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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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**Entasis Therapeutics Holdings Inc.**

(Exact name of registrant as specified in its charter)

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**Delaware**  
(State or other jurisdiction of  
incorporation or organization)  
  
**35 Gatehouse Drive**  
**Waltham, MA**  
(Address of Principal Executive Offices)

**82-4592913**  
(IRS employer  
identification number)

**02451**  
(Zip Code)

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**2018 Equity Incentive Plan**  
**2018 Employee Stock Purchase Plan**  
(Full title of the plans)

**Manoussos Perros, Ph.D.**  
**Chief Executive Officer**  
**Entasis Therapeutics Holdings Inc.**  
**35 Gatehouse Drive**  
**Waltham, MA 02451**  
(name and address of agent for service)  
**(781) 810-0120**  
(Telephone number, including area code, of agent for service)

**Copies to:**

**Michael Gutch**  
Entasis Therapeutics Holdings Inc.  
35 Gatehouse Drive  
Waltham, MA 02451  
(781) 810-8901

**Matthew C. Franker**  
Covington & Burling LLP  
One CityCenter  
850 Tenth Street, NW  
Washington, D.C. 20001  
(202) 662-6000

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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	<input type="checkbox"/>	Accelerated filer	<input type="checkbox"/>
Non-accelerated filer	<input checked="" type="checkbox"/>	Smaller reporting company	<input checked="" type="checkbox"/>
Emerging growth company	<input checked="" type="checkbox"/>		

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**

Title of Securities To Be Registered	Amount To Be Registered <sup>(1)</sup>	Proposed Maximum Offering Price Per Share	Proposed Maximum Aggregate Offering Price	Amount of Registration Fee
<b>Common Stock, par value \$0.001 per share</b> (2018 Equity Incentive Plan)	1,465,494	\$ 2.82 <sup>(2)</sup>	\$ 4,132,693.08 <sup>(2)</sup>	\$ 450.88
<b>Common Stock, par value \$0.001 per share</b> (2018 Employee Stock Purchase Plan)	250,000	\$ 2.40 <sup>(3)</sup>	\$ 600,000.00 <sup>(3)</sup>	\$ 65.46
<b>TOTAL</b>	1,715,494		\$ 4,732,693.08	\$ 516.34

- (1) Pursuant to Rule 416(a) under the Securities Act of 1933, as amended, or the Securities Act, this Registration Statement shall also cover any additional shares of common stock that become issuable under the above-named plans by reason of any stock dividend, stock split, recapitalization or any other similar transaction.
- (2) Estimated pursuant to Rule 457(c) and Rule 457(h) of the Securities Act solely for the purpose of calculating the registration fee, based on the average of the high and low sale prices of the registrant's common stock as reported on The Nasdaq Global Market on March 19, 2021.
- (3) Estimated pursuant to Rule 457(c) and Rule 457(h) of the Securities Act solely for the purpose of calculating the registration fee, based on 85% of the average of the high and low sale prices of the registrant's common stock as reported on The Nasdaq Global Market on March 19, 2021. Pursuant to the registrant's 2018 Employee Stock Purchase Plan, the purchase price of shares of registrant's common stock reserved for issuance thereunder will be not less than the lesser of an amount equal to 85% of the fair market value on (i) the offering date or (ii) the purchase date.

## EXPLANATORY NOTE

This Registration Statement on Form S-8, or the Registration Statement, is filed by Entasis Therapeutics Holdings Inc., or the Company, for the purpose of registering additional shares of its common stock, par value \$0.001 per share, or the Common Stock, under the Company's 2018 Equity Incentive Plan, or the 2018 Plan and the Company's 2018 Employee Stock Purchase Plan, or the ESPP.

The number of shares of Common Stock available for issuance under the 2018 Plan is subject to an automatic annual increase on January 1st of each year, for a period of not more than 10 years, commencing on January 1, 2019 and ending on (and including) January 1, 2028, in an amount equal to the lesser of: (a) 4% of the total number of shares of capital stock outstanding on December 31st of the preceding calendar year and (b) a number of shares of Common Stock designated by action of the Company's board of directors prior to the first day of any calendar year, or the 2018 Plan Provision. Accordingly, the number of shares of Common Stock available for issuance under the 2018 Plan was increased by 1,465,494 shares effective January 1, 2021. This Registration Statement registers the 1,465,494 additional shares of Common Stock available for issuance under the 2018 Plan as a result of the 2018 Plan Provision.

