insofar as they purport to describe the provisions of the laws and documents referred to therein, are accurate and complete summaries in all material respects;

(xxi) The Company and the Subsidiaries own or possess all licenses, inventions, copyrights, know-how (including trade secrets and other unpatented and/or unpatentable proprietary or confidential information, systems or procedures), trademarks, service marks and trade names, patents, patent applications and patent rights material to carrying on their businesses as described in the Registration Statement, the Pricing Disclosure Package or the Prospectus (collectively "Intellectual Property"), except where the failure to own or possess such Intellectual Property would not, individually or in the aggregate, reasonably be expected to result in a Material Adverse Effect, and neither the Company nor any Subsidiary has received any correspondence relating to any Intellectual Property or notice of infringement of or conflict with asserted rights of

others with respect to any Intellectual Property which would render any Intellectual Property invalid or inadequate to protect the interest of the Company and the Subsidiaries and which infringement or conflict (if the subject of any unfavorable decision, ruling or finding) or invalidity or inadequacy, individually or in the aggregate, would have or may reasonably be expected to have a Material Adverse Effect; to the knowledge of the

Company, the patents, copyrights and trademarks owned by or licensed to the Company and included within the Intellectual Property are valid, enforceable, and subsisting; other than as disclosed in the Registration Statement, the Pricing Disclosure Package and the Prospectus, (i) neither the Company nor any Subsidiary is obligated under any arrangement or agreement to pay a material royalty, grant a license to any material portion of the Intellectual Property, or provide other material consideration to any third party in connection with the Intellectual Property, (ii) neither the Company nor any of its Subsidiaries has received any notice of any claim of infringement, misappropriation or conflict with any asserted rights of others with respect to any of the Company's products, proposed products, processes or Intellectual Property, (iii) no action, suit, claim or other proceeding is pending, or to the Company's knowledge, is threatened, alleging that the Company is infringing, misappropriating, diluting or otherwise violating any asserted rights of others with respect to any of the Company's product candidates, processes or Intellectual Property, (iv) no action, suit, claim, or other proceeding is pending, or to the Company's knowledge, is threatened, challenging the validity, enforceability, scope, registration, ownership or use of any of the Intellectual Property that is, singly or in the aggregate, necessary to the business of the Company and its Subsidiaries, (v) to the knowledge of the Company, neither the sale nor any current or contemplated use of any of the products, proposed products or processes of the Company referred to in the Registration Statement, the Pricing Disclosure Package or the Prospectus do or will, to the knowledge of the Company, infringe, misappropriate or violate any valid right or valid patent claim of any third party, (vi) to the knowledge of the Company, no third party has any ownership right in or to any Intellectual Property that is owned by the Company, other than any co-owner of any patent constituting Intellectual Property who is listed on the records of the U.S. Patent and Trademark Office (the "USPTO") and any co-owner of any patent application constituting Intellectual Property who is named in such patent application, and (vii) except as would not, individually or in the aggregate, reasonably be expected to result in a Material Adverse Effect, the Company and its Subsidiaries have taken reasonable measures to protect, maintain and safeguard the Intellectual Property, including the execution of appropriate nondisclosure and confidentiality agreements;

(xxii) All patents and patent applications owned by or licensed to the Company or its Subsidiaries or under which the Company has rights have, to the knowledge of the Company, been duly and properly filed and maintained; to the knowledge of the Company, the parties prosecuting such patents and applications have complied with their duty of candor and disclosure to the USPTO in connection with such patents and applications; and the Company is not aware of any facts required to be disclosed to the USPTO that were not disclosed to the USPTO and which would preclude the grant of a patent in connection with any such application or would reasonably be expected to form the basis of a finding of invalidity with respect to any patents that have issued with respect to such applications;

(xxiii) No material labor dispute with the employees of the Company or the Subsidiaries exists, or, to the knowledge of the Company, is imminent. The Company is not aware of any existing or imminent labor disturbance by the employees of any of its or any Subsidiary's principal suppliers, manufacturers, customers or contractors, which, individually or in the aggregate, may reasonably be expected to result in a Material Adverse Effect;

(xxiv) The Company and its Subsidiaries are insured by insurers of recognized financial responsibility against such losses and risks and in such amounts as are prudent and customary in the businesses in which they are engaged; neither the Company nor any Subsidiary has been refused any insurance coverage sought or applied for; and the Company has no reason to believe that either it or any Subsidiary will not be able to renew its existing insurance coverage as and when such coverage expires or to obtain similar coverage from similar insurers as may be necessary to continue its business at a cost that would not, individually or in the aggregate, reasonably be expected to result in Material Adverse Effect;

(xxv) The Company and each of its Subsidiaries have made and keep books, records and accounts, which, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the Company and its Subsidiaries. The Company maintains a system of internal accounting controls sufficient to provide reasonable assurance that (1) transactions are executed in accordance with management's general or specific authorizations; (2) transactions are recorded as necessary to permit preparation of financial statements in conformity with generally accepted accounting principles and to maintain accountability for assets; (3) access to assets is permitted only in accordance with management's general or specific authorization; (4) the recorded accountability for assets is compared with the existing assets at reasonable intervals and appropriate action is taken with respect to any differences; and (5) the interactive data in eXtensible Business Reporting Language included or incorporated by reference in the Registration Statement is in conformity with generally accepted accounting principles and is updated as necessary to comply in all material respects with the requirements of the Securities Act and the Commission's rules and guidelines applicable thereto and present fairly the consolidated financial position, results of operations and changes in financial position of the Company and the Subsidiaries on the basis stated in the Registration Statement at the respective dates or for the respective periods to which they apply;

(xxvi) The Company (i) does not have any material lending or other relationship with any bank or lending affiliate of the Underwriters and (ii) does not intend to use any of the proceeds from the sale of the Shares hereunder to repay any outstanding debt owed to any affiliate of the Underwriters;

(xxvii) Since the date of the latest audited financial statements included in the Pricing Prospectus, (a) the Company has not been advised of (1) any significant deficiencies in the design or operation of internal controls that could adversely affect the ability of the Company and each of its Subsidiaries to record, process, summarize and report financial data, or any material weaknesses in internal controls and (2) any fraud, whether or not material, that involves management or other employees who have a significant role in the internal controls of the Company and each of its Subsidiaries, and (b) since that date, there has been no change in the Company's internal control over financial reporting that has materially affected, or is reasonably likely to materially affect, the Company's internal control over financial reporting;

(xxviii) The Company maintains disclosure controls and procedures (as such term is defined in Rule 13a-15 (e) of the Exchange Act) that comply with the requirements of the Exchange Act; such disclosure controls and procedures are effective;

(xxix) All United States federal income tax returns of the Company and the Subsidiaries required by law to be filed have been filed and all taxes shown by such returns or otherwise assessed, which are due and payable, have been paid, except assessments against which appeals have been or will be promptly taken and as to which adequate reserves have been provided. The Company and the Subsidiaries have filed all other material tax returns that are required to have been filed by them pursuant to applicable foreign, state, local or other law, except insofar as the failure to file such returns, individually or in the aggregate, would not result in a Material Adverse Effect, and have paid all taxes due pursuant to such returns or pursuant to any assessment received by the Company or any Subsidiary except for such taxes, if any, as are being contested in good faith and as to which adequate reserves have been provided. The charges, accruals and reserves on the books of the Company and the Subsidiaries in respect of any income and corporation tax liability for any years not finally determined are adequate to meet any assessments or re-assessments for additional income tax for any years not finally determined;

(xxx) There are no statutes, regulations, documents or contracts of a character required to be described in the Registration Statement or the Pricing Prospectus or to be filed as an exhibit to the Registration Statement which are not described or filed as required;

(xxxi) Neither the Company nor any of the Subsidiaries is in violation of any statute or any rule, regulation, decision or order of any governmental agency or body or any court, domestic or foreign, relating to the use, production, disposal or release of hazardous or toxic substances or relating to the protection or restoration of the environment or human exposure to hazardous or toxic substances (collectively, "environmental laws"), owns or operates any real property contaminated with any substance that is subject to any environmental laws, is liable for any off-site disposal or contamination pursuant to any environmental laws, or is subject to any claim relating to any

environmental laws, which violation, contamination, liability or claim, individually or in the aggregate, would reasonably be expected to have a Material Adverse Effect; and the Company is not aware of any pending investigation which might reasonably be expected to lead to such a claim;

(xxxii) Each employee benefit plan, within the meaning of Section 3(3) of the Employee Retirement Income Security Act of 1974, as amended ("ERISA"), that is maintained, administered or contributed to by the Company or any Subsidiary for employees or former employees of the Company and its affiliates has been maintained in compliance with its terms and the requirements of any applicable statutes, orders, rules and regulations, including but not limited to ERISA and the Internal Revenue Code of 1986, as amended (the "Code"), except to the extent that failure to so comply, individually or in the aggregate, would not reasonably be expected to have a Material Adverse Effect. No prohibited transaction, within the meaning of Section 406 of ERISA or Section 4975 of the Code has occurred with respect to any such plan excluding transactions effected pursuant to a statutory or administrative exemption;

(xxxiii) None of the following events has occurred or is reasonably likely to occur: (i) a material increase in the aggregate amount of contributions required to be made to all Plans in the current fiscal year of the Company as compared to the amount of such

contributions made in the most recently completed fiscal year of the Company; (ii) a material increase in the "accumulated post-retirement benefit obligations" (within the meaning of Statement of Financial Accounting Standards 106) of the Company as compared to the amount of such obligations in the most recently completed fiscal year of the Company; (iii) any event or condition giving rise to a liability under Title IV of ERISA that would reasonably be expected to have a Material Adverse Effect; or (iv) the filing of a claim by one or more employees or former employees of the Company related to their employment that would reasonably be expected to have a Material Adverse Effect. For purposes of this paragraph, the term "Plan" means a plan (within the meaning of Section 3(3) of ERISA) subject to Title IV of ERISA with respect to which the Company may have any liability;

(xxxiv) Neither the Company nor any of its Subsidiaries, or, to the Company's knowledge, any director, officer, agent, employee or affiliate of the Company or any of its Subsidiaries, has (i) used any corporate funds for any unlawful contribution, gift, entertainment or other unlawful expense relating to political activity; (ii) made any direct or indirect unlawful payment to any foreign or domestic government official or employee from corporate funds, (iii) violated or is in violation of any provision of the Foreign Corrupt Practices Act of 1977, or (iv) made any bribe, unlawful rebate, payoff, influence payment, kickback or other unlawful payment;

(xxxv) The operations of the Company are and have been conducted at all times in compliance with applicable financial recordkeeping and reporting requirements and the money laundering statutes and the rules and regulations thereunder and any related or similar rules, regulations or guidelines, issued, administered or enforced by any governmental agency (collectively, the "Money Laundering Laws") and no action, suit or proceeding by or before any court or governmental agency, authority or body or any arbitrator involving the Company with respect to the Money Laundering Laws is pending or, to the knowledge of the Company, threatened;

(xxxvi) Neither the Company nor any of its Subsidiaries, or, to the Company's knowledge, any director, officer, agent, employee or affiliate of the Company or any of its Subsidiaries (i) is currently subject to any sanctions administered imposed by the United States (including any administered or enforced by the Office of Foreign Assets Control of the U.S. Treasury Department ("OFAC") or (ii) will, directly or indirectly, use the proceeds of this offering, or lend, contribute or otherwise make available such proceeds to any subsidiary, joint venture partner or other person in any manner that will result in a violation of any economic sanctions imposed by the United States (including any administered or enforced by OFAC, the U.S. Department of State, or the Bureau of Industry and Security of the U.S. Department of Commerce), the United Nations Security Council, the European Union, or the United Kingdom (including sanctions administered or controlled by Her Majesty's Treasury) (collectively, "Sanctions" and such persons, "Sanctioned Persons");

(xxxvii) Neither the Company nor any of its Subsidiaries, or, to the Company's knowledge, any director, officer, agent, employee or affiliate of the Company or any of its Subsidiaries, is a person that is (i) the subject of any Sanctions or (ii) located, organized or resident in a country or territory that is, or whose government is, the subject of Sanctions or

located, organized or resident in Cuba, Iran, North Korea, Sudan and Syria (collectively, "Sanctioned Countries" and each, a "Sanctioned Country");

(xxxviii) The Company has not engaged in any dealings or transactions with or for the benefit of a Sanctioned Person, or with or in a Sanctioned Country, in the preceding three years, nor does the Company have any plans to increase its dealings or transactions with Sanctioned Persons, or with or in Sanctioned Countries;

(xxxix) There is, and has been, no failure on the part of the Company or, to the Company's knowledge, any of the Company's directors or officers, in their capacities as such, to comply in all material respects with any provision of the Sarbanes-Oxley Act of 2002 and the rules and regulations promulgated in connection therewith, including Section 402 related to loans and Sections 302 and 906 related to certifications;

(xxxl) The Company is not and, after giving effect to the offering and sale of the Shares as contemplated herein and the application of the net proceeds therefrom as described in the Pricing Prospectus, will not be an "investment company", as such term is defined in the Investment Company Act of 1940, as amended (the "Investment Company Act");

(xli) The Company has not distributed and, prior to the later to occur of the Closing Date (as defined in Section 4 hereof) and completion of distribution of the Shares, will not distribute any offering materials in connection with the offering and sale of the Shares, other than the Pricing Prospectus, the Prospectus and, subject to compliance with Section 6 hereof, any Issuer Free Writing Prospectus; and the Company has not taken and will not take, directly or indirectly, any action designed to cause or result in, or which constitutes or might reasonably be expected to constitute, the stabilization or manipulation of the price of any security of the Company to facilitate the sale of the Shares. The Company (a) has not alone engaged in any Testing-the-Waters Communication other than Testing-the-Waters Communications with the consent of the Representatives with entities that are qualified institutional buyers within the meaning of Rule 144A under the Securities Act or institutions that are accredited investors within the meaning of Rule 501 under the Securities Act and (b) has not authorized anyone other than the Representatives to engage in Testing-the-Waters Communications. The Company reconfirms that the Representatives have been authorized to act on its behalf in undertaking Testing-the-Waters Communications. The Company has not distributed any Written Testing-the-Waters Communications other than those listed on Schedule II hereto. "Written Testing-the-Waters Communication" means any Testing-the-Waters Communication that is a written communication within the meaning of Rule 405 under the Securities Act;

(xlii) The statistical and market and industry-related data included in the Pricing Prospectus and the Prospectus are based on or derived from sources which the Company believes to be reliable and accurate or represent the Company's good faith estimates that are made on the basis of data derived from such sources, and the Company has obtained the written consent to the use of such data from sources to the extent required;

(xliii) There are no persons with registration rights or other similar rights to have securities registered pursuant to the Registration Statement or otherwise to be registered by the Company under the Securities Act that have not been effectively waived.

[(xlii)] The audiovisual presentation made available to the public by the Company at [http://www.netroadshow.com/[address]][or Company address] is a "bona fide electronic roadshow" for purposes of Rule 433(d)(8)(ii) of the Securities Act, and such presentation, together with the Pricing Prospectus, does not contain any untrue statement of material fact or omit to state a material fact necessary to make the statements therein, in light of the circumstances under which they were made, not misleading, except that the representations and warranties set forth in this paragraph do not apply to statements in or omissions from such presentation or Pricing Prospectus made in reliance upon and in strict conformity with information furnished to the Company in writing by any Underwriter through the Representatives expressly for use therein; and]

(xliii) Any certificate signed by any officer of the Company delivered to the Underwriters or to counsel for the Underwriters shall be deemed a representation and warranty by the Company to the Underwriters as to the matters covered thereby.

2. Subject to the terms and conditions herein set forth, (a) the Company agrees to sell to each of the Underwriters, and each of the Underwriters agrees, severally and not jointly, to purchase from the Company, at a purchase price per share of $[·] (the "Purchase Price"), the number of Firm Shares (to be adjusted by you so as to eliminate fractional shares) determined by multiplying the aggregate number of Firm Shares to be sold by the Company hereunder by a fraction, the numerator of which is the aggregate number of Firm Shares to be purchased by such Underwriter as set forth opposite the name of such Underwriter in Schedule I hereto and the denominator of which is the aggregate number of Firm Shares to be purchased by all of the Underwriters from the Company hereunder and (b) in the event and to the extent that the Underwriters shall exercise the election to purchase Option Shares as provided below, the Company agrees to sell to each of the Underwriters, and each of the Underwriters agrees, severally and not jointly, to purchase from the Company, at the Purchase Price, the number of Option Shares (to be adjusted by you so as to eliminate fractional shares) determined by multiplying (x) the number of Option Shares as to which such election shall have been exercised by (y) the fraction set forth in clause (a) above.

The Company hereby grants to the Underwriters the right to purchase at their election up to [·] Option Shares, at the Purchase Price, for the sole purpose of covering over-allotments in connection with the sale of the Firm Shares. The Underwriters may exercise their option to acquire Option Shares in whole or in part from time to time only by written notice from the Representatives to the Company, given within a period of 30 calendar days after the date of this Agreement and setting forth the aggregate number of Option Shares to be purchased and the date on which such Option Shares are to be delivered, as determined by the Representatives but in no event earlier than the Closing Date or, unless the Representatives and the Company otherwise agree in writing, earlier than two or later than ten business days after the date of such notice.

3. It is understood that the several Underwriters propose to offer the Firm Shares for sale to the public upon the terms and conditions set forth in the Prospectus.

4. The Company will deliver the Firm Shares to the Representatives through the facilities of the Depository Trust Company ("DTC") for the accounts of the Underwriters, against payment of the purchase price therefor in Federal (same day) funds by official bank check or checks or wire transfer drawn to the order of the Company at the offices of Bingham McCutchen LLP, One Federal Street, Boston, MA 02110, at 10:00 A.M., New York time, on [·], 2014, or at such other time not later than seven full business days thereafter as the Representatives and the Company determine, such time being herein referred to as the "Closing Date". For purposes of Rule 15c6-1 under the Exchange Act, the Closing Date (if later than the otherwise applicable settlement date) shall be the settlement date for payment of funds and delivery of securities for all the Firm Shares. The certificates for the Firm Shares so to be delivered will be in definitive form, in such denominations and registered in such names as the Representatives request and will be made available for checking and packaging at the above office of Bingham McCutchen LLP at least 24 hours prior to the Closing Date.

Each time for the delivery of and payment for the Option Shares, being herein referred to as an "Option Closing Date", which may be the Closing Date, shall be determined by the Representatives as provided above. The Company will deliver the Option Shares being purchased on each Option Closing Date to the Representatives through the facilities of DTC for the accounts of the Underwriters, against payment of the purchase price therefor in Federal (same day) funds by official bank check or checks or wire transfer drawn to the order of the Company at the above office of Bingham McCutchen LLP, at 10:00 A.M., New York time on the applicable Option Closing Date. The certificates for the Option Shares so to be delivered will be in definitive form, in such denominations and registered in such names as the Representatives request and will be made available for checking and packaging at the above office of Bingham McCutchen LLP at least 24 hours prior to such Option Closing Date.

5. The Company covenants and agrees with each of the Underwriters as follows:

(a) The Company, subject to Section 5(b), will comply with the requirements of Rule 430A under the Securities Act, and will notify the Representatives immediately, and confirm the notice in writing (which may occur by email), (i) when any post-effective amendment to the Registration Statement shall become effective, or any supplement to the Prospectus or any amended prospectus shall have been filed, furnish the Representatives with copies thereof, and file promptly all material required to be filed by the Company with the Commission pursuant to Rule 433(d) under the Securities Act, (ii) of the receipt of any comments from the Commission, (iii) of any request by the Commission for any amendment to the Registration Statement or any amendment or supplement to the Prospectus or for additional information, (iv) of the issuance by the Commission of any stop order suspending the effectiveness of the Registration Statement or of any order preventing or suspending the use of any Preliminary Prospectus, or of the suspension of the qualification of the Shares for offering or sale in any jurisdiction, or of the initiation or threatening of any proceedings for any of such purposes; and (v) if the Company ceases to be an Emerging Growth Company at any time prior to the later of (A) completion of the distribution of the Shares within the meaning of the

Securities Act and (B) completion of the 180-day restricted period referred to in Section 5(j) hereof. The Company will promptly effect the filings necessary pursuant to Rule 424(b) under the Securities Act and will take such steps as it deems necessary to ascertain promptly whether the form of prospectus transmitted for filing under Rule 424(b) was received for filing by the Commission and, in the event that it was not, it will promptly file such prospectus. The Company will make every reasonable effort to prevent the issuance of any stop order and, if any stop order is issued, to obtain the lifting thereof at the earliest possible moment.

(b) The Company will give the Representatives notice of its intention to file or prepare any amendment to the Registration Statement (including any filing under Rule 462(b) under the Securities Act), or any amendment, supplement or revision to the Prospectus, or any Issuer Free Writing Prospectus, will furnish the Representatives with copies of any such documents a reasonable amount of time prior to such proposed filing or use, as the case may be, and will not file or use any such document to which the Representatives or counsel for the Underwriters shall reasonably object.

(c) The Company will use its best efforts to qualify the Shares for offering and sale under the securities laws of such jurisdictions as you may reasonably request and to comply with such laws so as to permit the continuance of sales and dealings therein in such jurisdictions for as long as may be necessary to complete the distribution of the Shares, provided that nothing in this Section 5(c) shall require the Company to qualify as a foreign corporation in any jurisdiction in which it is not already so qualified, or to file a general consent to service of process in any jurisdiction or subject itself to taxation in any jurisdiction if it is not otherwise so subject.

(d) The Company has furnished or will deliver to the Representatives, without charge, three signed copies of the Initial Registration Statement as originally filed, any Rule 462(b) Registration Statement and of each amendment to each (including exhibits filed therewith or incorporated by reference therein) and signed copies of all consents and certificates of experts, and will also, upon your request, deliver to the Representatives, without charge, a conformed copy of the Registration Statement as originally filed and of each amendment thereto (without exhibits) for each of the Underwriters. The copies of the Registration Statement and each amendment thereto furnished to the Underwriters will be identical to the electronically transmitted copies thereof filed with the Commission pursuant to EDGAR, except to the extent permitted by Regulation S-T.

(e) The Company has delivered to each Underwriter, without charge, as many written and electronic copies of each Preliminary Prospectus as such Underwriter reasonably requested, and the Company hereby consents to the use of such copies for purposes permitted by the Securities Act. The Company will furnish to each

Underwriter, without charge, prior to 5:00 P.M. (New York time) on the business day next succeeding the date of this Agreement and from time to time thereafter during the period when the Prospectus is required to be delivered in connection with sales of the Shares under the Securities Act or the Exchange Act or in lieu thereof, the notice referred to in Rule 173(a) under the Securities Act, such number of written and electronic copies of the Prospectus (as amended or supplemented) as such Underwriter may reasonably request. The Prospectus and any amendments or supplements thereto furnished to the

Underwriters will be identical to the electronically transmitted copies thereof filed with the Commission pursuant to EDGAR, except to the extent permitted by Regulation S-T.

(f) The Company will comply with the Securities Act and the Rules and Regulations so as to permit the completion of the distribution of the Shares as contemplated in this Agreement and in the Prospectus. If at any time when, in the opinion of counsel for the Underwriters, a prospectus is required to be delivered in connection with sales of the Shares under the Securities Act or the Exchange Act (or in lieu thereof, the notice referred to in Rule 173(a) under the Securities Act), any event shall occur or condition shall exist as a result of which it is necessary, in the opinion of counsel for the Underwriters or for the Company, to amend the Registration Statement or amend or supplement the Prospectus in order that the Prospectus will not include any untrue statements of a material fact or omit to state a material fact necessary in order to make the statements therein not misleading in the light of the circumstances existing at the time it (or in lieu thereof, the notice referred to in Rule 173(a) under the Securities Act) is delivered to a purchaser, or if it shall be necessary, in the opinion of either such counsel, at any such time to amend the Registration Statement or amend or supplement the Prospectus in order to comply with the requirements of the Securities Act or the Rules and Regulations, the Company will promptly prepare and file with the Commission, subject to Section 5(b), such amendment or supplement as may be necessary to correct such statement or omission or to make the Registration Statement or the Prospectus comply with such requirements, and the Company will furnish to the Underwriters such number of written and electronic copies of such amendment or supplement as the Underwriters may reasonably request. The Company will provide the Representatives with notice of the occurrence of any event during the period specified above that may give rise to the need to amend or supplement the Registration Statement or the Prospectus as provided in the preceding sentence promptly after the occurrence of such event. If at any time following the distribution of any Written Testing-the-Waters Communication there occurred or occurs an event or development as a result of which such Written Testing-the-Waters Communication included or would include an untrue statement of a material fact or omitted or would omit to state a material fact necessary in order to make the statements therein, in the light of the circumstances existing at that subsequent time, not misleading, the Company will promptly notify the Representatives and will promptly amend or supplement, at its own expense, such Written Testing-the-Waters Communication to eliminate or correct such untrue statement or omission.

(g) The Company will make generally available (within the meaning of Section 11(a) of the Securities Act) to its security holders and to the Representatives as soon as practicable, but not later than 45 days after the end of its fiscal quarter in which the first anniversary date of the effective date of the Registration Statement occurs, an earnings statement (in form complying with the provisions of Rule 158 under the Securities Act) covering a period of at least twelve consecutive months beginning after the effective date of the Registration Statement.

(h) The Company will use the net proceeds received by it from the sale of the Shares in the manner specified in the Pricing Prospectus under the heading “Use of Proceeds”.

(i) The Company will use its best efforts to effect and maintain the listing of the Common Stock (including the Shares) on the NASDAQ Global Market.

(j) During a period of 180 days from the date of the Prospectus, the Company will not, without the prior written consent of the Representatives, (i) 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, lend or otherwise transfer or dispose of, directly or indirectly, any Common Stock or any securities convertible into or exercisable or exchangeable for Common Stock or (ii) enter into any swap or other agreement that transfers, in whole or in part, any of the economic consequences of ownership of Common Stock, whether any such transaction described in clause (i) or (ii) above is to be settled by delivery of Common Stock or such other securities, in cash or otherwise, other than (1) the Shares to be sold hereunder, (2) the issuance of options to acquire shares of Common Stock granted pursuant to the Company’s benefit plans existing on the date hereof that are referred to in the Prospectus, as such plans may be amended or (3) the issuance of shares of Common Stock upon the exercise of any such options.

(k) If the Representatives, in their sole discretion, agree to release or waive the restrictions set forth in a “lock-up” agreement described in Section 8(l) hereof for an officer or director of the Company and provides the Company with notice of the impending release or waiver at least three business days before the effective date of the release or waiver, the Company agrees to announce the impending release or waiver by a press release substantially in the form of Exhibit E hereto through a major news service at least two business days before the effective date of the release or waiver.

(l) The Company, during the period when the Prospectus is required to be delivered in connection with sales of the Shares under the Securities Act or the Exchange Act (or in lieu thereof, the notice referred to in Rule 173(a) under the Securities Act), will file all documents required to be filed with the Commission pursuant to the Exchange Act within the time periods required by the Exchange Act and the rules and regulations of the Commission thereunder.

(m) The Company will file with the Commission such information on Form 10-Q or Form 10-K as may be required pursuant to Rule 463 under the Securities Act.

(n) During a period of three years from the effective date of the Registration Statement, the Company will furnish to you copies of all reports or other communications (financial or other) furnished to shareholders generally, and to deliver to you as soon as they are available, copies of any reports and financial statements furnished to or filed with the Commission or any national securities exchange on which any class of securities of the Company is listed; provided that the Company will be deemed to have furnished such reports and such financial statements to the extent they are filed on EDGAR.

(o) If the Company elects to rely upon Rule 462(b) under the Securities Act, the Company will file a Rule 462(b) Registration Statement with the Commission in compliance with Rule 462(b) by 10:00 P.M., Washington, D.C. time, on the date of this Agreement, and at

the time of filing either pay to the Commission the filing fee for the Rule 462(b) Registration Statement or give irrevocable instructions for the payment of such fee pursuant to Rule 111(b) under the Securities Act.

(p) If so requested by the Representatives, the Company shall cause to be prepared and delivered, at its expense, within one business day from the effective date of this Agreement, to the Representatives an “electronic Prospectus” to be used by the Underwriters in connection with the offering and sale of the Shares. As used herein, the term “electronic Prospectus” means a form of the most recent Preliminary Prospectus, any Issuer Free Writing Prospectus or the Prospectus, and any amendment or supplement thereto, that meets each of the following conditions: (i) it shall be encoded in an electronic format, satisfactory to the Representatives, that may be transmitted electronically by the Representatives and the other Underwriters to offerees and purchasers of the Shares, (ii) it shall disclose the same information as such paper Preliminary Prospectus, Issuer Free Writing Prospectus or the Prospectus, as the case may be; and (iii) it shall be in or convertible into a paper format or an electronic format, satisfactory to the Representatives, that will allow investors to store and have continuously ready access to such Preliminary Prospectus, Issuer Free Writing Prospectus or the Prospectus at any future time, without charge to investors (other than any fee charged for subscription to the Internet generally). The Company hereby confirms that, if so requested by the

Representatives, it has included or will include in the Prospectus filed with the Commission an undertaking that, upon receipt of a request by an investor or his or her representative, the Company shall transmit or cause to be transmitted promptly, without charge, a paper copy of such paper Preliminary Prospectus, Issuer Free Writing Prospectus or the Prospectus to such investor or representative.

6. (a) The Company represents and agrees that, without the prior consent of the Representatives, it has not made and will not make any offer relating to the Shares that would constitute a "free writing prospectus" as defined in Rule 405 under the Securities Act; each Underwriter represents and agrees that, without the prior consent of the Company and the Representatives, it has not made and will not make any offer relating to the Shares that would constitute a free writing prospectus; any such free writing prospectus the use of which has been consented to by the Company and the Representatives is listed on Schedule II hereto;

(b) The Company has complied and will comply with the requirements of Rule 433 under the Securities Act applicable to any Issuer Free Writing Prospectus, including timely filing with the Commission or retention where required and legending; the Company represents that it has satisfied and agrees that it will satisfy the conditions under Rule 433 under the Securities Act to avoid a requirement to file with the Commission any electronic road show;

(c) The Company agrees that if at any time following issuance of an Issuer Free Writing Prospectus any event occurred or occurs as a result of which such Issuer Free Writing Prospectus would conflict with the information in the Registration Statement, the Pricing Prospectus or the Prospectus or would include an untrue statement of a material fact or omit to state any material fact necessary in order to make the statements therein, in light of the circumstances then prevailing, not misleading, the Company will give prompt notice thereof to the Representatives and, if requested by the Representatives, will prepare and furnish without charge to each Underwriter an Issuer Free Writing Prospectus or other document which will

correct such conflict, statement or omission; provided, however, that this representation and warranty shall not apply to any statements or omissions in an Issuer Free Writing Prospectus made in reliance upon and in strict conformity with information furnished in writing to the Company by an Underwriter through the Representatives expressly for use therein.

7. The Company covenants and agrees with the several Underwriters that, whether or not the transactions contemplated by this Agreement are consummated, the Company will pay or cause to be paid all expenses incident to the performance of its obligations under this Agreement, including (i) the fees, disbursements and expenses of the Company's counsel, accountants and other advisors; (ii) filing fees and all other expenses in connection with the preparation, printing and filing of the Registration Statement, each Preliminary Prospectus, any Issuer Free Writing Prospectus and the Prospectus and amendments and supplements thereto and the mailing and delivering of copies thereof to the Underwriters and dealers; (iii) the cost of printing or producing this Agreement, closing documents (including any compilations thereof) and such other documents as may be required in connection with the offering, purchase, sale and delivery of the Shares; (iv) all expenses in connection with the qualification of the Shares for offering and sale under state securities laws as provided in Section 5(c), including filing fees and the reasonable fees and disbursements of counsel for the Underwriters in connection with such qualification and in connection with the Blue Sky survey; (v) all fees and expenses in connection with listing the Common Stock (including the Shares) on the NASDAQ Global Market; (vi) the filing fees incident to, and the reasonable fees and disbursements of counsel for the Underwriters in connection with, securing any required review by the Financial Industry Regulatory Authority ("FINRA") of the terms of the sale of the Shares (not to exceed $30,000); (vii) all fees and expenses in connection with the preparation, issuance and delivery of the certificates representing the Shares to the Underwriters, including any stock or other transfer taxes and any stamp or other duties payable upon the sale, issuance or delivery of the Shares to the Underwriters; (viii) the cost and charges of any transfer agent or registrar; (ix) the transportation and other expenses incurred by the Company in connection with presentations to prospective purchasers of Shares (provided, however, that the Underwriters and the Company shall each pay 50% of the cost of chartering any aircraft to be used in connection with the road show by the Company and the Underwriters that is required for making road show meetings); and (xi) all other costs and expenses incident to the performance of its obligations hereunder which are not otherwise specifically provided for in this Section. It is understood that, subject to Sections 7 and 12, the Underwriters will pay all of their costs and expenses associated with the transactions contemplated hereunder, including all fees and disbursements of their counsel.

8. The several obligations of the Underwriters hereunder to purchase the Shares on the Closing Date or each Option Closing Date, as the case may be, are subject to the performance by the Company of its obligations hereunder and to the following additional conditions:

(a) The Prospectus shall have been filed with the Commission pursuant to Rule 424(b) under the Securities Act within the applicable time period prescribed for such filing by the Rules and Regulations and in accordance with Section 5(a); all material required to be filed by the Company pursuant to Rule 433(d) under the Securities Act shall have been filed with the Commission within the applicable time period prescribed for such filing by Rule 433 under the Securities Act; if the Company has elected to rely upon Rule 462(b) under the Securities Act,

the Rule 462(b) Registration Statement shall have become effective by 10:00 P.M., Washington, D.C. time, on the date of this Agreement; no stop order suspending the effectiveness of the Registration Statement or any part thereof or the Prospectus or any part thereof or any Issuer Free Writing Prospectus shall have been issued and no proceeding for that purpose shall have been initiated or threatened by the Commission or any state securities commission; and all requests for additional information on the part of the Commission shall have been complied with to your reasonable satisfaction.

(b) The representations and warranties of the Company contained herein are true and correct on and as of the Closing Date or the Option Closing Date, as the case may be, as if made on and as of the Closing Date or the Option Closing Date, as the case may be, and the Company shall have complied with all agreements and all conditions on its part to be performed or satisfied hereunder at or prior to the Closing Date or the Option Closing Date, as the case may be.

(c) (i) Neither the Company nor any Subsidiary shall have sustained since the date of the latest audited financial statements included in the Pricing Prospectus any material loss or interference with its business from fire, explosion, flood or other calamity, whether or not covered by insurance, or from any labor dispute or court or governmental action, order or decree, otherwise than as set forth or contemplated in the Pricing Prospectus, and (ii) since the respective dates as of which information is given in the Registration Statement and the Prospectus and except as described in the Registration Statement and Prospectus, (1) there shall not have been any change in the capital stock (other than the issuance of shares of Common Stock upon the exercise or conversion of securities described as outstanding in, or the grant of options, restricted stock or other equity-based awards under the Company's existing equity incentive plans described in the Pricing Prospectus) or long-term debt of the Company or any Subsidiary or (2) there shall not have been any material adverse change, or any development that would reasonably be expected to result in a prospective material adverse change, in or affecting the general affairs, business, prospects, management, financial position, shareholders' equity or results of operations of the Company and the Subsidiaries, considered as one enterprise, the effect of which, in any such case described in clause (i) or (ii), is in the judgment of the Representatives so material and adverse as to make it impracticable or inadvisable to proceed with the public offering or the delivery of the Shares being delivered at such Closing Date or Option Closing Date, as the case may be, on the terms and in the manner contemplated in the Pricing Prospectus.

(d) the Representatives shall have received on and as of the Closing Date or the Option Closing Date, as the case may be, a certificate of two executive officers of the Company, at least one of whom has specific knowledge about the Company's financial matters, satisfactory to the Representatives, to the effect (1) set forth in Sections 8(b) (with respect to the respective representations, warranties, agreements and conditions of the Company) and 8(c), (2) that none of the situations set forth in clause (i) or (ii) of Section 8(d) shall have occurred and (3) that no stop order suspending the effectiveness of the Registration Statement has been issued and to the knowledge of the Company, no proceedings for that purpose have been instituted or are pending or contemplated by the Commission.

(e) On the Closing Date or Option Closing Date, as the case may be, Bingham McCutchen LLP, counsel for the Company, shall have furnished to the Representatives their favorable written opinion, dated the Closing Date or the Option Closing Date, as the case may be, in form and substance satisfactory to counsel for the Underwriters, to the effect set forth in Exhibit A hereto and to such further effect as counsel for the Underwriters may reasonably request.

(f) On the effective date of the Registration Statement and, if applicable, the effective date of the most recently filed post-effective amendment to the Registration Statement, Ernst & Young LLP shall have furnished to the Representatives a letter, dated the date of delivery thereof, in form and substance satisfactory to the Representatives, containing statements and information of the type customarily included in accountants' "comfort letters" to underwriters with respect to the financial statements and certain financial information contained in the Registration Statement and the Prospectus.

(g) On the Closing Date or Option Closing Date, as the case may be, the Representatives shall have received from Ernst & Young LLP a letter, dated the Closing Date or such Option Closing Date, as the case may be, to the effect that they reaffirm the statements made in the letter or letters furnished pursuant to Section 8(g), except that the specified date referred to shall be a date not more than three business days prior to the Closing Date or such Option Closing Date, as the case may be.

(h) On the Closing Date or Option Closing Date, as the case may be, Ropes & Gray LLP, counsel for the Underwriters, shall have furnished to the Representatives their favorable opinion dated the Closing Date or the Option Closing Date, as the case may be, with respect to the due authorization and valid issuance of the Shares, the Registration Statement, the Prospectus and other related matters as the Representatives may reasonably request, and such counsel shall have received such papers and information as they may reasonably request to enable them to pass upon such matters.

(i) The Shares to be delivered on the Closing Date or Option Closing Date, as the case may be, shall have been approved for listing on the NASDAQ Global Market, subject to official notice of issuance.

(j) FINRA shall have confirmed that it has not raised any objection with respect to the fairness and reasonableness of the underwriting terms and conditions.

(k) The Representatives shall have received "lock-up" agreements, each substantially in the form of Exhibit D hereto, from all officers and directors of the Company and the shareholders of substantially all of the securities of the Company, and such agreements shall be in full force and effect on the Closing Date or Option Closing Date, as the case may be.

(l) On or prior to the Closing Date or Option Closing Date, as the case may be, the Company shall have furnished to the Representatives such further information, certificates and documents as the Representatives shall reasonably request.

(m) On or after the Applicable Time there shall not have occurred any of the following: (i) a suspension or material limitation in trading in securities generally on the NASDAQ Global Market; (ii) a suspension or material limitation in trading in the Company's securities on the NASDAQ Global Market; (iii) a general moratorium on commercial banking activities declared by any of Federal, Maryland or New York State authorities or a material disruption in commercial banking or securities settlement or clearance services in the United States; (iv) the outbreak or escalation of hostilities involving the United States or the declaration by the United States of a national emergency or war or (v) the occurrence of any other calamity or crisis or any change in financial, political or economic conditions in the United States or elsewhere, if the effect of any such event specified in clause (iv) or (v) in the judgment of the Representatives makes it impracticable or inadvisable to proceed with the public offering or the delivery of the Shares being delivered at such Closing Date or Option Closing Date, as the case may be, on the terms and in the manner contemplated in the Prospectus;

If any condition specified in this Section 8 shall not have been fulfilled when and as required to be fulfilled, this Agreement may be terminated, subject to the provisions of Section 12, by the Representatives by notice to the Company at any time at or prior to the Closing Date or Option Closing Date, as the case may be, and such termination shall be without liability of any party to any other party, except as provided in Section 12.

(n) On the Closing Date or Option Closing Date, as the case may be, each of Biospark Intellectual Property Law and Hughes, Hubbard & Reed LLP, both intellectual property counsel for the Company, shall each have furnished to the Representatives their favorable written opinion, dated the Closing Date or the Option Closing Date, as the case may be, in form and substance satisfactory to counsel for the Underwriters, to the effect set forth in Exhibit B-1 and Exhibit B-2 hereto and to such further effect as counsel for the Underwriters may reasonably request.

(o) On the Closing Date or Option Closing Date, as the case may be, Hyman, Phelps, & McNamara, PC, regulatory counsel for the Company, shall have furnished to the Representatives their favorable written opinion, dated the Closing Date or the Option Closing Date, as the case may be, in form and substance satisfactory to counsel for the Underwriters, to the effect set forth in Exhibit C hereto and to such further effect as counsel for the Underwriters may reasonably request.

