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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**  
(Address of principal executive offices)

**02135**  
(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**  
**Senior Vice President, Legal Affairs**  
**Proteostasis Therapeutics, Inc.**  
**80 Guest Street, Suite 500**  
**Boston, Massachusetts, 02135**

**Marc Recht**  
**Courtney T. Thorne**  
**Cooley LLP**  
**500 Boylston Street**  
**Boston, Massachusetts 02116**  
**(617) 937-2300**

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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   
Non-accelerated filer

Accelerated filer   
Smaller reporting company   
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**

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Title 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
2016 Stock Option and Incentive Plan Common Stock, \$0.001 par value per share	1,563,498 shares(3)	\$1.05	\$1,641,672.90	\$213.09
2016 Employee Stock Purchase Plan Common Stock, \$0.001 par value per share	138,757 shares(4)	\$1.05	\$145,694.85	\$18.91
<b>Total</b>	1,702,255 shares			\$232.00

- (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.
- (2) Estimated solely for the purpose of calculating the registration fee pursuant to Rule 457(c) and Rule 457(h) of the Securities Act, and based on \$1.05, the average of the high and low sale prices of the registrant's common stock as reported on the Nasdaq Global Market on March 12, 2020.
- (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, 2020. 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. 222-210521), June 7, 2017 (Registration No. 333-218544), March 15, 2018 (Registration No. 333-223664) and March 8, 2019 (Registration No. 333-230155).
- (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, 2020. 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), June 7, 2017 (Registration No. 333-218544), March 15, 2018 (Registration No. 333-223664) and March 8, 2019 (Registration No. 333-230155).

## EXPLANATORY NOTE

This Registration Statement registers additional securities of the same class as other securities for which previous registration statements filed on Form S-8 of the Registrant is effective. The information contained in the Registrant's registration statements on Form S-8 filed with the Securities and Exchange Commission on [March 31, 2016](#) (Registration No. 333-210521), [June 7, 2017](#) (Registration No. 333-218544), [March 15, 2018](#) (Registration No. 333-223664) and [March 8, 2019](#) (Registration No. 333-230155) are hereby incorporated by reference pursuant to General Instruction E.

### PART II

#### INFORMATION REQUIRED IN THE REGISTRATION STATEMENT

##### Item 8. Exhibits.

<u>Exhibit No.</u>	<u>Description of Exhibit</u>
4.1	<a href="#">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).</a>
4.2	<a href="#">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).</a>
4.3	<a href="#">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).</a>
4.4	<a href="#">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).</a>
4.5	<a href="#">Form of Preferred Stock Warrant (Incorporated by reference to Exhibit 4.3 to the Registrant's Registration Statement on Form S-1 (333-208735).</a>
5.1*	<a href="#">Opinion of Cooley LLP.</a>
23.1*	<a href="#">Consent of PricewaterhouseCoopers LLP.</a>
23.2*	<a href="#">Consent of Cooley LLP (included in Exhibit 5.1).</a>
24.1*	<a href="#">Power of Attorney (included as part of the signature page to this Registration Statement).</a>
99.1	<a href="#">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).</a>
99.2	<a href="#">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).</a>

\* Filed herewith.

## 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 13, 2020.

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 13, 2020
<u>/s/ Eric Larson</u> Eric Larson	Controller (Principal Financial and Accounting Officer)	March 13, 2020
<u>/s/ Franklin M. Berger</u> Franklin M. Berger, CFA	Chairman of the Board of Directors	March 13, 2020
<u>Badrul Chowdhury</u> Badrul Chowdhury	Director	March 13, 2020
<u>/s/ Jeffrey W. Kelly</u> Jeffery W. Kelly, Ph.D.	Director	March 13, 2020
<u>/s/ Kim C. Drapkin</u> Kim C. Drapkin	Director	March 13, 2020
<u>/s/ Emmanuel Dulac</u> Emmanuel Dulac	Director	March 13, 2020
<u>/s/ David Arkowitz</u> David Arkowitz	Director	March 13, 2020



Marc Recht  
+1 617 937 2316  
mrecht@cooley.com

March 13, 2020

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

Ladies and Gentlemen:

You have requested our opinion, as counsel to Proteostasis Therapeutics, Inc., a Delaware corporation (the “**Company**”), in connection with the filing by the Company of a Registration Statement on Form S-8 (the “**Registration Statement**”) with the Securities and Exchange Commission covering the offering of up to 1,702,255 shares (the “**Shares**”) consisting of (a) 1,563,498 shares of the Company’s Common Stock, par value \$0.001 per share (the “**Common Stock**”), pursuant to the Company’s 2016 Stock Option and Incentive Plan (the “**2016 Plan**”), and (b) 138,757 shares of Common Stock pursuant to the Company’s 2016 Employee Stock Purchase Plan (together with the 2016 Plan, the “**Plans**”).

In connection with this opinion, we have examined and relied upon (a) the Registration Statement and the related prospectuses, (b) the Company’s Fifth Amended and Restated Certificate of Incorporation, as amended, and the Company’s Second Amended and Restated Bylaws, each as currently in effect, (c) the Plans and (d) originals or copies certified to our satisfaction of such records, documents, certificates, memoranda and other instruments as in our judgment are necessary or appropriate to enable us to render the opinion expressed below. We have assumed the genuineness and authenticity of all documents submitted to us as originals, the conformity to originals of all documents submitted to us as copies, the accuracy, completeness and authenticity of certificates of public officials; and the due authorization, execution and delivery of all documents by all persons other than the Company where authorization, execution and delivery are prerequisites to the effectiveness of such documents. As to certain factual matters, we have relied upon a certificate of an officer of the Company and have not sought independently to verify such matters.

Our opinion is expressed only with respect to the General Corporation Law of the State of Delaware. We express no opinion to the extent that any other laws are applicable to the subject matter hereof and express no opinion and provide no assurance as to compliance with any federal or state securities law, rule or regulation.

On the basis of the foregoing, and in reliance thereon, we are of the opinion that the Shares, when sold and issued in accordance with their respective Plans, the Registration Statement and the related prospectuses, will be validly issued, fully paid and nonassessable (except as to shares issued pursuant to certain deferred payment arrangements, which will be fully paid and nonassessable when such deferred payments are made in full).

Our opinion is limited to the matters stated herein and no opinion is implied or may be inferred beyond the matters expressly stated and is based on those laws as in effect on the date hereof, and we disclaim any obligation to advise you of facts, circumstances, events or developments which hereafter may be brought to our attention and which may alter, affect or modify the opinion expressed herein.

Cooley LLP 500 Boylston Street Boston, MA 02116-3736  
t: (617) 937-2300 f: (617) 937-2400 cooley.com



Proteostasis Therapeutics, Inc.  
March 13, 2020  
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We consent to the filing of this opinion as an exhibit to the Registration Statement.

Sincerely,

COOLEY LLP

By: /s/ Marc Recht

Marc Recht, Partner

Cooley LLP 500 Boylston Street Boston, MA 02116-3736  
t: (617) 937-2300 f: (617) 937-2400 cooley.com

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 10, 2020 relating to the financial statements, which appears in Proteostasis Therapeutics, Inc.'s Annual Report on Form 10-K for the year ended December 31, 2019.

/s/ PricewaterhouseCoopers LLP

Boston, Massachusetts  
March 13, 2020