The number of shares of Common Stock available for issuance under the ESPP is subject to an automatic annual increase on January 1st of each year for a period of up to 10 years, commencing on January 1, 2019 and ending on (and including) January 1, 2028. The number of shares added each year will be equal to the lesser of: (a) 1% of the total number of shares of the Company's capital stock outstanding on December 31 of the preceding calendar year; (b) 250,000 shares of Common Stock and (c) a number of shares of Common Stock designated by action of the Company's board of directors prior to the first day of any calendar year, or the ESPP Provision. Accordingly, the number of shares of Common Stock available for issuance under the ESPP was increased by 250,000 shares effective January 1, 2021. This Registration Statement registers the 250,000 additional shares of Common Stock available for issuance under the ESPP as a result of the ESPP Provision.

Pursuant to General Instruction E to Form S-8 under the Securities Act, the contents of the Company's Registration Statements on Form S-8 filed with the Securities and Exchange Commission, or the SEC, on [November 14, 2018 \(File No. 333-228384\)](#), [March 29, 2019 \(File No. 333-230593\)](#), [May 7, 2020 \(File No. 333-238076\)](#) and [August 6, 2020 \(File No. 333-241672\)](#), are incorporated by reference into this Registration Statement.

## PART II

### INFORMATION REQUIRED IN THE REGISTRATION STATEMENT

#### Item 3. Incorporation of Documents by Reference.

The following documents (File No. 001-38670) previously filed with the SEC are hereby incorporated by reference:

- (a) [the Company's Annual Report on Form 10-K for the year ended December 31, 2020, filed with the SEC on March 23, 2021;](#)
- (b) [The description of the Company's Common Stock contained in Exhibit 4.3 to the Company's Annual Report on Form 10-K for the year ended December 31, 2019, filed with the SEC on March 11, 2020, including any amendments or reports filed for the purposes of updating this description.](#)

All documents subsequently filed by the Company pursuant to Section 13(a), 13(c), 14 or 15(d) of the Exchange Act, prior to the filing of a post-effective amendment which indicates that all securities offered hereby have been sold or which deregisters all securities then remaining unsold, shall be deemed to be incorporated by reference into this Registration Statement and to be a part hereof from the date of filing such documents, except as to specific sections of such documents as set forth therein.

Unless expressly incorporated into this Registration Statement, a report furnished on Form 8-K (or any portion thereof so furnished) prior or subsequent to the date hereof shall not be incorporated by reference into this Registration Statement. Any statement contained in a document incorporated or deemed to be incorporated by reference herein shall be deemed to be modified or superseded for purposes of this Registration Statement to the extent that a statement herein or in any subsequently filed document which also is or is deemed to be incorporated by reference herein modifies or supersedes such statement. Any such statement so modified or superseded shall not constitute a part of this Registration Statement, except as so modified or superseded.

**Item 8. Exhibits.**

<b>Exhibit Number</b>	<b>Exhibit Description</b>
3.1	<a href="#"><u>Amended and Restated Certificate of Incorporation (incorporated herein by reference to Exhibit 3.1 to the Company's Current Report on Form 8-K (File No. 001-38670), filed with the SEC on September 28, 2018).</u></a>
3.1.1	<a href="#"><u>Certificate of Amendment to the Amended and Restated Certificate of Incorporation of the Company (incorporated herein by reference to Exhibit 3.1 to the Company's Current Report on Form 8-K (File No. 001-38670), filed with the SEC on June 11, 2020).</u></a>
3.2	<a href="#"><u>Amended and Restated Bylaws (incorporated herein by reference to Exhibit 3.2 to the Company's Current Report on Form 8-K (File No. 001-38670), filed with the SEC on September 28, 2018).</u></a>
4.1	<a href="#"><u>Specimen common stock certificate (incorporated herein by reference to Exhibit 4.1 to the Company's Registration Statement on Form S-1 (File No. 333-226920), filed with the SEC on August 17, 2018).</u></a>
4.2	<a href="#"><u>2018 Equity Incentive Plan (incorporated herein by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q (File No. 001-38670), filed with the SEC on November 14, 2018).</u></a>
4.2.1	<a href="#"><u>First Amendment to 2018 Equity Incentive Plan (incorporated herein by reference to Exhibit 10.3 to the Company's Quarterly Report on Form 10-Q (File No. 001-38670), filed with the SEC on August 6, 2020).</u></a>
4.3	<a href="#"><u>Forms of Stock Option Grant Notice and Stock Option Agreement under 2018 Equity Incentive Plan (incorporated herein by reference to Exhibit 10.10 to the Company's Registration Statement on Form S-1 (File No. 333-226920), filed with the SEC on August 17, 2018).</u></a>
4.4	<a href="#"><u>2018 Employee Stock Purchase Plan (incorporated herein by reference to Exhibit 10.4 to the Company's Quarterly Report on Form 10-Q (File No. 001-38670), filed with the SEC on November 14, 2018).</u></a>
5.1*	<a href="#"><u>Opinion of Covington &amp; Burling LLP.</u></a>
23.1*	<a href="#"><u>Consent of KPMG LLP, independent registered public accounting firm.</u></a>
23.2*	Consent of Covington & Burling LLP (included in Exhibit 5.1).
24.1*	Power of Attorney (included on the signature page to this Registration Statement).