9. (a) The Company agrees to indemnify and hold harmless each Underwriter and each person, if any, who controls any Underwriter within the meaning of Section 15 of the Securities Act or Section 20(a) of the Exchange Act against any and all losses, liabilities, claims, damages and expenses whatsoever as incurred (including without limitation, reasonable attorneys' fees and any and all reasonable expenses whatsoever incurred in investigating, preparing or defending against any litigation, commenced or threatened, or any claim whatsoever, and any and all amounts paid in settlement of any claim or litigation), joint or several, to which they or any of them may become subject under the Securities Act, the Exchange Act or otherwise, insofar as such losses, liabilities, claims, damages or expenses (or actions in respect thereof) arise out of or are based upon any untrue statement or alleged untrue statement of a material fact contained in the Initial Registration Statement, as originally filed or

any amendment thereof, the Registration Statement, or any post-effective amendment thereof, any Preliminary Prospectus, the Pricing Prospectus or the Prospectus, or in any supplement thereto or amendment thereof, any Issuer Free Writing Prospectus, any Written Testing-the-Waters Communication, or any "issuer information" filed or required to be filed pursuant to Rule 433(d) under the Securities Act, or arise out of or are based upon the omission or alleged omission to state therein a material fact required to be stated therein or necessary to make the statements therein, in the light of the circumstances under which they were made, not misleading; provided, however, that the Company will not be liable in any such case to the extent that any such loss, liability, claim, damage or expense arises out of or is based upon any such untrue statement or alleged untrue statement or omission or alleged omission made in the Initial Registration Statement, as originally filed or any amendment thereof, the Registration Statement, or any post-effective amendment thereof, any Preliminary Prospectus, the Pricing Prospectus or the Prospectus, or in any supplement thereto or amendment thereof, any Issuer Free Writing Prospectus, or any Written Testing-the-Waters Communication in reliance upon and in strict conformity with written information furnished to the Company by or on behalf of any Underwriter through the Representatives expressly for use therein, it being understood and agreed that the only such information furnished by any Underwriter is the information described as such in Section 9(b) below.

(b) Each Underwriter severally, and not jointly, agrees to indemnify and hold harmless the Company, each of the directors of the Company, each of the officers of the Company who shall have signed the Registration Statement, and each other person, if any, who controls the Company within the meaning of Section 15 of the Securities Act or Section 20(a) of the Exchange Act, against any losses, liabilities, claims, damages and expenses whatsoever as incurred (including without limitation, reasonable attorneys' fees and any and all reasonable expenses whatsoever incurred in investigating, preparing or defending against any litigation, commenced or threatened, or any claim whatsoever, and any and all amounts paid in settlement of any claim or litigation), joint or several, to which they or any of them may become subject under the Act, the Exchange Act or otherwise, insofar as such losses, liabilities, claims, damages or expenses (or actions in respect thereof) arise out of or are based upon any untrue statement or alleged

untrue statement of a material fact contained in the Initial Registration Statement, as originally filed or any amendment thereof, the Registration Statement, or any post-effective amendment thereof, or any Preliminary Prospectus, the Pricing Prospectus or the Prospectus, or in any supplement thereto or amendment thereof, any Issuer Free Writing Prospectus or any Written Testing-the-Waters Communication, or arise out of or are based upon the omission or alleged omission to state therein a material fact required to be stated therein or necessary to make the statements therein, in the light of the circumstances under which they were made, not misleading, in each case to the extent, but only to the extent, that any such loss, liability, claim, damage or expense arises out of or is based upon any such untrue statement or alleged untrue statement or omission or alleged omission made therein in reliance upon and in strict conformity with written information furnished to the Company by or on behalf of such Underwriter through the Representatives expressly for use therein, it being understood and agreed that the only such information furnished by or on behalf of any Underwriter consists of the following information in the Prospectus furnished on behalf of each Underwriter: [the last paragraph at the bottom of the cover page concerning the terms of the offering by the Underwriters, the concession and

reallowance figures appearing in the [·] paragraph under the caption "Underwriting" and the information contained in the [·] and [·] paragraphs under the caption "Underwriting"].

(c) Promptly after receipt by an indemnified party under Section 9(a) or 9(b) of notice of the commencement of any action, such indemnified party shall, if a claim in respect thereof is to be made against the indemnifying party under such Section, notify each party against whom indemnification is to be sought in writing of the commencement thereof (but the failure so to notify an indemnifying party shall not relieve it from any liability which it may have under this Section 9). In case any such action is brought against any indemnified party, and it notifies an indemnifying party of the commencement thereof, the indemnifying party will be entitled to participate therein, and jointly with any other indemnifying party similarly notified, to the extent it may elect by written notice delivered to the indemnified party promptly after receiving the aforesaid notice from such indemnified party, to assume the defense thereof with counsel reasonably satisfactory to such indemnified party (who shall not, except with the consent of the indemnified party, be counsel to the indemnified party). Notwithstanding the foregoing, the indemnified party or parties shall have the right to employ its or their own counsel in any such case, but the fees and expenses of such counsel shall be at the expense of such indemnified party or parties unless (i) the employment of such counsel shall have been authorized in writing by one of the indemnifying parties in connection with the defense of such action, (ii) the indemnifying parties shall not have employed counsel to have charge of the defense of such action within a reasonable time after notice of commencement of the action, or (iii) such indemnified party or parties shall have reasonably concluded that there may be defenses available to it or them which are different from or additional to those available to one or all of the indemnifying parties (in which case the indemnifying parties shall not have the right to direct the defense of such action on behalf of the indemnified party or parties), in any of which events such fees and expenses shall be borne by the indemnifying parties. In no event shall the indemnifying parties be liable for fees and expenses of more than one counsel (in addition to any local counsel) separate from their own counsel for all indemnified parties in connection with any one action or separate but similar or related actions in the same jurisdiction arising out of the same general allegations or circumstances, which counsel, in the event of indemnified parties under Section 9(a), shall be selected by the Representatives. No indemnifying party shall, without the written consent of the indemnified party, effect the settlement or compromise of, or consent to the entry of any judgment with respect to, any pending or threatened action or claim in respect of which indemnification or contribution may be sought hereunder (whether or not the indemnified party is an actual or potential party to such action or claim) unless such settlement, compromise or judgment (i) includes an unconditional release of the indemnified party from all liability arising out of such action or claim and (ii) does not include a statement as to or an admission of fault, culpability or a failure to act, by or on behalf of any indemnified party.

(d) If the indemnification provided for in this Section 9 is unavailable to or insufficient to hold harmless an indemnified party under Section 9(a) or 9(b) in respect of any losses, liabilities, claims, damages or expenses (or actions in respect thereof) referred to therein, then each indemnifying party shall contribute to the amount paid or payable by such indemnified party as a result of such losses, liabilities, claims, damages or expenses (or actions in respect thereof) in such proportion as is appropriate to reflect the relative benefits received by the Company on the one hand and the Underwriters on the other from the offering of the Shares. If,

however, the allocation provided by the immediately preceding sentence is not permitted by applicable law, then each indemnifying party shall contribute to such amount paid or payable by such indemnified party in such proportion as is appropriate to reflect not only such relative benefits but also the relative fault of the Company on the one hand and the Underwriters on the other in connection with the statements or omissions which resulted in such losses, liabilities, claims, damages or expenses (or actions in respect thereof), as well as any other relevant equitable considerations. The relative benefits received by the Company on the one hand and the Underwriters on the other from the offering of the Shares shall be deemed to be in the same proportion as the total net proceeds from the offering (before deducting expenses) received by the Company bear to the total underwriting discounts and commissions received by the Underwriters, in each case as set forth in the table on the cover page of the Prospectus. The relative fault shall be determined by reference to, among other things, whether the untrue or alleged untrue statement of a material fact or the omission or alleged omission to state a material fact relates to information supplied by the Company on the one hand or the Underwriters on the other and the parties' relative intent, knowledge, access to information and opportunity to correct or prevent such statement or omission.

The Company and the Underwriters agree that it would not be just and equitable if contributions pursuant to this Section 9(d) were determined by pro rata allocation (even if the Underwriters were treated as one entity for such purpose) or by any other method of allocation which does not take account of the equitable considerations referred to above in this Section 9(d). The amount paid or payable by an indemnified party as a result of the losses, liabilities, claims, damages or expenses (or actions in respect thereof) referred to above in this Section 9(d) shall be deemed to include any legal or other expenses reasonably incurred by such indemnified party in connection with investigating or defending any such action or claim. Notwithstanding the provisions of this Section 9(d), no Underwriter shall be required to contribute any amount in excess of the amount by which the total price at which the Shares underwritten by it and distributed to the public were offered to the public exceeds the amount of any damages which such Underwriter has otherwise been required to pay by reason of such untrue or alleged untrue statement or omission or alleged omission.

No person guilty of fraudulent misrepresentation (within the meaning of Section 11(f) of the Securities Act) shall be entitled to contribution from any person who was not guilty of such fraudulent misrepresentation. The Underwriters' obligations in this Section 9(d) to contribute are several in proportion to their respective underwriting obligations and not joint.

(e) The obligations of the parties to this Agreements contained in this Section 9 are not exclusive and shall not limit any rights or remedies which may otherwise be available to any indemnified party at law or in equity.

10. If any Underwriter or Underwriters default in its or their obligations to purchase Shares hereunder on the Closing Date or any Option Closing Date and the aggregate number of Shares that such defaulting Underwriter or Underwriters agreed but failed to purchase does not exceed 10% of the total number of Shares that the Underwriters are obligated to purchase on such Closing Date or Option Closing Date, as the case may be, the Representatives may make arrangements satisfactory to the Company for the purchase of such Shares by other persons,

including any of the Underwriters, but if no such arrangements are made by such Closing Date or Option Closing Date, as the case may be, the non-defaulting Underwriters shall be obligated severally, in proportion to their respective commitments hereunder, to purchase the Shares that such defaulting Underwriters agreed but failed to purchase on such Closing Date or Option Closing Date, as the case may be. If any Underwriter or Underwriters so default and the aggregate number of Shares with respect to which such default or defaults occur exceeds 10% of the total number of Shares that the Underwriters are obligated to purchase on such Closing Date or Option Closing Date, as the case may be, and arrangements satisfactory to the Representatives and the Company for the purchase of such Shares by other persons are not made within 36 hours after such default, this

Agreement will terminate, subject to the provisions of Section 12, without liability on the part of any non-defaulting Underwriter or the Company, except as provided in Section 12. Nothing herein will relieve a defaulting Underwriter from liability for its default.

In the event of any such default which does not result in a termination of this Agreement, either the Representatives or the Company shall have the right to postpone the Closing Date or the relevant Option Closing Date, as the case may be, for a period not exceeding seven days in order to effect any required changes in the Registration Statement or Prospectus or in any other documents or arrangements. As used in this Agreement, the term "Underwriter" includes any person substituted for an Underwriter under this Section 10.

11. Notwithstanding anything herein contained, this Agreement (or the obligations of the several Underwriters with respect to any Option Shares which have yet to be purchased) may be terminated, subject to the provisions of Section 12, in the absolute discretion of the Representatives, by notice given to the Company, if after the execution and delivery of this Agreement and prior to the Closing Date or the Option Closing Date, as the case may be, (a) trading generally on the American Stock Exchange or the New York Stock Exchange or on the NASDAQ Global Select Market or the NASDAQ Global Market shall have been suspended or materially limited, or minimum or maximum prices for trading have been fixed, or maximum ranges for prices have been required, by any of said exchanges or by such system or by order of the Commission, FINRA or any other governmental or regulatory authority, (b) trading of any securities of or guaranteed by the Company or any Subsidiary shall have been suspended on any exchange or in any over-the-counter market, (c) a general moratorium on commercial banking activities in New York or Maryland shall have been declared by Federal, New York State or Maryland State authorities or a new restriction materially adversely affecting the distribution of the Firm Shares or the Option Shares, as the case may be, shall have become effective, or (d) there has occurred any material adverse change in the financial markets in the United States or the international financial markets, any outbreak of hostilities or escalation thereof or other calamity or crisis or any change or development involving a prospective change in national or international political, financial or economic conditions, in each case the effect of which is such as to make it, in the judgment of the Representatives, impracticable to market the Shares to be delivered on the Closing Date or Option Closing Date, as the case may be, or to enforce contracts for the sale of the Shares.

If this Agreement is terminated pursuant to this Section 11, such termination will be without liability of any party to any other party except as provided in Section 12 hereof.

12. The respective indemnities, agreements, representations, warranties and other statements of the Company or its officers and of the several Underwriters set forth in or made pursuant to this Agreement will remain in full force and effect, regardless of any investigation, or statement as to the results thereof, made by or on behalf of any Underwriter, the Company or any of their respective representatives, officers or directors or any controlling person, and will survive delivery of and payment for the Shares. If this Agreement is terminated pursuant to Section 8, 10 or 11 or, if for any reason, the purchase of any of the Shares by the Underwriters is not consummated, the Company shall remain responsible for the expenses to be paid or reimbursed by it pursuant to Section 7, the respective obligations of the Company and the Underwriters pursuant to Section 9and the provisions of Sections 12, 13 and 16 shall remain in effect and, if any Shares have been purchased hereunder the representations and warranties in Section 1 and all obligations under Section 5, Section 6 and Section 7 shall also remain in effect. If this Agreement shall be terminated by the Underwriters, or any of them, under Section 8 or otherwise because of any failure or refusal on the part of the Company to comply with the terms or to fulfill any of the conditions of this Agreement (other than solely by reason of the failure of any Underwriter in performing its obligations hereunder), or if for any reason the Company shall be unable to perform its obligations under this Agreement (other than solely by reason of the failure of any Underwriter in performing its obligations hereunder) or any condition of the Underwriters' obligations cannot be fulfilled, the Company agrees to reimburse the Underwriters or such Underwriters as have so terminated this Agreement with respect to themselves, severally, for all out-of-pocket expenses (including the fees and expenses of its counsel) reasonably incurred by the Underwriter in connection with this Agreement or the offering contemplated hereunder.

13. This Agreement shall inure to the benefit of and be binding upon the Company and the Underwriters, the officers and directors of the Company referred to herein, any controlling persons referred to herein and their respective successors and assigns. Nothing expressed or mentioned in this Agreement is intended or shall be construed to give any other person, firm or corporation any legal or equitable right, remedy or claim under or in respect of this Agreement or any provision herein contained. No purchaser of Shares from any Underwriter shall be deemed to be a successor or assign by reason merely of such purchase.

14. All notices and other communications hereunder shall be in writing and shall be deemed to have been duly given upon receipt thereof by the recipient if mailed or transmitted by any standard form of telecommunication. Notices to the Underwriters shall be given to the Representatives, c/o Stifel, Nicolaus & Company, Incorporated, 237 Park Avenue, 8th Floor, New York, New York 10017 (fax no.: (212) 355-3333); Attention: General Counsel and c/o JMP Securities, LLC, Incorporated, [Address] (fax no.: [·]); Attention: [·]. Notices to the Company shall be given to it at Proteon Therapeutics, Inc., 200 West Street, Waltham, MA, 02451, (fax no.: (781) 487-6729); Attention: Chief Executive Officer.

15. This Agreement may be signed in counterparts, each of which shall be an original and all of which together shall constitute one and the same instrument.

16. THIS AGREEMENT SHALL BE GOVERNED BY AND CONSTRUED IN ACCORDANCE WITH THE LAWS OF THE STATE OF NEW YORK, WITHOUT REGARD TO SUCH STATE'S PRINCIPLES OF CONFLICTS OF LAWS.

17. The parties hereby submit to the jurisdiction of and venue in the federal courts located in the City of New York, New York in connection with any dispute related to this Agreement, any transaction contemplated hereby, or any other matter contemplated hereby.

18. The Company acknowledges and agrees that (i) the purchase and sale of the Shares pursuant to this Agreement, including the determination of the public offering price of the Shares and any related discounts and commissions, is an arm's-length commercial transaction between the Company on the one hand, and the several Underwriters, on the other, (ii) in connection therewith and with the process leading to such transaction each Underwriter is acting solely as a principal and not the agent or fiduciary of the Company or its respective stockholders, creditors, employees or any other party, (iii) no Underwriter has assumed an advisory or fiduciary responsibility in favor of the Company with respect to the offering contemplated hereby or the process leading thereto (irrespective of whether such Underwriter has advised or is currently advising the Company on other matters) or any other obligation to the Company except the obligations expressly set forth in this Agreement, and (iv) the Company has consulted its own legal and financial advisors to the extent it deemed appropriate. The Company agrees that it will not claim that the Underwriters, or any of them, has rendered advisory services of any nature or respect, or owes a fiduciary or similar duty to the Company, in connection with such transaction or the process leading thereto.

19. The Company acknowledges that the Underwriters' research analysts and research departments are required to be independent from their respective investment banking divisions and are subject to certain regulations and internal policies, and that such Underwriters' research analysts may hold views and make statements or investment recommendations and/or publish research reports with respect to the Company and/or the offering that differ from the views of their respective investment banking divisions. The Company hereby waives and releases, to the fullest extent permitted by law, any claims that the Company may have against the Underwriters with respect to any conflict of interest that may arise from the fact that the views expressed by their independent research analysts and research departments may be different from or inconsistent with the views or advice communicated to the Company by such Underwriters' investment banking divisions. The Company acknowledges that each of the Underwriters is a full service securities firm and as such from time to time, subject to applicable securities laws, may effect transaction for its own account or the account of its customers and hold long or short positions in debt or equity securities of the companies that may be the subject of the transactions contemplated by this Agreement.

20. Notwithstanding anything herein to the contrary, the Company is authorized to disclose to any persons the U.S. federal and state income tax treatment and tax structure of the potential transaction and all materials of any kind (including tax opinions and other tax analyses) provided to the Company relating to that treatment and structure, without the Underwriters imposing any limitation of any kind. However, any information relating to the tax treatment and

tax structure shall remain confidential (and the foregoing sentence shall not apply) to the extent necessary to enable any person to comply with securities laws. For this purpose, "tax structure" is limited to any facts that may be relevant to that treatment.

21. This Agreement supersedes all prior agreements and understandings (whether written or oral) between the Company and the Underwriters, or any of them, with respect to the subject matter hereof.

22. The Company and each of the Underwriters hereby irrevocably waives, to the fullest extent permitted by applicable law, any and all right to trial by jury in any legal proceeding arising out of or relating to this Agreement or the transactions contemplated hereby.

[*Signature Page Follows*]

If the foregoing is in accordance with your understanding of our agreement, please sign and return to the Company a counterpart hereof, whereupon this instrument will become a binding agreement among the Company and the Underwriters.

Very truly yours,

PROTEON THERAPEUTICS, INC.

By: _____
Name:
Title:

Accepted as of the date hereof:

STIFEL, NICOLAUS & COMPANY, INCORPORATED
JMP SECURITIES, LLC

By: Stifel, Nicolaus & Company, Incorporated

By: _____
Name:
Title:

By: JMP Securities, LLC

By: _____
Name:
Title:

For themselves and as Representatives of the
other Underwriters named in Schedule I hereto

[Signature Page to Underwriting Agreement]

SCHEDULE I

Underwriter	**Number of Firm Shares to be Purchased**
Stifel, Nicolaus & Company, Incorporated	
JMP Securities, LLC	
Robert W. Baird & Co	
Oppenheimer & Co	
Total:	

SCHEDULE II

Free Writing Prospectuses
and
Written Testing-the-Waters Communications

[to come]

EXHIBIT A

OPINION OF COUNSEL TO THE COMPANY

[to come]

EXHIBIT B-1

OPINION OF BIOSPARK INTELLECTUAL PROPERTY LAW
INTELLECTUAL PROPERTY COUNSEL TO COMPANY

[to come]

EXHIBIT B-2

OPINION OF HUGHES, HUBBARD & REED LLP
INTELLECTUAL PROPERTY COUNSEL TO COMPANY

[to come]

EXHIBIT C

OPINION OF REGULATORY COUNSEL TO COMPANY

[to come]

EXHIBIT D

LOCK-UP AGREEMENT

Proteon Therapeutics, Inc.
200 West Street
Waltham, MA 02451

STIFEL, NICOLAUS & COMPANY, INCORPORATED
JMP SECURITIES, LLC
As Representatives of the several Underwriters
named in the Underwriting Agreement referred to
below

c/o Stifel, Nicolaus & Company, Incorporated
One South Street, 15th Floor
Baltimore, Maryland 21202

c/o JMP Securities, LLC
600 Montgomery Street, Suite 1100
San Francisco, CA 94111

Ladies and Gentlemen:

The undersigned refers to the proposed Underwriting Agreement (the "**Underwriting Agreement**") among Proteon Therapeutics, Inc., a Delaware corporation (the "**Company**"), Stifel, Nicolaus & Company, Incorporated ("**Stifel**") and JMP Securities, LLC ("**JMP**"), as representatives ("**Representatives**") of the several underwriters named therein (together with the Representatives, the "**Underwriters**"). As an inducement to the Underwriters to execute the Underwriting Agreement in connection with the proposed initial public offering of shares of the Company's common stock, par value $0.001 per share ("**Common Stock**"), pursuant to a Registration Statement on Form S-1 (the "**Offering**"), the undersigned hereby agrees that from the date hereof and until 180 days after the initial public offering date set forth on the final prospectus used to sell the Common Stock (the "**Public Offering Date**") pursuant to the Underwriting Agreement (such 180 day period being referred to herein as the "**Lock-Up Period**"), to which you are or expect to become parties, the undersigned will not (and will cause any spouse, domestic partner or immediate family member of the spouse, domestic partner or the undersigned living in the undersigned's household, any partnership, corporation, limited liability company or other entity within the undersigned's control, and any trustee of any trust that holds Common Stock or other securities of the Company for the benefit of the undersigned or such spouse, domestic partner or family member not to) offer, sell, contract to sell (including any short sale), pledge, hypothecate, establish an open "put equivalent position" within the meaning of Rule 16a-1(h) under the Securities Exchange Act of 1934, as amended (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, or otherwise encumber,

dispose of or transfer, or grant any rights with respect to, directly or indirectly, any shares of Common Stock or securities convertible into or exchangeable or exercisable for any shares of 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 the Common Stock, whether any such aforementioned transaction is to be settled by delivery of the Common Stock or such other securities, in cash or otherwise, or publicly disclose the intention to make any such offer, sale, pledge or disposition, or to enter into any such transaction, swap, hedge or other arrangement, without, in each case, the prior written consent of the Representatives, which consent may be withheld in the Representatives' sole discretion.

If the undersigned is an officer or director of the Company, (i) the undersigned agrees that the foregoing restrictions shall be equally applicable to any issuer-directed or "friends and family" shares of Common Stock that the undersigned may purchase in the Offering; (ii) the Representatives agree that, at least three business days before the effective date of any release or waiver of the foregoing restrictions in connection with a transfer of shares of Common Stock, the Representatives will notify the Company of the impending release or waiver, and (iii) the Company has agreed in the Underwriting Agreement to announce the impending release or waiver by press release through a major news service at least two business days before the effective date of the release or waiver. Any release or waiver granted by the Representatives hereunder to any such officer or director shall only be effective two business days after the publication date of such press release. The provisions of this paragraph will not apply if (a) the release or waiver is effected solely to permit a transfer not for consideration and (b) the transferee has agreed in writing to be bound by the same terms described in this Agreement to the extent and for the duration that such terms remain in effect at the time of the transfer.

The foregoing restrictions shall not apply to *bona fide* gifts by the undersigned or to any transfer made by the will or intestate succession upon the death of the undersigned, provided that (a) each resulting transferee of the Company's securities executes and delivers to the Representatives an agreement satisfactory to the Representatives certifying that such transferee is bound by the terms of this Agreement and has been in compliance with the terms hereof since the date first above written as if it had been an original party hereto and (b) to the extent any interest in the Company's securities is retained by the undersigned (or such spouse, domestic partner or family member), such securities shall remain subject to the restrictions contained in this Agreement.

In addition, the undersigned agrees that, during the period commencing on the date hereof and ending 180 days after the Public Offering Date, without the prior written consent of the Representatives (which consent may be withheld in their sole discretion): (a) the undersigned will not request, make any demand for or exercise any right with respect to, the registration of any Common Stock or any security convertible into or exercisable or exchangeable for Common Stock and (b) the undersigned waives any and all notice requirements and rights with respect to the registration of any such security pursuant to any agreement, understanding or otherwise to which the undersigned is a party.

Any Common Stock received upon exercise of options granted to the undersigned will also be subject to this Agreement. Any Common Stock acquired by the undersigned in the open market on or after the Public Offering Date (except Common Stock acquired pursuant to a "friends and family" or directed share program) will not be subject to this Agreement. A transfer of Common Stock or other

securities convertible into or exercisable or exchangeable for Common Stock may be made (i) to a family member or a trust for the benefit of the undersigned or a family member, (ii) to any corporation, partnership, limited liability company or other entity all of the beneficial ownership interests of which are held by the undersigned or the immediate family of the undersigned, (iii) if the undersigned is a corporation, partnership, limited liability company, trust or other business entity, to the stockholders or other equity holders of the undersigned or any other corporation, partnership, limited liability company, trust or other business entity that is a direct or indirect affiliate (as defined in Rule 405 promulgated under the Securities Act of 1933, as amended) of the undersigned, (iv) pursuant to a trading plan established pursuant to Rule 10b5-1 under the Exchange Act for the transfer of shares of Common Stock, provided that such plan does not provide for the transfer of shares of Common Stock during the Lock-Up Period and no public announcement or filing under the Exchange Act regarding the establishment of such plan or such transfer shall be required or shall be voluntarily made by or on behalf of the undersigned, the Company or any other person during the Lock-Up Period, (v) to the Company (A) upon a vesting event of the Company's securities or the exercise of options issued pursuant to the Company's equity incentive plans in full or partial payment of taxes or tax withholding obligations required to be paid or satisfied upon such vesting or exercise or (B) in exercise of the Company's right to repurchase or reacquire the undersigned's securities pursuant to agreements entered into pursuant to the Company's equity incentive plans, as described in the final prospectus used to sell the Common Stock, that permit the Company to repurchase or reacquire such securities upon termination of the undersigned's services to the Company, or (vi) solely by operation of law, such as pursuant to a qualified domestic order or in connection with a divorce settlement, provided, in the case of clauses (i), (ii), (iii) or (vi), that the transferee agrees in writing prior to such transfer to be bound by the terms of this Agreement as if it were a party hereto, provided further, in the case of clauses (i) — (v), that no filing under the Exchange Act or other public announcement, reporting a reduction in beneficial ownership of shares of Common Stock, shall be required or shall be voluntarily made during the Lock-Up Period and provided further that in the case of clauses (i) — (iii), it shall be a condition to the transfer or distribution that any such transfer shall not involve a disposition for value.

In furtherance of the foregoing, the Company and its transfer agent and registrar are hereby authorized to (a) decline to make any transfer of shares of Common Stock if such transfer would constitute a violation or breach of this Agreement and (b) place legends and stop transfer instructions on any such shares of Common Stock owned or beneficially owned by the undersigned.

If (i) the Company notifies you in writing that it does not intend to proceed with the Offering, (ii) the registration statement filed with the Commission with respect to the Offering is withdrawn or (iii) for any reason the underwriting agreement with respect to the Offering shall be terminated prior to the Closing Date (as defined in the Underwriting Agreement), this Lock-Up Agreement shall be terminated and the undersigned shall be released from its obligations hereunder.

[*The remainder of this page is intentionally left blank.*
Signature on following page.]

This Agreement is irrevocable and shall be binding on the undersigned and the successors, heirs, personal representatives and assigns of the undersigned. This Agreement shall be governed by and construed in accordance with the laws of the State of New York, without regard to choice of law rules. This Agreement shall lapse and become null and void if the Public Offering Date shall not have occurred on or before March 31, 2015.

Very truly yours,

EXHIBIT E

[Form of Press Release]

Proteon Therapeutics, Inc.
[Date]

("Proteon Therapeutics, Inc.") announced today that Stifel, Nicolaus & Company, Incorporated and JMP Securities, LLC, the book-running managing underwriters in the Company's recent public offering of _____ shares of common stock, is [waiving] [releasing] a lock-up restriction with respect to _____ shares of the Company's

common stock held by [certain officers or directors] [an officer or director] of the Company. The [waiver] [release] will take effect on _____, 20___, and the shares may be sold on or after such date.

This press release is not an offer or sale of the securities in the United States or in any other jurisdiction where such offer or sale is prohibited, and such securities may not be offered or sold in the United States absent registration or an exemption from registration under the United States Securities Act of 1933, as amended.

SIXTH AMENDED AND RESTATED
CERTIFICATE OF INCORPORATION OF
PROTEON THERAPEUTICS, INC.

Proteon Therapeutics, Inc., a corporation organized and existing under the laws of the State of Delaware (the "Corporation"), **DOES HEREBY CERTIFY:**

FIRST: The name of the Corporation is "Proteon Therapeutics, Inc." The date of filing the original Certificate of Incorporation of the Corporation with the Secretary of State of the State of Delaware was March 24, 2006.

SECOND: This Sixth Amended and Restated Certificate of Incorporation (this "Restated Certificate") has been duly approved by the Board of Directors of the Corporation.

THIRD: This Restated Certificate has been duly adopted by the stockholders of the Corporation in accordance with the provisions of Sections 228, 242 and 245 of the General Corporation Law of the State of Delaware (the "DGCL"), and notice thereof has been given in accordance with the provisions of Section 228 of the DGCL.

FOURTH: The Fifth Amended and Restated Certificate of Incorporation of this Corporation, as previously amended, is hereby amended, integrated and restated to read as follows:

ARTICLE ONE

The name of the Corporation is Proteon Therapeutics, Inc.

ARTICLE TWO

The address of the Corporation's registered office is 1209 Orange Street, in the City of Wilmington, New Castle County, Delaware 19801. The name of the registered agent in charge thereof is The Corporation Trust Company.

ARTICLE THREE

The nature of the business or purpose of the Corporation is to engage in any lawful act or activity for which corporations may be organized under the DGCL.

ARTICLE FOUR

Section 1. Authorized Shares. The total number of shares of all classes of capital stock which the Corporation shall have authority to issue is One Hundred Tem million (110,000,000) shares, consisting of:

(a) One Hundred million (100,000,000) shares of common stock, par value $0.001 per share ("Common Stock"); and

(b) Ten million (10,000,000) shares of undesignated preferred stock, par value $0.001 per share (the "Preferred Stock").

Such stock may be issued from time to time by the Corporation for such consideration as may be fixed by the board of directors of the Corporation (the "Board of Directors"). The following is a statement

---

of the powers, designations, preferences, privileges, and relative rights in respect of each class of capital stock of the Corporation.

Section 2. Common Stock.

(a) General. The voting, dividend and liquidation rights of the holders of Common Stock are subject to and qualified by the rights of the holders of Preferred Stock.

(b) Voting. Except as otherwise provided by the DGCL or this Restated Certificate and subject to the rights of holders of any series of Preferred Stock, all of the voting power of the stockholders of the Corporation shall be vested in the holders of the Common Stock, and each holder of Common Stock shall have one vote for each share held by such holder on all matters voted upon by the stockholders of the Corporation; provided, however, that, except as otherwise required by law, holders of Common Stock, as such, shall not be entitled to vote on any amendment to this Restated Certificate (or on any amendment to a certificate of designations of any series of Preferred Stock) that alters or changes the powers, preferences, rights or other terms of one or more outstanding series of Preferred Stock if the holders of such affected series of Preferred Stock are entitled to vote, either separately or together with the holders of one or more other such series, on such amendment pursuant to this Restated Certificate (or pursuant to a certificate of designations of any series of Preferred Stock) or pursuant to the DGCL. There shall be no cumulative voting.

(c) Dividends. Except as otherwise provided by the DGCL or this Restated Certificate, dividends may be declared and paid on the Common Stock from funds lawfully available therefor if, as and when determined by the Board of Directors and subject to any preferential dividend rights of any then outstanding shares of Preferred Stock.

(d) No Preemptive Rights. The holders of the Common Stock shall have no preemptive rights to subscribe for any shares of any class of stock of the Corporation whether now or hereafter authorized.

(e) No Conversion Rights. The Common Stock shall not be convertible into, or exchangeable for, shares of any other class or classes or of any other series of the same class of the Corporation's capital stock.

(f) Liquidation. Upon the dissolution or liquidation or winding up of the affairs of the Corporation, whether voluntary or involuntary, holders of Common Stock will be entitled to receive all assets of the Corporation available for distribution to its stockholders equally on a per share basis, subject to any preferential rights of any then outstanding shares of Preferred Stock and after payment or provision for payment of the Corporation's debts.

Section 3. Preferred Stock. To the fullest extent authorized by the DGCL, shares of Preferred Stock may be issued from time to time in one or more series, each of such series to have such powers, designations, preferences, and relative, participating, optional, or other special rights, if any, and such qualifications and restrictions, if any, as are stated or expressed in the resolution or resolutions of the Board of Directors providing for such series of Preferred Stock. Different series of Preferred Stock shall not be construed to constitute different classes of shares for the purposes of voting by classes unless expressly so provided in such resolution or resolutions.

Authority is hereby granted to the Board of Directors, acting by resolution or resolutions adopted at any time and from time to time, to create, provide for, designate and issue, out of the authorized but unissued shares of Preferred Stock, one or more series of Preferred Stock, and, in connection with the creation of any such series of Preferred Stock, to determine and fix the powers, designations,

---

preferences, and relative, participating, optional, or other special rights, if any, and the qualifications and restrictions, if any, including without limitation dividend rights, conversion rights, voting rights (if any), redemption privileges, and liquidation preferences, of such series of Preferred Stock (which need not be uniform among series), all to the fullest extent now or hereafter permitted by the DGCL. Without limiting the generality of the foregoing, the resolution or resolutions providing for the creation or issuance of any series of Preferred Stock may provide that such series shall be superior to, rank equally with, or be junior to any other series of Preferred Stock, all to the fullest extent permitted by law. No resolution, vote, or consent of the holders of the capital stock of the Corporation shall be required in connection with the creation or issuance of any shares of any series of Preferred Stock authorized by and complying with the conditions of this Restated Certificate, the right to any such resolution, vote, or consent being expressly waived by all present and future holders of the capital stock of the Corporation.

Any resolution or resolutions adopted by the Board of Directors pursuant to the authority vested in them by this Section 3 of Article Four shall be set forth in a certificate of designation along with the number of shares of such series of Preferred Stock as to which the resolution or resolutions shall apply and such certificate shall be executed, acknowledged, filed, recorded, and shall become effective, in accordance with Section 103 of the DGCL. Unless otherwise provided in any such resolution or resolutions, the number of shares of any such series of Preferred Stock to which such resolution or resolutions apply may be increased (but not above the total number of authorized shares of Preferred Stock) or decreased (but not below the number of shares of such series of Preferred Stock then outstanding) by a certificate likewise executed, acknowledged, filed and recorded, setting forth a statement that a specified increase or decrease therein has been authorized and directed by a resolution or resolutions likewise adopted by the Board of Directors. In case the number of such shares shall be decreased, the number of shares so specified in the certificate shall resume the status which they had prior to the adoption of the first resolution or resolutions. When no shares of any such series of Preferred Stock are outstanding, either because none were issued or because none remain outstanding, a certificate setting forth a resolution or resolutions adopted by the Board of Directors that none of the authorized shares of such series of Preferred Stock are outstanding, and that none will be issued subject to the certificate of designations previously filed with respect to such series of Preferred Stock, may be executed, acknowledged, filed and recorded in the same manner as previously described and it shall have the effect of eliminating from this Restated Certificate all matters set forth in the certificate of designations with respect to such series of Preferred Stock. If no shares of any such series of Preferred Stock established by a resolution or resolutions adopted by the Board of Directors have been issued, the voting powers, designations, preferences and relative, participating, optional or other rights, if any, with the qualifications, limitations or restrictions thereof, may be amended by a resolution or resolutions adopted by the Board of Directors. In the event of any such amendment, a certificate which (i) states that no shares of such series of Preferred Stock have been issued, (ii) sets forth the copy of the amending resolution or resolutions and (iii) if the designation of such series of Preferred Stock is being changed, indicates the original designation and the new designation, shall be executed, acknowledged, filed, recorded, and shall become effective, in accordance with Section 103 of the DGCL.

ARTICLE FIVE

The Corporation is to have perpetual existence.

ARTICLE SIX

Section 1. Classification of Directors. Effective as of the closing (the "IPO Closing") of the Corporation's first public offering of shares of Common Stock registered pursuant to the Securities Act of 1933, as amended, the Board of Directors shall be divided into three classes of directors, Class I, Class II, and Class III, such classes to be as nearly equal in number of directors as possible, having staggered

---

three-year terms of office (except to the extent otherwise provided in the next sentence with respect to the initial term of the first and second of such classes of directors). The initial term of office of the directors of Class I shall expire as of the first annual meeting of the Corporation's stockholders following the IPO Closing; the initial term of office of the directors of Class II shall expire as of the second annual meeting of the Corporation's stockholders following the IPO Closing; and the initial term of office of the directors of Class III shall expire as of the third annual meeting of the Corporation's stockholders following the IPO Closing. At each annual meeting of stockholders of the Corporation after the IPO Closing, nominees will stand for election to succeed those directors whose terms are to expire as of such annual meeting of stockholders, and such nominees elected at such annual meeting of stockholders shall be elected for a term expiring at the third annual meeting of stockholders following their election. Directors shall hold office until the annual meeting of stockholders in which their term is scheduled to expire as set forth above in this Section 1 of Article Six and until their respective successors are duly elected or qualified or until their earlier death, incapacity, resignation or removal. Those directors already in office immediately prior to the IPO Closing shall be allocated among the three classes of directors contemplated under this Section 1 of Article Six pursuant to a resolution or resolutions adopted by the Board of Directors prior to the IPO Closing.

Section 2. Removal. Subject to the special rights of the holders of any series of Preferred Stock to elect directors, the directors of the Corporation may be removed only for cause by the affirmative vote of the holders of at least seventy-five percent (75%) of the outstanding shares of capital stock of the Corporation entitled to vote in the election of directors or class of directors, voting together as a single class, at a meeting of the stockholders called for that purpose.

Section 3. Vacancies. Except as the DGCL may otherwise require, any new directorships or vacancies in the Board of Directors, including new directorships resulting from any increase in the number of directors to serve in the Board of Directors and/or any unfilled vacancies by reason of death, resignation, disqualification, removal for cause, failure to elect or otherwise with respect to any director, may be filled only by the vote of a majority of the remaining directors then in office, although less than a quorum, or by the sole remaining director.

Section 4. Number of Directors. Subject to the special rights of the holders of any series of Preferred Stock to elect directors, the number of directors which shall constitute the Board of Directors shall be fixed exclusively by the Board of Directors from time to time in accordance with the by-laws of the Corporation. No decrease in the number of directors constituting the whole board shall shorten the term of any incumbent director.

ARTICLE SEVEN

The Board of Directors shall have the power and authority: (i) to adopt, amend or repeal the Corporation's by-laws, subject to the power of the stockholders of the Corporation entitled to vote with respect thereto to make, alter, amend or repeal the bylaws; provided , that with respect to the powers of stockholders entitled to vote with respect thereto to make, alter, amend or repeal the bylaws, in addition to any other vote otherwise required by law, the affirmative vote of the holders of at least seventy-five percent (75%) of the outstanding shares of capital stock of the Corporation entitled to vote in the election of directors or class of directors, voting together as a single class, shall be required to make, alter, amend or repeal the bylaws of the Corporation; and (ii) to the full extent permitted or not prohibited by law, and without the consent of or other action by the stockholders, to authorize or create mortgages, pledges or other liens or encumbrances upon any or all of the assets, real, personal or mixed, and franchises of the Corporation, including after-acquired property, and to exercise all of the powers of the Corporation in connection therewith.

ARTICLE EIGHT

Except as otherwise provided for by any resolutions of the Board of Directors providing for the issuance of any series of Preferred Stock, effective as of the IPO Closing, any action required or permitted to be taken by the stockholders of the Corporation may be taken only at a duly called annual or special meeting of the stockholders in which such action is properly brought before such meeting, and not by written consent in lieu of such a meeting. Subject to any special rights of the holders of any series of Preferred Stock, and to the requirements of applicable law, special meetings of stockholders of the Corporation may 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. Any business transacted at any special meeting of stockholders shall be limited to matters relating to the purpose or purposes stated in the notice of meeting

ARTICLE NINE

The Corporation reserves the right to amend, alter, change or repeal any provision contained in this Restated Certificate, in the manner now or hereafter prescribed by the DGCL, and all rights conferred upon stockholders herein are granted subject to this reservation. Notwithstanding anything to the contrary contained in this Restated Certificate, and notwithstanding that a lesser percentage may be permitted from time to time by applicable law, the affirmative vote of the holders of at least seventy-five percent (75%) of the outstanding shares of capital stock of the Corporation entitled to vote with in the election of directors or class of directors, voting together as a single class (in addition to any separate class vote that may in the future be required pursuant to the terms of any outstanding Preferred Stock), shall be required to amend or repeal the provisions of Articles Four (only to the extent it relates to the authority of the Board of Directors to issue shares of Preferred Stock in one or more series, the terms of which may be determined by the Board of Directors), Six, Seven, Eight, Nine, Ten or Eleven of this Restated Certificate or to reduce the numbers of authorized shares of Common Stock or Preferred Stock.

ARTICLE TEN

Section 1. Limitation of Liability. To the fullest extent permitted by the DGCL as it now exists or may hereafter be amended (but, in the case of any such amendment, only to the extent that such amendment permits the Corporation to provide broader indemnification rights than permitted prior thereto), no director of the Corporation shall be personally liable to the Corporation or to any of its stockholders for monetary damages for breach of fiduciary duty as a director, notwithstanding any provision of law imposing such liability; provided, however, that to the extent required from time to time by applicable law, this Article Ten shall not eliminate or limit the liability of a director, to the extent such liability is provided by applicable law, (i) for any breach of the director's duty of loyalty to the corporation or its stockholders, (ii) for acts or omissions not in good faith or which involve intentional misconduct or a knowing violation of law, (iii) under Section 174 of the DGCL, or (iv) for any transactions from which the director derived an improper personal benefit.

