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**UNITED STATES  
SECURITIES AND EXCHANGE COMMISSION  
WASHINGTON, D.C. 20549**

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**FORM S-8  
REGISTRATION STATEMENT  
UNDER  
THE SECURITIES ACT OF 1933**

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**PROTEOSTASIS THERAPEUTICS, INC.**  
(Exact name of registrant as specified in its charter)

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**Delaware**  
(State or other jurisdiction of  
incorporation or organization)

**20-8436652**  
(I.R.S. Employer  
Identification No.)

**80 Guest Street, Suite 500,  
Boston, Massachusetts, 02135**  
(Address of principal executive offices) (Zip Code)

**Proteostasis Therapeutics, Inc. 2016 Stock Option and Incentive Plan  
Proteostasis Therapeutics, Inc. 2016 Employee Stock Purchase Plan**  
(Full title of the plan)

**Meenu Chhabra**  
**President and Chief Executive Officer**  
**Proteostasis Therapeutics, Inc.**  
**80 Guest Street, Suite 500**  
**Boston, Massachusetts**  
(Name and address of agent for service)

**(617) 225-0096**  
(Telephone number, including area code, of agent for service)

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*With copies to:*

**Janet Smart**  
**VP, Intellectual Property and Legal Affairs**  
**Proteostasis Therapeutics, Inc.**  
**80 Guest Street, Suite 500**  
**Boston, Massachusetts, 02135**

**Mitchell S. Bloom, Esq.**  
**John M. Mutkoski, Esq.**  
**Goodwin Procter LLP**  
**100 Northern Avenue**  
**Boston, Massachusetts 02109**  
**(617) 570-1000**

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

Large accelerated filer  Accelerated filer  Smaller reporting company   
Non-accelerated filer  Emerging growth company

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 7(a)(2)(B) of the Securities Act.

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**CALCULATION OF REGISTRATION FEE**

<b>Title of securities to be registered</b>	<b>Amount to be registered<sup>(1)</sup></b>	<b>Proposed maximum offering price per share<sup>(2)</sup></b>	<b>Proposed maximum aggregate offering price<sup>(2)</sup></b>	<b>Amount of registration fee<sup>(2)</sup></b>
<b>2016 Stock Option and Incentive Plan</b>				
Common Stock, \$0.001 par value per share	1,524,252 shares <sup>(3)</sup>	\$4.23	\$6,447,585.96	\$781.45
<b>2016 Employee Stock Purchase Plan</b>				
Common Stock, \$0.001 par value per share	138,757 shares <sup>(4)</sup>	\$4.23	\$586,942.11	\$71.14
<b>Total</b>	<b>1,663,009 shares</b>			<b>\$852.59</b>

- (1) Pursuant to Rule 416 under the Securities Act of 1933, as amended (the "Securities Act"), this Registration Statement shall also cover any additional shares of common stock which become issuable under the above-named plans by reason of any stock dividend, stock split, recapitalization or any other similar transaction effected without the receipt of consideration which results in an increase in the number of our outstanding shares of common stock. Pursuant to Rule 416(c) under the Securities Act, this Registration Statement shall also cover an indeterminate amount of interests to be offered or sold pursuant to the employee benefit plans described herein.
- (2) Estimated solely for the purpose of calculating the registration fee pursuant to Rule 457 of the Securities Act, and based on \$4.23, the average of the high and low sale prices of the registrant's common stock as reported on the Nasdaq Global Market on March 6, 2019.
- (3) Represents an automatic increase to the number of shares available for issuance under the registrant's 2016 Stock Option and Incentive Plan (the "Plan"), effective as of January 1, 2018. Shares available for issuance under the Plan were previously registered on registration statements on Form S-8 filed with the Securities and Exchange Commission on March 31, 2016 (Registration No. 333-210521).
- (4) Represents an automatic increase to the number of shares available for issuance under the registrant's 2016 Employee Stock Purchase Plan (the "ESPP"), effective as of January 1, 2018. Shares available for issuance under the ESPP were previously registered on registration statements on Form S-8 filed with the Securities and Exchange Commission on March 31, 2016 (Registration No. 333-210521).

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**EXPLANATORY NOTE**

This Registration Statement registers additional securities of the same class as other securities for which a registration statement filed on Form S-8 (Registration No. 333-210521) of the Registrant is effective. The information contained in the Registrant's registration statement on Form S-8 (Registration No. 333-210521) is hereby incorporated by reference pursuant to General Instruction E.

**PART II**

**INFORMATION REQUIRED IN THE REGISTRATION STATEMENT**

**Item 8. Exhibits.**

See the Exhibit Index on the page immediately preceding the exhibits for a list of exhibits filed as part of this registration statement, which Exhibit Index is incorporated herein by reference.

