
UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM S-1

REGISTRATION STATEMENT
Under
The Securities Act of 1933

Proteon Therapeutics, Inc.

(Exact name of Registrant as specified in its charter)

Delaware (State or Other Jurisdiction of Incorporation or Organization)	2836 (Primary Standard Industrial Classification Code Number)	20-4580525 (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.

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. 333-198777

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.

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.

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

Accelerated filer

Non-accelerated filer
(Do not check if a
smaller reporting company)

Smaller reporting company

Title of Each Class of Securities to be Registered	Amount to be Registered(1)	Proposed Maximum Offering Price per Share(2)	Proposed Maximum Aggregate Offering Price(2)	Amount of Registration Fee(3)
Common Stock, \$0.001 par value per share	1,621,500	\$10.00	\$16,215,000	\$1,885

- (1) The Registrant is registering 1,621,500 shares, including 211,500 shares of common stock issuable upon exercise of the underwriters' option to purchase additional shares, pursuant to this Registration Statement which shares are in addition to the 5,405,000 shares registered pursuant to the Registration Statement on Form S-1, as amended (File No. 333-198777).
- (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) The registration fee is based upon the public offering price.

This Registration Statement shall become effective upon filing in accordance with Rule 462(b) under the Securities Act of 1933.

EXPLANATORY NOTE AND INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

Pursuant to Rule 462(b) under the Securities Act of 1933, as amended, Proteon Therapeutics, Inc. (the "**Registrant**") is filing this Registration Statement on Form S-1 (this "**Registration Statement**") with the Securities and Exchange Commission (the "**Commission**"). This Registration Statement relates to the public offering of securities contemplated by the Registration Statement on Form S-1, as amended (File No. 333-198777) (the "**Prior Registration Statement**"), which the Registrant originally filed with the Commission on September 16, 2014, and which the Commission declared effective on October 21, 2014.

The Registrant is filing this Registration Statement for the sole purpose of increasing the aggregate number of shares of common stock offered by the Registrant by 1,621,500 shares, 211,500 of which may be sold by the Registrant in the event the underwriters exercise their option to purchase additional shares of the Registrant's common stock. The additional shares that are being registered for issuance and sale are in an amount and at a price that together represent no more than 20% of the maximum aggregate offering price set forth in the Calculation of Registration Fee table contained in the Prior Registration Statement. The information set forth in the Prior Registration Statement and all exhibits to the Prior Registration Statement are hereby incorporated by reference into this Registration Statement.

The required opinion and consents are listed on the Exhibit Index attached hereto and filed herewith.

SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, as amended, the Registrant has duly caused this registration statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the city of Waltham, Commonwealth of Massachusetts on October 21, 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 registration statement has been signed by the following persons in the capacities and on the dates indicated.

<u>Name</u>	<u>Title</u>	<u>Date</u>
/s/ TIMOTHY P. NOYES _____ Timothy P. Noyes	President, Chief Executive Officer and Director (<i>Principal Executive Officer</i>)	October 21, 2014
/s/ GEORGE ELDRIDGE _____ George Eldridge	Senior Vice President, Chief Financial Officer, Treasurer and Secretary (<i>Principal Financial Officer and Principal Accounting Officer</i>)	October 21, 2014
* _____ Hubert Birner, Ph.D.	Director	October 21, 2014
* _____ John G. Freund, M.D.	Director	October 21, 2014
* _____ Tim Haines	Director	October 21, 2014
* _____ Dmitry Kobzyev, Ph.D.	Director	October 21, 2014
* _____ Brendan M. O'Leary, Ph.D.	Director	October 21, 2014
* _____ Gregory D. Phelps	Director	October 21, 2014
* _____ Garen Bohlin	Director	October 21, 2014

*By: /s/ TIMOTHY P. NOYES

Timothy P. Noyes
Attorney-in-fact

EXHIBIT INDEX

Exhibit No.	Description
5.1	Opinion of Bingham McCutchen LLP.
23.1	Consent of Ernst & Young LLP, Independent Registered Public Accounting Firm.
23.2	Consent of Bingham McCutchen LLP (included in Exhibit 5.1).
24.1	Power of Attorney (incorporated by reference to Exhibit 24.1 of the Registration Statement on Form S-1, as amended (File No. 333-198777)).

QuickLinks

[EXPLANATORY NOTE AND INCORPORATION OF CERTAIN INFORMATION BY REFERENCE](#)

[SIGNATURES](#)

[EXHIBIT INDEX](#)

October 21, 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 filed with the Securities and Exchange Commission on October 21, 2014 (the "Registration Statement"), under the Securities Act of 1933, as amended (the "Act"), pursuant to Rule 462(b) of the Act. The Registration Statement relates to the registration of the offer and sale of up to 1,621,500 shares of the Company's Common Stock, par value \$0.001 per share (the "Common Stock"), including up to 211,500 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 a Registration Statement on Form S-1, as amended (File No. 333-198777), 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

QuickLinks

[Exhibit 5.1](#)

Consent of Independent Registered Public Accounting Firm

We consent to the incorporation by reference in the Registration Statement on Form S-1 filed pursuant to Rule 462(b) of the Securities Act of 1933 of the reference to our firm under the caption "Experts" and our report dated June 25, 2014 (except for Note 15, as to which the date is October 6, 2014) relating to the financial statements of Proteon Therapeutics, Inc. included in Amendment No. 1 to the Registration Statement (Form S-1 No. 333-198777) and related Prospectus of Proteon Therapeutics, Inc. for the registration of its common stock.

/s/ Ernst & Young LLP

Boston, Massachusetts
October 21, 2014

QuickLinks

[Exhibit 23.1](#)