Section 2. Indemnification. The Corporation shall, to the fullest extent permitted by Section 145 of the DGCL and as further provided in the Corporation's by-laws, each as amended from time to time, indemnify each person who was or is a party or is threatened to be made a party to any threatened, pending or completed action, suit or proceeding, whether civil, criminal, administrative or investigative, by reason of the fact that such person is or was, or has agreed to become, a director or officer of the Corporation, or is or was serving, or has agreed to serve, at the request of the Corporation, as a director, officer or trustee of, or in a similar capacity with, another corporation, partnership, joint venture, trust or other enterprise (including any employee benefit plan), or by reason of any action alleged to have been taken or omitted in such capacity, against all expenses (including attorneys' fees), judgments, fines and

---

amounts paid in settlement actually and reasonably incurred by him or her or on his or her behalf in connection with such action, suit or proceeding and any appeal therefrom.

Indemnification may include payment by the Corporation of expenses in defending an action or proceeding in advance of the final disposition of such action or proceeding upon receipt of an undertaking by the person indemnified to repay such payment if it is ultimately determined that such person is not entitled to indemnification under this Article Ten, which undertaking may be accepted without reference to the financial ability of such person to make such repayment.

The Corporation shall not indemnify any such person seeking indemnification in connection with a proceeding (or part thereof) initiated by such person unless the initiation thereof was approved by the Board of Directors or except and to the extent otherwise permitted in the Corporation's by-laws or in an agreement between the Corporation and such person.

The indemnification rights provided in this Article Ten (i) shall not be deemed exclusive of any other rights to which those indemnified may be entitled under the Corporation's by-laws, any law, agreement or vote of stockholders or disinterested directors or otherwise, and (ii) shall inure to the benefit of the heirs, executors and administrators of such persons. The Corporation may, to the extent authorized from time to time by its Board of Directors, grant indemnification rights to other employees or agents of the Corporation or other persons serving the Corporation and such rights may be equivalent to, or greater or less than, those set forth in this Article Ten.

Section 3. Merger or Consolidation. For purposes of this Article Ten, references to the "Corporation" shall include, in addition to the resulting corporation, any constituent corporation (including any constituent of a constituent) absorbed in a consolidation or merger which, if its separate existence had continued, would have had power and authority to indemnify its directors, officers and employees or agents, so that any person who is or was a director, officer, employee or agent of such constituent corporation, or is or was serving at the request of such constituent corporation as a director, officer, employee or agent of another corporation, partnership, joint venture, trust or other enterprise, shall stand in the same position under this Article Ten with respect to the resulting or surviving corporation as he or she would have with respect to such constituent corporation if its separate existence had continued.

Section 4. Amendment or Repeal. No amendment to or repeal of this Article Ten shall apply to or have any effect on the liability or alleged liability of any director for or with respect to any acts or omissions of such director occurring prior to the effective date of such amendment or repeal.

ARTICLE ELEVEN

Unless the Corporation, as authorized by the Board of Directors, consents in writing to the selection of one or more alternative forums, the Court of Chancery of the State of Delaware shall be the sole and exclusive forum for a stockholder (including a beneficial owner) to bring (i) any derivative action or proceeding brought on behalf of the Corporation, (ii) any action asserting a claim of breach of a fiduciary duty owed by any director, officer or other employee of the Corporation to the Corporation or the Corporation's stockholders, (iii) any action asserting a claim against the Corporation arising pursuant to any provision of the DGCL or this Restated Certificate or the Corporation's Bylaws or (iv) any action asserting a claim against the Corporation, its directors, officers or employees governed by the internal affairs doctrine, except for, as to each of (i) through (iv), any claim as to which the Court of Chancery determines that there is an indispensable party not subject to the jurisdiction of the Court of Chancery (and the indispensable party does not consent to the personal jurisdiction of the Court of Chancery within ten days following such determination), which is vested in the exclusive jurisdiction of a court or forum

---

other than the Court of Chancery, or for which the Court of Chancery does not have subject matter jurisdiction. Any person or entity purchasing or otherwise acquiring any interest in shares of capital stock of the Corporation (including, without limitation, shares of Common Stock) shall, and shall be deemed to, have notice of and to have consented to the provisions of this Article Eleven.

ARTICLE TWELVE

If any provision or provisions of this Restated Certificate shall be held to be invalid, illegal or unenforceable as applied to any circumstance for any reason whatsoever: (i) the validity, legality and enforceability of such provisions in any other circumstance and of the remaining provisions of this Restated Certificate (including, without limitation, each portion of any paragraph of this Restated Certificate containing any such provision held to be invalid, illegal or unenforceable that is not itself held to be invalid, illegal or unenforceable) shall not in any way be affected or impaired thereby and (ii) to the fullest extent possible, the provisions of this Restated Certificate (including, without limitation, each such portion of any paragraph of this Restated Certificate containing any such provision held to be invalid, illegal or unenforceable) shall be construed so as to permit the Corporation to protect its directors, officers, employees and agents from personal liability in respect of their good faith service to or for the benefit of the Corporation to the fullest extent permitted by law.

[The remainder of this page is left intentionally blank.]

IN WITNESS WHEREOF, this Sixth Amended and Restated Certificate of Incorporation has been executed by a duly authorized officer of this Corporation on this day of , 2014.

PROTEON THERAPEUTICS, INC.

By: _____
Name: Timothy Noyes
Title: President and Chief Executive Officer

PROTEON THERAPEUTICS, INC.

AMENDED AND RESTATED BY-LAWS

Article I. - General.

1.1. Offices. The registered office of Proteon Therapeutics. (the "Company") shall be in the City of Wilmington, County of New Castle, State of Delaware. The Company may also have offices at such other places both within and without the State of Delaware as the board of directors of the Company (the "Board of Directors") may from time to time determine or the business of the Company may require.

1.2. Seal. The seal, if any, of the Company shall be in the form of a circle and shall have inscribed thereon the name of the Company, the year of its organization and the words "Corporate Seal, Delaware."

1.3. Fiscal Year. The fiscal year of the Company shall be fixed by resolution of the Board of Directors.

Article II. - Stockholders.

2.1. Place of Meetings. Each meeting of the stockholders shall be held upon notice as hereinafter provided, at such place as the Board of Directors shall have determined and as shall be stated in such notice, either within or outside the State of Delaware.

2.2. Annual Meeting. The annual meeting of the stockholders shall be held each year on such date and at such time as the Board of Directors may determine. At each annual meeting the stockholders entitled to vote shall elect such members of the Board of Directors as are standing for election, by plurality vote by ballot, and they may transact such other corporate business as may properly be brought before the meeting. At the annual meeting any business may be transacted, irrespective of whether the notice calling such meeting shall have contained a reference thereto, except where notice is required by law, the Company's Seventh Amended and Restated Certificate of Incorporation (as amended from time to time, the "Certificate of Incorporation"), or these By-laws.

2.3. Quorum and Adjournment. At all meetings of the stockholders the holders of a majority of the stock issued and outstanding and entitled to vote thereat, present in person or represented by proxy, shall constitute a quorum requisite for the transaction of business except as otherwise provided by law, the Company's Certificate of Incorporation, or these By-laws. Whether or not there is such a quorum at any meeting, the presiding officer of the meeting may adjourn the meeting from time to time without notice other than announcement at the meeting. If the adjournment is for more than thirty (30) days, or if after the adjournment a new record date is fixed for the adjourned meeting, a notice of the adjourned meeting shall be given to each stockholder of record entitled to vote at the meeting. At such adjourned meeting, at which the requisite amount of voting stock shall be represented, any business may be transacted that might have been transacted if the meeting had been held as originally called. The stockholders present in person or by proxy at a duly called meeting at which a quorum is present may continue to transact business until adjournment, notwithstanding the withdrawal of enough stockholders to leave less than a quorum.

2.4. Right to Vote; Proxies. Subject to the provisions of the Company's Certificate of Incorporation, each holder of a share or shares of capital stock of the Company having the right to vote at any meeting shall be entitled to one vote for each such share of stock held by such stockholder. Any stockholder entitled to vote at any meeting of stockholders may vote either in person or by proxy, but no

---

proxy that is dated more than three (3) years prior to the meeting at which it is offered shall confer the right to vote thereat unless the proxy provides that it shall be effective for a longer period. A proxy may be granted by a writing executed by the stockholder or his or her authorized agent or by transmission or authorization of transmission by other means of electronic transmission to the person who will be the holder of the proxy or to a proxy solicitation firm, proxy support service organization, or like agent duly authorized by the person who will be the holder of the proxy to receive such transmission, subject to the conditions set forth in Section 212 of the Delaware General Corporation Law, as it may be amended from time to time (the "DGCL").

2.5. Voting. At all meetings of stockholders, except as otherwise expressly provided for by statute, the Company's Certificate of Incorporation or these By-laws, (i) in all matters other than the election of directors, the affirmative vote of a majority of shares present in person or represented by proxy at the meeting and entitled to vote on such matter shall be the act of the stockholders and (ii) directors shall be elected by a plurality of the votes of cast, present in person or represented by proxy at the meeting and entitled to vote on the election of directors.

2.6. Notice of Annual Meetings. Written notice of the annual meeting of the stockholders shall be mailed to each stockholder of record entitled to vote thereat at such address as appears on the stock books of the Company at least ten (10) days (and not more than sixty (60) days) prior to the meeting. The Board of Directors may postpone any annual meeting of the stockholders at its discretion, even after notice thereof has been mailed. It shall be the duty of every stockholder to furnish to the Secretary of the Company or to the transfer agent, if any, of the class of stock owned by him or her and such stockholder's post-office address, and to notify the Secretary of any change therein. Notice need not be given to any stockholder who submits a written waiver of notice signed by him or her before or after the time stated therein. Attendance of a stockholder at a meeting of stockholders shall constitute a waiver of notice of such meeting, except when the stockholder attends the meeting for the express purpose of objecting, at the beginning of the meeting, to the transaction of any business because the meeting is not lawfully called or convened. Neither the business to be transacted at, nor the purpose of, any regular or special meeting of the stockholders need be specified in any written waiver of notice.

2.7. Stockholders' List. A complete list of the stockholders entitled to vote at any meeting of stockholders, arranged in alphabetical order and showing the address of each stockholder, and the number of shares registered in the name of each stockholder, shall be prepared by the Secretary and shall be open to the examination of any stockholder, for any purpose germane to the meeting for a period of at least ten (10) days before such meeting (i) on a reasonably accessible electronic network, provided that the information required to gain access to such list is provided with the notice of the meeting, or (ii) during ordinary business hours, at the principal place of business of the Company, and said list shall be produced and kept at the time and place of such meeting during the whole time of said meeting, and may be inspected by any stockholder who is present at the place of said meeting, or, if the meeting is to be held solely by means of remote communication, on a reasonably accessible electronic network and the information required to access such list shall be provided with the notice of the meeting.

2.8. Special Meetings. Special meetings of the stockholders for any purpose or purposes, unless otherwise provided by law, may be called only in the manner set forth in the Certificate of Incorporation. Any such person or persons that has or have called a special meeting of stockholders in the manner set forth in the Certificate of Incorporation may postpone or cancel any special meeting of the stockholders at its or their discretion, even after notice thereof has been mailed.

2.9. Notice of Special Meetings. Written notice of a special meeting of stockholders, stating the time and place and purpose or purposes thereof, shall be mailed, postage prepaid, not less than ten (10) nor more than sixty (60) days before such meeting, to each stockholder entitled to vote thereat, at

such address as appears on the books of the Company. No business may be transacted at such meeting except that referred to in said notice, or in a supplemental notice given also in compliance with the provisions hereof, or such other business as may be germane or supplementary to that stated in said notice or notices. The individual or group calling such meeting shall have exclusive authority to determine the business included in such notice. Notice need not be given to any stockholder who submits a written waiver of notice signed by him or her before or after the time stated therein. Attendance of a stockholder at a meeting of stockholders shall constitute a waiver of notice of such meeting, except when the stockholder attends the meeting for the express purpose of objecting, at the beginning of the meeting, to the transaction of any business because the meeting is not lawfully called or convened. Neither the business to be transacted at, nor the purpose of, any regular or special meeting of the stockholders need be specified in any written waiver of notice.

2.10. Inspectors of Elections; Opening and Closing the Polls.

(a) One or more inspectors may be appointed by the Board of Directors before or at any meeting of stockholders, or, if no such appointment shall have been made, the presiding officer may make such appointment at the meeting. At the meeting for which the inspector or inspectors are appointed, he, she or they shall open and close the polls, receive and take charge of the proxies and ballots, and decide all questions touching on the qualifications of voters, the validity of proxies, and the acceptance and rejection of votes. If any inspector previously appointed shall fail to attend or refuse or be unable to serve, the presiding officer shall appoint an inspector in his or her place.

(b) At any time at which the Company has a class of voting stock that is (i) listed on a national securities exchange, (ii) authorized for quotation on an inter-dealer quotation system of a registered national securities association, or (iii) held of record by more than 2,000 stockholders, the provisions of Section 231 of the DGCL with respect to inspectors of election and voting procedures shall apply, in lieu of the provisions of paragraph (a) of this Section 2.10.

2.11. Stockholders' Consent in Lieu of Meeting. Unless otherwise provided in the Company's Certificate of Incorporation, any action required to be taken at any annual or special meeting of stockholders of the Company, or any action that may be taken at any annual or special meeting of such stockholders, may be taken only at such a meeting, and not by written consent of the stockholders.

2.12. Advance Notice of Stockholder Business and Nominations.

(a) Timely Notice. At a meeting of the stockholders, only such nominations of persons for the election of directors and such other business shall be conducted as shall have been properly brought before the meeting. To be properly brought before an annual meeting, nominations or such other business must be: (i) specified in the notice of meeting (or any supplement thereto) given by or at the direction of the Board of Directors or any committee thereof, (ii) otherwise properly brought before the meeting by or at the direction of the Board of Directors or any committee thereof, or (iii) otherwise properly brought before the meeting by a stockholder who is a stockholder of record of the Company at the time such notice of meeting is delivered, who is entitled to vote at the meeting and who complies with the notice procedures set forth in this Section 2.12. In addition, any proposal of business (other than the nomination of persons for election to the Board of Directors) must be a proper matter for stockholder action. For business (including, but not limited to, director nominations) to be properly brought before an annual meeting by a stockholder, the stockholder or stockholders of record intending to propose the business (the "Proposing Stockholder") must have given timely notice thereof pursuant to this Section 2.12(a) or Section 2.12(c) below, as applicable, in writing to the Secretary of the Company even if such matter is already the subject of any notice to the stockholders or a disclosure made in a press release reported by the Dow Jones News Services, The Associated Press or a comparable national news service or in a

document filed by the Company with the Securities and Exchange Commission pursuant to Section 13, 14 or 15(d) of the Securities Exchange Act of 1934, as amended (the "Exchange Act") from the Board of Directors (a "Public Disclosure"). To be timely, a Proposing Stockholder's notice must be delivered to or mailed and received at the principal executive offices of the Company: (x) not later than the close of business on the 90th day, nor earlier than the close of business on the 120th day in advance of the anniversary of the previous year's annual meeting if such meeting is to be held on a day which is not more than 30 days in advance of the anniversary of the previous year's annual meeting or not later than 70 days after the anniversary of the previous year's annual meeting; and (y) with respect to any other annual meeting of stockholders, the close of business on the tenth (10th) day following the date of Public Disclosure of the date of such meeting. In no event shall the Public Disclosure of an adjournment or postponement of an annual meeting commence a new notice time period (or extend any notice time period).

(b) Stockholder Nominations. For the nomination of any person or persons for election to the Board of Directors, a Proposing Stockholder's notice to the Secretary of the Company shall set forth (i) the name, age, business address and residence address of each nominee proposed in such notice, (ii) the principal occupation or employment of each such nominee, (iii) the number of shares of capital stock of the Company which are owned of record and beneficially by each such nominee (if any), (iv) such other information concerning each such nominee as would be required to be disclosed in a proxy statement soliciting proxies for the election of such nominee as a director in an election contest (even if an election contest is not involved) or that is otherwise required to be disclosed, under Section 14(a) of the Exchange Act and the rules and regulations promulgated thereunder, (v) the consent of the nominee to being named in the proxy statement as a nominee and to serving as a director if elected, and (vi) as to the Proposing Stockholder: (A) the name and address of the Proposing Stockholder as they appear on the Company's books and of the beneficial owner, if any, on whose behalf the nomination is being made, (B) the class and number of shares of the Company which are owned by the Proposing Stockholder (beneficially and of record) and owned by the beneficial owner, if any, on whose behalf the nomination is being made, as of the date of the Proposing Stockholder's notice, and a representation that the Proposing Stockholder will notify the Company in writing of the class and number of such shares owned of record and beneficially as of the record date for the meeting promptly following the later of the record date or the date notice of the record date is first publicly disclosed, (C) a description of any agreement, arrangement or understanding with respect to such nomination between or among the Proposing Stockholder and the beneficial owner, if any, on whose behalf the nomination is being made, and any of their affiliates or associates, and any others (including their names) acting in concert with any of the foregoing, and a representation that the Proposing Stockholder will notify the Company in writing of any such agreement, arrangement or understanding in effect as of the record date for the meeting promptly following the later of the record date or the date notice of the record date is first publicly disclosed, (D) a description of any agreement, arrangement or understanding (including any derivative or short positions, profit interests, options, hedging transactions, and borrowed or loaned shares) that has been entered into as of the date of the Proposing Stockholder's notice by, or on behalf of, the Proposing Stockholder or any of its affiliates or associates, the effect or intent of which is to mitigate loss to, manage risk or benefit of share price changes for, or increase or decrease the voting power of the Proposing Stockholder, or any such beneficial owner, or any of its affiliates or associates with respect to shares of stock of the Company, and a representation that the Proposing Stockholder will notify the Company in writing of any such agreement, arrangement or understanding in effect as of the record date for the meeting promptly following the later of the record date or the date notice of the record date is first publicly disclosed, (E) a representation that the Proposing Stockholder is a holder of record of shares of the Company entitled to vote at the meeting and intends to appear in person or by proxy at the meeting to nominate the person or persons specified in the notice, and (F) a representation whether the Proposing Stockholder intends to deliver a proxy statement and/or form of proxy to holders of at least the percentage of the Company's outstanding capital stock required to approve the nomination and/or otherwise to solicit proxies from stockholders in support

of the nomination. The Company may require any proposed nominee to furnish such other information as it may reasonably require to determine the eligibility of such proposed nominee to serve as an independent director of the Company or that could be material to a reasonable stockholder's understanding of the independence, or lack thereof, of such nominee.

(c) Other Stockholder Proposals. For all business other than director nominations, a Proposing Stockholder's notice to the Secretary of the Company shall set forth as to each matter the Proposing Stockholder proposes to bring before the annual meeting: (i) a brief description of the business desired to be brought before the annual meeting and the reasons for conducting such business at the annual meeting, (ii) any other information relating to such stockholder and beneficial owner, if any, on whose behalf the proposal is being made, required to be disclosed in a proxy statement or other filings required to be made in connection with solicitations of proxies for the proposal and pursuant to and in accordance with Section 14(a) of the Exchange Act and the rules and regulations promulgated thereunder and (iii) the information required by Section 2.12(b)(vi) above.

(d) Proxy Rules. Notwithstanding the foregoing provisions of this Section 2.12, a stockholder shall comply with all applicable requirements of the Exchange Act and the rules and regulations thereunder with respect to the matters set forth in this Section 2.12, including, by way of illustration and not of limitation, the requirements of Rule 14a-8 under the Exchange Act, as applicable. Accordingly, any stockholder exercising rights under Rule 14a-8 or any other rule under the Exchange Act shall comply with all requirements of that Rule or rule, including by way of illustration requirements for timely notice, notwithstanding any different or inconsistent provisions of this Section 2.12. Nothing in this Section 2.12 shall be deemed to affect any rights of stockholders to request inclusion of proposals in the Company's proxy statement pursuant to Rule 14a-8 under the Exchange Act or any other rights conferred on stockholders by a rule under the Exchange Act.

(e) Special Meetings of Stockholders. Only such business shall be conducted at a special meeting of stockholders as shall have been brought before the meeting pursuant to the Company's notice of meeting. Nominations of persons for election to the Board of Directors may be made at a special meeting of stockholders at which directors are to be elected pursuant to the Company's notice of meeting (x) by or at the direction of the Board of Directors or any committee thereof or (y) provided that the Board of Directors has determined that directors shall be elected at such meeting, by any stockholder of the Company who is a stockholder of record at the time the notice provided for in this Section 2.12 is delivered to the Secretary of the Company, who is entitled to vote at the meeting and upon such election and who complies with the notice procedures set forth in this Section 2.12. In the event the Company calls a special meeting of stockholders for the purpose of electing one or more directors to the Board of Directors, any such stockholder entitled to vote in such election of directors may nominate a person or persons (as the case may be) for election to such position(s) as specified in the Company's notice of meeting, if the stockholder's notice required by this Section 2.12 shall be delivered to the Secretary at the principal executive offices of the Company not later than the later of the close of business on the 90th day prior to such special meeting or the tenth (10th) day following the date of Public Disclosure of the date of the special meeting and of the nominees proposed by the Board of Directors to be elected at such meeting and not earlier than the close of business on the 120th day prior to such special meeting. In no event shall the Public Disclosure of an adjournment or postponement of a special meeting commence a new time period (or extend any notice time period).

(f) Effect of Noncompliance. Notwithstanding anything in these By-laws to the contrary: (i) no nominations shall be made or business shall be conducted at any annual meeting except in accordance with the procedures set forth in this Section 2.12, and (ii) unless otherwise required by law, if a Proposing Stockholder intending to propose business or make nominations at an annual meeting pursuant to this Section 2.12 does not provide the information required under this Section 2.12 to the Company promptly

following the later of the record date or the date notice of the record date is first publicly disclosed, or the Proposing Stockholder (or a qualified representative of the Proposing Stockholder) does not appear at the meeting to present the proposed business or nominations, such business or nominations shall not be considered, notwithstanding that proxies in respect of such business or nominations may have been received by the Company. The requirements of this Section 2.12 shall apply to any business or nominations to be brought before an annual meeting by a stockholder whether such business or nominations are to be included in the Company's proxy statement pursuant to Rule 14a-8 of the Exchange Act or presented to stockholders by means of an independently financed proxy solicitation. The requirements of Section 2.12 are included to provide the Company notice of a stockholder's intention to bring business or nominations before an annual meeting and shall in no event be construed as imposing upon any stockholder the requirement to seek approval from the Company as a condition precedent to bringing any such business or make such nominations before an annual meeting.

Article III. - Directors.

3.1. Number of Directors.

(a) Except as otherwise provided by law, the Company's Certificate of Incorporation, or these By-laws, the property and business of the Company shall be managed by or under the direction of the Board of Directors. Directors need not be stockholders, residents of Delaware, or citizens of the United States. The use of the phrase "whole board" herein refers to the total number of directors which the Company would have if there were no vacancies.

(b) Subject to the special rights of the holders of any series of Preferred Stock to elect directors, the number of directors constituting the full Board of Directors shall be as determined by the Board of Directors from time to time by resolution adopted by the affirmative vote of at least a majority of the directors then in office.

(c) Effective as of the closing (the "IPO Closing") of the Company's first public offering of shares of Common Stock registered pursuant to the Securities Act of 1933, as amended, the Board of Directors shall be divided into three classes of directors, such classes to be as nearly equal in number of directors as possible, having staggered three-year terms of office (except to the extent otherwise provided in the next sentence with respect to the initial term of the first and second of such classes of directors). The initial term of office of the directors of the first such class shall expire as of the first annual meeting of the Company's stockholders following the IPO Closing; the initial term of office of the directors of the second such class shall expire as of the second annual meeting of the Company's stockholders following the IPO Closing; and the initial term of office of the directors of the third such class shall expire as of the third annual meeting of the Company's stockholders following the IPO Closing. At each annual meeting of stockholders of the Company after the IPO Closing, nominees will stand for election to succeed those directors whose terms are to expire as of such annual meeting of stockholders, and such nominees elected at such annual meeting of stockholders shall be elected for a term expiring at the third annual meeting of stockholders following their election.

(d) Directors shall hold office until the annual meeting of stockholders in which their term is scheduled to expire as set forth above in this Section 3.1 and until their respective successors are duly elected or qualified or until their earlier death, incapacity, resignation or removal. Any director serving as such pursuant to this Section 3.1 may be removed pursuant to Section 3.3. Those directors already in office immediately prior to the IPO Closing shall be allocated among the three (3) classes of directors contemplated under this Section 3.1 pursuant to a resolution or resolutions adopted by the Board of Directors prior to the IPO Closing.

(e) Except as the DGCL or the Company's Certificate of Incorporation may otherwise require, any new directorships or vacancies in the Board of Directors, including new directorships resulting from any increase in the number of directors to serve on the whole board and/or any unfilled vacancies by reason of death, resignation, disqualification, removal for cause, failure to elect or otherwise with respect to any director, may be filled by only the vote of a majority of the remaining directors then in office, although less than a quorum, or by the sole remaining director.

(f) No decrease in the number of directors constituting the whole board shall shorten the term of any incumbent director.

3.2. Resignation. Any director of the Company may resign at any time by giving notice in writing or by electronic transmission to the Chairperson of the Board, the President, or the Secretary of the Company. Such resignation shall take effect at the time specified therein, at the time of receipt if no time is specified therein and at the time of acceptance if the effectiveness of such resignation is conditioned upon its acceptance. Unless otherwise specified therein, the acceptance of such resignation shall not be necessary to make it effective.

3.3. Removal. Except as may otherwise be provided by the DGCL or the Company's Certificate of Incorporation, any director or the entire Board of Directors may be removed only for cause and only by the vote of the holders of at least seventy-five percent (75%) of the outstanding shares of capital stock of the Company entitled to vote for the election of directors or class of directors, voting together as single class, at a meeting of the stockholders called for that purpose.

3.4. Place of Meetings and Books. The Board of Directors may hold their meetings and keep the books of the Company outside the State of Delaware, at such places as they may from time to time determine.

3.5. General Powers. In addition to the powers and authority expressly conferred upon them by these By-laws, the Board of Directors may exercise all such powers of the Company and do all such lawful acts and things as are not by statute or by the Company's Certificate of Incorporation or by these By-laws directed or required to be exercised or done by the stockholders.

3.6. Committees. The Board of Directors may designate one or more committees, by resolution or resolutions passed by at least a majority vote of the Board of Directors; such committee or committees shall consist of one or more directors of the Company, and to the extent provided in the resolution or resolutions designating them, shall have and may exercise specific powers of the Board of Directors in the management of the business and affairs of the Company to the extent permitted by statute and shall have power to authorize the seal of the Company to be affixed to all papers that may require it. Such committee or committees shall have such name or names as may be determined from time to time by resolution adopted by the Board of Directors.

3.7. Powers Denied to Committees. Committees of the Board of Directors shall not, in any event, have any power or authority to amend the Company's Certificate of Incorporation (except that a committee may, to the extent authorized in the resolution or resolutions providing for the issuance of shares adopted by the Board of Directors as provided in Section 151(a) of the DGCL, fix the designations and any of the preferences or rights of such shares relating to dividends, redemption, dissolution, any distribution of assets of the Company or the conversion into, or the exchange of such shares for, shares of any other class or classes or any other series of the same or any other class or classes of stock of the Company or fix the number of shares of any series of stock or authorize the increase or decrease of the shares of any series), adopt an agreement of merger or consolidation, recommend to the stockholders the sale, lease, or exchange of all or substantially all of the Company's property and assets, recommend to the

stockholders a dissolution of the Company or a revocation of a dissolution, or amend the By-laws of the Company. Further, no committee of the Board of Directors shall have the power or authority to declare a dividend, to authorize the issuance of stock, or to adopt a certificate of ownership and merger pursuant to Section 253 of the DGCL, unless the resolution or resolutions designating such committee expressly so provides.

3.8. Substitute Committee Member. In the absence or on the disqualification of a member of a committee, the member or members thereof present at any meeting and not disqualified from voting, whether or not he or they constitute a quorum, may unanimously appoint another member of the Board of Directors to act at the meeting in the place of such absent or disqualified member. Any committee shall keep regular minutes of its proceedings and report the same to the Board of Directors as may be required by the Board of Directors.

3.9. Compensation of Directors. The Board of Directors shall have the power to fix the compensation of directors and members of committees of the Board. The directors may be paid their expenses, if any, of attendance at each meeting of the Board of Directors and may be paid a fixed sum for attendance at each meeting of the Board of Directors, a stated amount per annum as director and/or other forms of compensation as the Board of Directors may approve. No such payment shall preclude any director from serving the Company in any other capacity and receiving compensation therefor. Members of special or standing committees may be allowed like compensation for attending committee meetings.

3.10. Regular Meetings. No notice shall be required for regular meetings of the Board of Directors for which the time and place have been fixed.

3.11. Special Meetings. Special meetings of the board may be called by the Chairperson of the Board of Directors, if any, or the President, on two (2) days notice, which may be written, oral or by electronic transmission, to each director, or such shorter period of time before the meeting as will nonetheless be sufficient for the convenient assembly of the directors so notified; special meetings shall be called by the Secretary in like manner and on like notice, on the written request of two (2) or more directors.

3.12. Quorum. At all meetings of the Board of Directors, a majority of the members of the Board of Directors shall be necessary and sufficient to constitute a quorum for the transaction of business, and the act of a majority of the directors present at any meeting at which there is a quorum shall be the act of the Board of Directors, except as may be otherwise specifically permitted or provided by statute, or by the Company's Certificate of Incorporation, or by these By-laws. If at any meeting of the Board of Directors there shall be less than a quorum present, a majority of those present may adjourn the meeting from time to time until a quorum is obtained, and no further notice thereof need be given other than by announcement at said meeting that shall be so adjourned.

3.13. Telephonic Participation in Meetings. Members of the Board of Directors or any committee designated by the Board of Directors may participate in a meeting of the Board of Directors or committee by means of conference telephone or similar communications equipment by means of which all persons participating in the meeting can hear one another, and participation in a meeting pursuant to this section shall constitute presence in person at such meeting.

3.14. Action by Consent. Unless otherwise restricted by the Company's Certificate of Incorporation or these By-laws, any action required or permitted to be taken at any meeting of the Board of Directors or of any committee thereof may be taken without a meeting, if written consent thereto is signed or submitted by electronic transmission by all members of the Board of Directors or of such

committee as the case may be, and such written consent is filed with the minutes of proceedings of the Board of Directors or committee.

3.15. Chairperson of the Board. The Board of Directors may elect or remove, by the affirmative vote of at least a majority of the directors then in office, a Chairperson. Any Chairperson must be a director of the Company. The Chairperson shall preside at all meetings of the Board of Directors and at all meetings of the stockholders and, subject to the provisions of these By-laws and the direction of the Board of Directors, the Chairperson shall have such powers and perform such duties that are commonly incident to the position of chairperson of the board or as may be prescribed from time to time by the Board of Directors or provided in these By-laws.

Article IV. - Officers.

4.1. Selection; Statutory Officers. The officers of the Company shall be chosen by the Board of Directors. There shall be a President, a Secretary, and a Treasurer, and there may be a Chairperson of the Board of Directors, one or more Vice Presidents, one or more Assistant Secretaries, and one or more Assistant Treasurers, as the Board of Directors may elect. Any number of offices may be held by the same person.

4.2. Time of Election. The officers above named shall be chosen by the Board of Directors at its first meeting after each annual meeting of stockholders. Other than the Chairperson, none of said officers need be a director.

4.3. Additional Officers. The Board of Directors may appoint such other officers and agents as it shall deem necessary, who shall hold their offices for such terms and shall exercise such powers and perform such duties as shall be determined from time to time by the Board of Directors.

4.4. Terms of Office. Each officer of the Company shall hold office until such officer's successor is chosen and qualified, or until such officer's earlier death, resignation or removal. Any officer may be removed at any time by the Board of Directors.

4.5. Compensation of Officers. The Board of Directors shall have power to fix the compensation of all officers of the Company. It may authorize any officer, upon whom the power of appointing subordinate officers may have been conferred, to fix the compensation of such subordinate officers.

4.6. Chairperson of the Board. The Chairperson of the Board of Directors shall preside at all meetings of the stockholders and directors, and shall have such other duties as may be assigned to him or her from time to time by the Board of Directors.

4.7. President. Unless the Board of Directors otherwise determines, the President shall be the chief executive officer and head of the Company and his or her title shall be any of the following: President; Chief Executive Officer; President and Chief Executive Officer; or Chief Executive Officer and President. Unless there is a Chairperson of the Board, the President shall preside at all meetings of directors and stockholders. Under the supervision of the Board of Directors, the President shall have the general control and management of its business and affairs, subject, however, to the right of the Board of Directors to confer any specific power, except such as may be by statute exclusively conferred on the President, upon any other officer or officers of the Company. The President shall perform and do all acts and things incident to the position of President and such other duties as may be assigned to such officer from time to time by the Board of Directors.

4.8. Vice-Presidents. The Vice-Presidents shall perform such of the duties of the President on behalf of the Company as may be respectively assigned to them from time to time by the Board of Directors or by the President. The Board of Directors may designate one of the Vice-Presidents as the Executive Vice-President, and in the absence or inability of the President to act, such Executive Vice-President shall have and possess all of the powers and discharge all of the duties of the President, and when so acting, shall be subject to the control of the Board of Directors.

4.9. Treasurer. The Treasurer shall have the care and custody of all the funds and securities of the Company that may come into his or her hands as Treasurer, and the power and authority to endorse checks, drafts and other instruments for the payment of money for deposit or collection when necessary or proper and to deposit the same to the credit of the Company in such bank or banks or depository as the Board of Directors, or the officers or agents to whom the Board of Directors may delegate such authority, may designate, and such officer may endorse all commercial documents requiring endorsements for or on behalf of the Company. The Treasurer may sign all receipts and vouchers for the payments made to the Company. The Treasurer shall render an account of such officer's transactions to the Board of Directors as often as the Board of Directors or the committee shall require the same. The Treasurer shall enter regularly in the books to be kept by such officer for that purpose full and adequate account of all moneys received and paid by him or her on account of the Company. The Treasurer shall perform all acts incident to the position of Treasurer, subject to the control of the Board of Directors. The Treasurer shall when requested, pursuant to vote of the Board of Directors, give a bond to the Company conditioned for the faithful performance of such officer's duties, the expense of which bond shall be borne by the Company.

4.10. Secretary. The Secretary shall keep the minutes of all meetings of the Board of Directors and of the stockholders; such officer shall attend to the giving and serving of all notices of the Company. Except as otherwise ordered by the Board of Directors, such officer shall attest the seal of the Company upon all contracts and instruments executed under such seal and shall affix the seal of the Company thereto and to all certificates of shares of capital stock of the Company. The Secretary shall have charge of the stock certificate book, transfer book and stock ledger, and such other books and papers as the Board of Directors may direct. The Secretary shall, in general, perform all the duties of Secretary, subject to the control of the Board of Directors.

4.11. Assistant Secretary. The Board of Directors or any two of the officers of the Company acting jointly may appoint or remove one or more Assistant Secretaries of the Company. Any Assistant Secretary upon such officer's appointment shall perform such duties of the Secretary, and also any and all such other duties as the Board of Directors or the President or the Executive Vice-President or the Treasurer or the Secretary may designate.

4.12. Assistant Treasurer. The Board of Directors or any two of the officers of the Company acting jointly may appoint or remove one or more Assistant Treasurers of the Company. Any Assistant Treasurer upon such officer's appointment shall perform such of the duties of the Treasurer, and also any and all such other duties as the Board of Directors or the President or the Executive Vice-President or the Treasurer or the Secretary may designate.

4.13. Subordinate Officers. The Board of Directors may select such subordinate officers as it may deem desirable. Each such officer shall hold office for such period, have such authority, and perform such duties as the Board of Directors may prescribe. The Board of Directors may, from time to time, authorize any officer to appoint and remove subordinate officers and to prescribe the powers and duties thereof.

4.14. Delegation of Authority. The Board of Directors may from time to time delegate the powers or duties of any officer to any other officer or agent, notwithstanding any provision hereof.

4.15. Removal. The Board of Directors may remove any officer of the Company at any time, with or without cause.

Article V. - Stock.

5.1. Stock. The shares of the Company's capital stock may be certificated or uncertificated and shall be entered in the books of the Company and registered as they are issued. Any certificate representing shares of stock issued to a stockholder of the Company (i) shall be numbered, (ii) shall certify the holder's name, the number of shares and the class or series of stock, (iii) shall otherwise be in such form as the Board of Directors shall prescribe, (iv) shall be signed by both of (a) either the President or a Vice-President, and (b) any one of the Treasurer or an Assistant Treasurer or the Secretary or an Assistant Secretary, and (v) shall be sealed with the corporate seal of the Company, if any. If such certificate is countersigned (l) by a transfer agent other than the Company or its employee, or, (2) by a registrar other than the Company or its employee, the signature of the officers of the Company and the corporate seal may be facsimiles. In case any officer or officers who shall have signed, or whose facsimile signature or signatures shall have been used on, any such certificate or certificates shall cease to be such officer or officers of the Company, whether because of death, resignation or otherwise, before such certificate or certificates shall have been delivered by the Company, such certificate or certificates may nevertheless be adopted by the Company and be issued and delivered as though the person or persons who signed such certificate or certificates or whose facsimile signature shall have been used thereon had not ceased to be such officer or officers of the Company.

5.2. Fractional Share Interests. The Company may, but shall not be required to, issue fractions of a share. If the Company does not issue fractions of a share, it shall (i) arrange for the disposition of fractional interests by those entitled thereto, (ii) pay in cash the fair value of fractions of a share as of the time when those entitled to receive such fractions are determined, or (iii) issue scrip or warrants in registered or bearer form that shall entitle the holder to receive a certificate for a full share upon the surrender of such scrip or warrants aggregating a full share. A certificate for a fractional share shall, but scrip or warrants shall not unless otherwise provided therein, entitle the holder to exercise voting rights, to receive dividends thereon, and to participate in any of the assets of the Company in the event of liquidation. The Board of Directors may cause scrip or warrants to be issued subject to the conditions that they shall become void if not exchanged for certificates representing full shares before a specified date, or subject to the conditions that the shares for which scrip or warrants are exchangeable may be sold by the Company and the proceeds thereof distributed to the holders of scrip or warrants, or subject to any other conditions that the Board of Directors may impose.

5.3. Transfers of Stock.

Subject to any transfer restrictions then in force, the shares of stock of the Company shall be transferable only upon its books by the holders thereof in person or by their duly authorized attorneys or legal representatives.

If the shares of stock of the Company to be transferred are certificated shares, then, subject to the provisions of Section 5.7 below, the holder of the certificate or certificates representing such shares shall surrender to the Company or the transfer agent of the Company such certificate or certificates duly endorsed or accompanied by proper evidence of

succession, assignation or authority to transfer, and, subject to any transfer restrictions then in force, the Company or the transfer agent of the Company shall cancel such certificate or certificates upon receipt thereof or upon compliance by such holder with the provisions of Section 5.7 below and (i) deliver to the applicable stockholder transferee either a new certificate or certificates representing the number of shares transferred or appropriate documentation evidencing the applicable stockholder transferee's record ownership of a number of uncertificated shares

equal to the number of shares transferred, and, if applicable, (ii) deliver to the applicable stockholder transferor a new certificate or certificates representing the number of shares not transferred that were previously represented by the certificate or certificates so surrendered or appropriate documentation evidencing the applicable stockholder transferor's record ownership of a number of uncertificated shares equal to such number of shares not transferred. Any transfer or transfers in compliance with the provisions of this paragraph shall be recorded upon the books of the Company.

If the shares of stock of the Company to be transferred are uncertificated shares, then the registered owner of such shares shall deliver to the Company or the transfer agent of the Company proper transfer instructions, with such proof of authenticity of signature as the Company or its transfer agent or registrar may reasonably require, and, subject to any transfer restrictions then in force that are applicable to such shares, the Company or the transfer agent of the Company shall cancel such shares upon receipt of such transfer instructions and (i) deliver to the applicable stockholder transferee either a new certificate or certificates representing such shares or appropriate documentation evidencing the applicable stockholder transferee's record ownership of such shares in uncertificated form, and, if applicable and required, (ii) deliver to the applicable stockholder transferor appropriate documentation evidencing that the applicable stockholder transferor is no longer the record owner of such shares so transferred. Any transfer or transfers in compliance with the provisions of this paragraph shall be recorded upon the books of the Company.

The Company shall be entitled to treat the holder of record of any share or shares of stock as the holder in fact thereof and accordingly shall not be bound to recognize any equitable or other claim to or interest in such share on the part of any other person whether or not it shall have express or other notice thereof save as expressly provided by the laws of Delaware.