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## INDEX TO EXHIBITS

<u>Exhibit No.</u>	<u>Description of Exhibit</u>
3.1	<a href="#"><u>Fifth Amended and Restated Certificate of Incorporation of the Registrant (Incorporated by reference to Exhibit 3.1 to the Registrant's Registration Statement on Form S-3, as amended (333-208735) filed on November 23, 2018).</u></a>
3.2	<a href="#"><u>Second Amended and Restated By-laws of the Registrant (Incorporated by reference to Exhibit 3.2 to the Registrant's Registration Statement on Form S-1, as amended (333-208735) filed on February 1, 2016).</u></a>
4.1	<a href="#"><u>Specimen Common Stock Certificate (Incorporated by reference to Exhibit 4.1 to the Registrant's Registration Statement on Form S-1, as amended (333-208735) filed on February 1, 2016).</u></a>
4.2	<a href="#"><u>Third Amended and Restated Stockholders' Agreement of the Company (Incorporated by reference to Exhibit 4.2 to the Registrant's Registration Statement on Form S-1, as amended (333-208735) filed on February 1, 2016).</u></a>
4.3	<a href="#"><u>Form of Preferred Stock Warrant (Incorporated by reference to Exhibit 4.3 to the Registrant's Registration Statement on Form S-1 (333-208735) filed on February 1, 2016).</u></a>
5.1*	<a href="#"><u>Opinion of Goodwin Procter LLP.</u></a>
23.1*	<a href="#"><u>Consent of PricewaterhouseCoopers LLP.</u></a>
23.2*	<a href="#"><u>Consent of Goodwin Procter LLP (included in Exhibit 5.1).</u></a>
24.1*	<a href="#"><u>Power of Attorney (included as part of the signature page to this Registration Statement).</u></a>
99.1	<a href="#"><u>2016 Stock Option and Incentive Plan and forms of award agreements thereunder (Incorporated by reference to Exhibit 10.6 to the Registrant's Registration Statement on Form S-1, as amended (File No. 333-208735) filed on February 1, 2016).</u></a>
99.2	<a href="#"><u>2016 Employee Stock Purchase Plan (Incorporated by reference to Exhibit 10.15 to the Registrant's Registration Statement on Form S-1, as amended (File No. 333-208735) filed on February 1, 2016).</u></a>

\* Filed herewith.

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## SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, the registrant certifies that it has reasonable grounds to believe that it meets all of the requirements for filing on Form S-8 and has duly caused this Registration Statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of Boston, State of Massachusetts, on March 8, 2019.

PROTEOSTASIS THERAPEUTICS, INC.

By: /s/ Meenu Chhabra  
Meenu Chhabra  
President and Chief Executive Officer

## POWER OF ATTORNEY

We, the undersigned officers and directors of Proteostasis Therapeutics, Inc., hereby severally constitute and appoint Meenu Chhabra, our true and lawful attorney-in-fact and agent, with full power of substitution and resubstitution for her and in her name, place and stead, and in any and all capacities, to sign any and all amendments (including post-effective amendments) to this registration statement, and to file the same, with all exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorney-in-fact and agent, full power and authority to do and perform each and every act and thing requisite or necessary to be done in and about the premises, as full to all intents and purposes as she might or could do in person, hereby ratifying and confirming all that said attorney-in-fact and agent or her substitute or substitutes, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Act of 1933, as amended, this Registration Statement has been signed by the following persons in the capacities and on the date indicated.

<u>/s/ Meenu Chhabra</u> Meenu Chhabra	President, Chief Executive Officer and Director (Principal Executive Officer)	March 8, 2019
<u>/s/ Sandra Zimmerman</u> Sandra Zimmerman	Interim Vice President of Finance (Principal Financial and Accounting Officer)	March 8, 2019
<u>/s/ M. James Barrett</u> M. James Barrett, Ph.D.	Chairman of the Board of Directors	March 8, 2019
<u>/s/ Franklin M. Berger</u> Franklin M. Berger, CFA	Director	March 8, 2019
<u>/s/ Jeffrey W. Kelly</u> Jeffery W. Kelly, Ph.D.	Director	March 8, 2019
<u>/s/ Kim C. Drapkin</u> Kim C. Drapkin	Director	March 8, 2019
<u>/s/ Emmanuel Dulac</u> Emmanuel Dulac	Director	March 8, 2019
<u>/s/ David Arkowitz</u> David Arkowitz	Director	March 8, 2019



Goodwin Procter LLP  
100 Northern Avenue  
Boston, MA 02210

goodwinlaw.com  
+1 617 570 1000

March 8, 2019

Proteostasis Therapeutics, Inc.  
80 Guest Street  
Suite 500  
Boston, Massachusetts 02135

Re: Securities Being Registered under Registration Statement on Form S-8

Ladies and Gentlemen:

We have acted as counsel to you in connection with your filing of a Registration Statement on Form S-8 (the "Registration Statement") pursuant to the Securities Act of 1933, as amended (the "Securities Act"), on or about the date hereof relating to an aggregate of 1,663,009 shares (the "Shares") of Common Stock, \$0.001 par value per share ("Common Stock"), of Proteostasis Therapeutics, Inc., a Delaware corporation (the "Company"), that may be issued pursuant to the Company's 2016 Stock Option and Incentive Plan and 2016 Employee Stock Purchase Plan (collectively, the "Plans").

We have reviewed such documents and made such examination of law as we have deemed appropriate to give the opinions set forth below. We have relied, without independent verification, on certificates of public officials and, as to matters of fact material to the opinion set forth below, on certificates of officers of the Company.

The opinion set forth below is limited to the Delaware General Corporation Law.

For purposes of the opinion set forth below, we have assumed that no event occurs that causes the number of authorized shares of Common Stock available for issuance by the Company to be less than the number of then unissued Shares.

Based on the foregoing, we are of the opinion that the Shares have been duly authorized and, upon issuance and delivery against payment therefor in accordance with the terms of the Plans, will be validly issued, fully paid and nonassessable.

We hereby consent to the inclusion of this opinion as Exhibit 5.1 to the Registration Statement. In giving our consent, we do not admit that we are in the category of persons whose consent is required under Section 7 of the Securities Act or the rules and regulations thereunder.



Proteostasis Therapeutics, Inc.  
March 8, 2019  
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Very truly yours,

/s/ GOODWIN PROCTER LLP

GOODWIN PROCTER LLP

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We hereby consent to the incorporation by reference in this Registration Statement on Form S-8 of Proteostasis Therapeutics, Inc., of our report dated March 8, 2019 relating to the financial statements, which appears in Proteostasis Therapeutics, Inc.'s Annual Report on Form 10-K for the year ended December 31, 2018.

/s/ PricewaterhouseCoopers LLP  
Boston, Massachusetts  
March 8, 2019