5.4. Record Date. For the purpose of determining the stockholders entitled to notice of or to vote at any meeting of stockholders or any adjournment thereof, or entitled to receive payment of any dividend or other distribution or the allotment of any rights, or entitled to exercise any rights in respect of any change, conversion, or exchange of stock or for the purpose of any other lawful action, the Board of Directors may fix, in advance, a record date, that shall not be more than sixty (60) days nor less than ten (10) days before the date of such meeting, nor more than sixty (60) days prior to any other action. If no such record date is fixed by the Board of Directors, the record date for determining stockholders entitled to notice of or to vote at a meeting of stockholders shall be at the close of business on the day before the day on which notice is given, or, if notice is waived, at the close of business on the day before the day on which the meeting is held; the record date for determining stockholders for any other purpose shall be at the close of business on the day on which the Board of Directors adopts the resolution relating thereto. A determination of stockholders of record entitled to notice of or to vote at any meeting of stockholders shall apply to any adjournment of the meeting; provided, however, that the Board of Directors may fix a new record date for the adjourned meeting.

5.5. Transfer Agent and Registrar. The Board of Directors may appoint one or more transfer agents or transfer clerks and one or more registrars and may require all certificates of stock to bear the signature or signatures of any of them.

5.6. Dividends.

(a) Power to Declare. Dividends upon the capital stock of the Company, subject to the provisions of the Company's Certificate of Incorporation, if any, may be declared by the Board of Directors at any regular or special meeting, pursuant to law. Dividends may be paid in cash, in property, or in shares of the capital stock, subject to the provisions of the Company's Certificate of Incorporation and the laws of Delaware.

(b) Reserves. Before payment of any dividend, there may be set aside out of any funds of the Company available for dividends such sum or sums as the directors from time to time, in their absolute discretion, think proper as a reserve or reserves to meet contingencies, or for equalizing dividends, or for repairing or maintaining any property of the Company, or for such other purpose as the directors shall think conducive to the interest of the Company, and the directors may modify or abolish any such reserve in the manner in which it was created.

5.7. Lost, Stolen, or Destroyed Certificates. No certificates for shares of stock of the Company shall be issued in place of any certificate alleged to have been lost, stolen, or destroyed, except upon production of such evidence of the loss, theft, or destruction and upon indemnification of the Company and its agents to such extent and in such manner as the officers of the Company may from time to time prescribe. Upon compliance with the foregoing provisions of this Section 5.7, the Company may issue (i) a new certificate or certificates of stock or (ii) uncertificated shares, in place of any certificate or certificates previously issued by the Company alleged to have been lost, stolen or destroyed.

5.8. Inspection of Books. The stockholders of the Company, by a majority vote at any meeting of stockholders duly called, or in case the stockholders shall fail to act, the Board of Directors shall have power from time to time to determine whether and to what extent and at what times and places and under what conditions and regulations the accounts and books of the Company (other than the stock ledger) or any of them, shall be open to inspection of stockholders; and no stockholder shall have any right to inspect any account or book or document of the Company except as conferred by statute or authorized by the Board of Directors or by a resolution of the stockholders.

Article VI. - Miscellaneous Management Provisions.

6.1. Checks, Drafts, and Notes. All checks, drafts, or orders for the payment of money, and all notes and acceptances of the Company shall be signed by such officer or officers, or such agent or agents, as the officers of the Company may designate.

6.2. Notices.

(a) Notices to directors may, and notices to stockholders shall, be in writing or by electronic transmission, and delivered personally, electronically transmitted or mailed to the directors or stockholders at their postage or electronic mail addresses appearing on the books of the Company. Notice by mail and electronic transmission shall be deemed to be given at the time when the same shall be mailed or transmitted. Notice to directors may also be given by telegram, telecopy or orally, by telephone or in person.

(b) Whenever any notice is required to be given under the provisions of any applicable statute or of the Company's Certificate of Incorporation or of these By-laws, an electronic transmission or written waiver of notice, signed by the person or persons entitled to said notice, whether before or after the time stated therein or the meeting or action to which such notice relates, shall be deemed equivalent to notice. Attendance of a person at a meeting shall constitute a waiver of notice of such meeting except when the person attends a meeting for the express purpose of objecting, at the beginning of the meeting, to the transaction of any business because the meeting is not lawfully called or convened.

6.3. Conflict of Interest. No contract or transaction between the Company and one or more of its directors or officers, or between the Company and any other corporation, partnership, association, or other organization in which one or more of its directors or officers are directors or officers, or have a financial interest, shall be void or voidable solely for this reason, or solely because the director or officer

is present at or participates in the meeting of the Board of Directors or committee thereof that authorized the contract or transaction, or solely because his, her or their votes are counted for such purpose, if: (i) the material facts as to his or her relationship or interest and as to the contract or transaction are disclosed or are known to the Board of Directors or the committee and the Board of Directors or committee in good faith authorizes the contract or transaction by the affirmative vote of a majority of the disinterested directors, even though the disinterested directors be less than a quorum; or (ii) the material facts as to his or her relationship or interest and as to the contract or transaction are disclosed or are known to the stockholders of the Company entitled to vote thereon, and the contract or transaction as specifically approved in good faith by vote of such stockholders; or (iii) the contract or transaction is fair as to the Company as of the time it is authorized, approved, or ratified, by the Board of Directors, a committee or the stockholders. Common or interested directors may be counted in determining the presence of a quorum at a meeting of the Board of Directors or of a committee that authorizes the contract or transaction.

6.4. Voting of Securities owned by the Company. Subject always to the specific directions of the Board of Directors, (i) any shares or other securities issued by any other corporation and owned or controlled by the Company may be voted in person at any meeting of security holders of such other corporation by the President of the Company if he or she is present at such meeting, or in his or her absence by the Treasurer of the Company if he or she is present at such meeting, and (ii) whenever, in the judgment of the President, it is desirable for the Company to execute a proxy or written consent in respect to any shares or other securities issued by any other corporation and owned by the Company, such proxy or consent shall be executed in the name of the Company by the President, without the necessity of any authorization by the Board of Directors, affixation of corporate seal or countersignature or attestation by another officer, provided that if the President is unable to execute such proxy or consent by reason of sickness, absence from the United States or other similar cause, the Treasurer may execute such proxy or consent. Any person or persons designated in the manner above stated as the proxy or proxies of the Company shall have full right, power and authority to vote the shares or other securities issued by such other corporation and owned by the Company the same as such shares or other securities might be voted by the Company.

Article VII. - Indemnification.

7.1. Right to Indemnification. Each person who was or is made a party or is threatened to be made a party to or is otherwise involved in any action, suit or proceeding, whether civil, criminal, administrative or investigative (a "Proceeding"), by reason of being or having been a director or officer of the Company or serving or having served at the request of the Company as a director, trustee, officer, employee or agent of another corporation or of a partnership, joint venture, trust or other enterprise, including service with respect to an employee benefit plan (an "Indemnitee"), whether the basis of such proceeding is alleged action or failure to act in an official capacity as a director, trustee, officer, employee or agent or in any other capacity while serving as a director, trustee, officer, employee or agent, shall be indemnified and held harmless by the Company to the fullest extent authorized by the DGCL, as the same exists or may hereafter be amended (but, in the case of any such amendment, only to the extent that such amendment permits the Company to provide broader indemnification rights than permitted prior thereto) (as used in this Article 7, the "Delaware Law"), against all expense, liability and loss (including attorneys' fees, judgments, fines, ERISA excise taxes or penalties and amounts paid in settlement) reasonably incurred or suffered by such Indemnitee in connection therewith and such indemnification shall continue as to an Indemnitee who has ceased to be a director, trustee, officer, employee, or agent and shall inure to the benefit of the Indemnitee's heirs, executors, and administrators; provided, however, that, except as provided in Section 7.2 hereof with respect to Proceedings to enforce rights to indemnification, the Company shall indemnify any such Indemnitee in connection with a Proceeding (or part thereof) initiated by such Indemnitee only if such Proceeding (or part thereof) was authorized by the Board of Directors of

the Company. The right to indemnification conferred in this Article 7 shall be a contract right and shall include the right to be paid by the Company the expenses (including attorneys' fees) incurred in defending any such Proceeding in advance of its final disposition (an "Advancement of Expenses"); provided, however, that, if the Delaware Law so requires, an Advancement of Expenses incurred by an Indemnitee shall be made only upon delivery to the Company of an undertaking (an "Undertaking"), by or on behalf of such Indemnitee, to repay all amounts so advanced if it shall ultimately be determined by final judicial decision from which there is no further right to appeal (a "Final Adjudication") that such Indemnitee is not entitled to be indemnified for such expenses under this Article 7 or otherwise.

7.2. Right of Indemnitee to Bring Suit. If a claim under Section 7.1 hereof is not paid in full by the Company within sixty (60) days after a written claim has been received by the Company, except in the case of a claim for an Advancement of Expenses, in which case the applicable period shall be twenty (20) days, the Indemnitee may at any time thereafter bring suit against the Company to recover the unpaid amount of the claim. If successful in whole or in part in any such suit, or in a suit brought by the Company to recover an Advancement of Expenses pursuant to the terms of an Undertaking, the Indemnitee shall be entitled to be paid also the expense of prosecuting or defending such suit. In any suit brought by the Indemnitee to enforce a right to indemnification hereunder (but not in a suit brought by the Indemnitee to enforce a right to an Advancement of Expenses) it shall be a defense that the Indemnitee has not met the applicable standard of conduct set forth in the Delaware Law. In addition, any suit by the Company to recover an Advancement of Expenses pursuant to the terms of an Undertaking the Company shall be entitled to recover such expenses upon a Final Adjudication that, the Indemnitee has not met the applicable standard of conduct set forth in the Delaware Law. Neither the failure of the Company (including its Board of Directors, independent legal counsel, or its stockholders) to have made a determination prior to the commencement of such suit that indemnification of the Indemnitee is proper in the circumstances because the Indemnitee has met the applicable standard of conduct set forth in the Delaware Law, nor an actual determination by the Company (including its Board of Directors, independent legal counsel, or its stockholders) that the Indemnitee has not met such applicable standard of conduct, shall create a presumption that the Indemnitee has not met the applicable standard of conduct or, in the case of such a suit brought by the Indemnitee, be a defense to such suit. In any suit brought by the Indemnitee to enforce a right to indemnification or to an Advancement of Expenses hereunder, or by the Company to recover an Advancement of Expenses pursuant to the terms of an Undertaking, the burden of proving that the Indemnitee is not entitled to be indemnified, or to such Advancement of Expenses, under this Article 7 or otherwise shall be on the Company.

7.3. Non-Exclusivity of Rights. The rights to indemnification and to the Advancement of Expenses conferred in this Article 7 shall not be exclusive of any other right that any person may have or hereafter acquire under any statute, the Company's Certificate of Incorporation, by law, agreement, vote of stockholders or disinterested directors or otherwise.

7.4. Insurance. The Company may maintain insurance, at its expense, to protect itself and any director, officer, employee or agent of the Company or another corporation, partnership, joint venture, trust or other enterprise against any expense, liability or loss, whether or not the Company would have the power to indemnify such person against such expense, liability or loss under this Article 7 or under the Delaware Law.

7.5. Indemnification of Employees and Agents of the Company. The Company may, to the extent authorized from time to time by the Board of Directors, grant rights to indemnification, and to the Advancement of Expenses, to any employee or agent of the Company to the fullest extent of the provisions of this Article 7 with respect to the indemnification and Advancement of Expenses of directors and officers of the Company.

7.6. Merger or Consolidation. For purposes of this Article 7, references to the "Company" shall include, in addition to the resulting corporation, any constituent corporation (including any constituent of a constituent) absorbed in a consolidation or merger which, if its separate existence had continued, would have had power and authority to indemnify its directors, officers and employees or agents, so that any person who is or was a director, officer, employee or agent of such constituent corporation, or is or was serving at the request of such constituent corporation as a director, officer, employee or agent of another corporation, partnership, joint venture, trust or other enterprise, shall stand in the same position under this Section 6 with respect to the resulting or surviving corporation as he or she would have with respect to such constituent corporation if its separate existence had continued

7.7. Savings Clause. If this Article7 or any portion hereof shall be invalidated on any ground by any court of competent jurisdiction, then the Company shall nevertheless indemnify and advance expenses to each person entitled to indemnification under Article 7 as to all expense, liability and loss (including attorneys' fees and related disbursements, judgments, fines, ERISA excise taxes and penalties, penalties and amounts paid or to be paid in settlement) actually and reasonably incurred or suffered by such person and for which indemnification or advancement of expenses is available to such person pursuant to this Article 7 to the fullest extent permitted by any applicable portion of this Article 7 that shall not have been invalidated and to the fullest extent permitted by applicable law.

Article VIII. - Amendments.

8.1 Amendments. Subject always to any limitations imposed by the Company's Certificate of Incorporation, these By-laws and any amendment thereof may be altered, amended or repealed, or new by-laws may be adopted, by the Board of Directors at any regular or special meeting by the affirmative vote of a majority of all of the members of the Board of Directors, provided in the case of any special meeting at which all of the members of the Board of Directors are not present, that the notice of such meeting shall have stated that the amendment of these By-laws was one of the purposes of the meeting; but these By-laws and any amendment thereof, including the By-laws adopted by the Board of Directors, may be altered, amended or repealed and other By-laws may be adopted by the affirmative vote of holders of at least seventy-five percent (75%) of the outstanding shares of capital stock of the Company entitled to vote in the election of directors or class of directors, voting together as a single class, provided, in the case of any special meeting, that notice of such proposed alteration, amendment, repeal or adoption is included in the notice of the meeting.

Exhibit 3.5

PROTEON THERAPEUTICS, INC.

Amendment No. 1
to
Fifth Amended and Restated Certificate of Incorporation

PROTEON THERAPEUTICS, INC., a corporation organized and existing under and by virtue of the provisions of the General Corporation Law of the State of Delaware (the "General Corporation Law"),

DOES HEREBY CERTIFY:

1. That the name of this corporation is Proteon Therapeutics, Inc. (the "Company"). The date of filing of the original certificate of incorporation of this corporation with the Secretary of State of the State of Delaware was on March 24, 2006.

2. That the Company filed a Fifth Amended and Restated Certificate of Incorporation with the Secretary of State of the State of Delaware on May 9, 2014.

3. This Amendment No. 1 to the Fifth Amended and Restated Certificate of Incorporation has been duly approved by the Board of Directors of the Company in accordance with Section 242 of the General Corporation Law.

4. This Amendment No. 1 to the Fifth Amended and Restated Certificate of Incorporation has been duly approved by the required vote of the stockholders of the Company in accordance with Section 228 of the General Corporation Law.

5. Section 3.2(a) of Division C of Article FOURTH of the Fifth Amended and Restated Certificate of Incorporation is hereby amended by deleting such section in its entirety and substituting said section with the following:

"*(a) The number of directors constituting the whole Board of Directors shall be no less than five (5) and no greater than ten (10).*"

[The Following Page is the Signature Page]

IN WITNESS WHEREOF, this Amendment No. 1 to the Fifth Amended and Restated Certificate of Incorporation has been executed by a duly authorized officer of this corporation on this 3rd day of September, 2014.

By: /s/ Timothy Noyes.
Timothy Noyes
President and Chief Executive Officer

SIGNATURE PAGE TO AMENDMENT NO. 1 TO
FIFTH AMENDED AND RESTATED CERTIFICATE OF INCORPORATION

Exhibit 3.6

PROTEON THERAPEUTICS, INC.

Amendment No. 2
to
Fifth Amended and Restated Certificate of Incorporation

PROTEON THERAPEUTICS, INC., a corporation organized and existing under and by virtue of the provisions of the General Corporation Law of the State of Delaware (the "General Corporation Law"),

DOES HEREBY CERTIFY:

1. That the name of this corporation is Proteon Therapeutics, Inc. (the "Company"). The date of filing of the original certificate of incorporation of this corporation with the Secretary of State of the State of Delaware was on March 24, 2006.

2. That the Company filed a Fifth Amended and Restated Certificate of Incorporation with the Secretary of State of the State of Delaware on May 9, 2014, as amended by Amendment No. 1 filed with the Secretary of State of the State of Delaware on September 3, 2014.

3. This Amendment No. 2 to the Fifth Amended and Restated Certificate of Incorporation has been duly approved by the Board of Directors of the Company in accordance with Section 242 of the General Corporation Law.

4. This Amendment No. 2 to the Fifth Amended and Restated Certificate of Incorporation has been duly approved by the required vote of the stockholders of the Company in accordance with Section 228 of the General Corporation Law.

5. The Fifth Amended and Restated Certificate of Incorporation, as previously amended, is hereby further amended by adding the following paragraphs immediately following the first sentence of Article Fourth:

"Effective on the filing of this Amendment No. 2 to the Fifth Amended and Restated Certificate of Incorporation with the Office of the Secretary of State of the State of Delaware (the "Effective Time"), a 1-for-15.87 reverse stock split of the Corporation's Common Stock (as defined in this Article) shall become effective, pursuant to which each 15.87 shares of Common Stock outstanding and held of record by each stockholder of the Corporation (including treasury shares) immediately prior to the Effective Time shall be reclassified and combined into one validly issued, fully-paid and nonassessable share of Common Stock automatically and without any action by the holder thereof upon the Effective Time and shall represent one share of Common Stock from and after the Effective Time (such reclassification and combination of shares, the "Reverse Stock Split"). The par value of the Common Stock and the Preferred Stock following the Reverse Stock Split shall remain at $0.001 per share. No fractional shares of Common Stock shall be issued as a result of the Reverse Stock Split and, in lieu thereof, upon surrender after the Effective Time of a certificate which formerly represented shares of Common Stock that were issued and outstanding immediately prior to the Effective Time, any person who would otherwise be entitled to a fractional share of Common Stock as a result of the Reverse Stock Split, following the Effective Time, shall be entitled to receive a cash payment equal to the fraction of which such holder would otherwise be entitled multiplied by the fair value per share as determined by the Board of Directors.

Each stock certificate that, immediately prior to the Effective Time, represented shares of Common Stock that were issued and outstanding immediately prior to the Effective Time

---

shall, from and after the Effective Time, automatically and without the necessity of presenting the same for exchange, represent that number of whole shares of Common Stock after the Effective Time into which the shares formerly represented by such certificate have been reclassified (as well as the right to receive cash in lieu of fractional shares of Common Stock after the Effective Time); provided, however, that each person of record holding a certificate that represented shares of Common Stock that were issued and outstanding immediately prior to the Effective Time shall receive, upon surrender of such certificate, a new certificate evidencing and representing the number of whole shares of Common Stock after the Effective Time into which the shares of Common Stock formerly represented by such certificate shall have been reclassified; and provided further, however, that whether or not fractional shares would be issuable as a result of the Reverse Stock Split shall be determined on the basis of (i) the total number of shares of Common Stock that were issued and outstanding immediately prior to the Effective Time formerly represented by certificates that the holder is at the time surrendering for a new certificate evidencing and representing the number of whole shares of Common Stock after the Effective Time and (ii) the aggregate number of shares of Common Stock after the Effective Time into which the shares of Common Stock formerly represented by such certificates shall have been reclassified."

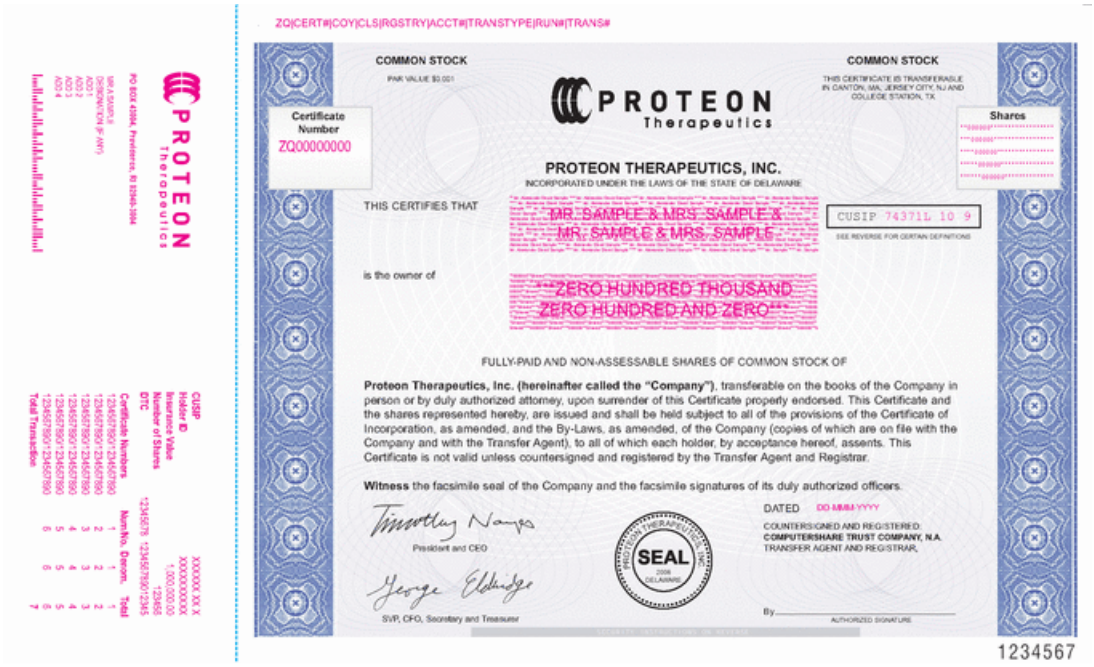
[The Following Page is the Signature Page]

IN WITNESS WHEREOF, this Amendment No. 2 to the Fifth Amended and Restated Certificate of Incorporation has been executed by a duly authorized officer of this corporation on this 6th day of October, 2014.

By: /s/ Timothy Noyes
Timothy Noyes
President and Chief Executive Officer

SIGNATURE PAGE TO AMENDMENT NO. 2 TO
FIFTH AMENDED AND RESTATED CERTIFICATE OF INCORPORATION

Exhibit 4.1



ZQ|CERT#|COY|CLS|RGSTRY|ACCT#|TRANSTYPE|RUN#|TRANS#

COMMON STOCK

PAR VALUE $0.001

COMMON STOCK

THIS CERTIFICATE IS TRANSFERABLE IN CANTON, MA, JERSEY CITY, NJ AND COLLEGE STATION, TX

PROTEON Therapeutics

Certificate Number

ZQ00000000

Shares

PROTEON THERAPEUTICS, INC.

INCORPORATED UNDER THE LAWS OF THE STATE OF DELAWARE

THIS CERTIFIES THAT

MR. SAMPLE & MRS. SAMPLE &
MR. SAMPLE & MRS. SAMPLE

CUSIP 74371L 10 9

SEE REVERSE FOR CERTAIN DEFINITIONS

is the owner of

ZERO HUNDRED THOUSAND ZERO HUNDRED AND ZERO

FULLY-PAID AND NON-ASSESSABLE SHARES OF COMMON STOCK OF

Proteon Therapeutics, Inc. (hereinafter called the "Company"), transferable on the books of the Company in person or by duly authorized attorney, upon surrender of this Certificate properly endorsed. This Certificate and the shares represented hereby, are issued and shall be held subject to all of the provisions of the Certificate of Incorporation, as amended, and the By-Laws, as amended, of the Company (copies of which are on file with the Company and with the Transfer Agent), to all of which each holder, by acceptance hereof, assents. This Certificate is not valid unless countersigned and registered by the Transfer Agent and Registrar.

Witness the facsimile seal of the Company and the facsimile signatures of its duly authorized officers.

Timothy Nayer

President and CEO

George Eldridge

SVP, CFO, Secretary and Treasurer

SEAL

DATED DD-MMM-YYYY

COUNTERSIGNED AND REGISTERED:
COMPUTERSHARE TRUST COMPANY, N.A.
TRANSFER AGENT AND REGISTRAR,

By_____
AUTHORIZED SIGNATURE

1234567

PROTEON Therapeutics

PO BOX 43004, Providence, RI 02940-3004

SAMPLE

SAMPLE

ADD1

ADD2

ADD3

ADD4

CUSIP
Holder ID
Insurance Value
Number of Shares
DTC
Certificate Numbers
Num
No.
Denom.
Total

XXXXXX XX X
XXXXXXXXXX
1,000,000.00
12345678
12345678012345
12345678012345678012345
1 1 1
2 2 2
3 3 3
4 4 4
5 5 5
6 6 6
7

PROTEON THERAPEUTICS, INC.

THE COMPANY WILL FURNISH WITHOUT CHARGE TO EACH SHAREHOLDER WHO SO REQUESTS, A SUMMARY OF THE POWERS, DESIGNATIONS, PREFERENCES AND RELATIVE, PARTICIPATING, OPTIONAL OR OTHER SPECIAL RIGHTS OF EACH CLASS OF STOCK OF THE COMPANY AND THE QUALIFICATIONS, LIMITATIONS OR RESTRICTIONS OF SUCH PREFERENCES AND RIGHTS, AND THE VARIATIONS IN RIGHTS, PREFERENCES AND LIMITATIONS DETERMINED FOR EACH SERIES, WHICH ARE FIXED BY THE CERTIFICATE OF INCORPORATION OF THE COMPANY, AS AMENDED, AND THE RESOLUTIONS OF THE BOARD OF DIRECTORS OF THE COMPANY, AND THE AUTHORITY OF THE BOARD OF DIRECTORS TO DETERMINE VARIATIONS FOR FUTURE SERIES. SUCH REQUEST MAY BE MADE TO THE OFFICE OF THE SECRETARY OF THE COMPANY OR TO THE TRANSFER AGENT. THE BOARD OF DIRECTORS MAY REQUIRE THE OWNER OF A LOST OR DESTROYED STOCK CERTIFICATE, OR HIS LEGAL REPRESENTATIVES, TO GIVE THE COMPANY A BOND TO INDEMNIFY IT AND ITS TRANSFER AGENTS AND REGISTRARS AGAINST ANY CLAIM THAT MAY BE MADE AGAINST THEM ON ACCOUNT OF THE ALLEGED LOSS OR DESTRUCTION OF ANY SUCH CERTIFICATE.

The following abbreviations, when used in the inscription on the face of this certificate, shall be construed as though they were written out in full according to applicable laws or regulations:

TEN COM	- as tenants in common	UNIF GIFT MIN ACT	- ..... (Cust) Custodian ..... (Minor) under Uniform Gifts to Minors Act ..... (State)
TEN ENT	- as tenants by the entireties		
JT TEN	- as joint tenants with right of survivorship and not as tenants in common	UNIF TRF MIN ACT	- ..... (Cust) Custodian (until age .....) ..... (Minor) under Uniform Transfers to Minors Act ..... (State)

Additional abbreviations may also be used though not in the above list.

For value received, _____ hereby sell, assign and transfer unto

PLEASE INSERT SOCIAL SECURITY OR OTHER IDENTIFYING NUMBER OF ASSIGNEE

_____

(PLEASE PRINT OR TYPEWRITE NAME AND ADDRESS, INCLUDING POSTAL ZIP CODE, OF ASSIGNEE)

_____

_____

_____ Shares

of the common stock represented by the within Certificate, and do hereby irrevocably constitute and appoint

_____ Attorney

to transfer the said stock on the books of the within-named Company with full power of substitution in the premises.

Dated: _____ 20_____

Signature: _____

Signature: _____

Notice: The signature to this assignment must correspond with the name as written upon the face of the certificate, in every particular, without alteration or enlargement, or any change whatever.

Signature(s) Guaranteed: Medallion Guarantee Stamp

THE SIGNATURE(S) SHOULD BE GUARANTEED BY AN ELIGIBLE GUARANTOR INSTITUTION (Banks, Stockbrokers, Savings and Loan Associations and Credit Unions) WITH MEMBERSHIP IN AN APPROVED SIGNATURE GUARANTEE MEDALLION PROGRAM, PURSUANT TO S.E.C. RULE 17Ad-15.

SECURITY INSTRUCTIONS

THIS IS WATERMARKED PAPER. DO NOT ACCEPT WITHOUT NOTING WATERMARK. HOLD TO LIGHT TO VERIFY WATERMARK.

The IRS requires that we report the cost basis of certain shares acquired after January 1, 2011. If your shares were covered by the legislation and you have sold or transferred the shares and requested a specific cost basis calculation method, we have processed as requested. If you did not specify a cost basis calculation method, we have defaulted to the first in, first out (FIFO) method. Please visit our website or consult your tax advisor if you need additional information about cost basis.

If you do not keep in contact with us or do not have any activity in your account for the time periods specified by state law, your property could become subject to state unclaimed property laws and transferred to the appropriate state.

1534201

Exhibit 5.1

Bingham McCutchen LLP
One Federal Street
Boston, Massachusetts 02110
Tel: 617-951-8000

October 7, 2014

Proteon Therapeutics, Inc.
200 West Street
Waltham, MA 02451

Re: Registration Statement on Form S-1

Ladies and Gentlemen:

We have acted as counsel to Proteon Therapeutics, Inc., a Delaware corporation (the "Company"), in connection with the Company's registration statement on Form S-1 (Registration No. 333-198777) initially filed with the Securities and Exchange Commission on September 16, 2014, as amended to date (the "Registration Statement"), under the Securities Act of 1933, as amended (the "Act"). The Registration Statement relates to the registration of the offer and sale of up to 4,700,000 shares of the Company's Common Stock, par value $0.001 per share (the "Common Stock"), including up to 705,000 shares of Common Stock that may be offered and sold by the Company to cover over-allotments pursuant to the Registration Statement (together, the "Shares").

We have reviewed the corporate proceedings of the Company with respect to the authorization of the issuance of the Shares. As such counsel, we have also examined originals, or copies certified or otherwise identified to our satisfaction, of the Registration Statement and the exhibits thereto and such other documents, corporate records and other instruments as we have deemed necessary or appropriate for the purpose of this opinion. As to questions of fact material to this opinion, we have relied on certificates or comparable documents of public officials and of officers and representatives of the Company. In rendering the opinion expressed below, we have assumed without verification the genuineness of all signatures, the legal capacity of natural persons, the authenticity of all documents submitted to us as originals, the conformity to the originals of all documents submitted to us as copies and the authenticity of the originals of such copies. We have also assumed that an Underwriting Agreement substantially in the form of Exhibit 1.1 to the Registration Statement, by and among the Company and the underwriters named therein (the "Underwriting Agreement"), will have been duly executed and delivered pursuant to the authorizing resolutions of the Board of Directors of the Company and the pricing committee thereof.

We have also assumed that, at or prior to the time of the issuance and delivery of any Shares, the Registration Statement will have been declared effective under the Act, that the Shares will have been registered under the Act pursuant to the Registration Statement and that such Registration Statement will not have been modified or rescinded, and that there will not have occurred any change in law affecting the validity of the issuance of the Shares.

This opinion is limited solely to the Delaware General Corporation Law, as applied by courts located in Delaware.

Based upon and subject to the foregoing, we are of the opinion that, upon the effectiveness of the Company's Sixth Amended and Restated Certificate of Incorporation with the Secretary of State of the State of Delaware, a form of which has been filed as an exhibit to the Registration Statement, the Shares

---

to be issued and sold by the Company under the Underwriting Agreement will have been duly authorized, and when delivered and paid for by the Underwriters (as such term is defined in the Underwriting Agreement) in accordance with the terms of the Underwriting Agreement, will be validly issued, fully paid and nonassessable.

We hereby consent to the filing of this opinion as an exhibit to the Registration Statement and to the reference to this firm under the heading "Legal Matters" in the Prospectus included in the Registration Statement. In giving this consent, we do not admit that we are in the category of persons whose consent is required under Section 7 of the Act, or the rules and regulations promulgated thereunder. In rendering the opinions set forth above, we are opining only as to the specific legal issues expressly set forth therein, and no opinion shall be inferred as to any other matter or matters.

This opinion is intended solely for use in connection with the issuance and sale of the Shares subject to the Registration Statement and is not to be relied upon for any other purpose.

Very truly yours,

/s/ Bingham McCutchen LLP

BINGHAM MCCUTCHEN LLP

PROTEON THERAPEUTICS, INC.

AMENDED AND RESTATED
2006 EQUITY INCENTIVE PLAN

ADOPTED: AUGUST 21, 2014
APPROVED BY STOCKHOLDERS: OCTOBER 3, 2014
TERMINATION DATE: MARCH 23, 2016

1. PURPOSES.

(a) Eligible Stock Award Recipients. The persons eligible to receive Stock Awards are Employees, Directors and Consultants.

(b) Available Stock Awards. The purpose of the Plan is to provide a means by which eligible recipients of Stock Awards may be given an opportunity to benefit from increases in value of the Common Stock through the granting of the following Stock Awards: (i) Incentive Stock Options, (ii) Nonstatutory Stock Options, (iii) stock bonuses, (iv) rights to acquire restricted stock, (v) Stock Appreciation Rights and (vi) Phantom Stock Awards.

(c) General Purpose. The Company, by means of the Plan, seeks to retain the services of the group of persons eligible to receive Stock Awards, to secure and retain the services of new members of this group and to provide incentives for such persons to exert maximum efforts for the success of the Company and its Affiliates.

2. DEFINITIONS.

(a) *"Affiliate"* means any parent corporation or subsidiary corporation of the Company, whether now or hereafter existing, as those terms are defined in Sections 424(e) and (f), respectively, of the Code.

(b) *"Board"* means the Board of Directors of the Company.

(c) *"Capitalization Adjustment"* has the meaning ascribed to that term in Section 11(a).

(d) *"Change in Control"* means the occurrence, in a single transaction or in a series of related transactions, of any one or more of the following events:

(i) any Exchange Act Person becomes the Owner, directly or indirectly, of securities of the Company representing more than fifty percent (50%) of the combined voting power of the Company's then outstanding securities other than by virtue of a merger, consolidation or similar transaction;

(ii) there is consummated a merger, consolidation or similar transaction involving (directly or indirectly) the Company if, immediately after the consummation of such merger, consolidation or similar transaction, the stockholders of the Company immediately prior thereto do not Own, directly or indirectly, either (A) outstanding voting securities representing

more than fifty percent (50%) of the combined outstanding voting power of the surviving Entity in such merger, consolidation or similar transaction or (B) more than fifty percent (50%) of the combined outstanding voting power of the parent of the surviving Entity in such merger, consolidation or similar transaction;

(iii) the stockholders of the Company approve or the Board approves a plan of complete dissolution or liquidation of the Company, or a complete dissolution or liquidation of the Company shall otherwise occur;

(iv) there is consummated a sale, lease, license or other disposition of all or substantially all of the consolidated assets of the Company and its Subsidiaries, other than a sale, lease, license or other disposition of all or substantially all of the consolidated assets of the Company and its Subsidiaries to an Entity, more than fifty percent (50%) of the combined voting power of the voting securities of which are Owned by stockholders of the Company in substantially the same proportion as their Ownership of the Company immediately prior to such sale, lease, license or other disposition; or

(v) a majority of the Board votes in favor of a decision that a Change of Control has occurred, which vote may adopted by the Board with the intention that such vote become effective subject to and contingent upon the occurrence of certain events, in which case such Change of Control shall not be deemed to have occurred unless and until such vote becomes effective in accordance with its terms.

The term Change in Control shall not include a sale of assets, merger or other transaction effected exclusively for the purpose of changing the domicile of the Company, or for primarily fundraising purposes.

Notwithstanding the foregoing or any other provision of this Plan, the definition of Change in Control (or any analogous term) in an individual written agreement between the Company or any Affiliate and the Participant shall supersede the foregoing definition with respect to Stock Awards subject to such agreement (it being understood, however, that if no definition of Change in Control or any analogous term is set forth in such an individual written agreement, the foregoing definition shall apply).

(e) *"Code"* means the Internal Revenue Code of 1986, as amended.

(f) *"Committee"* means a committee of one or more members of the Board appointed by the Board in accordance with Section 3(c).

(g) *"Common Stock"* means the common stock of the Company.

(h) *"Company"* means Proteon Therapeutics, Inc., a Delaware corporation.

(i) *"Consultant"* means any person, including an advisor, (i) engaged by the Company or an Affiliate to render consulting or advisory services and who is compensated for such services or (ii) serving as a member of the Board of Directors of an Affiliate and who is compensated for such services. However, the term "Consultant" shall not include Directors who

are not compensated by the Company for their services as Directors, and the payment of a director's fee by the Company for services as a Director shall not cause a Director to be considered a "Consultant" for purposes of the Plan.

(j) ***"Continuous Service"*** means that the Participant's service with the Company or an Affiliate, whether as an Employee, Director or Consultant, is not interrupted or terminated. A change in the capacity in which the Participant renders service to the Company or an Affiliate as an Employee, Consultant or Director or a change in the entity for which the Participant renders such service, provided that there is no interruption or termination of the Participant's service with the Company or an Affiliate, shall not terminate a Participant's Continuous Service. For example, a change in status from an employee of the Company to a consultant to an Affiliate or to a Director shall not constitute an interruption of Continuous Service. The Board, in its sole discretion, may determine whether Continuous Service shall be considered interrupted in the case of any leave of absence approved by that party, including sick leave, military leave or any other personal leave. Notwithstanding the foregoing, a leave of absence shall be treated as Continuous Service for purposes of vesting in a Stock Award only to such extent as may be provided in the Company's leave of absence policy or in the written terms of the Participant's leave of absence.

(k) ***"Corporate Transaction***" means the occurrence, in a single transaction or in a series of related transactions, of any one or more of the following events:

(i) a sale or other disposition of all or substantially all, as determined by the Board in its discretion, of the consolidated assets of the Company and its Subsidiaries;

(ii) a sale or other disposition of at least ninety percent (90%) of the outstanding securities of the Company;

(iii) a merger, consolidation or similar transaction following which the Company is not the surviving corporation; or

(iv) a merger, consolidation or similar transaction following which the Company is the surviving corporation but the shares of Common Stock outstanding immediately preceding the merger, consolidation or similar transaction are converted or exchanged by virtue of the merger, consolidation or similar transaction into other property, whether in the form of securities, cash or otherwise.

(l) ***"Director"*** means a member of the Board.

(m) ***"Disability"*** means the inability of a person, in the opinion of a qualified physician acceptable to the Company, to perform the major duties of that person's position with the Company or an Affiliate because of the sickness or injury of the person.

(n) ***"Employee"*** means any person employed by the Company or an Affiliate. Service as a Director or payment of a director's fee by the Company for such service or for service as a

member of the Board of Directors of an Affiliate shall not be sufficient to constitute "employment" by the Company or an Affiliate.

(o) ***"Entity"*** means a corporation, partnership or other entity.

(p) ***"Exchange Act"*** means the Securities Exchange Act of 1934, as amended.

(q) ***"Exchange Act Person"*** means any natural person, Entity or "group" (within the meaning of Section 13(d) or 14(d) of the Exchange Act), except that "Exchange Act Person" shall not include (A) the Company or any Subsidiary of the Company, (B) any employee benefit plan of the Company or any Subsidiary of the Company or any trustee or other fiduciary holding securities under an employee benefit plan of the Company or any Subsidiary of the Company, (C) an underwriter temporarily holding securities pursuant to an offering of such securities, or (D) an Entity Owned, directly or indirectly, by the stockholders of the Company in substantially the same proportions as their Ownership of stock of the Company.

(r) ***"Fair Market Value"*** means, as of any date, the value of the Common Stock determined in good faith by the Board, and if required by applicable law, in a manner consistent with Section 260.140.50 of Title 10 of the California Code of Regulations.

(s) ***"Incentive Stock Option"*** means an Option intended to qualify as an incentive stock option within the meaning of Section 422 of the Code and the regulations promulgated thereunder.

(t) ***"Nonstatutory Stock Option***" means an Option not intended to qualify as an Incentive Stock Option.

(u) ***"Officer"*** means any person designated by the Company as an officer.

(v) ***"Option"*** means an Incentive Stock Option or a Nonstatutory Stock Option granted pursuant to the Plan.

(w) ***"Option Agreement***" means a written agreement between the Company and an Optionholder evidencing the terms and conditions of an individual Option grant. Each Option Agreement shall be subject to the terms and conditions of the Plan.

(x) ***"Optionholder***" means a person to whom an Option is granted pursuant to the Plan or, if applicable, such other person who holds an outstanding Option.

(y) ***"Own," "Owned," "Owner," "Ownership"*** A person or Entity shall be deemed to "Own," to have "Owned," to be the "Owner" of, or to have acquired "Ownership" of securities if such person or Entity, directly or indirectly, through any contract, arrangement, understanding, relationship or otherwise, has or shares voting power, which includes the power to vote or to direct the voting, with respect to such securities.

(z) ***"Participant"*** means a person to whom a Stock Award is granted pursuant to the Plan or, if applicable, such other person who holds an outstanding Stock Award.

(aa) ***"Phantom Stock Award"*** means an award of a specified number of units of value granted under the Plan, which, when redeemed, shall be a right to receive cash from the Company in an amount equal to the Fair Market Value of the Common Stock as determined in accordance with this Plan.

(bb) ***"Plan"*** means this Amended and Restated Proteon Therapeutics, Inc. 2006 Equity Incentive Plan.

(cc) ***"Restricted Stock Award"*** means an award of shares of Common Stock that is granted pursuant to the terms and conditions of Section 7(b).

(dd) ***"Securities Act"*** means the Securities Act of 1933, as amended.

(ee) **"*Stock Appreciation Right*" or "SAR"** means a single unit of value granted under the Plan, which, when redeemed, shall be a right to receive cash from the Company in an amount equal to the Fair Market Value of the Common Stock, as determined in accordance with this Plan, minus the exercise price, if any, of the SAR.

(ff) **"*Stock Award*"** means any right granted under the Plan, including an Option, a stock bonus and a right to acquire restricted stock.

(gg) **"*Stock Award Agreement*"** means a written agreement between the Company and a holder of a Stock Award evidencing the terms and conditions of an individual Stock Award grant. Each Stock Award Agreement shall be subject to the terms and conditions of the Plan.

(hh) **"*Subsidiary*"** means, with respect to the Company, (i) any corporation of which more than fifty percent (50%) of the outstanding capital stock having ordinary voting power to elect a majority of the board of directors of such corporation (irrespective of whether, at the time, stock of any other class or classes of such corporation shall have or might have voting power by reason of the happening of any contingency) is at the time, directly or indirectly, Owned by the Company, and (ii) any partnership in which the Company has a direct or indirect interest (whether in the form of voting or participation in profits or capital contribution) of more than fifty percent (50%).

(ii) **"Ten Percent Stockholder"** means a person who Owns (or is deemed to Own pursuant to Section 424(d) of the Code) stock possessing more than ten percent (10%) of the total combined voting power of all classes of stock of the Company or of any of its Affiliates.

3. ADMINISTRATION.

(a) **Administration by Board.** The Board shall administer the Plan unless and until the Board delegates administration to a Committee, as provided in Section 3(c).

(b) **Powers of Board.** The Board shall have the power, subject to, and within the limitations of, the express provisions of the Plan:

(i) To determine from time to time which of the persons eligible under the Plan shall be granted Stock Awards; when and how each Stock Award shall be granted; what type or combination of types of Stock Award shall be granted; the provisions of each Stock Award granted (which need not be identical), including the time or times when a person shall be permitted to receive Common Stock pursuant to a Stock Award; and the number of shares of Common Stock, or units of value for Stock Appreciation Rights or Phantom Stock Awards, with respect to which a Stock Award shall be granted to each such person.

(ii) To construe and interpret the Plan and Stock Awards granted under it, and to establish, amend and revoke rules and regulations for its administration. The Board, in the exercise of this power, may correct any defect, omission or inconsistency in the Plan or in any Stock Award Agreement, in a manner and to the extent it shall deem necessary or expedient to make the Plan fully effective.

(iii) To effect, at any time and from time to time, with the consent of any adversely affected Optionholder, (1) the reduction of the exercise price of any outstanding Option under the Plan, (2) the cancellation of any outstanding Option under the Plan and the grant in substitution therefor of (A) a new Option under the Plan or another equity plan of the Company covering the same or a different number of shares of Common Stock, (B) a Restricted Stock Award (including a stock bonus), (C) a Stock Appreciation Right, (D) cash (E) Phantom Stock Awards and/or (F) other valuable consideration (as determined by the Board, in its sole discretion), or (3) any other action that is treated as a repricing under generally accepted accounting principles.

(iv) To amend the Plan or a Stock Award as provided in Section 12.

(v) To terminate or suspend the Plan as provided in Section 13.

(vi) Generally, to exercise such powers and to perform such acts as the Board deems necessary or expedient to promote the best interests of the Company and that are not in conflict with the provisions of the Plan.

(c) **Delegation to Committee.** The Board may delegate administration of the Plan to a Committee or Committees of three (3) or more members of the Board, and the term "Committee" shall apply to any person or persons to whom such authority has been delegated. If administration is delegated to a Committee, the Committee shall have, in connection with the administration of the Plan, the powers theretofore possessed by the Board, including the power to delegate to a subcommittee any of the administrative powers the Committee is authorized to exercise (and references in this Plan to the Board shall thereafter be to the Committee or subcommittee), subject, however, to such resolutions, not inconsistent with the provisions of the Plan, as may be adopted from time to time by the Board. The Board may abolish the Committee at any time and revest in the Board the administration of the Plan.

(d) **Delegation to an Officer.** The Board may delegate to one or more Officers of the Company the authority to do one or both of the following: (i) designate Officers and Employees of the Company or any of its Subsidiaries to be recipients of Stock Awards and (ii) determine the

number of shares of Common Stock to be subject to such Stock Awards granted to such Officers and Employees of the Company; *provided, however,* that the Board resolutions regarding such delegation shall specify the total number of shares of Common Stock that may be subject to the Stock Awards granted by such Officer and that such Officer may not grant a Stock Award to himself or herself. Notwithstanding the foregoing, the Board may not delegate authority to an Officer to determine the Fair Market Value of the Common Stock.

(e) **Effect of Board's Decision.** All determinations, interpretations and constructions made by the Board in good faith shall not be subject to review by any person and shall be final, binding and conclusive on all persons.

4. SHARES SUBJECT TO THE PLAN.

(a) **Share Reserve**. Subject to the provisions of Section 11(a) relating to Capitalization Adjustments, the Common Stock and units of value for Stock Appreciation Rights or Phantom Stock Awards that may be issued pursuant to Stock Awards shall not exceed in the aggregate eighteen million two hundred twenty-two thousand one hundred fifty-seven (18,222,157) shares of Common Stock.

(b) **Reversion of Shares to the Share Reserve**. If any Stock Award shall for any reason expire or otherwise terminate, in whole or in part, without having been exercised or redeemed in full, the shares of Common Stock not acquired under such Stock Award shall revert to and again become available for issuance under the Plan.

(c) **Source of Shares**. The shares of Common Stock subject to the Plan may be unissued shares or reacquired shares, bought on the market or otherwise.

(d) **Share Reserve Limitation**. To the extent that it may be required by Section 260.140.45 of Title 10 of the California Code of Regulations, the total number of shares of Common Stock issuable upon exercise of all outstanding Options and the total number of shares of Common Stock provided for under any stock bonus or similar plan

of the Company shall not exceed the applicable percentage as calculated in accordance with the conditions and exclusions of Section 260.140.45 of Title 10 of the California Code of Regulations, based on the shares of Common Stock of the Company that are outstanding at the time the calculation is made.

5. ELIGIBILITY.

(a) Eligibility for Specific Stock Awards. Incentive Stock Options may be granted only to Employees. Stock Awards other than Incentive Stock Options may be granted to Employees, Directors and Consultants.

(b) Ten Percent Stockholders.

(i) A Ten Percent Stockholder shall not be granted an Incentive Stock Option unless the exercise price of such Option is at least one hundred ten percent (110%) of the Fair Market Value of the Common Stock on the date of grant and the Option is not exercisable after the expiration of five (5) years from the date of grant.

(ii) A Ten Percent Stockholder shall not be granted a Nonstatutory Stock Option unless the exercise price of such Option is at least (i) one hundred ten percent (110%) of the Fair Market Value of the Common Stock on the date of grant or (ii) such lower percentage of the Fair Market Value of the Common Stock on the date of grant as is permitted by Section 260.140.41 of Title 10 of the California Code of Regulations at the time of the grant of the Option, if applicable.

(iii) A Ten Percent Stockholder shall not be granted a restricted stock award unless the purchase price of the restricted stock is at least (i) one hundred percent (100%) of the Fair Market Value of the Common Stock on the date of grant or (ii) such lower percentage of the Fair Market Value of the Common Stock on the date of grant as is permitted by Section 260.140.42 of Title 10 of the California Code of Regulations at the time of the grant of the restricted stock award, if applicable.

(c) Consultants. A Consultant shall not be eligible for the grant of a Stock Award if, at the time of grant, either the offer or the sale of the Company's securities to such Consultant is not exempt under Rule 701 of the Securities Act ("Rule 701") because of the nature of the services that the Consultant is providing to the Company, because the Consultant is not a natural person, or because of some other provision of Rule 701, unless the Company determines that such grant need not comply with the requirements of Rule 701 and will satisfy another exemption under the Securities Act as well as comply with the securities laws of all other relevant jurisdictions, if applicable.

6. OPTION PROVISIONS.

Each Option shall be in such form and shall contain such terms and conditions as the Board shall deem appropriate. All Options shall be separately designated Incentive Stock Options or Nonstatutory Stock Options at the time of grant, and, if certificates are issued, a separate certificate or certificates shall be issued for shares of Common Stock purchased on exercise of each type of Option. The provisions of separate Options need not be identical, but each Option shall include (through incorporation of provisions hereof by reference in the Option or otherwise) the substance of each of the following provisions:

(a) Term. Subject to the provisions of Section 5(b) regarding Ten Percent Stockholders, no Option shall be exercisable after the expiration of ten (10) years from the date it was granted.

(b) Exercise Price of an Incentive Stock Option. Subject to the provisions of Section 5(b) regarding Ten Percent Stockholders, the exercise price of each Incentive Stock Option shall be not less than one hundred percent (100%) of the Fair Market Value of the Common Stock subject to the Option on the date the Option is granted. Notwithstanding the foregoing, an Incentive Stock Option may be granted with an exercise price lower than that set forth in the preceding sentence if such Option is granted pursuant to an assumption or substitution for another option in a manner satisfying the provisions of Section 424(a) of the Code.

(c) Exercise Price of a Nonstatutory Stock Option. Subject to the provisions of Section 5(b) regarding Ten Percent Stockholders, the exercise price of each Nonstatutory Stock Option shall be not less than eighty-five percent (85%) of the Fair Market Value of the Common Stock subject to the Option on the date the Option is granted. Notwithstanding the foregoing, a Nonstatutory Stock Option may be granted with an exercise price lower than that set forth in the preceding sentence if such Option is granted pursuant to an assumption or substitution for another option in a manner satisfying the provisions of Section 424(a) of the Code.

(d) Consideration. The purchase price of Common Stock acquired pursuant to an Option shall be paid, to the extent permitted by applicable statutes and regulations, either (i) in cash at the time the Option is exercised, or (ii) at the discretion of the Board at the time of the grant of the Option (or subsequently in the case of a Nonstatutory Stock Option) (1) by delivery to the Company of other Common Stock, (2) according to a deferred payment or other similar arrangement with the Optionholder or (3) in any other form of legal consideration that may be acceptable to the Board. Unless otherwise specifically provided in the Option, the purchase price of Common Stock acquired pursuant to an Option that is paid by delivery to the Company of other Common Stock acquired, directly or indirectly from the Company, shall be paid only by shares of the Common Stock of the Company that have been held for more than six (6) months (or such longer or shorter period of time required to avoid a charge to earnings for financial accounting purposes). At any time that the Company is incorporated in Delaware, payment of the Common Stock's "par value," as defined in the Delaware General Corporation Law, shall not be made by deferred payment.

In the case of any deferred payment arrangement, interest shall be compounded at least annually and shall be charged at the minimum rate of interest necessary to avoid (1) the treatment as interest, under any applicable provisions of the Code, of any amounts other than amounts stated to be interest under the deferred payment arrangement and (2) the treatment of the Option as a variable award for financial accounting purposes.

If the Common Stock is traded on an established market, payment of any exercise price may also be made through and under the terms and conditions of any formal cashless exercise program authorized by the Company entailing the sale of the Common Stock subject to an Option in a brokered transaction (other than to the Company), provided, that, such formal cashless exercise program shall not be applicable to any Option unless and until the holder of such Option shall have agreed in writing that such formal cashless exercise program shall be applicable to such Option.

(e) Transferability of an Incentive Stock Option. An Incentive Stock Option shall not be transferable except by will or by the laws of descent and distribution and shall be exercisable during the lifetime of the Optionholder only by the Optionholder. Notwithstanding the foregoing, the Optionholder may, by delivering written notice to the Company, in a form satisfactory to the Company, designate a third party who, in the event of the death of the Optionholder, shall thereafter be entitled to exercise the Option.

(f) Transferability of a Nonstatutory Stock Option. A Nonstatutory Stock Option shall not be transferable except by will or by the laws of descent and distribution and, to the

extent provided in the Option Agreement, to such further extent as permitted by Section 260.140.41(d) of Title 10 of the California Code of Regulations, if applicable at the time of the grant of the Option, and shall be exercisable during the lifetime of the Optionholder only by the Optionholder. If the Nonstatutory Stock Option does not provide for transferability, then the Nonstatutory Stock Option shall not be transferable except by will or by the laws of descent and distribution and shall be exercisable during the lifetime of the Optionholder only by the Optionholder. Notwithstanding the foregoing, the Optionholder may, by delivering written notice to the Company, in a form satisfactory to the Company, designate a third party who, in the event of the death of the Optionholder, shall thereafter be entitled to exercise the Option.

(g) Vesting Generally. The total number of shares of Common Stock subject to an Option may, but need not, vest and therefore become exercisable in periodic installments that may, but need not, be equal. The Option may be subject to such other terms and conditions on the time or times when it may be exercised (which may be based on performance or other criteria) as the Board may deem appropriate. The vesting provisions of individual Options may vary. The provisions of this Section 6(g) are subject to any Option provisions governing the minimum number of shares of Common Stock as to which an Option may be exercised.

(h) Minimum Vesting. Notwithstanding the foregoing Section 6(g), to the extent that the following restrictions on vesting are required by Section 260.140.41(f) of Title 10 of the California Code of Regulations at the time of the grant of the Option, then:

(i) Options granted to an Employee who is not an Officer, Director or Consultant shall provide for vesting of the total number of shares of Common Stock at a rate of at least twenty percent (20%) per year over five (5) years from the date the Option was granted, subject to reasonable conditions such as continued employment; and

(ii) Options granted to Officers, Directors or Consultants may be made fully exercisable, subject to reasonable conditions such as continued employment, at any time or during any period established by the Company.

(i) Termination of Continuous Service. In the event that an Optionholder's Continuous Service terminates (other than upon the Optionholder's death or Disability), the Optionholder may exercise his or her Option (to the extent that the Optionholder was entitled to exercise such Option as of the date of termination) but only within such period of time ending on the earlier of (i) the date three (3) months following the termination of the Optionholder's Continuous Service (or such longer or shorter period specified in the Option Agreement), or (ii) the expiration of the term of the Option as set forth in the Option Agreement. If, after termination, the Optionholder does not exercise his or her Option within the time specified in the Option Agreement, the Option shall terminate.

(j) Extension of Termination Date. An Optionholder's Option Agreement may also provide that if the exercise of the Option following the termination of the Optionholder's Continuous Service (other than upon the Optionholder's death or Disability) would be prohibited at any time solely because the issuance of shares of Common Stock would violate the registration requirements under the Securities Act, then the Option shall terminate on the earlier

of (i) the expiration of the term of the Option set forth in Section 6(a) or (ii) the expiration of a period of three (3) months after the termination of the Optionholder's Continuous Service during which the exercise of the Option would not be in violation of such registration requirements.

(k) Disability of Optionholder. In the event that an Optionholder's Continuous Service terminates as a result of the Optionholder's Disability, the Optionholder may exercise his or her Option (to the extent that the Optionholder was entitled to exercise such Option as of the date of termination), but only within such period of time ending on the earlier of (i) the date twelve (12) months following such termination (or such longer or shorter period specified in the Option Agreement, which period shall not be less than six (6) months) or (ii) the expiration of the term of the Option as set forth in the Option Agreement. If, after termination, the Optionholder does not exercise his or her Option within the time specified herein, the Option shall terminate.

(l) Death of Optionholder. In the event that (i) an Optionholder's Continuous Service terminates as a result of the Optionholder's death or (ii) the Optionholder dies within the period (if any) specified in the Option Agreement after the termination of the Optionholder's Continuous Service for a reason other than death, then the Option may be exercised (to the extent the Optionholder was entitled to exercise such Option as of the date of death) by the Optionholder's estate, by a person who acquired the right to exercise the Option by bequest or inheritance or by a person designated to exercise the option upon the Optionholder's death pursuant to Section 6(e) or 6(f), but only within the period ending on the earlier of (1) the date eighteen (18) months following the date of death (or such longer or shorter period specified in the Option Agreement, which period shall not be less than six (6) months) or (2) the expiration of the term of such Option as set forth in the Option Agreement. If, after death, the Option is not exercised within the time specified herein, the Option shall terminate.

(m) Early Exercise. The Option may, but need not, include a provision whereby the Optionholder may elect at any time before the Optionholder's Continuous Service terminates to exercise the Option as to any part or all of the shares of Common Stock subject to the Option prior to the full vesting of the Option. Subject to the "Repurchase Limitation" in Section 10(h), any unvested shares of Common Stock so purchased may be subject to a repurchase option in favor of the Company or to any other restriction the Board determines to be appropriate. Provided that the "Repurchase Limitation" in Section 10(h) is not violated, the Company will not exercise its repurchase option until at least six (6) months (or such longer or shorter period of time required to avoid a charge to earnings for financial accounting purposes) have elapsed following exercise of the Option unless the Board otherwise specifically provides in the Option.

7. PROVISIONS OF STOCK AWARDS OTHER THAN OPTIONS.

(a) Stock Bonus Awards. Each stock bonus agreement shall be in such form and shall contain such terms and conditions as the Board shall deem appropriate. The terms and conditions of stock bonus agreements may change from time to time, and the terms and conditions of separate stock bonus agreements need not be identical, but each stock bonus agreement shall include (through incorporation of provisions hereof by reference in the agreement or otherwise) the substance of each of the following provisions:

(i) Consideration. A stock bonus may be awarded in consideration for past services actually rendered to the Company or an Affiliate for its benefit.

(ii) Vesting. Subject to the "Repurchase Limitation" in Section 10(h), shares of Common Stock awarded under the stock bonus agreement may, but need not, be subject to a share repurchase option in favor of the Company in accordance with a vesting schedule to be determined by the Board.

(iii) Termination of Participant's Continuous Service. Subject to the "Repurchase Limitation" in Section 10(h), in the event that a Participant's Continuous Service terminates, the Company may reacquire any or all of the shares of Common Stock held by the Participant that have not vested as of the date of termination under the terms of the stock bonus agreement. Provided that the "Repurchase Limitation" in Section 10(h) is not violated, the Company will not exercise its repurchase option until at least six (6) months (or such longer or shorter period of time required to avoid a charge to earnings for financial accounting purposes) have elapsed following receipt of the stock bonus unless otherwise specifically provided in the stock bonus agreement.

(iv) Transferability. Rights to acquire shares of Common Stock under the stock bonus agreement shall not be transferable except by will or by the laws of descent and distribution and shall be exercisable during the lifetime of the Participant only by the Participant.

(b) Restricted Stock Awards. Each restricted stock purchase agreement shall be in such form and shall contain such terms and conditions as the Board shall deem appropriate. The terms and conditions of the restricted stock purchase agreements may change from time to time, and the terms and conditions of separate restricted stock purchase agreements need not be identical, but each restricted stock purchase agreement shall include (through incorporation of provisions hereof by reference in the agreement or otherwise) the substance of each of the following provisions:

(i) **Purchase Price**. Subject to the provisions of Section 5(b) regarding Ten Percent Stockholders, the purchase price of restricted stock awards shall not be less than eighty-five percent (85%) of the Common Stock's Fair Market Value on the date such award is made or at the time the purchase is consummated.

(ii) **Consideration**. The purchase price of Common Stock acquired pursuant to the restricted stock purchase agreement shall be paid either: (i) in cash at the time of purchase; (ii) at the discretion of the Board, according to a deferred payment or other similar arrangement with the Participant; or (iii) in any other form of legal consideration that may be acceptable to the Board in its discretion; *provided*, *however*, that at any time that the Company is incorporated in Delaware, then payment of the Common Stock's "par value," as defined in the Delaware General Corporation Law, shall not be made by deferred payment.

(iii) **Vesting**. Subject to the "Repurchase Limitation" in Section 10(h), shares of Common Stock acquired under the restricted stock purchase agreement may, but need not, be

subject to a share repurchase option in favor of the Company in accordance with a vesting schedule to be determined by the Board.

(iv) **Termination of Participant's Continuous Service**. Subject to the "Repurchase Limitation" in Section 10(h), in the event that a Participant's Continuous Service terminates, the Company may repurchase or otherwise reacquire any or all of the shares of Common Stock held by the Participant that have not vested as of the date of termination under the terms of the restricted stock purchase agreement. Provided that the "Repurchase Limitation" in Section 10(h) is not violated, the Company will not exercise its repurchase option until at least six (6) months (or such longer or shorter period of time required to avoid a charge to earnings for financial accounting purposes) have elapsed following the purchase of the restricted stock unless otherwise specifically provided in the restricted stock purchase agreement.

(v) **Transferability**. Rights to acquire shares of Common Stock under the restricted stock purchase agreement shall not be transferable except by will or by the laws of descent and distribution and shall be exercisable during the lifetime of the Participant only by the Participant.

(c) **Stock Appreciation Rights and Phantom Stock Awards**. Each SAR and Phantom Stock Award agreement shall be in such form and shall contain such terms and conditions as the Board shall deem appropriate. The terms and conditions of SAR and Phantom Stock Award agreements may change from time to time, and the terms and conditions of separate SAR and Phantom Stock Award agreements need not be identical, but each SAR and Phantom Stock Award agreement shall include (through incorporation of provisions hereof by reference in the agreement or otherwise) the substance of each of the following provisions:

(i) **Grants**. SARs and Phantom Stock Awards granted to a Participant shall be credited to a bookkeeping account to be maintained for such Participant. A Participant may be granted more than one SAR or Phantom Stock Award under the Plan, and such Participant shall be notified of each such grant in writing within thirty (30) days of the date of grant, or within such other time period as the Board shall determine is appropriate.

(ii) **Term**. Each SAR and Phantom Stock Award granted pursuant to the Plan shall have a term of ten (10) years. A SAR or Phantom Stock Award not redeemed prior to the payment shall be made to the Participant holding such SAR or Phantom Stock Award in accordance with this Section 7(c).

(iii) **Vesting and Forfeiture**. SARs and the units subject to each Phantom Stock Award shall become vested and redeemable in periodic installments that may, but need not, be equal. The SAR or Phantom Stock Award may be subject to such other terms and conditions on the time or times when it may be redeemed (which may be based on performance or other criteria) as the Board may deem appropriate. The vesting provisions of individual SARs and Phantom Stock Awards may vary.

A Participant's SARs or Phantom Stock Awards shall continue to vest until either (i) the Participant's Continuous Service terminates for any reason, or (ii) all SARs or units subject to

the Phantom Stock Award under the Participant's grant become fully vested. Only SARs and units subject to the Phantom Stock Awards that are vested may be redeemed.

If a Participant's Continuous Service terminates for any reason before all SARs or units subject to a Phantom Stock Award held by such Participant have vested, the portion of those SARs or Phantom Stock Awards that has not vested as of the date of such termination of Continuous Service shall be forfeited and canceled as of such date. Such Participant's SARs and vested units subject to the Phantom Stock Award that have vested automatically shall be redeemed on the date of his or her termination, and the Participant shall receive a cash payment for such automatically redeemed vested SARs and Phantom Stock Awards in accordance with Section 7(c)(iv).

If a Participant's Continuous Service with the Company is interrupted for a period of three (3) months or more in a calendar year for any reason, including such Participant's sick leave, maternity leave, military leave, or other leave of absence approved by the Company, before all SARs or units subject to a Phantom Stock Award held by such Participant have vested, then upon the occurrence of such interruption, further vesting of the SARs and Phantom Stock Awards shall cease until the Participant resumes Continuous Service. The unvested SARs and Phantom Stock Awards thereafter shall vest on the basis set forth in the Participant's SAR or Phantom Stock Award agreement, with no vesting credit given for the period during which the vesting ceased.

Notwithstanding the foregoing, the Board shall have the power to accelerate the time of vesting for any Participant or Participants under this Section 7(c), including in the event of a Change in Control or a Participant's termination of Continuous Service.

(iv) **Redemption**. SARs and Phantom Stock Awards shall entitle the holder to receive a cash payment from the Company upon redemption in an amount equal to the Fair Market Value per share of the Common Stock (or such other value per share as may be set forth in the SAR or Phantom Stock Award agreement), multiplied by the number of SARs or units as to which the Phantom Stock Award is redeemed, less the applicable exercise price, if any, and applicable withholding taxes and authorized payroll deductions. Such payments shall be made as soon as reasonably practicable following the redemption of a SAR or Phantom Stock Award. Notwithstanding the foregoing a SAR or Phantom Stock Award agreement may provide that the Company may, in its sole discretion, make payment following a redemption of a SAR or Phantom Stock Award pursuant to a deferred payment schedule. Such deferred payment schedule shall provide that the Company shall pay the Participant the payment due with respect to the redemption within a period certain not to exceed two years from the date of the redemption. Payments made pursuant to a deferred payment schedule will include an interest payment by the Company in an amount equal to the mid-term Applicable Federal Rate established by the Internal Revenue Service, compounded annually, on the unpaid balance of the payment over the actual term of the payment.

At the time of the redemption of a SAR or Phantom Stock Award, the Participant shall execute such additional documents as the Company may then require in order to administer properly the terms of the grant and redemption.

(v) **Transferability**. SARs and Phantom Stock Awards shall not be transferable or assignable in any manner by a Participant. During the lifetime of a Participant, vested SARs and units subject to Phantom Stock Awards held by such Participant shall be redeemed only by such Participant or his or her guardian or legal

representative. In the case of the death of a Participant who holds vested SARs or units subject to Phantom Stock Awards, such vested SARs or units subject to Phantom Stock Awards automatically shall be redeemed as of the Participant's date of death, and payment shall be made to such Participant's designated beneficiary or, in the absence of designation, to such Participant's beneficiary by will or by the laws of descent and distribution upon sufficient legal proof of entitlement, in accordance with Section 7(c)(iv) of the Plan.

(vi) Funding. SARs and Phantom Stock Awards shall not be funded, the Company shall not be required to segregate any funds representing the value of SARs or Phantom Stock Awards granted to Participants, and nothing in the Plan shall be construed as providing for such segregation. A Participant's rights to amounts received upon the redemption of SARs or Phantom Stock Awards under the Plan shall be those of an unsecured general creditor of the Company. The liability for payment upon the redemption of a SAR or Phantom Stock Award shall be a liability of the Company alone and shall not be a liability of any officer, director, shareholder or affiliate of the Company.

8. COVENANTS OF THE COMPANY.

(a) Availability of Shares. During the terms of the Stock Awards, the Company shall keep available at all times the number of shares of Common Stock required to satisfy such Stock Awards.

(b) Securities Law Compliance. The Company shall seek to obtain from each regulatory commission or agency having jurisdiction over the Plan such authority as may be required to grant Stock Awards and to issue and sell shares of Common Stock upon exercise of the Stock Awards; *provided, however*, that this undertaking shall not require the Company to register under the Securities Act the Plan, any Stock Award or any Common Stock issued or issuable pursuant to any such Stock Award. If, after reasonable efforts, the Company is unable to obtain from any such regulatory commission or agency the authority which counsel for the Company deems necessary for the lawful issuance and sale of Common Stock under the Plan, the Company shall be relieved from any liability for failure to issue and sell Common Stock upon exercise of such Stock Awards unless and until such authority is obtained.

9. USE OF PROCEEDS FROM STOCK

Proceeds from the sale of Common Stock pursuant to Stock Awards shall constitute general funds of the Company.

10. MISCELLANEOUS.

(a) Acceleration of Exercisability or Redemption and Vesting. The Board shall have the power to accelerate the time at which a Stock Award may first be exercised or

redeemed or the time during which a Stock Award or any part thereof will vest in accordance with the Plan, notwithstanding the provisions in the Stock Award stating the time at which it may first be exercised or redeemed or the time during which it will vest; *provided, however,* that in the case of an Incentive Stock Option, any such acceleration of the Option would not cause the Option to fail to comply with the provisions of Section 422 of the Code or the Optionholder consents to the acceleration.

(b) Stockholder Rights. No Participant shall be deemed to be the holder of, or to have any of the rights of a holder with respect to, any shares of Common Stock subject to such Stock Award unless and until such Participant has satisfied all requirements for exercise of the Stock Award pursuant to its terms.

(c) No Employment or other Service Rights. Nothing in the Plan or any instrument executed or Stock Award granted pursuant thereto shall confer upon any Participant any right to continue to serve the Company or an Affiliate in the capacity in effect at the time the Stock Award was granted or shall affect the right of the Company or an Affiliate to terminate (i) the employment of an Employee with or without notice and with or without cause, (ii) the service of a Consultant pursuant to the terms of such Consultant's agreement with the Company or an Affiliate or (iii) the service of a Director pursuant to the Bylaws of the Company or an Affiliate, and any applicable provisions of the corporate law of the state in which the Company or the Affiliate is incorporated, as the case may be.

(d) Incentive Stock Option $100,000 Limitation. To the extent that the aggregate Fair Market Value (determined at the time of grant) of Common Stock with respect to which Incentive Stock Options are exercisable for the first time by any Optionholder during any calendar year (under all plans of the Company and its Affiliates) exceeds one hundred thousand dollars ($100,000) (the "***ISO Limit***"), the Options or portions thereof that exceed the ISO Limit (according to the order in which they were granted) shall be treated as Nonstatutory Stock Options, notwithstanding any contrary provision of a Stock Award Agreement; provided however, that to the extent that applicable law is amended to increase or decrease the incentive stock option value limitation, the ISO Limit shall be deemed to be such amended value.

(e) Investment Assurances. The Company may require a Participant, as a condition of exercising or acquiring Common Stock under any Stock Award, (i) to give written assurances satisfactory to the Company as to the Participant's knowledge and experience in financial and business matters and/or to employ a purchaser representative reasonably satisfactory to the Company who is knowledgeable and experienced in financial and business matters and that he or she is capable of evaluating, alone or together with the purchaser representative, the merits and risks of exercising the Stock Award; and (ii) to give written assurances satisfactory to the Company stating that the Participant is acquiring Common Stock subject to the Stock Award for the Participant's own account and not with any present intention of selling or otherwise distributing the Common Stock. The foregoing requirements, and any assurances given pursuant to such requirements, shall be inoperative if (1) the issuance of the shares of Common Stock upon the exercise or acquisition of Common Stock under the Stock Award has been registered under a then currently effective registration statement under the Securities Act or (2) as to any particular requirement, a determination is made by counsel for the Company that such

requirement need not be met in the circumstances under the then applicable securities laws. The Company may, upon advice of counsel to the Company, place legends on stock certificates issued under the Plan as such counsel deems necessary or appropriate in order to comply with applicable securities laws, including, but not limited to, legends restricting the transfer of the Common Stock.

(f) Withholding Obligations. To the extent provided by the terms of a Stock Award Agreement, a Participant may satisfy any federal, state or local tax withholding obligation relating to the exercise or acquisition of Common Stock under a Stock Award or redemption of a SAR or Phantom Stock Award by any of the following means (in addition to the Company's right to withhold from any compensation paid to the Participant by the Company) or by a combination of such means: (i) tendering a cash payment; (ii) authorizing the Company to withhold shares of Common Stock from the shares of Common Stock otherwise issuable to the Participant as a result of the exercise or acquisition of Common Stock under the Stock Award; *provided, however*, that no shares of Common Stock are withheld with a value exceeding the minimum amount of tax required to be withheld by law (or such lower amount as may be necessary to avoid variable award accounting); or (iii) delivering to the Company owned and unencumbered shares of Common Stock.

(g) Information Obligation. To the extent required by Section 260.140.46 of Title 10 of the California Code of Regulations, the Company shall deliver financial statements to Participants at least annually. This Section 10(g) shall not apply to key Employees whose duties in connection with the Company assure them access to equivalent information.

(h) Repurchase Limitation. The terms of any repurchase option shall be specified in the Stock Award, and the repurchase price may be either the Fair Market Value of the shares of Common Stock on the date of termination of Continuous Service or the lower of (i) the Fair Market Value of the shares of Common Stock on the date of repurchase or (ii) their original purchase price. To the extent required by Section 260.140.41 and Section 260.140.42 of Title 10 of the California Code of Regulations at the time a Stock Award is made, any repurchase option contained in a Stock Award granted to a person who is not an Officer, Director or Consultant shall be upon the terms described below:

(i) Fair Market Value. If the repurchase option gives the Company the right to repurchase the shares of Common Stock upon termination of Continuous Service at not less than the Fair Market Value of the shares of Common Stock to be purchased on the date of termination of Continuous Service, then (i) the right to repurchase shall be exercised for cash or cancellation of purchase money indebtedness for the shares of Common Stock within ninety (90) days of termination of Continuous Service (or in the case of shares of Common Stock issued upon exercise of Stock Awards after such date of termination, within ninety (90) days after the date of the exercise) or such longer period as may be agreed to by the Company and the Participant (for example, for purposes of satisfying the requirements of Section 1202(c)(3) of the Code regarding "qualified small business stock") and (ii) the right terminates when the shares of Common Stock become publicly traded.

(ii) Original Purchase Price. If the repurchase option gives the Company the right to repurchase the shares of Common Stock upon termination of Continuous Service at the lower of (i) the Fair Market Value of the shares of Common Stock on the date of repurchase or (ii) their original purchase price, then (x) the right to repurchase at the original purchase price shall lapse at the rate of at least twenty percent (20%) of the shares of Common Stock per year over five (5) years from the date the Stock Award is granted (without respect to the date the Stock Award was exercised or became exercisable) and (y) the right to repurchase shall be exercised for cash or cancellation of purchase money indebtedness for the shares of Common Stock within ninety (90) days of termination of Continuous Service (or in the case of shares of Common Stock issued upon exercise of Options after such date of termination, within ninety (90) days after the date of the exercise) or such longer period as may be agreed to by the Company and the Participant (for example, for purposes of satisfying the requirements of Section 1202(c)(3) of the Code regarding "qualified small business stock").

11. ADJUSTMENTS UPON CHANGES IN STOCK

(a) Capitalization Adjustments. If any change is made in, or other event occurs with respect to, the Common Stock subject to the Plan or subject to any Stock Award without the receipt of consideration by the Company (through merger, consolidation, reorganization, recapitalization, reincorporation, stock dividend, dividend in property other than cash, stock split, liquidating dividend, combination of shares, exchange of shares, change in corporate structure or other transaction not involving the receipt of consideration by the Company (each a "Capitalization Adjustment"), the Plan will be appropriately adjusted in the class(es) and maximum number of securities subject to the Plan pursuant to Sections 4(a) and 4(b) and the maximum number of securities subject to award to any person pursuant to Section 5(c), and the outstanding Stock Awards will be appropriately adjusted in the class(es) and number of securities and price per share of Common Stock subject to such outstanding Stock Awards. The Board shall make such adjustments, and its determination shall be final, binding and conclusive. (The conversion of any convertible securities of the Company shall not be treated as a transaction "without receipt of consideration" by the Company.)

(b) Dissolution or Liquidation. In the event of a dissolution or liquidation of the Company, then all outstanding Options shall terminate immediately prior to the completion of such dissolution or liquidation, and shares of Common Stock subject to the Company's repurchase option may be repurchased by the Company notwithstanding the fact that the holder of such stock is still in Continuous Service.

(c) Corporate Transaction. In the event of a Corporate Transaction, any surviving corporation or acquiring corporation may assume or continue any or all Stock Awards outstanding under the Plan or may substitute similar stock awards for Stock Awards outstanding under the Plan (it being understood that similar stock awards include, but are not limited to, awards to acquire the same consideration paid to the stockholders or the Company, as the case may be, pursuant to the Corporate Transaction), and any reacquisition or repurchase rights held by the Company in respect of Common Stock issued pursuant to Stock Awards may be assigned by the Company to the successor of the Company (or such successor's parent company), if any, in connection with such Corporate Transaction. In the event that any surviving corporation or

acquiring corporation does not assume or continue any or all such outstanding Stock Awards or substitute similar stock awards for such outstanding Stock Awards, then with respect to Stock Awards that have not been assumed, continued or substituted and that are held by Participants whose Continuous Service has not terminated prior to the effective time of the Corporate Transaction, the vesting of such Stock Awards (and, if applicable, the time at which such Stock Awards may be exercised or redeemed) shall (contingent upon the effectiveness of the Corporate Transaction) be accelerated in full to a date prior to the effective time of such Corporate Transaction as the Board shall determine (or, if the Board shall not determine such a date, to the date that is five (5) days prior to the effective time of the Corporate Transaction), the Stock Awards shall terminate if not exercised or redeemed (if applicable) at or prior to such effective time, and any reacquisition or repurchase rights held by the Company with respect to such Stock Awards held by Participants whose Continuous Service has not terminated shall (contingent upon the effectiveness of the Corporate Transaction) lapse. With respect to any other Stock Awards outstanding under the Plan that have not been assumed, continued or substituted, the vesting of such Stock Awards (and, if applicable, the time at which such Stock Award may be exercised or redeemed) shall not be accelerated, unless otherwise provided in a written agreement between the Company or any Affiliate and the holder of such Stock Award, and such Stock Awards shall terminate if not exercised or redeemed (if applicable) prior to the effective time of the Corporate Transaction.

(d) Change in Control. A Stock Award held by any Participant whose Continuous Service has not terminated prior to the effective time of a Change in Control may be subject to additional acceleration of vesting and exercisability or redemption upon or after such event as may be provided in the Stock Award Agreement for such Stock Award or as may be provided in any other written agreement between the Company or any Affiliate and the Participant, but in the absence of such provision, no such acceleration shall occur. Notwithstanding the foregoing, upon the occurrence of a Change of Control, to the extent that the surviving entity declines to continue, convert, assume or replace any outstanding Options, then such Options, to the extent not already exercisable in full, shall accelerate with respect to 100% of the shares for which such Options are not then exercisable.

12. AMENDMENT OF THE PLAN AND STOCK AWARDS.

(a) Amendment of Plan. The Board at any time, and from time to time, may amend the Plan. However, except as provided in Section 11(a) relating to Capitalization Adjustments, no amendment shall be effective unless approved by the stockholders of the Company to the extent stockholder approval is necessary to satisfy the requirements of Section 422 of the Code.

(b) Stockholder Approval. The Board, in its sole discretion, may submit any other amendment to the Plan for stockholder approval.

(c) Contemplated Amendments. It is expressly contemplated that the Board may amend the Plan in any respect the Board deems necessary or advisable to provide eligible Employees with the maximum benefits provided or to be provided under the provisions of the Code and the regulations promulgated thereunder relating to Incentive Stock Options and/or to bring the Plan and/or Incentive Stock Options granted under it into compliance therewith.

(d) **No Impairment of Rights**. Rights under any Stock Award granted before amendment of the Plan shall not be impaired by any amendment of the Plan unless (i) the Company requests the consent of the Participant and (ii) the Participant consents in writing.

(e) **Amendment of Stock Awards**. The Board at any time, and from time to time, may amend the terms of any one or more Stock Awards; *provided, however*, that the rights under any Stock Award shall not be impaired by any such amendment unless (i) the Company requests the consent of the Participant and (ii) the Participant consents in writing.

13. **TERMINATION OR SUSPENSION OF THE PLAN**.

(a) **Plan Term**. The Board may suspend or terminate the Plan at any time. Unless sooner terminated, the Plan shall terminate on the day before the tenth (10th) anniversary of the date the Plan is adopted by the Board or approved by the stockholders of the Company, whichever is earlier. No Stock Awards may be granted under the Plan while the Plan is suspended or after it is terminated.

(b) **No Impairment of Rights**. Suspension or termination of the Plan shall not impair rights and obligations under any Stock Award granted while the Plan is in effect except with the written consent of the Participant.

14. **EFFECTIVE DATE OF PLAN**.

The Plan shall become effective as determined by the Board.

15. **CHOICE OF LAW**.

The law of the State of Delaware shall govern all questions concerning the construction, validity and interpretation of this Plan, without regard to such state's conflict of laws rules.

****

PROTEON THERAPEUTICS, INC.

2014 EQUITY INCENTIVE PLAN

TABLE OF CONTENTS

PROTEON THERAPEUTICS, INC.

2014 EQUITY INCENTIVE PLAN

1. Purpose

This Plan is intended to provide incentives that will attract, retain and motive highly competent officers, directors, employees, consultants and advisors to promote the success of the Company's business and align employees' interests with stockholders' interests. The Plan is intended to be an incentive stock option plan within the meaning of Section 422 of the Code, but not all Awards are required to be Incentive Options.

2. Definitions

As used in this Plan, the following terms shall have the respective meanings set out below, unless the context clearly requires otherwise:

2.1. Accelerate, Accelerated, and Acceleration, means: (a) when used with respect to an Option or Stock Appreciation Right, that as of the time of reference such Option or Stock Appreciation Right will become exercisable with respect to some or all of the shares of Stock for which it was not then otherwise exercisable by its terms; (b) when used with respect to Restricted Stock or Restricted Stock Units, that the Risk of Forfeiture otherwise applicable to such Restricted Stock or Restricted Stock Units shall expire with respect to some or all of such shares of Restricted Stock or such Restricted Stock Units then still otherwise subject to the Risk of Forfeiture; and (c) when used with respect to Performance Units, that the applicable Performance Goals or other business objectives shall be deemed to have been met as to some or all of such Performance Units.

2.2. Affiliate means any corporation, partnership, limited liability company, business trust, or other entity controlling, controlled by or under common control with the Company.

2.3. Award means any grant or sale pursuant to the Plan of Options, Stock Appreciation Rights, Performance Units, Restricted Stock, Restricted Stock Units, Stock Grants or any of the foregoing intended to constitute Qualified Performance-Based Awards.

2.4. Award Agreement means an agreement between the Company and the recipient of an Award, or other notice of grant of an Award, setting forth the terms and conditions of the Award.

2.5. Board means the Company's Board of Directors.

2.6. Change of Control means the occurrence of any of the following after the date of the approval of the Plan by the Board:

(a) a Transaction (as defined in Section 8.4), unless securities possessing more than 50% of the total combined voting power of the survivor's or acquiror's outstanding securities (or the securities of any parent thereof) are held by a person or persons who held securities possessing more than 50% of the total combined voting power of the Company's outstanding securities immediately prior to that Transaction, or

(b) any person or group of persons (within the meaning of Section 13(d)(3) of the Securities Exchange Act of 1934, as amended and in effect from time to time) that, directly or indirectly, acquires, including but not limited to by means of a merger or consolidation, beneficial ownership (determined pursuant to Securities and Exchange Commission Rule 13d-3 promulgated under the said Exchange Act) of securities possessing more than 50% of the total combined voting power of the Company's outstanding securities unless pursuant to a tender or exchange offer made directly to the Company's stockholders that the Board recommends such stockholders accept, other than (i) the Company or any of its Affiliates, (ii) an employee benefit plan of the Company or any of its Affiliates, (iii) a trustee or other fiduciary holding securities under an employee benefit plan of the Company or any of its Affiliates, or (iv) an underwriter temporarily holding securities pursuant to an offering of such securities, or

(c) over a period of thirty-six (36) consecutive months or less, there is a change in the composition of the Board such that a majority of the Board members (rounded up to the next whole number, if a fraction) ceases, by reason of one or more proxy contests for the election of Board members, 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 Board members described in the preceding clause (i) who were still in office at the time that election or nomination was approved by the Board; or

(d) a majority of the Board votes in favor of a decision that a Change of Control has occurred, which vote may adopted by the Board with the intention that such vote become effective subject to and contingent upon the occurrence of certain events, in which case such Change of Control shall not be deemed to have occurred unless and until such vote becomes effective in accordance with its terms.

2.7. Code means the Internal Revenue Code of 1986, as amended from time to time, or any successor statute thereto, and any regulations issued from time to time thereunder.

2.8. Committee means the Compensation Committee of the Board, which in general is responsible for the administration of the Plan, as provided in Section 5 of this Plan. For any period during which no such committee is in existence "Committee" shall mean the Board and all authority and responsibility assigned to the Committee under the Plan shall be exercised, if at all, by the Board.

2.9. Company means Proteon Therapeutics, Inc., a corporation organized under the laws of the State of Delaware.

2.10. "Forfeiture," "forfeit," and derivations thereof, when used in respect of Restricted Stock purchased by a Participant, includes the Company's repurchase of such Restricted Stock at less than its then Market Value as a means intended to effect a forfeiture of value.

2.11. Grant Date means the date as of which an Option is granted, as determined under Section 7.1(a).

2.12. Incentive Option means an Option which by its terms is to be treated as an "incentive stock option" within the meaning of Section 422 of the Code.

2.13. Market Value means the value of a share of Stock on a particular date determined by such methods or procedures as may be established by the Committee. Unless otherwise determined by the Committee, the Market Value of Stock as of any date is the closing price for the Stock as reported on the New York Stock Exchange (or on any other national securities exchange on which the Stock is then listed) for that date or, if no closing price is reported for that date, the closing price on the first following date for which a closing price is reported. For purposes of Awards effective as of the effective date of the Company's initial public offering, Market Value of Stock shall be the price at which the Company's Stock is offered to the public in its initial public offering.

2.14. Nonstatutory Option means any Option that is not an Incentive Option.

2.15. Option means an option to purchase shares of Stock.

2.16. Optionee means an eligible individual to whom an Option shall have been granted under the Plan.

2.17. Participant means any holder of an outstanding Award under the Plan.

2.18. Performance Criteria and Performance Goals have the meanings given such terms in Section 7.7(f).

2.19. Performance Period means the one or more periods of time, which may be of varying and overlapping durations, selected by the Committee, over which the attainment of one or more Performance Goals or other business objectives will be measured for purposes of determining a Participant's right to, and the payment of, an Award.

2.20. Performance Unit means a right granted to a Participant under Section 7.5, to receive cash, Stock or other Awards, the payment of which is contingent on achieving Performance Goals or other business objectives established by the Committee.

2.21. Plan means this 2014 Equity Incentive Plan of the Company, as amended from time to time, and including any attachments or addenda hereto.

2.22. Qualified Performance-Based Awards means Awards intended to qualify as "performance-based compensation" under Section 162(m) of the Code.

2.23. Restricted Stock means a grant or sale of shares of Stock to a Participant subject to a Risk of Forfeiture.

2.24. Restricted Stock Units means rights to receive shares of Stock at the close of a Restriction Period, subject to a Risk of Forfeiture.

2.25. Restriction Period means the period of time, established by the Committee in connection with an Award of Restricted Stock or Restricted Stock Units, during which the shares of Restricted Stock or Restricted Stock Units are subject to a Risk of Forfeiture described in the applicable Award Agreement.

2.26. Risk of Forfeiture means a limitation on the right of the Participant to retain Restricted Stock or Restricted Stock Units, including a right of the Company to reacquire shares

of Restricted Stock at less than their then Market Value, arising because of the occurrence or non-occurrence of specified events or conditions.

2.27. Stock means common stock, par value $0.001 per share, of the Company, and such other securities as may be substituted for such common stock pursuant to Section 8.

2.28. Stock Appreciation Right means a right to receive any excess in the Market Value of shares of Stock (except as otherwise provided in Section 7.2(c)) over a specified exercise price.

2.29. Stock Grant means the grant of shares of Stock not subject to restrictions or other forfeiture conditions.

2.30. Stockholders' Agreement means any agreement by and among the holders of at least a majority of the outstanding voting securities of the Company and setting forth, among other provisions, restrictions upon the transfer of shares of Stock or on the exercise of rights appurtenant thereto (including but not limited to voting rights).

2.31. Ten Percent Owner means a person who owns, or is deemed within the meaning of Section 422(b)(6) of the Code to own, stock possessing more than 10% of the total combined voting power of all classes of stock of the Company (or any parent or subsidiary corporations of the Company, as defined in Sections 424(e) and (f), respectively, of the Code). Whether a person is a Ten Percent Owner shall be determined with respect to an Option based on the facts existing immediately prior to the Grant Date of the Option.

3. Term of the Plan

Unless the Plan shall have been earlier terminated by the Board, Awards may be granted under this Plan at any time in the period commencing on the date of approval of the Plan by the Board and ending immediately prior to the tenth anniversary of the earlier of the adoption of the Plan by the Board and approval of the Plan by the Company's stockholders. Awards granted pursuant to the Plan within that period shall not expire solely by reason of the termination of the Plan. Awards of Incentive Options granted prior to stockholder approval of the Plan are expressly conditioned upon such approval, but in the event of the failure of the stockholders to approve the Plan shall thereafter and for all purposes be deemed to constitute Nonstatutory Options.

4. Stock Subject to the Plan

4.1. Plan Share Limitations.

(a) Limitation. At no time shall the number of shares of Stock issued pursuant to or subject to outstanding Awards granted under the Plan (including pursuant to Incentive Options), nor the number of shares of Stock issued pursuant to Incentive Options, exceed 704,000 shares of Stock provided, however, that beginning on January 1, 2015, the number of shares of Stock authorized under this Section 4.1(a) of the Plan will be increased each January 1 by an amount equal to four percent (4%) of outstanding Stock as of the end of the immediately preceding fiscal year. Notwithstanding the foregoing, the Board may act prior to January 1 of a given year to provide that there will be no such January 1 increase in the number of shares of Stock authorized under this Section 4.1(a) of the Plan for such year or that the increase in the number of shares of

Stock authorized under this Section 4.1(a) of the Plan for such year will be a lesser number than would otherwise occur pursuant to the preceding sentence. Notwithstanding the preceding sentences, in no event shall the number of shares available for issuance pursuant to Incentive Options exceed 14,080,000 shares of Stock.

(b) Application. For purposes of applying the foregoing limitation of Section 4.1(a), (i) if any Option or Stock Appreciation Right expires, terminates, or is cancelled for any reason without having been exercised in full, or if any other Award is forfeited, the shares of Stock not purchased by the holder or which are forfeited, as the case may be, shall again be available for Awards to be granted under the Plan, (ii) if any Option is exercised by delivering previously owned shares of Stock in payment of the exercise price therefor, only the net number of shares, that is, the number of shares of Stock issued minus the number received by the Company in payment of the exercise price, shall be considered to have been issued pursuant to an Award granted under the Plan, and (iii) any shares of Stock either delivered to or withheld by the Company in satisfaction of tax withholding obligations of the Company or an Affiliate with respect to an Award shall again be available for Awards to be granted under the Plan. In addition, settlement of any Award shall not count against the foregoing limitations except to the extent settled in the form of Stock. Shares of Stock issued pursuant to the Plan may be either authorized but unissued shares or shares held by the Company in its treasury.

4.2. Per Person Limitations. The maximum number of shares of Stock that may be subject to Options or Stock Appreciation Rights or any combination thereof granted to any one Participant during any single calendar year shall be 1,408,000. The maximum number of shares of Stock that may be subject to all other Awards or any combination thereof granted to any one Participant during any single calendar year that are intended to be Qualified Performance-Based Awards shall be 1,408,000. The maximum value of awards denominated in cash granted to any one person during any single calendar year and that are intended to be Qualified Performance-Based Awards shall be $30,000,0000**.** Each of the foregoing limitations shall be doubled with respect to awards granted to an individual during the first calendar year in which he or she commences employment. The per Participant limits described in this Section 4.2 shall be construed and applied consistent with Section 162(m) of the Code.

4.3. Adjustment of Limitations. Each of the share limitations of this Section 4 shall be subject to adjustment pursuant to Section 8 of the Plan, but in the case of the limitations of Section 4.2, only if and to the extent consistent with Section 162(m) of the Code.

5. Administration

The Plan shall be administered by the Committee; *provided, however*, that at any time and on any one or more occasions the Board may itself exercise any of the powers and responsibilities assigned the Committee under the Plan and when so acting shall have the benefit of all of the provisions of the Plan pertaining to the Committee's exercise of its authorities hereunder; and *provided further, however,* that the Committee may delegate to an executive officer or officers the authority to grant Awards hereunder to employees who are not officers, and to consultants, up to such maximum number and in accordance with such other guidelines as the Committee shall specify by resolution at any time or from time to time. Any such delegation may not include the authority to grant Restricted Stock, unless the delegate is a committee of the Board, including a committee consisting solely of an executive officer who is a Board member. Subject to the provisions of the Plan, the Committee shall have complete authority, in its discretion, to make or to select the manner of making all determinations with respect to each

Award to be granted by the Company under the Plan including the officer, employee, consultant, advisor or director to receive the Award and the form of Award. In making such determinations, the Committee may take into account the nature of the services rendered by the respective officers, employees, consultants, advisors and directors, their present and potential contributions to the success of the Company and its Affiliates, and such other factors as the Committee in its discretion shall deem relevant. Subject to the provisions of the Plan, the Committee shall also have complete authority to interpret the Plan, to prescribe, amend and rescind rules and regulations relating to it, to determine the terms and provisions of the respective Award Agreements (which need not be identical), and to make all other determinations necessary or advisable for the administration of the Plan. The Committee's determinations made in good faith on matters referred to in the Plan shall be final, binding and conclusive on all participants, beneficiaries, heirs, assigns or other persons having or claiming any interest under the Plan or an Award made pursuant hereto.

6. Authorization of Grants

6.1. Eligibility. The Committee may grant from time to time and at any time prior to the termination of the Plan one or more Awards, either alone or in combination with any other Awards, to any officer or employee of or consultant or advisor to one or more of the Company and its Affiliates or to any non-employee member of the Board or of any board of directors (or similar governing authority) of any Affiliate. However, only employees of the Company, and of any parent or subsidiary corporations of the Company, as defined in Sections 424(e) and (f), respectively, of the Code, shall be eligible for the grant of an Incentive Option.

6.2. General Terms of Awards. Each grant of an Award shall be subject to all applicable terms and conditions of the Plan (including but not limited to any specific terms and conditions applicable to that type of Award set out in the following Section), and such other terms and conditions, not inconsistent with the terms of the Plan, as the Committee may prescribe. No prospective Participant shall have any rights with respect to an Award, unless and until such Participant shall have complied with the applicable terms and conditions of such Award (including if applicable delivering a fully executed copy of any agreement evidencing an Award to the Company).

6.3. Effect of Termination of Employment, Etc. Unless the Committee shall provide otherwise with respect to any Award (including, but not limited to, in a Participant's Award Agreement), if the Participant's employment or other association with the Company and its Affiliates ends for any reason, including because of the Participant's employer ceasing to be an Affiliate, (a) any outstanding Option or Stock Appreciation Right of the Participant shall cease to be exercisable in any respect not later than ninety (90) days following that event and, for the period it remains exercisable following that event, shall be exercisable only to the extent exercisable at the date of that event, and (b) any other outstanding Award of the Participant to the extent that it is then still subject to Risk of Forfeiture shall be forfeited or otherwise subject to return to or repurchase by the Company on the terms specified in the applicable Award Agreement. Cessation of the performance of services in one capacity, for example, as an employee, shall not result in termination of an Award while the Participant continues to perform services in another capacity, for example as a director. Military or sick leave or other bona fide leave shall not be deemed a termination of employment or other association, *provided* that it does not exceed the longer of ninety (90) days or the period during which the absent Participant's reemployment rights, if any, are guaranteed by statute or by contract. To the extent consistent with applicable law, the Committee may provide that Awards continue to vest for some or all of

the period of any such leave, or that their vesting shall be tolled during any such leave and only recommence upon the Participant's return from leave, if ever.

6.4. Non-Transferability of Awards. Except as otherwise provided in this Section 6.4, Awards shall not be transferable, and no Award or interest therein may be sold, transferred, pledged, assigned, or otherwise alienated or hypothecated, other than by will or by the laws of descent and distribution. The provisions of the immediately preceding sentence shall not be applicable to Stock Grants which shall not be subject to any transfer restrictions under this Section 6.4. All of a Participant's rights in any Award may be exercised during the life of the Participant only by the Participant or the Participant's legal representative. However, the Committee may, at or after the grant of an Award of a Nonstatutory Option, or shares of Restricted Stock, provide that such Award may be transferred by the recipient to a family member; *provided*, *however*, that any such transfer is without payment of any consideration whatsoever and that no transfer shall be valid unless first approved by the Committee, acting in its sole discretion. For this purpose, "family member" means any child, stepchild, grandchild, parent, grandparent, stepparent, spouse, former spouse, sibling, niece, nephew, mother-in-law, father-in-law, son-in-law, daughter-in-law, brother-in-law, or sister-in-law, including adoptive relationships, any person sharing the employee's household (other than a tenant or employee), a trust in which the foregoing persons have more than fifty (50) percent of the beneficial interests, a foundation in which the foregoing persons (or the Participant) control the management of assets, and any other entity in which these persons (or the Participant) own more than fifty (50) percent of the voting interests.

7. Specific Terms of Awards

7.1. Options.

(a) Date of Grant. The granting of an Option shall take place at the time specified in the Award Agreement.

(b) Exercise Price. The price at which shares of Stock may be acquired under each Incentive Option shall be not less than 100% of the Market Value of Stock on the Grant Date, or not less than 110% of the Market Value of Stock on the Grant Date if the Optionee is a Ten Percent Owner. The price at which shares of Stock may be acquired under each Nonstatutory Option shall not be so limited solely by reason of this Section.

(c) Option Period. No Incentive Option may be exercised on or after the tenth anniversary of the Grant Date, or on or after the fifth anniversary of the Grant Date if the Optionee is a Ten Percent Owner. The Option period under each Nonstatutory Option shall not be so limited solely by reason of this Section.

(d) Exercisability. An Option may be immediately exercisable or become exercisable in such installments, cumulative or non-cumulative, as the Committee may determine. In the case of an Option not otherwise immediately exercisable in full, the Committee may Accelerate such Option in whole or in part at any time; *provided*, *however*, that in the case of an Incentive Option, any such Acceleration of the Option would not cause the Option to fail to comply with the provisions of Section 422 of the Code or the Optionee consents to the Acceleration.

(e) Method of Exercise. An Option may be exercised by the Optionee giving written notice, in the manner provided in Section 17, specifying the number of shares of Stock with respect to which the Option is then being exercised. The notice shall be accompanied by payment in the form of cash or check payable to the order of the Company in an amount equal to the exercise price of the shares of Stock to be purchased or, subject in each instance to the Committee's approval, acting in its sole discretion, and to such conditions, if any, as the Committee may deem necessary to avoid adverse accounting effects to the Company,

(i) by delivery to the Company of shares of Stock having a Market Value equal to the exercise price of the shares to be purchased, or

(ii) by surrender of the Option as to all or part of the shares of Stock for which the Option is then exercisable in exchange for shares of Stock having an aggregate Market Value equal to the difference between (*1*) the aggregate Market Value of the surrendered portion of the Option, and (*2*) the aggregate exercise price under the Option for the surrendered portion of the Option, or

(iii) unless prohibited by applicable law, by delivery to the Company of the Optionee's executed promissory note in the principal amount equal to the exercise price of the shares of Stock to be purchased and otherwise in such form as the Committee shall have approved.

If the Stock is traded on an established market, payment of any exercise price may also be made through and under the terms and conditions of any formal cashless exercise program authorized by the Company entailing the sale of the Stock subject to an Option in a brokered transaction (other than to the Company). Receipt by the Company of such notice and payment in any authorized or combination of authorized means shall constitute the exercise of the Option. Within thirty (30) days thereafter but subject to the remaining provisions of the Plan, the Company shall deliver or cause to be delivered to the Optionee or his agent a certificate or certificates or shall cause the Stock to be held in book-entry position through the direct registration system of the Company's transfer agent for the number of shares then being purchased. Such shares of Stock shall be fully paid and nonassessable.

(f) Limit on Incentive Option Characterization. An Incentive Option shall be considered to be an Incentive Option only to the extent that the number of shares of Stock for which the Option first becomes exercisable in a calendar year do not have an aggregate Market Value (as of the date of the grant of the Option) in excess of the

"current limit". The current limit for any Optionee for any calendar year shall be $100,000 *minus* the aggregate Market Value at the date of grant of the number of shares of Stock available for purchase for the first time in the same year under each other Incentive Option previously granted to the Optionee under the Plan, and under each other incentive stock option previously granted to the Optionee under any other incentive stock option plan of the Company and its Affiliates, after December 31, 1986. Any shares of Stock which would cause the foregoing limit to be violated shall be deemed to have been granted under a separate Nonstatutory Option, otherwise identical in its terms to those of the Incentive Option.

(g) Notification of Disposition. Each person exercising any Incentive Option granted under the Plan shall be deemed to have covenanted with the Company to report to the Company any disposition of the shares of Stock issued upon such exercise prior to the

expiration of the holding periods specified by Section 422(a)(1) of the Code and, if and to the extent that the realization of income in such a disposition imposes upon the Company federal, state, local or other withholding tax requirements, or any such withholding is required to secure for the Company an otherwise available tax deduction, to remit to the Company an amount in cash sufficient to satisfy those requirements.

7.2. Stock Appreciation Rights.

(a) Tandem or Stand-Alone. Stock Appreciation Rights may be granted in tandem with an Option (at or, in the case of a Nonstatutory Option, after, the award of the Option), or alone and unrelated to an Option. Stock Appreciation Rights in tandem with an Option shall terminate to the extent that the related Option is exercised, and the related Option shall terminate to the extent that the tandem Stock Appreciation Rights are exercised.

(b) Exercise Price. Stock Appreciation Rights shall have an exercise price of not less than one hundred percent (100%) of the Market Value of the Stock on the date of award, or in the case of Stock Appreciation Rights in tandem with Options, the exercise price of the related Option.

(c) Other Terms. Except as the Committee may deem inappropriate or inapplicable in the circumstances, Stock Appreciation Rights shall be subject to terms and conditions substantially similar to those applicable to a Nonstatutory Option. In addition, a Stock Appreciation Right related to an Option which can only be exercised during limited periods following a Change of Control may entitle the Participant to receive an amount based upon the highest price paid or offered for Stock in any transaction relating to the Change of Control or paid during the thirty (30) day period immediately preceding the occurrence of the Change of Control in any transaction reported in the stock market in which the Stock is normally traded.

7.3. Restricted Stock.

(a) Purchase Price. Shares of Restricted Stock shall be issued under the Plan for such consideration, if any, in cash, other property or services, or any combination thereof, as is determined by the Committee.

(b) Issuance of Stock. Each Participant receiving a Restricted Stock Award, subject to subsection (c) below, shall be issued a stock certificate in respect of such shares of Restricted Stock or the shares shall be held in book-entry position through the direct registration system of the Company's transfer agent. If a certificate is issued, such certificate shall be registered in the name of such Participant, and, if applicable, shall bear an appropriate legend referring to the terms, conditions, and restrictions applicable to such Award substantially in the following form:

> The shares evidenced by this certificate are subject to the terms and conditions of Proteon Therapeutics, Inc.'s 2014 Equity Incentive Plan and an Award Agreement entered into by the registered owner and Proteon Therapeutics, Inc., copies of which will be furnished by the Company to the holder of the shares evidenced by this certificate upon written request and without charge.

If the Stock is in book-entry position through the direct registration system of the Company's transfer agent, the restrictions will be appropriately noted.

(c) Escrow of Shares. The Committee may require that any stock certificates evidencing shares of Restricted Stock be held in custody by a designated escrow agent (which may but need not be the Company) until the restrictions thereon shall have lapsed, and that the Participant deliver a stock power, endorsed in blank, relating to the Stock covered by such Award.

(d) Restrictions and Restriction Period. During the Restriction Period applicable to shares of Restricted Stock, such shares shall be subject to limitations on transferability and a Risk of Forfeiture arising on the basis of such conditions related to the performance of services, Company or Affiliate performance or otherwise as the Committee may determine and provide for in the applicable Award Agreement. Any such Risk of Forfeiture may be waived or terminated, or the Restriction Period shortened, at any time by the Committee on such basis as it deems appropriate.

(e) Rights Pending Lapse of Risk of Forfeiture or Forfeiture of Award. Except as otherwise provided in the Plan or the applicable Award Agreement, the Participant shall have all of the rights of a stockholder of the Company with respect to any outstanding shares of Restricted Stock, including the right to vote, and the right to receive any dividends with respect to, the shares of Restricted Stock (but any dividends or other distributions payable in shares of Stock or other securities of the Company shall constitute additional Restricted Stock, subject to the same Risk of Forfeiture as the shares of Restricted Stock in respect of which such shares of Stock or other securities are paid). The Committee, as determined at the time of Award, may permit or require the payment of cash dividends to be deferred and, if the Committee so determines, reinvested in additional Restricted Stock to the extent shares of Stock are available under Section 4.

(f) Lapse of Restrictions. If and when the Restriction Period expires without a prior forfeiture, any certificates for such shares shall be delivered to the Participant promptly if not theretofore so delivered.

7.4. Restricted Stock Units.

(a) Character. Each Restricted Stock Unit shall entitle the recipient to a share of Stock at a close of such Restriction Period as the Committee may establish and subject to a Risk of Forfeiture arising on the basis of such conditions relating to the performance of services, Company or Affiliate performance or otherwise as the Committee may determine and provide for in the applicable Award Agreement. Any such Risk of Forfeiture may be waived or terminated, or the Restriction Period shortened, at any time by the Committee on such basis as it deems appropriate.

(b) Form and Timing of Payment. Payment of earned Restricted Stock Units shall be made promptly following the close of the applicable Restriction Period. At the discretion of the Committee, Participants may be entitled to receive payments equivalent to any dividends declared with respect to Stock referenced in grants of Restricted Stock Units but only following the close of the applicable Restriction Period and then only if the underlying Stock shall have been earned. Unless the Committee shall provide otherwise, any such dividend equivalents shall be paid, if at all, without interest or other earnings.

7.5. Performance Units.

(a) Character. Each Performance Unit shall entitle the recipient to the value of a specified number of shares of Stock, over the initial value for such number of shares, if any, established by the Committee at the time of grant, at the close of a specified Performance Period to the extent specified business objectives, including but not limited to Performance Goals, shall have been achieved.

(b) Earning of Performance Units. The Committee shall set Performance Goals or other business objectives in its discretion which, depending on the extent to which they are met within the applicable Performance Period, will determine the number and value of Performance Units that will be paid out to the Participant. After the applicable Performance Period has ended, the holder of Performance Units shall be entitled to receive payout on the number and value of Performance Units earned by the Participant over the Performance Period, to be determined as a function of the extent to which the corresponding Performance Goals or other business objectives have been achieved.

(c) Form and Timing of Payment. Payment of earned Performance Units shall be made in a single lump sum following the close of the applicable Performance Period. At the discretion of the Committee, Participants may be entitled to receive any dividends declared with respect to Stock which have been earned in connection with grants of Performance Units which have been earned, but not yet distributed to Participants. The Committee may permit or, if it so provides at grant require, a Participant to defer such Participant's receipt of the payment of cash or the delivery of Stock that would otherwise be due to such Participant by virtue of the satisfaction of any requirements or goals with respect to Performance Units. If any such deferral election is required or permitted, the Committee shall establish rules and procedures for such payment deferrals.

7.6. Stock Grants. Stock Grants shall be awarded solely in recognition of significant prior or expected contributions to the success of the Company or its Affiliates, as an inducement to employment, in lieu of compensation otherwise already due and in such other limited circumstances as the Committee deems appropriate. Stock Grants shall be made without forfeiture conditions of any kind.

7.7. Qualified Performance-Based Awards.

(a) Purpose. The purpose of this Section 7.7 is to provide the Committee the ability to qualify Awards as "performance-based compensation" under Section 162(m) of the Code. If the Committee, in its discretion, decides to grant an Award as a Qualified Performance-Based Award, the provisions of this Section 7.7 will control over any contrary provision contained in the Plan. In the course of granting any Award, the Committee may specifically designate the Award as intended to qualify as a Qualified Performance-Based Award. However, no Award shall be considered to have failed to qualify as a Qualified Performance-Based Award solely because the Award is not expressly designated as a Qualified Performance-Based Award, if the Award otherwise satisfies the provisions of this Section 7.7 and the requirements of Section 162(m) of the Code applicable to "performance-based compensation."

(b) Authority. All grants of Awards intended to qualify as Qualified Performance-Based Awards and the determination of the terms applicable thereto shall be made by the Committee. If not all of the members thereof qualify as "outside directors" within the meaning of Section 162 of the Code, however, all grants of Awards intended to qualify as Qualified Performance-Based Awards and the determination of the terms applicable thereto shall

be made by a subcommittee of the Committee consisting of such of the members of the Committee as do so qualify. Any reference in this Section 7.7 to the Committee shall mean any such subcommittee if required under the preceding sentence, and any action by such a subcommittee shall be considered the action of the Committee for purposes of the Plan.

(c) Discretion of Committee with Respect to Qualified Performance-Based Awards. Any form of Award permitted under the Plan, other than a Stock Grant, may be granted as a Qualified Performance-Based Award. Options and Stock Appreciation Rights may be granted as Qualified Performance-Based Awards in accordance with Section 7.1 and 7.2, respectively, except that the exercise price of any Option or Stock Appreciation Right intended to qualify as a Qualified Performance-Based Award shall in no event be less that the Market Value of the Stock on the date of grant, and may become exercisable based on continued service, on satisfaction of Performance Goals or other business objectives, or on a combination thereof. Each other Award intended to qualify as a Qualified Performance-Based Award, such as Restricted Stock, Restricted Stock Units, or Performance Units, shall be subject to satisfaction of one or more Performance Goals except as otherwise provided in this Section 7.7. The Committee will have full discretion to select the length of any applicable Restriction Period or Performance Period, the kind and/or level of the applicable Performance Goal, and whether the Performance Goal is to apply to the Company, a subsidiary of the Company or any division or business unit or to the individual. Any Performance Goal or Goals applicable to Qualified Performance-Based Awards shall be objective, shall be established not later than ninety (90) days after the beginning of any applicable Performance Period (or at such other date as may be required or permitted for "performance-based compensation" under Section 162(m) of the Code) and shall otherwise meet the requirements of Section 162(m) of the Code, including the requirement that the outcome of the Performance Goal or Goals be substantially uncertain (as defined for purposes of Section 162(m) of the Code) at the time established.

(d) Payment of Qualified Performance-Based Awards. A Participant will be eligible to receive payment under a Qualified Performance-Based Award which is subject to achievement of a Performance Goal or Goals only if the applicable Performance Goal or Goals are achieved within the applicable Performance Period, as determined by the Committee, *provided*, that a Qualified Performance-Based Award may be deemed earned as a result of death, becoming disabled, or in connection with a change of control (within the meaning of Section 162(m) of the Code) if otherwise provided in the Plan or the applicable Award Agreement even if the Award would not constitute "performance-based compensation" under Section 162(m) of the Code following the occurrence of such an event. In determining the actual size of an individual Qualified Performance-Based Award, the Committee may reduce or eliminate the amount of the Qualified Performance-Based Award earned for the Performance Period, if in its sole and absolute discretion, such reduction or elimination is appropriate.

(e) Limitation on Adjustments for Certain Events. No adjustment of any Qualified Performance-Based Award pursuant to Section 8 shall be made except on such basis, if any, as will not cause such Award to provide other than "performance-based compensation" within the meaning of Section 162(m) of the Code.

(f) Definitions. For purposes of the Plan

(i) Performance Criteria means the criteria that the Committee selects for purposes of establishing the Performance Goal or Performance Goals for a Participant for a Performance Period. The Performance

Criteria used to establish Performance Goals are limited to: (i) net earnings (either before or after one or more of (A) interest, (B) taxes, (C) depreciation and (D) amortization), (ii) gross or net sales or revenue, (iii) net income (either before or after taxes), (iv) adjusted net income, (v) operating earnings or profit, (vi) cash flow (including, but not limited to, operating cash flow and free cash flow, (vii) return on assets, (viii) return on capital, (ix) return on stockholders' equity, (x) total stockholder return, (xi) return on sales, (xii) gross or net profit or operating margin, (xiii) costs, (xiv) expenses, (xv) working capital, (xvi) earnings per share, (xvii) adjusted earnings per share, (xviii) price per share, (xix) regulatory body approval for commercialization of a product, (xx) implementation, completion or attainment of objectives relating to research, development, regulatory, commercial, or strategic milestones or developments; (xxi) market share, (xxii) economic value, (xxiii) revenue, (xxiv) revenue growth and (xxv) operational and organizational metrics.

(ii) Performance Goals means, for a Performance Period, the written goal or goals established by the Committee for the Performance Period based upon one or more of the Performance Criteria. The Performance Goals may be expressed in terms of overall Company performance or the performance of a division, business unit, subsidiary, or an individual, either individually, alternatively or in any combination, applied to either the Company as a whole or to a business unit or Affiliate, either individually, alternatively or in any combination, and measured either quarterly, annually or cumulatively over a period of years, on an absolute basis or relative to a pre-established target, to previous years' results or to a designated comparison group, in each case as specified by the Committee. The Committee will objectively define the manner of calculating the Performance Goal or Goals it selects to use for such Performance Period for such Participant, including whether or to what extent there shall not be taken into account any of the following events that occurs during a Performance Period: (i) asset write-downs, (ii) litigation, claims, judgments or settlements, (iii) the effect of changes in tax law, accounting principles or other such laws or provisions affecting reported results, (iv) accruals for reorganization and restructuring programs and (v) any extraordinary, unusual, non-recurring or non-comparable items (A) as described in Accounting Standard Codification Section 225-20, (B) as described in management's discussion and analysis of financial condition and results of operations appearing in the Company's Annual Report to stockholders for the applicable year, or (C) publicly announced by the Company in a press release or conference call relating to the Company's results of operations or financial condition for a completed quarterly or annual fiscal period.

7.8. Awards to Participants Outside the United States. The Committee may modify the terms of any Award under the Plan granted to a Participant who is, at the time of grant or during the term of the Award, resident or primarily employed outside of the United States in any manner deemed by the Committee to be necessary or appropriate in order that the Award shall conform to laws, regulations, procedures, and customs of the country in which the Participant is then resident or primarily employed, or so that the value and other benefits of the Award to the Participant, as affected by foreign tax laws and other restrictions applicable as a result of the Participant's residence or employment abroad, shall be as comparable as practicable to the value of such an Award to a Participant who is resident or primarily employed in the United States.

The Committee may establish supplements or sub-plans to, or amendments, restatements, or alternative versions of, the Plan for the purpose of granting and administrating any such modified Award. No such modification, supplement, sub-plan, amendment, restatement or alternative version may increase the share limit of Section 4.

8. Adjustment Provisions

8.1. Adjustment for Corporate Actions. All of the share numbers set forth in the Plan reflect the capital structure of the Company as of October __, 2014. If subsequent to that date the outstanding shares of Stock (or any other securities covered by the Plan by reason of the prior application of this Section) are increased, decreased, or exchanged for a different number or kind of shares or other securities, or if additional shares or new or different shares or other securities are distributed with respect to shares of Stock, as a result of a reorganization, recapitalization, reclassification, stock dividend, stock split, reverse stock split, or other similar distribution with respect to such shares of Stock, an appropriate and proportionate adjustment will be made in (i) the maximum numbers and kinds of shares provided in Section 4, (ii) the numbers and kinds of shares or other securities subject to the then outstanding Awards, (iii) the exercise price for each share or other unit of any other securities subject to then outstanding Options and Stock Appreciation Rights (without change in the aggregate purchase price as to which such Options or Rights 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.

8.2. Adjustment of Awards Upon the Occurrence of Certain Unusual or Nonrecurring Events. In the event of any corporate action not specifically covered by the preceding Section, including but not limited to an extraordinary cash distribution on Stock, a corporate separation or other reorganization or liquidation, the Committee may make such adjustment of outstanding Awards and their terms, if any, as it, in its sole discretion, may deem equitable and appropriate in the circumstances. The Committee may make adjustments in the terms and conditions of, and the criteria included in, Awards in recognition of unusual or nonrecurring events (including, without limitation, the events described in this Section) affecting the Company or the financial statements of the Company or of changes in applicable laws, regulations, or accounting principles, whenever the Committee determines that such adjustments are appropriate in order to prevent dilution or enlargement of the benefits or potential benefits intended to be made available under the Plan.

8.3. Related Matters. Any adjustment in Awards made pursuant to Section 8.1 or 8.2 shall be determined and made, if at all, by the Committee, acting in its sole discretion, and shall include any correlative modification of terms, including of Option exercise prices, rates of vesting or exercisability, Risks of Forfeiture, applicable repurchase prices for Restricted Stock, and Performance Goals and other business objectives which the Committee may deem necessary or appropriate so as to ensure the rights of the Participants in their respective Awards are not substantially diminished nor enlarged as a result of the adjustment and corporate action other than as expressly contemplated in this Section 8. The Committee, in its discretion, may determine that no fraction of a share of Stock shall be purchasable or deliverable upon exercise, and in that event if any adjustment hereunder of the number of shares of Stock covered by an Award would cause such number to include a fraction of a share of Stock, such number of shares of Stock shall be adjusted to the nearest smaller whole number of shares. No adjustment of an Option exercise price per share pursuant to Sections 8.1 or 8.2 shall result in an exercise price which is less than the par value of the Stock.

8.4. Transactions.

(a) Definition of Transaction. In this Section 8.4, "Transaction" means (1) any merger or consolidation of the Company with or into another entity as a result of which the Stock of the Company is converted into or exchanged for the right to receive cash, securities or other property or is cancelled, (2) any sale or exchange of all or substantially all of the outstanding Stock of the Company for cash, securities or other property, (3) any sale, transfer, or other disposition of all or substantially all of the Company's assets to one or more other persons in a single transaction or series of related transactions or (4) any liquidation or dissolution of the Company.

(b) Treatment of Awards. In a Transaction, the Committee may take any one or more of the following actions as to all or any (or any portion of) outstanding Awards, subject to the provisions of Section 9 of this Plan.

(1) Provide that any Awards shall be assumed, or substantially equivalent rights shall be provided in substitution therefor, by the acquiring or succeeding entity (or an affiliate thereof).

(2) Upon written notice to the holders, provide that all or any of the holders' unexercised outstanding Options and Stock Appreciation Rights (collectively, "Rights") will terminate immediately prior to the consummation of such Transaction unless exercised within a specified period following the date of such notice.

(3) Provide that all or any Awards that are subject to Risk of Forfeiture will terminate immediately prior to the consummation of such Transaction.

(4) Provide that all or any outstanding Rights shall Accelerate so as to become exercisable prior to or upon such Transaction with respect to some or all of the shares of Stock for which any such Rights would not then otherwise be exercisable by their terms.

(5) Provide that outstanding all or any Awards that are subject to Risk of Forfeiture shall Accelerate so that the Risk of Forfeiture otherwise applicable to such Awards shall expire prior to or upon such Transaction with respect to any such Awards that would then still otherwise be subject to the Risk of Forfeiture.

(6) Provide for cash payments, net of applicable tax withholdings, to be made to holders equal to the excess, if any, of (A) the acquisition price times the number of shares of Stock subject to an Option (to the extent the exercise price does not exceed the acquisition price) over (B) the aggregate exercise price for all such shares of Stock subject to the Option, in exchange for the termination of such Option; provided, that if the acquisition price does not exceed the exercise price of any such Option, the Committee may cancel that Option without the payment of any consideration therefore prior to or upon the Transaction. For purposes of this paragraph 6 and paragraph 7 below, "acquisition price" means the amount of cash, and market value of any other consideration, received in payment for a share of Stock surrendered in a

Transaction but need not take into account any deferred consideration unless and until received.

(7) Provide for cash payments, net of applicable tax withholdings, to be made to holder or holders of all or any Awards (other than Options) equal to the acquisition price times the number of shares of Stock subject to any such Awards, in exchange for the termination of any such Awards; provided, that the Committee may cancel, pursuant to paragraph 3 above, any such Award that is subject to a Risk of Forfeiture at the time of the consummation of such Transaction without the payment of any consideration therefor prior to or upon the Transaction.

(8) Provide that, in connection with a liquidation or dissolution of the Company, all or any Awards (other than Restricted Stock or Stock Grants) shall convert into the right to receive liquidation proceeds net of the exercise price thereof and any applicable tax withholdings.

(9) Any combination of the foregoing.

In the event that the Committee determines in its discretion to take the actions contemplated under paragraph (1) above of this Section 8.4(b) with respect to all or any Awards, the Committee shall ensure that, upon consummation of the Transaction, any such Awards are assumed and/or exchanged or replaced with another similar award issued by the acquiring or succeeding entity (or an affiliate thereof) and that, as a result of such assumption and/or exchange or replacement, the holder of such assumed Award and/or such exchanged or replaced similar award has the right to purchase or receive the value of, for each share of Stock subject to such Award immediately prior to the consummation of the Transaction, the consideration (whether cash, securities or other property) received as a result of the Transaction by holders of Stock for each share of Stock held immediately prior to the consummation of the Transaction (and if holders were offered a choice of consideration, the type of consideration chosen by the holders of a majority of the outstanding shares of Stock); *provided*, *however*, that if such consideration received as a result of the Transaction is not solely common stock (or its equivalent) of the acquiring or succeeding entity (or an affiliate thereof), the Committee may, with the consent of the acquiring or succeeding entity (or an affiliate thereof), provide for the consideration to be received with respect to such assumed Award and/or such exchanged or replaced similar award to consist of or be based solely on common stock (or its equivalent) of the acquiring or succeeding entity (or an affiliate thereof) equivalent in value to the per share consideration received by holders of outstanding shares of Stock as a result of the Transaction; and *provided*, *further*, that if such Award is an Option, the holder of such Option must exercise the Option and make payment of the applicable exercise price in connection therewith in order to receive such consideration.

(c) Treatment of Other Awards. Upon the occurrence of a Transaction other than a liquidation or dissolution of the Company which is not part of another form of Transaction, then, subject to the provisions of Section 9 below, with respect to all outstanding Awards (other than Options and Share Appreciation Rights) that are not terminated prior to or upon such Transaction, the repurchase and other rights of the Company under each such Award shall inure to the benefit of the Company's successor and shall, unless the Committee determines otherwise, apply to the cash, securities or other property which the Stock was converted into or exchanged for pursuant to such Transaction in the same manner and to the same extent as they applied to the Award.

(d) Related Matters. In taking any of the actions permitted under this Section 8.4, the Committee shall not be obligated to treat all Awards, all Awards held by a Participant, or all Awards of the same type, identically. Any determinations required to carry out the foregoing provisions of this Section 8.4, including but not limited to the market value of other consideration received by holders of Stock in a Transaction and whether substantially equivalent Rights have been substituted, shall be made by the Committee acting in its sole discretion. In connection with any action or actions taken by the Committee in respect of Awards and in connection with a Transaction, the Committee may require such acknowledgements of satisfaction and releases from Participants as it may determine.

9. Change of Control

Except as otherwise provided below, upon the occurrence of a Change of Control, to the extent that the surviving entity declines to continue, convert, assume or replace outstanding Awards, then, notwithstanding anything express or implied to the contrary in Section 8.4 above:

(a) any and all Options and Stock Appreciation Rights not already exercisable in full shall Accelerate with respect to 100% of the shares for which such Options or Stock Appreciation Rights are not then exercisable;

(b) any Risk of Forfeiture applicable to Restricted Stock and Restricted Stock Units which is not based on achievement of Performance Goals or other business objectives shall lapse with respect to 100% of the Restricted Stock and Restricted Stock Units still subject to such Risk of Forfeiture immediately prior to the Change of Control; and

(c) all outstanding Awards of Restricted Stock and Restricted Stock Units conditioned on the achievement of Performance Goals or other business objectives and the payouts attainable under outstanding Performance Units shall be deemed to have been satisfied as of the effective date of the Change of Control, except if and to the extent otherwise determined by the Committee in its sole discretion at any time prior to, or upon, such Change of Control.

All such Awards of Performance Units and Restricted Stock Units shall be paid to the extent earned to Participants in accordance with their terms within thirty (30) days following the effective date of the Change of Control. None of the foregoing shall apply, however, (i) in the case of any Award pursuant to an Award Agreement requiring other or additional terms upon a Change of Control (or similar event), (ii) if specifically prohibited under applicable laws, or by the rules and regulations of any governing governmental agencies or national securities exchanges, or (iii) as otherwise provided in Section 7.7, concerning Qualified Performance-Based Awards.

10. Settlement of Awards

10.1. In General. Options and Restricted Stock shall be settled in accordance with their terms. All other Awards may be settled in cash, Stock, or other Awards, or a combination thereof, as determined by the Committee at or after grant and subject to any contrary Award Agreement. The Committee may not require settlement of any Award in Stock pursuant to the immediately preceding sentence to the extent issuance of such Stock would be prohibited or unreasonably delayed by reason of any other provision of the Plan.

10.2. Violation of Law. Notwithstanding any other provision of the Plan or the relevant Award Agreement, if, at any time, in the reasonable opinion of the Company, the issuance of shares of Stock covered by an Award may constitute a violation of law, then the Company may delay such issuance until (i) approval shall have been obtained from such governmental agencies, other than the Securities and Exchange Commission, as may be required under any applicable law, rule, or regulation and (ii) in the case where such issuance would constitute a violation of a law administered by or a regulation of the Securities and Exchange Commission, one of the following conditions shall have been satisfied:

(a) the shares of Stock are at the time of the issue of such shares effectively registered under the Securities Act of 1933, as amended; or

(b) the Company shall have determined, on such basis as it deems appropriate (including an opinion of counsel in form and substance satisfactory to the Company) that the sale, transfer, assignment, pledge, encumbrance or other disposition of such shares does not require registration under the Securities Act of 1933, as amended or any applicable State securities laws.

Furthermore, the inability of the Company to obtain or maintain, or the impracticability of it obtaining or maintaining, authority from any governmental agency having jurisdiction, which authority is deemed by the Company's counsel to be necessary to the lawful issuance of any Stock hereunder, shall relieve the Company of any liability in respect of the failure to issue such Stock as to which such requisite authority shall not have been obtained, and shall constitute circumstances in which the Committee may determine to amend or cancel Awards pertaining to such Stock, with or without consideration to the affected Participants.

10.3. Corporate Restrictions on Rights in Stock. Any Stock to be issued pursuant to Awards granted under the Plan shall be subject to all restrictions upon the transfer thereof which may be now or hereafter imposed by the charter, certificate or articles, and by-laws, of the Company. Whenever Stock is to be issued pursuant to an Award, if the Committee so directs at or after grant, the Company shall be under no obligation to issue such shares until such time, if ever, as the recipient of the Award (and any person who exercises any Option, in whole or in part), shall have become a party to and bound by the Stockholders' Agreement, if any.

10.4. Investment Representations. The Company shall be under no obligation to issue any shares of Stock covered by any Award unless the shares to be issued pursuant to Awards granted under the Plan have been effectively registered under the Securities Act of 1933, as amended, or the Participant shall have made such written representations to the Company (upon which the Company believes it may reasonably rely) as the Company may deem necessary or appropriate for purposes of confirming that the issuance of such shares will be exempt from the registration requirements of that Act and any applicable state securities laws and otherwise in compliance with all applicable laws, rules and regulations of any jurisdiction in which Participants may reside or primarily work, including but not limited to that the Participant is acquiring the shares for his or her own account for the purpose of investment and not with a view to, or for sale in connection with, the distribution of any such shares.

10.5. Registration. If the Company shall deem it necessary or desirable to register under the Securities Act of 1933, as amended, or other applicable statutes any shares of Stock issued or to be issued pursuant to Awards granted under the Plan, or to qualify any such shares of Stock for exemption from the Securities Act of 1933, as amended or other applicable statutes,

then the Company shall take such action at its own expense. The Company may require from each recipient of an Award, or each holder of shares of Stock acquired pursuant to the Plan, such information in writing for use in any registration statement, prospectus, preliminary prospectus or offering circular as is reasonably necessary for that purpose and may require reasonable indemnity to the Company and its officers and directors from that holder against all losses, claims, damage and liabilities arising from use of the information so furnished and caused by any untrue statement of any material fact therein or caused by the omission to state a material fact required to be stated therein or necessary to make the statements therein not misleading in the light of the circumstances under which they were made. In addition, the Company may require of any such person that he or she agree that, without the prior written consent of the Company or the managing underwriter in any public offering of shares of Stock, he or she will not sell, make any short sale of, loan, grant any option for the purchase of, pledge or otherwise encumber, or otherwise dispose of, any shares of Stock during the 180 day period commencing on the effective date of the registration statement relating to the underwritten public offering of securities (or during such shorter or longer period of time as the Committee shall determine in its sole discretion, which period of time shall commence from and after such effective date of such registration statement). Without limiting the generality of the foregoing provisions of this Section 10.5, if in connection with any underwritten public offering of securities of the Company the managing underwriter of such offering requires that the Company's directors and officers enter into a lock-up agreement containing provisions that are more restrictive than the provisions set forth in the preceding sentence, then (a) each holder of shares of Stock acquired pursuant to the Plan (regardless of whether such person has complied or complies with the provisions of clause (b) below) shall be bound by, and shall be deemed to have agreed to, the same lock-up terms as those to which the Company's directors and officers are required to adhere; and (b) at the request of the Company or such managing underwriter, each such person shall execute and deliver a lock-up agreement in form and substance equivalent to that which is required to be executed by the Company's directors and officers.

10.6. Placement of Legends; Stop Orders; etc. Each share of Stock to be issued pursuant to Awards granted under the Plan may bear a reference to the investment representations made in accordance with Section 10.4 in addition to any other applicable restrictions under the Plan, and the terms of the Award and under the Stockholders' Agreement and, if applicable, to the fact that no registration statement has been filed with the Securities and Exchange Commission in respect to such shares of Stock. All shares of Stock or other securities issued under the Plan shall be subject to such stop transfer orders and other restrictions as the Committee may deem advisable under the rules, regulations, and other requirements of any stock exchange upon which the Stock is then listed, and any applicable federal or state securities law, and the Committee may cause a legend or legends to be placed on any such certificates to make appropriate reference to such restrictions, or, if the Stock will be held in book-entry position through the direct registration system of the Company's transfer agent, the restrictions will be appropriately noted.

10.7. Tax Withholding. Whenever shares of Stock are issued or to be issued pursuant to Awards granted under the Plan, the Company shall have the right to require the recipient to remit to the Company an amount sufficient to satisfy federal, state, local, foreign or other withholding tax requirements if, when, and to the extent required by law (whether so required to secure for the Company an otherwise available tax deduction or otherwise) prior to the delivery of any certificate or certificates, held in book-entry position through the direct registration system of the Company's transfer agent, for such shares. The obligations of the Company under the Plan shall be conditional on satisfaction of all such withholding obligations and the Company shall, to

the extent permitted by law, have the right to deduct any such taxes from any payment of any kind otherwise due to a Participant or to utilize any other withholding method prescribed by the Committee from time to time. However, in such cases Participants may elect, subject to the approval of the Committee, acting in its sole discretion, to satisfy an applicable withholding requirement, in whole or in part, by having the Company withhold shares of Stock to satisfy their tax obligations. All elections shall be irrevocable, made in writing, signed by the Participant, and shall be subject to any restrictions or limitations that the Committee deems appropriate. If shares of Stock are withheld to satisfy an applicable withholding requirement, the shares of Stock withheld shall have a Market Value on the date the tax is to be determined equal to the minimum statutory total tax which could be imposed on the transaction, *provided, however*, if shares of Stock are withheld to satisfy a withholding requirement imposed by a country other than the United States, the amount withheld may exceed such minimum, provided that it is not in excess of the actual amount required to be withheld with respect to the Participant under applicable tax law or regulations.

10.8. Company Charter and By-Laws; Other Company Policies. This Plan and all Awards granted hereunder are subject to the charter and By-Laws of the Company, as they may be amended from time to time, and all other Company policies duly adopted by the Board, the Committee or any other committee of the Board and as in effect from time to time regarding the acquisition, ownership or sale of Stock by officers, employees, directors, consultants, advisors and other service providers, including, without limitation, policies intended to limit the potential for insider trading and to avoid or recover compensation payable or paid on the basis of inaccurate financial results or statements, employee conduct, and other similar events.

11. Reservation of Stock

The Company shall at all times during the term of the Plan and any outstanding Awards granted hereunder reserve or otherwise keep available such number of shares of Stock as will be sufficient to satisfy the requirements of the Plan (if then in effect) and the Awards and shall pay all fees and expenses necessarily incurred by the Company in connection therewith.

12. Limitation of Rights in Stock; No Special Service Rights

A Participant shall not be deemed for any purpose to be a stockholder of the Company with respect to any of the shares of Stock subject to an Award, unless and until a certificate shall have been issued therefor and delivered to the Participant or his agent, or the Stock shall be issued through the direct registration system of the Company's transfer agent. Any Stock to be issued pursuant to Awards granted under the Plan shall be subject to all restrictions upon the transfer thereof which may be now or hereafter imposed by the certificate or articles of incorporation and the by-laws of the Company. Nothing contained in the Plan or in any Award Agreement shall confer upon any recipient of an Award any right with respect to the continuation of his or her employment or other association with the Company (or any Affiliate), or interfere in any way with the right of the Company (or any Affiliate), subject to the terms of any separate employment or consulting agreement or provision of law or corporate articles or by-laws to the contrary, at any time to terminate such employment or consulting agreement or to increase or decrease, or otherwise adjust, the other terms and conditions of the recipient's employment or other association with the Company and its Affiliates.

13. Unfunded Status of Plan

The Plan is intended to constitute an "unfunded" plan for incentive compensation, and the Plan is not intended to constitute a plan subject to the provisions of the Employee Retirement Income Security Act of 1974, as amended. With respect to any payments not yet made to a Participant by the Company, nothing contained herein shall give any such Participant any rights that are greater than those of a general creditor of the Company. In its sole discretion, the Committee may authorize the creation of trusts or other arrangements to meet the obligations created under the Plan to deliver Stock or payments with respect to Awards hereunder, *provided, however*, that the existence of such trusts or other arrangements is consistent with the unfunded status of the Plan.

14. Nonexclusivity of the Plan

Neither the adoption of the Plan by the Board nor any action taken in connection with the adoption or operation of the Plan shall be construed as creating any limitations on the power of the Board to adopt such other incentive arrangements as it may deem desirable, including without limitation, the granting of stock options and restricted stock other than under the Plan, and such arrangements may be either applicable generally or only in specific cases.

15. No Guarantee of Tax Consequences

It is intended that all Awards shall be granted and maintained on a basis which ensures they are exempt from, or otherwise compliant with, the requirements of Section 409A of the Code, pertaining non-qualified plans of deferred compensation, and the Plan shall be governed, interpreted and enforced consistent with such intent. However, neither the Company nor any Affiliate, nor any director, officer, agent, representative or employee of either, guarantees to the Participant or any other person any particular tax consequences as a result of the grant of, exercise of rights under, or payment in respect of an Award, including but not limited to that an Option granted as an Incentive Option has or will qualify as an "incentive stock option" within the meaning of Section 422 of the Code or that the provisions and penalties of Section 409A of the Code will or will not apply and no person shall have any liability to a Participant or any other party if a payment under an Award that is intended to benefit from favorable tax treatment or avoid adverse tax treatment fails to realize such intention or for any action taken by the Board or the Committee with respect to the Award.

16. Termination and Amendment of the Plan

16.1. Termination or Amendment of the Plan. Subject to the limitations contained in Section 16.3 below, including specifically the requirement of stockholder approval, if applicable, the Board may at any time suspend or terminate the Plan or make such modifications of the Plan as it shall deem advisable. Unless the Board otherwise expressly provides, no amendment of the Plan shall affect the terms of any Award outstanding on the date of such amendment.

16.2. Termination or Amendment of Outstanding Awards; Assumptions. Subject to the limitations contained in Section 16.3 below, including specifically the requirement of stockholder approval, if applicable, the Committee may at any time:

(a) amend the terms of any Award theretofore granted, prospectively or retroactively, provided that the Award as amended is consistent with the terms of the Plan;

(b) within the limitations of the Plan, modify, extend or assume outstanding Awards or accept the cancellation of outstanding Awards or of outstanding stock options or other equity-based compensation awards granted by another issuer in return for the grant of new Awards for the same or a different number of shares of Stock and on the same or different terms and conditions (including but not limited to the exercise price of any Option); and

(c) offer to buy out for a payment in cash or cash equivalents an Award previously granted or authorize the recipient of an Award to elect to cash out an Award previously granted, in either case at such time and based upon such terms and conditions as the Committee shall establish.

16.3. Limitations on Amendments, Etc.

(a) Without the approval of the Company's stockholders, no amendment or modification of the Plan by the Board may (i) increase the number of shares of Stock which may be issued under the Plan, (ii) change the description of the persons eligible for Awards, or (iii) effect any other change for which stockholder approval is required by law or the rules of any relevant stock exchange.

(b) No action by the Board or the Committee pursuant to this Section 16 shall impair the rights of the recipient of any Award outstanding on the date of such amendment or modification of such Award, as the case may be, without the Participant's consent; *provided, however,* that no such consent shall be required (A) in the case of any amendment or termination of any outstanding Award that is permitted by any provision of this Plan that is set forth in Section 16.4 below, Section 8, Section 9 or in any other section of this Plan that is not Section 16.2 or (B) if the Board or Committee, as the case may be, (i) determines in its sole discretion and prior to the date of any Change of Control that such amendment or alteration either is required or advisable in order for the Company, the Plan or the Award to satisfy any law or regulation, including without limitation the provisions of Section 409A of the Code, or to meet the requirements of or avoid adverse financial accounting consequences under any accounting standard, (ii) determines in its sole discretion and prior to the date of any Change of Control that such amendment or alteration is not reasonably likely to significantly diminish the benefits provided under the Award, or that any such diminution has been adequately compensated, or (iii) reasonably determines on or after the date of Change of Control that such amendment or alteration either is required or advisable in order for the Company, the Plan or the Award to satisfy any law or regulation, including without limitation the provisions of Section 409A of the Code.

16.4 Option Repricing. Notwithstanding anything in Section 16.3 express or implied to the contrary, the Committee is expressly authorized to amend any or all outstanding Options at any time and from time to time to effect a repricing thereof by lowering the exercise price applicable to the shares of Stock subject to such Option or Options without the consent or approval of the stockholders of the Company or the holder or holders of such Option or Options, and, in connection with such repricing, to amend or modify any of the other terms of the Option or Options so repriced, including, without limitation, for purposes of reducing the number of shares subject to such Option or Options or for purposes of adversely affecting the provisions applicable to such Option or Options that relate to the vesting or exercisability thereof, in each case without the approval or consent of stockholders of the Company or the holder or holders of such Option or Options.

17. Notices and Other Communications

Any communication or notice required or permitted to be given under the Plan shall be in such form as the Committee may determine from time to time. If a notice, demand, request or other communication is required or permitted to be given in writing, then any such notice, demand, request or other communication hereunder to any party shall be deemed to be sufficient if contained in a written instrument delivered in person or duly sent by first class registered, certified or overnight mail, postage prepaid, or telecopied with a confirmation copy by regular, certified or overnight mail, addressed or telecopied, as the case may be, (i) if to the recipient of an Award, at his or her residence address last filed with the Company and (ii) if to the Company, at its principal place of business, addressed to the attention of its Treasurer, or to such other address or telecopier number, as the case may be, as the addressee may have designated by notice to the addressor. All such notices, requests, demands and other communications shall be deemed to have been received: (i) in the case of personal delivery, on the date of such delivery; (ii) in the case of mailing, when received by the addressee; and (iii) in the case of facsimile transmission, when confirmed by facsimile machine report.

18. Governing Law

The Plan and all Award Agreements and actions taken hereunder and thereunder shall be governed, interpreted and enforced in accordance with the laws of the Commonwealth of Massachusetts, without regard to the conflict of laws principles thereof.

[End of document.]

PROTEON THERAPEUTICS, INC.
2014 EQUITY INCENTIVE PLAN

STOCK OPTION AGREEMENT

THIS AGREEMENT dated as of _____ ___, 20__, between Proteon Therapeutics, Inc., a corporation organized under the laws of the State of Delaware (the "Company"), and the individual identified in paragraph 1 below, currently residing at the address set out at the end of this Agreement (the "Optionee").

1. Grant of Option. Pursuant and subject to the Company's 2014 Equity Incentive Plan (as the same may be amended from time to time, the "Plan"), the Company grants to you, the Optionee identified in the table below, an option (the "Option") to purchase from the Company all or any part of a total of the number of shares identified in the table below (the "Optioned Shares") of the common stock, par value $0.001 per share, in the Company (the "Stock"), at the exercise price per share set out in the table below.

Optionee	_____
Number of Shares	_____
Exercise Price Per Share	_____
Grant Date	_____
Expiration Date(1)	_____

2. Character of Option. This Option [*is/is not*](2) intended to be treated as an "incentive stock option" within the meaning of Section 422 of the Internal Revenue Code of 1986, as amended.

3. Expiration of Option. This Option shall expire at 5:00 p.m. Eastern Standard Time on the Expiration Date or, if earlier, the earliest of the dates specified in whichever of the following applies:

a) If the termination of your employment or other association is on account of your death or disability, the first anniversary of the date your employment ends.

b) If the termination of your employment or other association is due to any other reason, three (3) months after your employment or other association ends.

(1) For ISOs not later than the day immediately preceding the tenth anniversary of the Grant Date. NQSOs may have a later expiration date, if the Plan allows. But as a general matter, NQSOs will also have an expiration date of not later than the the day immediately preceding the tenth anniversary of the Grant Date.

(2) Either "is" or "is not", as the Committee has determined.

4. Exercise of Option.

a) You may exercise this Option as to the number of Optioned Shares which have vested (the "Vested Shares") under this paragraph 4, in full or in part and at any time prior to the Expiration Date. However, during any period that this Option remains outstanding after your employment or other association with the Company and its Affiliates ends, you may exercise it only to the extent of any remaining Vested Shares determined as of immediately prior to the end of your employment or other association. The procedure for exercising this Option is described in Section 7.1(e) of the Plan.

b) [*Time-based vesting:* That number of Optioned Shares specified in the table below shall become Vested Shares on the date set opposite such number in the table below:]

Number of Shares in Each Installment	Initial Vesting Date for Shares in Installment

c) [*Performance-based vesting*]

d) [*Other vesting, e.g., Change of Control*]

5. Transfer of Option. Except if and to the extent otherwise provided under the Plan, you may not transfer this Option except by will or the laws of descent and distribution, and, during your lifetime, only you may exercise this Option.

6. Incorporation of Plan Terms. This Option is granted subject to all of the applicable terms and provisions of the Plan, including but not limited to the limitations on the Company's obligation to deliver Optioned Shares upon exercise set forth in Section 10 (Settlement of Awards).

7. Tax Consequences. The Company makes no representation or warranty as to the tax treatment to you of your receipt or exercise of this Option or upon your sale or other disposition of the Optioned Shares. You should rely on your own tax advisors for such advice.

8. Acknowledgements. You acknowledge that you have reviewed and understand the Plan and this Agreement in their entirety, and have had an opportunity to obtain the advice of counsel prior to executing this Agreement. You hereby agree to accept as binding, conclusive and final all decisions or interpretations of the Committee upon any questions arising under the Plan or this Agreement.

9. Further Assurances. The parties agree to execute such further instruments and to take such action as may reasonably be necessary to carry out the intent of this Agreement.

[10. Community Property. Without prejudice to the actual rights of the spouses as between each other, for all purposes of this Agreement, you shall be treated as agent and attorney-in-fact for that interest held or claimed by your spouse with respect to this Option and any Optioned Shares and the parties hereto shall act in all matters as if the Optionee was the sole owner of this Option and (following exercise) any such Optioned Shares. This appointment is coupled with an interest and is irrevocable.](3)

11. Miscellaneous. This Agreement shall be construed and enforced in accordance with the laws of the Commonwealth of Massachusetts without regard to the conflict of laws principles thereof and shall be binding upon and inure to the benefit of any successor or assign of the Company and any executor, administrator, trustee, guardian, or other legal representative of you. Capitalized terms used but not defined herein shall have the meaning assigned under the Plan. This Agreement may be executed in one or more counterparts all of which together shall constitute but one instrument. In making proof of this Agreement it shall not be necessary to produce or account for more than one such counterpart.

[Signature page follows]

(3) Consider for inclusion for grants to California residents (and residents of other states with community property rules).

IN WITNESS WHEREOF, the parties have executed this Agreement as of the date first above written.

PROTEON THERAPEUTICS, INC.

By: _____

Title: _____

_____
Signature of Optionee

Optionee's Address:

_____

_____

_____

PROTEON THERAPEUTICS, INC.
2014 EQUITY INCENTIVE PLAN

OPTION EXERCISE FORM

Proteon Therapeutics, Inc.
200 West Street
Waltham, MA 02451

Attention: Chief Financial Officer

Dear Sir:

In accordance with and subject to the terms and conditions of the Proteon Therapeutics, Inc. 2014 Equity Incentive Plan, as amended, I hereby elect to exercise my option granted under the agreement dated _____, to purchase _____ (_____) shares of the common stock, par value $0.001 per share, in Proteon Therapeutics, Inc. (the "Company").

Enclosed herewith is payment to the Company in the amount of _____ Dollars ($ _____) in full payment of the option price for said shares. [*To be revised as necessary for non-cash payment of exercise price.*]

Sincerely yours,

_____
Name:

PROTEON THERAPEUTICS, INC.

2014 EMPLOYEE STOCK PURCHASE PLAN

1. Purpose and History

The purpose of this Plan is to give Employees wishing to do so a convenient means of purchasing Common Stock of the Company through payroll deductions. The Company believes that ownership of Common Stock by Employees will foster greater Employee interest in the Company's growth and development.

This Plan was adopted by the Board on August 21, 2014. It is the Company's intention that the Plan qualify as an "employee stock purchase plan" under Section 423 of the Code. The provisions of the Plan shall, accordingly, be construed in a manner consistent with the requirements of that Code section.

2. Definitions

As used in this Plan, the following terms shall have the following meanings:

2.1. Board means the Company's Board of Directors.

2.2. Business Day means a day on which the NASDAQ Global Market (or any other national securities exchange on which the Common Stock is then listed) is open for trading. Every date under this Plan that falls on a weekend, a holiday or any other day that is not a Business Day (and any event that occurs after 5 p.m. eastern time on any date) shall be deemed automatically to fall on the next Business Day.

2.3. Code means the Internal Revenue Code of 1986, as amended from time to time, or any successor statute thereto, and any regulations issued from time to time thereunder.

2.4. Committee means the Compensation Committee of the Board or such other committee delegated responsibility by the Board for the administration of the Plan, as provided in Section 5 of the Plan. For any period during which no such committee is in existence "Committee" shall mean the Board and all authority and responsibility assigned to the Committee under the Plan shall be exercised, if at all, by the Board.

2.5. Common Stock or Stock means the common stock, par value $0.001 per share, of the Company.

2.6. Company means Proteon Therapeutics, Inc., a corporation organized under the laws of the State of Delaware.

2.7. Compensation means an Employee's total compensation, including base pay or regular earnings plus commissions, bonuses, and overtime.

2.8. Continuous Status as an Employee means the absence of any interruption or termination of service as an Employee. Continuous Status as an Employee shall not be considered interrupted in the case of (i) sick leave; (ii) military leave; (iii) any other leave of absence approved by the Plan administrator, provided that such leave is for a period of not more than three

months, unless reemployment upon the expiration of such leave is guaranteed by contract or statute, or unless provided otherwise pursuant to Company policy adopted from time to time; or (iv) transfers between locations of the Company or between the Company and a Covered Entity.

2.9. Contributions means all amounts credited to the account of a Participating Employee pursuant to the Plan.

2.10. Corporate Transaction means any (1) merger or consolidation of the Company with or into another entity as a result of which the Stock of the Company is converted into or exchanged for the right to receive cash, securities or other property or is cancelled, (2) sale or exchange of all or substantially all of the Stock of the Company for cash, securities or other property, (3) sale, transfer, or other disposition of all or substantially all of the Company's assets to one or more other persons in a single transaction or series of related transactions or (4) liquidation or dissolution of the Company; except, in the case of clauses (1) and (2), for a transaction the principal purpose of which is to change the state in which the Company is incorporated.

2.11. Covered Entity means any Subsidiary that may adopt the Plan from time to time in accordance with the procedures set forth in Section 14 hereof with the Company's consent.

2.12. Effective Date means the IPO Date.

2.13. Employee means an employee of the Company or a Covered Entity who is customarily employed for at least 20 hours per week and more than five months in a calendar year.

2.14. Exchange Act means the Securities Exchange Act of 1934, as amended.

2.15. Fair Market Value has the meaning set forth in Section 6.4(c).

2.16. Initial Plan Period means the first Plan Period of the Plan.

2.17. IPO Date means the date of the closing of the initial public offering of shares of Common Stock.

2.18. New Plan Period Termination Date has the meaning set forth in Section 12.4.

2.19. Participating Employee means an Employee who elects to participate in the Plan pursuant to Section 6.2(b) or otherwise becomes a Participating Employee pursuant to Section 6.2(h).

2.20. Plan means this Proteon Therapeutics, Inc. 2014 Employee Stock Purchase Plan.

2.21. Plan Period Commencement Date means the first day of each Plan Period.

2.22. Plan Period Termination Date means the last day of each Plan Period.

2.23. Plan Period means each successive period described in Section 6.1, at the end of which each Participating Employee shall purchase Shares.

2.24. Purchase Price means with respect to a Plan Period an amount equal to eighty five percent (85%) of the Fair Market Value of a Share on the Plan Period Commencement Date or on the Plan Period Termination Date, whichever is lower.

2.25. Share means a share of Common Stock, as adjusted in accordance with Section 12 of the Plan.

2.26. Subsidiary means a corporation, in an unbroken chain of corporations beginning with the Company if, at the time of the granting of the option, each of the corporations other than the last corporation in the unbroken chain owns stock possessing fifty percent (50%) or more of the total combined voting power of all classes of stock in one of the other corporations in such chain.

3. Shares Reserved For The Plan

Subject to adjustment as provided in Section 12 hereof, the number of Shares reserved for issuance hereunder shall be One Hundred Forty Thousand Five Hundred (140,500), provided, however, that the number of Shares authorized under this Section 3 of the Plan will be increased each January 1, commencing on January 1 of the year following the year in which the IPO Date occurs and ending on (and including) January 1, 2024, by an amount equal to the lesser of (i) one percent (1%) of outstanding Shares as of the end of the immediately preceding fiscal year and (ii) 281,000. Notwithstanding the foregoing, the Board may act prior to January 1 of a given year to provide that there will be no such January 1 increase in the number of Shares authorized under this Section 3 of the Plan for such year or that the increase in the number of Shares authorized under this Section 3 of the Plan for such year will be a lesser number than would otherwise occur pursuant to the preceding sentence. For purposes of applying the foregoing limitation, if any option expires, terminates or is cancelled for any reason without having been exercised in full, the Shares not purchased or received by the Employee shall again be available for options to be granted under the Plan. Shares issued pursuant to the Plan may be either authorized but unissued shares or shares held by the Company in its treasury.

4. Administration

The Plan shall be administered by the Committee, *provided*, *however*, that at any time and on any one or more occasions the Board may itself exercise any of the powers and responsibilities assigned the Committee under the Plan and when so acting shall have the benefit of all of the provisions of the Plan pertaining to the Committee's exercise of its authorities hereunder; and *provided*, *further*, that the Committee may delegate its duties in order to facilitate the purchase and transfer of Shares and to provide for the day-to-day administration of the Plan with all powers necessary to enable the delegate to carry out its duties in that respect. Subject to the provisions of the Plan, the Committee shall have complete authority, in its discretion, to make or to select the manner of making all determinations with respect to each option to be granted by the Company under the Plan. In making such determinations, the Committee may take into account such factors as the Committee in its discretion shall deem relevant. Subject to the provisions of the Plan, the Committee shall also have complete authority to interpret the Plan, to prescribe, amend and rescind rules and regulations relating to it and to make all other determinations necessary or advisable for the administration of the Plan. The Committee's determinations made in good faith on matters referred to in the Plan shall be final, binding and conclusive on all persons having or claiming any interest under the Plan or an option granted pursuant hereto.

5. Eligibility for Awards

Subject to the requirements of Section 6.2 and the limitations imposed by Section 423(b) of the Code, any Employee shall be eligible to participate in a Plan Period under the Plan as of the applicable Plan Period Commencement Date. Notwithstanding any provision of the Plan to the contrary, no Employee shall be granted an option under the Plan (i) if, immediately after the grant, such Employee (taking into account stock which would be attributed to such Employee pursuant to Section 424(d) of the Code) would own capital stock of the Company and/or hold outstanding options to purchase stock possessing five percent (5%) or more of the total combined voting power or value of all classes of stock of the Company or of any Subsidiary of the Company, or (ii) if such option would permit his or her rights to purchase stock under all employee stock purchase plans (described in Section 423 of the Code) of the Company and its Subsidiaries to accrue at a rate which exceeds twenty-five thousand dollars ($25,000) of such stock (determined on the basis of the Fair Market Value of such stock on the date or dates such option was granted) for each calendar year in which such option is outstanding at any time.

6. Terms of Participation

6.1. Plan Periods. Each calendar year shall be divided into two six-month Plan Periods, the first beginning on January 1 and ending on the immediately following June 30, and the second beginning on July 1 and ending on the immediately following December 31. However, the Initial Plan Period shall commence on such date following the IPO Date as the Committee may determine in its sole discretion and continue until December 31, 2014.

6.2. Election to Participate and Plan Deductions.

(a) Shares shall be offered for purchase under the Plan through a series of successive, non-overlapping Plan Periods until such time as (i) the maximum number of Shares available for issuance under the Plan shall have been purchased or (ii) the Plan shall have been sooner terminated. At any time and from time to time, the Committee may change the duration and/or the frequency of Plan Periods or suspend operation of the Plan with respect to Plan Periods not yet commenced.

(b) An eligible Employee may become a Participating Employee in the Plan by completing an enrollment agreement provided by the Company and filing it with the Company at least three business days prior to the Plan Period Commencement Date for the Plan Period in which such Employee desires to participate, unless either an earlier or later time for filing the enrollment agreement is set by the Committee for all eligible Employees with respect to a given Plan Period. The enrollment agreement shall set forth the percentage of the Employee's Compensation (subject to Section 6.2(c) below) to be paid as Contributions pursuant to the Plan. Payroll deductions shall commence on the first payroll following the Plan Period Commencement Date and shall end on the last payroll paid on or prior to the Plan Period Termination Date, unless sooner terminated by the Participating Employee as provided in Section 6.7.

(c) A Participating Employee may elect to have payroll deductions taken from each payroll during any Plan Period in an amount, in whole percentages, not less than one percent (1%) and not more than fifteen percent (15%) (or such other percentage as the Committee may establish from time to time before any Plan Period Commencement Date) of such Participating Employee's Compensation on each payroll date during the Plan Period. All payroll deductions made by a Participating Employee shall be credited to his or her account under the

Plan. No interest shall accrue on Contributions to the Plan. A Participating Employee may not make any additional payments into such account.

(d) Unless the Committee announces otherwise before the start of a particular Plan Period, an eligible Employee's enrollment agreement in effect at the end of one Plan Period will remain in effect for each subsequent Plan Period.

(e) A Participating Employee may discontinue his or her participation in the Plan as provided in Section 6.7. An employee may choose to increase or decrease his or her deductions at any time during the specified enrollment period communicated to employees prior to the start of the Plan Period.

(f) Notwithstanding the foregoing, to the extent necessary to comply with Section 423(b)(8) of the Code and Section 5, a Participating Employee's payroll deductions may be decreased during any Plan Period to zero percent (0%). Payroll deductions reduced to zero percent (0%) in compliance with this Section 6.2(f) shall re-commence automatically at the rate provided in such Participating Employee's enrollment agreement at the beginning of the next Plan Period, unless terminated by the Participating Employee as provided in Section 6.7.

(g) Any amounts left over in a Participating Employee's account upon expiration or termination of the Plan (or upon a withdrawal by a Participating Employee or upon a Participating Employee purchasing the maximum dollar amount or number of shares hereunder) shall be returned to the Participating Employee.

6.3. Shares.

(a) If the Committee determines that, on a given Plan Period Termination Date, the number of shares with respect to which options are to be exercised may exceed (i) the number of Shares that were available for sale under the Plan on the Plan Period Commencement Date, or (ii) the number of shares available for sale under the Plan on such Plan Period Termination Date, then the Company shall make a pro rata allocation of the Shares available for purchase on such Plan Period Termination Date in as uniform a matter as shall be practicable and as it shall determine in its sole discretion to be equitable among all Participating Employees exercising options to purchase Common Stock on such Plan Period Termination Date. The Company shall make pro rata allocation of the Shares available on the Plan Period Commencement Date pursuant to the preceding sentence, notwithstanding any authorization of additional Shares for issuance under the Plan by the Company's stockholders subsequent to such Plan Period Commencement Date.

(b) The Participating Employee shall have no interest or voting right in Shares covered by his or her option until such option has been exercised.

(c) Shares to be delivered to a Participating Employee under the Plan will be registered in the name of the Participating Employee.

6.4. Grant of Options.

(a) A Participating Employee shall be granted a separate option for each Plan Period in which he or she participates. The option shall be granted on the Plan Period

Commencement Date for the Plan Period and shall provide the Participating Employee with the right to purchase Shares upon the terms set forth below.

(b) The number of Shares purchasable by a Participating Employee on each Plan Period Termination Date during the Plan Period, pursuant to Section 6.5 below, shall be determined by dividing such Employee's Contributions accumulated during such Plan Period prior to such Plan Period Termination Date and retained in the Participating Employee's account as of the Plan Period Termination Date by the applicable Purchase Price. However, the maximum number of Shares a Participating Employee may purchase during each Plan Period shall not exceed 10,000 Shares, or such other number as may be determined by the Committee and announced to Employees at least five days prior to the scheduled beginning of the next Plan Period to be affected by the Committee's determination, provided that such purchase shall be subject to the limitations set forth in Section 6.2(c).

(c) Except as provided in Section 6.2(h)(ii), the fair market value of the Shares on a given date (the "Fair Market Value") means the value of a share of Common Stock on a particular date determined by such methods or procedures as may be established by the Committee. Unless otherwise determined by the Committee, the Fair Market Value of the Common Stock as of any date, is (a) the closing price for the Common Stock as reported by the the NASDAQ Global Market (or on any other national securities exchange on which the Common Stock is then listed) for that date or, if no closing price is reported for that date, the closing price on the next preceding date for which a closing price was reported or (b) if the Common Stock is not traded on a national securities exchange but is traded over-the-counter, the closing or last price of the Common Stock on the composite tape or other comparable reporting system on that date or, if such date is not a trading day, the last market trading day prior to such date.

6.5. Exercise. Unless a Participating Employee withdraws from the Plan as provided in Section 6.7, each option shall be exercised automatically on each Plan Period Termination Date, and Shares shall accordingly be purchased on behalf of each Participating Employee on each such Plan Period Termination Date. The purchase shall be effected by applying the Participating Employee's payroll deductions for the Plan Period ending on such Plan Period Termination Date to the purchase of Shares (subject to the limitation on the maximum number of Shares purchasable per Participating Employee on any one Plan Period Termination Date) at the Purchase Price in effect for the Participating Employee for that Plan Period Termination Date. The Shares purchased upon exercise of an option hereunder shall be deemed to be transferred to the Participating Employee on the Plan Period Termination Date. During his or her lifetime, a Participating Employee's option to purchase Shares hereunder is exercisable only by him or her.

6.6. Delivery. As promptly as practicable after each Plan Period Termination Date, the Company shall arrange the delivery to each Participating Employee a certificate or certificates or book-entry authorization and instruction to the Company's transfer agent and registrar for the number of Shares purchased upon exercise of his or her option.

6.7. Voluntary Withdrawal; Termination of Employment.

(a) A Participating Employee may withdraw all but not less than all of the Contributions credited to his or her account under the Plan up to two weeks prior to the Plan Period Termination Date by giving written notice to the Company in accordance with the Company's policy regarding withdrawal from the Plan. All of the Participating Employee's

Contributions credited to his or her account will be paid to him or her promptly after receipt of his or her notice of withdrawal and his or her option for the current Plan Period will be automatically terminated, and no further Contributions for the purchase of Shares will be made (or will be permitted to be made) during the Plan Period.

(b) Upon termination of the Participating Employee's Continuous Status as an Employee prior to a Plan Period Termination Date for any reason, including retirement or death, the Contributions credited to his or her account will be returned to him or her or, in the case of his or her death, to the person or persons entitled thereto under Section 8, and his or her option will be automatically terminated.

(c) In the event a Participating Employee fails to remain in Continuous Status as an Employee of the Company for at least 20 hours per week during the Plan Period in which the Employee is a Participating Employee, he or she will be deemed to have elected to withdraw from the Plan and the Contributions credited to his or her account and remaining there will be returned to him or her and his or her option terminated.

(d) A Participating Employee's withdrawal during a Plan Period will not have any effect upon his or her eligibility to participate in a succeeding Plan Period or in any similar plan which may hereafter be adopted by the Company.

7. No Special Service Rights

Nothing contained in this Plan shall confer upon any Employee any right with respect to the continuation of his or her employment with the Company or any Covered Entity or any other entity, corporation, partnership, limited liability company or business trust controlling, controlled by or under common control with the Company, or interfere in any way with the right of any such entity, subject to the terms of any separate employment agreement or provision of law or the Company's charter or by-laws to the contrary, at any time to terminate such employment relationship or to increase or decrease, or otherwise adjust, the other terms and conditions of the Employee's employment.

8. Designation of Beneficiary

8.1. A Participating Employee may file a written designation of a beneficiary who is to receive any Shares and cash, if any, from the Participating Employee's account under the Plan in the event of such Participating Employee's death subsequent to the end of a Plan Period but prior to delivery to him or her of such Shares and cash. Any such beneficiary shall also be entitled to receive any cash from the Participating Employee's account under the Plan in the event of such Participating Employee's death during a Plan Period.

8.2. Such designation of beneficiary may be changed by the Participating Employee at any time by written notice. In the event of the death of a Participating Employee and in the absence of a beneficiary validly designated under the Plan who is living at the time of such Participating Employee's death, the Company shall deliver such Shares and/or cash to the executor or administrator of the estate of the Participating Employee, or if no such executor or administrator has been appointed (to the knowledge of the Company), the Company, in its discretion, may deliver such Shares and/or cash to the spouse or to any one or more dependents or relatives of the Participating Employee, or if no spouse, dependent or relative is known to the Company, then to such other person as the Company may designate.

9. Transferability of Options and Shares

Neither Contributions credited to a Participating Employee's account nor any rights with regard to the exercise of an option or to receive Shares under the Plan may be assigned, transferred, pledged or otherwise disposed of in any way (other than by will, the laws of descent and distribution, or as provided in Section 8) by the Participating Employee. Any such attempt at assignment, transfer, pledge or other disposition shall be without effect, except that the Company may treat such act as an election to withdraw funds in accordance with Section 6.7. In addition, if the Committee has so announced to Participating Employees at least five days prior to the scheduled beginning of the next Plan Period, any Shares acquired on the Plan Period Termination Date of such Plan Period may be subject to restrictions specified by the Committee on the transfer of such Shares. Any Participating Employee selling or transferring any or all of his or her Shares purchased pursuant to the Plan must provide written notice of such sale or transfer to the Company within five business days after the date of sale or transfer. Such notice to the Company shall include the gross sales price, if any, the Plan Period during which the Shares being sold were purchased by the Participating Employee, the number of Shares being sold or transferred and the date of sale or transfer.

10. Use of Funds

All Contributions received or held by the Company under the Plan may be used by the Company for any corporate purpose, and the Company shall not be obligated to segregate such Contributions from its other assets.

11. Reports

Individual accounts will be maintained for each Participating Employee in the Plan. Statements of account will be given to Participating Employees at least annually, which statements will set forth, with respect to the immediately prior calendar year, the amounts of Contributions, the per Share Purchase Price, the number of Shares purchased and the remaining cash balance, if any.

12. Adjustments Upon Changes in Capitalization; Corporate Transactions

12.1. Adjustment in General. All of the share numbers set forth in the Plan reflect the capital structure of the Company as of the Effective Date. If subsequent to that date the outstanding Shares (or any other securities covered by the Plan by reason of the prior application of this Section) are increased, decreased, or exchanged for a different number or kind of shares or other securities, or if additional shares or new or different shares or other securities are distributed with respect to Shares, as a result of a reorganization, recapitalization, reclassification, stock dividend, stock split, reverse stock split, or other similar distribution with respect to such Shares, an appropriate and proportionate adjustment will be made in (i) the maximum numbers and kinds of shares provided in Section 3, (ii) the numbers and kinds of shares or other securities subject to the then outstanding options, and (iii) the exercise price for each share or other unit of any other securities subject to then outstanding options.

12.2. Adjustment Upon the Occurrence of Certain Unusual or Nonrecurring Events. In the event of any corporate action not specifically covered by the preceding Section 12.1, including but not limited to an extraordinary cash distribution on Common Stock, a corporate

separation or other reorganization or liquidation, the Committee may make such adjustment of outstanding options and their terms, if any, as it, in its sole discretion, may deem equitable and appropriate in the circumstances. The Committee may make adjustments in the terms and conditions of, and the criteria included in, options in recognition of unusual or nonrecurring events (including, without limitation, the events described in this Section 12.2) affecting the Company or the financial statements of the Company or of changes in applicable laws, regulations, or accounting principles, whenever the Committee determines that such adjustments are appropriate in order to prevent dilution or enlargement of the benefits or potential benefits intended to be made available under the Plan.

12.3. Related Matters. Any adjustment in options made pursuant to Section 12.1 or 12.2 shall be determined and made, if at all, by the Committee, acting in its sole discretion, and shall include any correlative modification of terms which the Committee may deem necessary or appropriate so as to ensure the rights of the Participating Employees in their respective options are not substantially diminished nor enlarged as a result of the adjustment and corporate action other than as expressly contemplated in this Section 12.

12.4. Corporate Transactions. In the event of a Corporate Transaction that is a dissolution or liquidation of the Company, the Plan Period then in progress will terminate immediately prior to the consummation of such action, unless otherwise provided by the Committee. In the event of any other Corporate Transaction, each option outstanding under the Plan may be assumed or an equivalent option may be substituted by the successor corporation or a parent or subsidiary of such successor corporation. In the event that the successor corporation refuses to assume or substitute for outstanding options, the Plan Period then in progress shall be shortened and a new Plan Period Termination Date shall be set (the "New Plan Period Termination Date"), as of which date the Plan Period then in progress will terminate. The New Plan Period Termination Date shall be on

or before the date of consummation of the Corporate Transaction and the Committee shall notify each Participating Employee in writing, at least three Business Days prior to the New Plan Period Termination Date, that the Plan Period Termination Date for his or her option has been changed to the New Plan Period Termination Date and that his or her option will be exercised automatically on the New Plan Period Termination Date, unless prior to such date he or she has withdrawn from the Plan Period as provided in Section 6.7. For purposes of this Section 12.4, an option granted under the Plan shall be considered assumed, or a substantially equivalent award shall be considered to have been provided in substitution therefor, if following consummation of the Corporate Transaction, the option is assumed and/or exchanged or replaced with another option issued by the acquiring or succeeding entity (or an affiliate thereof) that confers the right to receive upon exercise of such option, for each share of Common Stock subject to the option immediately prior to the consummation of the Corporate Transaction, the consideration (whether cash, securities or other property) received as a result of the Corporate Transaction by holders of Common Stock for each share of Common Stock held immediately prior to the consummation of the Corporate Transaction (and if holders were offered a choice of consideration, the type of consideration chosen by the holders of a majority of the outstanding shares of Stock); *provided however* that if the consideration received in the transaction is not solely common stock of the successor corporation or its parent (as defined in Section 424(e) of the Code), the Committee may, with the consent of the successor corporation, provide for the consideration to be received upon exercise of the option to be solely common stock of the successor corporation or its parent equal in fair market value to the per Share consideration received by holders of Common Stock in the transaction.

13. Settlement of Awards

13.1. Violation of Law. Notwithstanding any other provision of the Plan to the contrary, if, at any time, in the reasonable opinion of the Company, the issuance of Shares pursuant to the Plan may constitute a violation of law, then the Company may delay such issuance of such Shares until (i) approval shall have been obtained from such governmental agencies, other than the Commission, as may be required under any applicable law, rule, or regulation and (ii) in the case where such issuance would constitute a violation of a law administered by or a regulation of the Commission, one of the following conditions shall have been satisfied:

(a) the Shares are, at the time of the issue of such Shares, effectively registered under the Securities Act; or

(b) the Company shall have determined, on such basis as it deems appropriate (including an opinion of counsel in form and substance satisfactory to the Company) that the sale, transfer, assignment, pledge, encumbrance or other disposition of such Shares or such beneficial interest, as the case may be, does not require registration under the Securities Act or any applicable State securities laws.

The Company shall make all reasonable efforts to bring about the occurrence of said events.

13.2. Corporate Restrictions on Rights in Stock. Any Shares to be issued pursuant to the Plan shall be subject to all restrictions upon the transfer thereof which may be now or hereafter imposed by the charter and by-laws of the Company.

13.3. Investment Representations. As a condition to the exercise of an option, the Company may require the person exercising such option to represent and warrant at the time of any such exercise that the Shares are being purchased only for investment and without any present intention to sell or distribute such Shares if, in the opinion of counsel for the Company, such a representation is required by any of the aforementioned applicable provisions of law. The Company shall be under no obligation to issue any Shares unless the Shares to be issued pursuant to the Plan have been effectively registered under the Securities Act.

13.4. Placement of Legends; Stop Orders; etc. Each Share to be issued pursuant to the Plan may bear a reference to any applicable restriction under the Plan. All Shares or other securities delivered under the Plan shall be subject to such stock transfer orders and other restrictions as the Committee may deem advisable under the rules, regulations, and other requirements of any stock exchange upon which the Common Stock is then listed, and any applicable federal or state securities law, and the Committee may cause a legend or legends to be put on any such certificates to make appropriate reference to such restrictions.

13.5. Company Charter and By-Laws; Other Company Policies. This Plan and all options granted under this Plan (including the exercise of an option) are subject to and must comply with the certificate of incorporation and bylaws of the Company, as they may be amended from time to time, and all other Company policies duly adopted by the Board, the Committee or any other committee of the Board as in effect from time to time regarding the acquisition, ownership or sale of Common Stock by employees, including, without limitation, policies intended to limit the potential for insider trading and to avoid or recover compensation payable or

paid on the basis of inaccurate financial results or statements, employee conduct, and other similar events.

14. Adopting Subsidiaries

Any Subsidiary of the Company may request that its Employees be allowed to participate in the Plan in accordance with procedures to be adopted by the Board. The Board may, in its sole discretion, approve or reject any such request. Any such Subsidiary whose request is approved by the Board shall be referred to herein as a "Covered Entity." In addition, the Board may determine, in its sole discretion, that a Subsidiary that is a Covered Entity will cease to be a Covered Entity with respect to Plan Periods not yet commenced.

15. Amendment and Termination

(a) The Board may at any time terminate the Plan or make such modifications of the Plan as it shall deem advisable. Except as provided in Section 12, no termination of the Plan may affect options previously granted, provided that the Plan or a Plan Period may be terminated by the Board on a Plan Period Termination Date or by the Board's setting a new Plan Period Termination Date with respect to a Plan Period then in progress if the Board determines that termination of the Plan and/or any Plan Period is in the best interests of the Company and its stockholders or if continuation of the Plan and/or a Plan Period would cause the Company to incur adverse accounting charges as a result of the Plan. Except as provided in Section 12 or this Section 15, no amendment to the Plan shall make any change in any option previously granted which adversely affects the rights of any Participating Employee.

(b) In addition to the foregoing, without stockholder consent and without regard to whether any Participating Employee rights may be considered to have been adversely affected, the Committee shall be entitled to change the Plan Periods, establish the exchange ratio applicable to amounts withheld in a currency other than U.S. dollars (if applicable), permit payroll withholding in excess of the amount designated by a Participating Employee to adjust for delays or mistakes in the Company's processing of properly completed withholding elections, establish reasonable waiting and adjustment periods and/or accounting and crediting procedures to ensure that amounts applied toward the purchase of Common Stock for each Participating Employee properly correspond with amounts withheld from the Participating Employee's Compensation, and establish such other limitations or procedures as the Committee determines in its sole discretion advisable which are consistent with the Plan.

16. Notices and Other Communications

Any notice, demand, request or other communication hereunder to any party shall be deemed to be sufficient if contained in a written instrument delivered in person or duly sent by first class registered, certified or overnight mail, postage prepaid, or telecopied with a confirmation copy by regular, certified or overnight mail, addressed or telecopied, as the case may be, (i) if to a Participating Employee, at his or her residence address last filed with the Company and (ii) if to the Company, at its principal place of business, addressed to the attention of its Chief Financial Officer, or to such other address or telecopier number, as the case may be, as the addressee may have designated by

notice to the addressor. All such notices, requests, demands and other communications shall be deemed to have been received: (i) in the case of personal delivery, on the date of such delivery; (ii) in the case of mailing, when received by the addressee; and (iii) in the case of facsimile transmission, when confirmed by facsimile machine

report. In addition, the Company may, in its sole discretion, deliver any documents related to the Plan by electronic means or request that Participating Employee communicate with the Company with respect to the Plan by electronic means. By participating in the Plan, each Participating Employee will have consented to receive such documents by electronic delivery and, if requested, to agree to participate in the Plan through an on-line or electronic system established and maintained by the Company or another third party designated by the Company, and such consent shall remain in effect throughout the Participating Employee's term of employment or service with the Company and thereafter until withdrawn in writing by Participant.

17. Governing Law

The Plan and all options and actions taken thereunder shall be governed, interpreted and enforced in accordance with the laws of the Commonweath of Massachusetts without regard to the conflict of laws principles thereof.

18. Term of Plan

The Plan shall become effective on the IPO Date and shall continue in effect until the tenth (10th) anniversary thereof, unless earlier terminated pursuant to Section 15.

SAMPLE

PROTEON THERAPEUTICS, INC.

2014 EMPLOYEE STOCK PURCHASE PLAN

ENROLLMENT AGREEMENT

o Original Application Enrollment Date: _____

o Change in Payroll Deduction Rate

o Change in Beneficiary(ies)

1. I, , hereby elect to participate in the Proteon Therapeutics, Inc. 2014 Employee Stock Purchase Plan, as amended (the "Purchase Plan"), and subscribe to purchase shares of the Company's Common Stock in accordance with this Enrollment Agreement and the Purchase Plan. Capitalized terms used (and not otherwise defined) in this enrollment agreement have the meanings assigned to them in the Purchase Plan.

2. I hereby authorize payroll deductions from each paycheck in the amount of % of my Compensation (from 1% to 15%) on each payroll date during the Plan Period in accordance with the Purchase Plan. (Please note that no fractional percentages are permitted.)

3. I understand that such payroll deductions will be accumulated for the purchase of shares of Common Stock at the applicable purchase price determined in accordance with the Purchase Plan. I understand that, if I do not withdraw from a Plan Period, any accumulated payroll deductions will be used to automatically purchase shares of Common Stock.

4. I understand that all my payroll deductions received or held by the Company under the Purchase Plan may be used by the Company for any corporate purpose, and the Company shall not be obligated to segregate such payroll deductions. Until shares are issued to me, I will only have the rights of an unsecured creditor with respect to such accumulated payroll deductions.

5. I have received a copy of the Purchase Plan Prospectus and the Purchase Plan document. I understand that my participation in the Purchase Plan is in all respects subject to the terms of the Purchase Plan.

6. Shares purchased for me under the Purchase Plan should be issued in the name(s) of (Employee or Employee and spouse only):

_____

7. I understand that if I dispose of any shares received by me pursuant to the Purchase Plan within two years after the Plan Period Commencement Date (the first day of a Plan Period during which I purchased such shares) or one year after the Plan Period Termination Date, I will be treated for federal income tax purposes as having received ordinary income at the time of such disposition in an amount equal to the excess of the fair market value of the shares at the time such shares were purchased by me over the price which I paid for the shares. **I hereby agree to notify the Company in writing within five (5) business days after the date of any disposition of my shares, and I will make adequate provision for federal, state or other tax withholding obligations, if any, which arise upon the disposition of the Common Stock**. The Company may, but will not be obligated to, withhold from my compensation the amount necessary to meet any applicable withholding obligation, including any withholding necessary to make available to the Company any tax deductions or benefits attributable to the sale or early disposition of Common Stock by me.

   If I dispose of such shares at any time after the expiration of the applicable holding periods, I understand that I will be treated for federal income tax purposes as having received income only at the time of such disposition, and that such income will be taxed as ordinary income only to the extent of an amount equal to the lesser of (a) the excess of the fair market value of the shares at the time of such disposition over the purchase price which I paid for the shares or (b) 15% of the fair market value of the shares on the first day of the Plan Period. The remainder of the gain, if any, recognized on such disposition will be taxed as capital gain.

8. I hereby agree to be bound by the terms of the Purchase Plan. The effectiveness of this Enrollment Agreement is dependent upon my eligibility to participate in the Purchase Plan.

9. I hereby agree to establish a brokerage account with and to fill out and submit the necessary forms to allow the Company to deposit shares purchased on my behalf under the Purchase Plan in such account, if I have not done so already.

10. In the event of my death, I hereby designate the following as my beneficiary(ies) to receive all payments and shares due me under the Purchase Plan:

BENEFICIARY NAME: (Please print) _____
(First) (Middle) (Last)

_____
Relationship

I UNDERSTAND THAT THIS ENROLLMENT AGREEMENT SHALL REMAIN IN EFFECT THROUGHOUT SUCCESSIVE PLAN PERIODS UNLESS TERMINATED BY ME.

Dated: _____

_____
Signature of Employee

_____
Print name

_____
Spouse's Signature
(If beneficiary other than spouse)

SAMPLE

PROTEON THERAPEUTICS, INC.

2014 EMPLOYEE STOCK PURCHASE PLAN

NOTICE OF WITHDRAWAL

The undersigned participant in the Proteon Therapeutics, Inc. 2014 Employee Stock Purchase Plan, hereby notifies the Company that he or she hereby withdraws from the Plan Period beginning _____. He or she hereby directs the Company to pay to the undersigned as promptly as practicable all the payroll deductions credited to his or her account with respect to such Plan Period. The undersigned understands and agrees that his or her option for such Plan Period will be automatically terminated, that no further payroll deductions will be made for the purchase of shares in the current Plan Period, and that the undersigned shall be eligible to participate in subsequent Plan Periods only by delivering to the Company a new Enrollment Agreement.

Name: _____

Signature: _____

Date: _____

Proteon Therapeutics, Inc.
200 West St.
Waltham, MA 02451

October 1, 2014

Mr. Timothy P. Noyes
5 Brigham Road
Lexington, MA 02420

Re: Employment with Proteon Therapeutics, Inc.

Dear Tim,

Reference is hereby made to that certain Employment Letter Agreement, dated as of April 14, 2006, between you and Proteon Therapeutics, Inc. (the "Company" or "Proteon"), as amended by that certain First Amendment thereto, dated as of April 29, 2009 (as amended, the "Original Employment Agreement"). This letter agreement (the "Agreement") amends and restates the Original Employment Agreement in its entirety. This letter contains the basic terms of your employment with the Company. 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. This Agreement shall be effective contingent upon, and from and after, the consummation of the Company's initial public offering (the "IPO") of its common stock, par value $0.001 per share ("Common Stock").

1. **Duties**. You will be employed as the Company's President and 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 and Chief Executive Officer. You will report directly to the Board of Directors ("Board") of the Company who will be responsible for evaluating your performance.

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**. You will be compensated at a base rate of $437,280 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 50% ("Bonus") of your Base Salary, subject to upward adjustments at the discretion of the Board typically made annually as part of the Company's annual compensation review process. The actual amount of this Bonus, if any and up to the full 50% target shall be determined by the Board, based on its assessment, in its discretion, of your and the Company's performance. 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. "Pro-Rata Bonus" means the Bonus that (but for the cessation of employment) would otherwise have been payable for the fiscal year in which the cessation occurs (based on actual performance outcomes for that year), multiplied by the following fraction: (i) the number of

---

days that you were employed by the Company during that fiscal year, divided by (ii) 365. For this purpose, the Bonus that would otherwise have been payable to you shall be determined by the Board in good faith and in the same manner applicable to active executive officers of the Company.

5. **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 executive.

6. **Vacation**. You will continue to accrue vacation on a monthly basis per standard Company policy. Your vacation benefit shall not be less than four (4) 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.

7. **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.

8. **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 being cured, is not cured within thirty (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 thirty (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 thirty (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 Section 18 below. In the event of your death or disability as provided in Section 8(b)(vi) or 8(b)(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 one hundred eighty (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 twelve (12) months of your Base Salary, at the rate in effect on the date of termination, plus your annual Bonus in respect of any calendar year that has been earned but not yet paid (for this purpose, the Bonus earned for such calendar year shall be determined by the Board in good faith and in the same manner applicable to active executive officers of the Company, your "Earned Unpaid Bonus") or, in the event Constructive Termination or a termination without Cause occurs within thirty (30) days prior to or three hundred sixty-five (365) days following a Corporate Transaction, eighteen (18) months of your Base Salary, as applicable, at the rate in effect on the date of termination plus, only following a Corporation Transaction, an amount equal to your Pro-Rata Bonus plus any Earned and Unpaid Bonus, 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 equal to the amount that the Company was paying for you under such group health insurance plans prior to the effective date of termination for twelve (12) months following (the "12-Month Tail Period") or, in the event Constructive Termination or a termination without Cause occurs within thirty (30) days prior to or three hundred sixty-five (365) days following a Corporate Transaction, eighteen (18) months following (the "18-Month Tail Period" and, collectively with the 12-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 or a termination without Cause, accelerated to one hundred percent (100%) vesting in the event Constructive Termination or a termination without Cause occurs within thirty (30) days prior to or three hundred sixty-five (365) days following a Corporate Transaction (as defined below) (the "Option Acceleration"); and (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 one hundred eighty (180) days following the termination (the "Option Extension"); provided, however, that the Option Extension period shall not be extended beyond the period of time that would enable the stock option to remain exempt under Section 409A (as defined below).

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 8(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 will be paid 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 11(d) hereof. The payment of the COBRA Premiums will commence on such later date as well. Notwithstanding the foregoing, if the Company determines that it cannot provide such reimbursement of premiums to you without potentially violating applicable law, the Company shall not be obligated to make any such payments or reimbursements to you.

The following shall constitute Constructive Termination:

(i) failure of the Company to provide you Base Salary (as may have been increased pursuant to Section 3) 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 (*e.g.*, 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, or a reduction in your Base Salary (as may have been increased pursuant to Section 3) without your prior written consent;

(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 one hundred eighty (180) consecutive days in any three hundred sixty-five (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) the Severance Payment less applicable

---

withholdings and deductions, paid in a lump sum as provided below; (ii) the COBRA Premiums; (iii) the Option Acceleration; and (iv) the Option Extension; provided, however, that the Option Extension period shall not be extended beyond the period of time that would enable the stock option to remain exempt under Section 409A.

Any obligation of the Company to you in Section 8(c) is conditioned upon you signing and returning to the Company a timely and effective Release of Claims. The Release of Claims required for separation benefits in accordance with this Section 8(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 will be paid 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 11(d) hereof. The payment of the COBRA Premiums will commence on such later date as well. Notwithstanding the foregoing, if the Company determines that it cannot provide such reimbursement of premiums to you without potentially violating applicable law, the Company shall not be obligated to make any such payments or reimbursements to you.

(d) Section 280G. 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.

9. **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, and without prior notice, 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.

10. **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.

11. **Tax Matters.**

(a) Subsections (a) through (e) of this Section 11 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 Company 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 (12) months after your employment ends, if your employment ends on account of your death or total and permanent disability, or

(ii) more than three (3) months after your employment ends, if your employment ends in any other circumstance.

12. **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 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 Section 12 survive any termination of your employment.

---

13. **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.

14. **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.

15. **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.

16. **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.

17. **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.

18. **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.

19. **Entire Agreement**. This Agreement, the Employee Confidentiality and Inventions Assignment Agreement that you have previously executed with the Company, 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.

20. **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.

[*The remainder of this page is intentionally left blank.*
Signatures on following page.]

Best Regards,

PROTEON THERAPEUTICS, INC.

By: /s/ George A. Eldridge
Name: George A. Eldridge,
Title: Chief Financial Officer

I have read, understand and accept the enclosed offer of employment with Proteon Therapeutics, Inc.

/s/ Timothy P. Noyes — October 1, 2014
Timothy P. Noyes — Date

EXHIBIT A

Release of Claims

In consideration of the promises and covenants recited in the Employment Agreement dated as of by and between Proteon Therapeutics, Inc. (the "Company") and Timothy P. Noyes (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

---

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 the Company's Chief Executive Officer 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.

Timothy P. Noyes

Timothy P. Noyes
Date:

Proteon Therapeutics, Inc.
200 West St.
Waltham, MA 02451

October 1, 2014

Mr. Steven K. Burke
82 Willis Road
Sudbury, MA 01776

Re: Employment with Proteon Therapeutics, Inc.

Dear Steve,

Reference is hereby made to that certain Employment Letter Agreement, dated as of July 25, 2006, between you and Proteon Therapeutics, Inc. (the "Company" or "Proteon"), as amended by that certain First Amendment dated as of April 29, 2009 (as amended, the "Original Employment Agreement"). This letter agreement (the "Agreement") amends and restates the Original Employment Agreement in its entirety. This letter contains the basic terms of your employment with the Company. 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. This Agreement shall be effective contingent upon, and from and after, the consummation of the Company's initial public offering (the "IPO") of its common stock, par value $0.001 per share ("Common Stock").

1. **Duties**. You will be employed as the Company's Senior Vice President and Chief Medical Officer. In this capacity, you will be responsible for all medical aspects of the Company and shall perform such duties as are ordinary, customary and necessary in your role as Senior Vice President and Chief Medical 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**. You will be compensated at a base rate of $378,100 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.

4. **Annual Bonus**. You will have an annual target bonus of 35% of your Base Salary ("Bonus"), subject to upward adjustments at the discretion of the Board typically made annually as part of the Company's annual compensation review process. The actual amount of this Bonus, if any and up to the full 35% target shall be determined by the Board, based on its assessment, in its discretion, of your and the Company's performance. 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. "Pro-Rata Bonus" means the Bonus that (but for the cessation of employment) would otherwise have been payable for the fiscal year in which the cessation occurs (based on actual performance outcomes for that year), multiplied by the following fraction: (i) the number of

---

days that you were employed by the Company during that fiscal year, divided by (ii) 365. For this purpose, the Bonus that would otherwise have been payable to you shall be determined by the Board in good faith and in the same manner applicable to active executive officers of the Company.

5. **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 executive.

6. **Vacation**. You will continue to accrue vacation on a monthly basis per standard Company policy. 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.

7. **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.

8. **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 being cured, is not cured within thirty (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 thirty (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 thirty (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 Section 18 below. In the event of your death or disability as provided in Section 8(b)(vi) or 8(b)(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 one hundred eighty (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 twelve (12) months of your Base Salary, at the rate in effect on the date of termination, plus your annual Bonus in respect of any Calendar year that has been earned but not yet paid (for this purpose the Bonus earned for such calendar year shall be determined by the Board in good faith and in the same manner applicable to executive officers of the Company, your "Earned and Unpaid Bonus") or, in the event Constructive Termination or a 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 plus, only following a Corporation Transaction, an amount equal to your Pro-Rata Bonus plus any Earned and Unpaid Bonus, 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 equal to the amount that the Company was paying for you under such group health insurance plans prior to the effective date of termination for twelve (12) months following 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 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 or a termination without Cause, accelerated to one hundred percent (100%) vesting in the event Constructive Termination or a termination without Cause occurs within thirty (30) days prior to or three hundred sixty-five (365) days following a Corporate Transaction (as defined below) (the "Option Acceleration"); and (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 one hundred eighty (180) days following the termination (the "Option Extension"); *provided*, *however*, that the Option Extension period shall not be extended beyond the period of time that would enable the stock option to remain exempt under Section 409A (as defined below).

Any obligation of the Company to you in Section 8(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 8(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 will be paid 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 11(d) hereof. The payment of the COBRA Premiums will commence on such later date as well. Notwithstanding the foregoing, if the Company determines that it cannot provide such reimbursement of premiums to you without potentially violating applicable law, the Company shall not be obligated to make any such payments or reimbursements to you.

The following shall constitute Constructive Termination:

(i) failure of the Company to provide you Base Salary (as may have been increased pursuant to Section 3) 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;

(iii) material diminution in the nature or scope of your responsibilities, duties or authority, or a reduction in your Base Salary (as may have been increased pursuant to Section 3) 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) 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 one hundred eighty (180) consecutive days in any three hundred sixty-five (365) consecutive calendar days.

"Constructive Termination" shall also mean failure by the Company, or a successor to the Company, prior to the one (1) year anniversary of a Corporation Transaction to offer you continued employment on mutually acceptable terms pursuant to the terms of a written agreement with the Company, any third party acquiror or any affiliate of the Company or such third party acquiror that contemplates or provides for your continued employment with the Company at any time from and after such Corporation Transaction or for your employment with such acquiror or any affiliate of such acquiror or the Company at any time from and after such Corporation Transaction.

(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) the Severance Payment less applicable withholdings and deductions, paid in a lump sum as provided below, (ii) the COBRA Premiums; (iii) the Option Acceleration; and (iv) the Option Extension; provided, however, that the Option Extension period shall not be extended beyond the period of time that would enable the stock option to remain exempt under Section 409A.

Any obligation of the Company to you in Section 8(c) is conditioned upon you signing and returning to the Company a timely and effective Release of Claims. The Release of Claims required for separation benefits in accordance with this Section 8(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 will be paid 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 11(d) hereof. The payment of the COBRA Premiums will commence on such later date as well. Notwithstanding the foregoing, if the Company determines that it cannot provide such reimbursement of premiums to you without potentially violating applicable law, the Company shall not be obligated to make any such payments or reimbursements to you.

(d) Section 280G. 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.

9. **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, and without prior notice, 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.

10. **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.

11. **Tax Matters**.

(a) Subsections (a) through (e) of this Section 11 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 Company 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 (12) months after your employment ends, if your employment ends on account of your death or total and permanent disability, or

(ii) more than three (3) months after your employment ends, if your employment ends in any other circumstance.

12. **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 PRT-201 that the Company is developing for the reduction of vascular access failure in patients receiving hemodialysis. Your obligations under this Section 12 survive any termination of your employment.

13. **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.

14. **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.

15. **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.

---

16. **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.

17. **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.

18. **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.

19. **Entire Agreement**. This Agreement, the Employee Confidentiality and Inventions Assignment Agreement that you have previously executed with the Company, 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.

20. **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.

[*The remainder of this page is intentionally left blank.*
Signatures on following page.]

Best Regards,

PROTEON THERAPEUTICS, INC.

By: /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 October 1, 2014

Steven K. Burke Date

EXHIBIT A

Release of Claims

In consideration of the promises and covenants recited in the Employment Agreement dated as of by and between Proteon Therapeutics, Inc. (the "Company") and Steven K. Burke (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 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 the Company's Chief Executive Officer 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.

Steven K. Burke

Steven K. Burke
Date:

Exhibit 10.28

Proteon Therapeutics, Inc.
200 West St.
Waltham, MA 02451

October 1, 2014

Mr. George A. Eldridge
64 Damien Road
Wellesley, MA 02481

Re: Employment with Proteon Therapeutics, Inc.

Dear George,

Reference is hereby made to that certain Employment Letter Agreement (the "Original Employment Agreement"), dated as of September 9, 2013, between you and Proteon Therapeutics, Inc. (the "Company" or "Proteon"). This letter agreement (the "Agreement") amends and restates the Original Employment Agreement in its entirety. This letter contains the basic terms of your employment with the Company. 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. This Agreement shall be effective contingent upon, and from and after, the consummation of the Company's initial public offering (the "IPO") of its common stock, par value $0.001 per share ("Common Stock").

1. **Duties**. 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**. You will be compensated at a base rate of $300,290 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.

4. **Annual Bonus**. You will have an annual target bonus of 35% of your Base Salary ("Bonus"), subject to upward adjustments at the discretion of the Board typically made annually as part of the Company's annual compensation review process. The actual amount of this Bonus, if any and up to the full 35% target shall be determined by the Board, based on its assessment, in its discretion, of your and the Company's performance. 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. "Pro-Rata Bonus" means the Bonus that (but for the cessation of employment) would otherwise have been payable for the fiscal year in which the cessation occurs (based on actual performance outcomes for that year), multiplied by the following fraction: (i) the number of days that you were employed by the Company during that fiscal year, divided by (ii) 365. For this

---

purpose, the Bonus that would otherwise have been payable to you shall be determined by the Board in good faith and in the same manner applicable to active executive officers of the Company.

5. **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 executive.

6. **Vacation**. You will continue to accrue vacation on a monthly basis per standard Company policy. 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.

7. **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.

8. **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 being cured, is not cured within thirty (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 thirty (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 thirty (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 Section 18 below. In the event of

your death or disability as provided in Section 8(b) (vi) or 8(b)(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 one hundred eighty 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 nine (9) months of your Base Salary, at the rate in effect on the date of termination, plus your annual Bonus in respect of any calendar year that has been earned but not yet paid (for this purpose the Bonus earned for such calendar year shall be determined by the Board in good faith and in the same manner applicable to active executive officers of the Company, your "Earned and Unpaid Bonus") or, in the event Constructive Termination or a 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, as applicable, at the rate in effect on the date of termination plus, only following a Corporation Transaction, an amount equal to your Pro-Rata Bonus plus any Earned and Unpaid Bonus, 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 equal to the amount that the Company was paying for you under such group health insurance plans prior to the effective date of termination for nine (9) months following (the "9-Month Tail Period") or, in the event Constructive Termination or a 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 9-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 or a termination without Cause, accelerated to one hundred percent (100%) vesting in the event Constructive Termination or a termination without Cause occurs within thirty (30) days prior to or three hundred sixty-five (365) days following a Corporate Transaction (as defined below) (the "Option Acceleration"); and (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 one hundred eighty (180) days following the termination (the "Option Extension"); provided, however, that the Option Extension period shall not be extended beyond the period of time that would enable the stock option to remain exempt under Section 409A (as defined below).

Any obligation of the Company to you in Section 8(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 8(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 will be paid 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 11(d) hereof. The payment of the COBRA Premiums will commence on such later date as well. Notwithstanding the foregoing, if the Company determines that it cannot provide such reimbursement of premiums to you without potentially violating applicable law, the Company shall not be obligated to make any such payments or reimbursements to you.

The following shall constitute Constructive Termination:

(i) failure of the Company to provide you Base Salary (as may have been increased pursuant to Section 3) 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;

(iii) material diminution in the nature or scope of your responsibilities, duties or authority, or a reduction in your Base Salary (as may have been increased pursuant to Section 3) 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) 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 one hundred eighty (180) consecutive days in any three hundred sixty-five (365) consecutive calendar days.

"Constructive Termination" shall also mean failure by the Company, or a successor to the Company, prior to the one (1) year anniversary of a Corporation Transaction to offer you continued employment on mutually acceptable terms pursuant to the terms of a written agreement with the Company, any third party acquiror or any affiliate of the Company or such third party acquiror that contemplates or provides for your continued employment with the Company at any time from and after such Corporation Transaction or for your employment with such acquiror or any affiliate of such acquiror or the Company at any time from and after such Corporation Transaction.

(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) the Severance Payment less applicable withholdings and deductions, paid in a lump sum as provided below; (ii) the COBRA Premiums; (iii) the Option Acceleration; and (iv) the Option Extension; provided, however, that the Option Extension period shall not be extended beyond the period of time that would enable the stock option to remain exempt under Section 409A.

Any obligation of the Company to you in Section 8(c) is conditioned upon you signing and returning to the Company a timely and effective Release of Claims. The Release of Claims required for

separation benefits in accordance with this Section 8(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 will be paid 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 11(d) hereof. The payment of the COBRA Premiums will commence on such later date as well. Notwithstanding the foregoing, if the Company determines that it cannot provide such reimbursement of premiums to you without potentially violating applicable law, the Company shall not be obligated to make any such payments or reimbursements to you.

(d) Section 280G. 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.

9. **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, and without prior notice, 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.

10. **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.

11. **Tax Matters**.

(a) Subsections (a) through (e) of this Section 11 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 Company 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 (12) months after your employment ends, if your employment ends on account of your death or total and permanent disability, or

(ii) more than three (3) months after your employment ends, if your employment ends in any other circumstance.

12. **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 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 Section 12 survive any termination of your employment.

13. **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.

14. **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.

15. **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.

16. **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.

17. **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.

18. **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.

19. **Entire Agreement**. This Agreement, the Employee Confidentiality and Inventions Assignment Agreement that you have previously executed with the Company, 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.

20. **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.

[*The remainder of this page is intentionally left blank.*
Signatures on following page.]

Best Regards,

PROTEON THERAPEUTICS, INC.

By: /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 A. Eldridge	October 1, 2014
George A. Eldridge	Date

EXHIBIT A

Release of Claims

In consideration of the promises and covenants recited in the Employment Agreement dated as of by and between Proteon Therapeutics, Inc. (the "Company") and George A. 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 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 the Company's Chief Executive Officer 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 A. Eldridge

George A. Eldridge
Date:

Proteon Therapeutics, Inc.
200 West St.
Waltham, MA 02451

October 1, 2014

Mr. Daniel Gottlieb
25 Suffolk Road
Sudbury, MA 01776

Re: Employment with Proteon Therapeutics, Inc.

Dear Daniel,

Reference is hereby made to that certain employment letter agreement, dated as of July 19, 2007, between you and Proteon Therapeutics, Inc. (the "Company" or "Proteon") and that certain severance agreement, dated as of September 23, 2013, between you and the Company (the "Original Employment Agreements"). This letter agreement (the "Agreement") amends and restates the Original Employment Agreements, as amended, in their entirety. This letter contains the basic terms of your employment with the Company. 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. This Agreement shall be effective contingent upon, and from and after, the consummation of the Company's initial public offering (the "IPO") of its common stock, par value $0.001 per share ("Common Stock").

1. **Duties**. You will be employed as the Company's Vice President, Marketing and Business Development. In this capacity, you shall perform such duties as are ordinary, customary and necessary in your role as Vice President, Marketing and Business Development. 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**. You will be compensated at a base rate of $221,230 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.

4. **Annual Bonus**. You will have an annual target bonus of 30% of your Base Salary ("Bonus"), subject to upward adjustments at the discretion of the Board typically made annually as part of the Company's annual compensation review process. The actual amount of this Bonus, if any and up to the full 30% target shall be determined by the Board, based on its assessment, in its discretion, of your and the Company's performance. 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. "Pro-Rata Bonus" means the Bonus that (but for the cessation of employment) would otherwise have been payable for the fiscal year in which the cessation occurs (based on actual performance outcomes for that year), multiplied by the following fraction: (i) the number of

---

days that you were employed by the Company during that fiscal year, divided by (ii) 365. For this purpose, the Bonus that would otherwise have been payable to you shall be determined by the Board in good faith and in the same manner applicable to active executive officers of the Company.

5. **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 executive.

6. **Vacation**. You will continue to accrue vacation on a monthly basis per standard Company policy. 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.

7. **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.

8. **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 being cured, is not cured within thirty (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 thirty (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 thirty (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 Section 18 below. In the event

of your death or disability as provided in Section 8(b)(vi) or 8(b)(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 one hundred eighty 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 nine (9) months of your Base Salary, at the rate in effect on the date of termination, plus your annual Bonus in respect of any calendar year that has been earned but not yet paid (for this purpose, the Bonus earned for such calendar year shall be determined by the Board in good faith and in the same manner applicable to active executive officers of the Company, your "Earned and Unpaid Bonus") or, in the event Constructive Termination or a 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, as applicable, at the rate in effect on the date of termination plus, only following a Corporation Transaction, an amount equal to your Pro-Rata Bonus plus any Earned and Unpaid Bonus, 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 equal to the amount that the Company was paying for you under such group health insurance plans prior to the effective date of termination for nine (9) months following (the "9-Month Tail Period") or, in the event Constructive Termination or a 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 9-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 or a termination without Cause, accelerated to one hundred percent (100%) vesting in the event Constructive Termination or a termination without Cause occurs within thirty (30) days prior to or three hundred sixty-five (365) days following a Corporate Transaction (as defined below) (the "Option Acceleration"); (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 one hundred eighty (180) days following the termination (the "Option Extension"); provided, however, that the Option Extension Period shall not be extended beyond the period of time that would enable the stock option to remain exempt under Section 409A (as defined below).

Any obligation of the Company to you in Section 8(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 8(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 will be paid 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 11(d) hereof. The payment of the COBRA Premiums will commence on such later date as well. Notwithstanding the foregoing, if the Company determines that it cannot provide such reimbursement of premiums to you without potentially violating applicable law, the Company shall not be obligated to make any such payments or reimbursements to you.

The following shall constitute Constructive Termination:

(i) failure of the Company to provide you Base Salary (as may have been increased pursuant to Section 3) 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;

(iii) material diminution in the nature or scope of your responsibilities, duties or authority, or a reduction in your Base Salary (as may have been increased pursuant to Section 3) 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) 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 one hundred eighty (180) consecutive days in any three hundred sixty-five (365) consecutive calendar days.

"Constructive Termination" shall also mean failure by the Company prior to the one (1) year anniversary of a Corporation Transaction to offer you continued employment on mutually acceptable terms pursuant to the terms of a written agreement with the Company, any third party acquiror or any affiliate of the Company or such third party acquiror that contemplates or provides for your continued employment with the Company at any time from and after such Corporation Transaction or for your employment with such acquiror or any affiliate of such acquiror or the Company at any time from and after such Corporation Transaction.

(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) the Severance Payment less applicable withholdings and deductions, paid in a lump sum as provided below; (ii) the COBRA Premiums; (iii) the Option Acceleration; and (iv) the Option Extension; provided, however, that the Option Extension period shall not be extended beyond the period of time that would enable the stock option to remain exempt under Section 409A.

Any obligation of the Company to you in Section 8(c) is conditioned upon you signing and returning to the Company a timely and effective Release of Claims. The Release of Claims required for separation benefits in accordance with this Section 8(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 will be paid 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 11(d) hereof. The payment of the COBRA Premiums will commence on such later date as well. Notwithstanding the foregoing, if the Company determines that it cannot provide such reimbursement of premiums to you without potentially violating applicable law, the Company shall not be obligated to make any such payments or reimbursements to you.

(d) Section 280G. 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.

9. **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, and without prior notice, 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.

10. **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.

11. **Tax Matters**.

(a) Subsections (a) through (e) of this Section 11 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 Company 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 (12) months after your employment ends, if your employment ends on account of your death or total and permanent disability, or

(ii) more than three (3) months after your employment ends, if your employment ends in any other circumstance.

12. **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 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 Section 12 survive any termination of your employment.

13. **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.

14. **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.

15. **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.

---

16. **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.

17. **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.

18. **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.

19. **Entire Agreement**. This Agreement, the Employee Confidentiality and Inventions Assignment Agreement that you have previously executed with the Company, 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.

20. **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.

[The remainder of this page is intentionally left blank.
Signatures on following page.]

Best Regards,

PROTEON THERAPEUTICS, INC.

By: /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/ Daniel Gottlieb	October 1, 2014
Daniel Gottlieb	Date

EXHIBIT A

Release of Claims

In consideration of the promises and covenants recited in the Employment Agreement dated as of by and between Proteon Therapeutics, Inc. (the "Company") and Daniel Gottlieb (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

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 the Company's Chief Executive Officer 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.

Daniel Gottlieb

Daniel Gottlieb
Date:

FORM OF AMENDED AND RESTATED

INDEMNIFICATION AGREEMENT

AMENDED AND RESTATED INDEMNIFICATION AGREEMENT

THIS AMENDED AND RESTATED INDEMNIFICATION AGREEMENT (the "**Agreement**") is made and entered into as of _____ ___, 2014 between **PROTEON THERAPEUTICS, INC.**, a Delaware corporation (the "**Company**"), and _____ ("**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, or is made (or asked to) respond to discovery requests, 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 a written 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 an officer or 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 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 an officer or director of the Company, and the Company acknowledges that Indemnitee is relying upon this Agreement in serving as an officer or 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, or responding to, or objecting to, a request to provide discovery in any Proceeding. Expenses also shall include Expenses incurred in connection with any appeal resulting from any Proceeding and any federal, state, local or foreign taxes imposed on the Indemnitee as a result of the actual or deemed receipt of any payments under this Agreement, including without limitation the premium, security for, and other costs relating to any cost bond, supersede as 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 an officer or director of the Company, by reason of any action taken by him or of any inaction on his part while acting as an officer or 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 Amended and Restated Indemnification Agreement on and as of the day and year first above written.

PROTEON THERAPEUTICS, INC.

By: _____
Name: _____
Title: _____

INDEMNITEE

_____
Name: _____

Address:

SIGNATURE PAGE TO INDEMNIFICATION AGREEMENT

Exhibit 23.2

Consent of Independent Registered Public Accounting Firm

We consent to the reference to our firm under the caption "Experts" and to the use of our report dated June 25, 2014 (except for Note 15, as to which the date is October 6, 2014) included in Amendment No. 1 to the Registration Statement (Form S-1 333-198777) and related Prospectus of Proteon Therapeutics, Inc. for the registration of shares of its common stock.

/s/ Ernst & Young LLP

Boston, Massachusetts

October 7, 2014

QuickLinks