\*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 Waltham, Commonwealth of Massachusetts on March 23, 2021.

### Entasis Therapeutics Holdings Inc.

By: /s/ Manoussos Perros, Ph.D.  
Manoussos Perros, Ph.D.  
President and Chief Executive Officer

## POWER OF ATTORNEY

**KNOW ALL PERSONS BY THESE PRESENTS**, that each person whose signature appears below constitutes and appoints Manoussos Perros, Ph.D. and Michael Gutch, Ph.D., and each or any one of them, his or her true and lawful attorney-in-fact and agent, with full power of substitution and resubstitution, for him or her and in his or her name, place and stead, in any and all capacities, to sign any and all amendments (including post-effective amendments) to this Registration Statement, and to file the same, with all exhibits thereto, and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing requisite and necessary to be done in connection therewith, as fully to all intents and purposes as he or she might or could do in person, hereby ratifying and confirming all that said attorneys-in-fact and agents, or any of them, or their or his or her substitutes or substitute, may lawfully do or cause to be done by virtue hereof.

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

<u>Signature</u>	<u>Title</u>	<u>Date</u>
<u>/s/ Manoussos Perros</u> Manoussos Perros, Ph.D.	President, Chief Executive Officer and Director ( <i>Principal Executive Officer</i> )	March 23, 2021
<u>/s/ Michael Gutch</u> Michael Gutch, Ph.D.	Chief Financial Officer and Chief Business Officer ( <i>Principal Financial and Accounting Officer</i> )	March 23, 2021
<u>/s/ David Meek</u> David Meek	Chairman of the Board	March 23, 2021
<u>/s/ Heather Behanna</u> Heather Behanna, Ph.D.	Director	March 23, 2021
<u>/s/ David C. Hastings</u> David C. Hastings	Director	March 23, 2021
<u>/s/ Heather Preston</u> Heather Preston, M.D.	Director	March 23, 2021
<u>/s/ Howard Mayer</u> Howard Mayer, M.D.	Director	March 23, 2021

**COVINGTON**BEIJING BRUSSELS DUBAI FRANKFURT JOHANNESBURG  
LONDON LOS ANGELES NEW YORK PALO ALTO  
SAN FRANCISCO SEOUL SHANGHAI WASHINGTONCovington & Burling LLP  
One CityCenter  
850 Tenth Street, NW  
Washington, DC 20001-4956  
T +1 202 662 6000

March 23, 2021

Entasis Therapeutics Holdings Inc.  
35 Gatehouse Drive  
Waltham, MA 02451

Ladies and Gentlemen:

We have acted as counsel to Entasis Therapeutics Holdings Inc., a Delaware corporation (the “Company”), in connection with the registration by the Company under the Securities Act of 1933, as amended (the “Act”), of 1,715,494 shares of the Company’s common stock, par value \$0.001 per share (the “Common Stock”), consisting of 1,465,494 shares of Common Stock (the “2018 Plan Shares”) issuable under the Company’s 2018 Equity Incentive Plan, as amended (the “2018 Plan”), and 250,000 shares of Common Stock (the “ESPP Shares,” and together with the 2018 Plan Shares, the “Shares”) issuable under the Company’s 2018 Employee Stock Purchase Plan (the “ESPP”), pursuant to the Registration Statement on Form S-8 filed with the Securities and Exchange Commission on the date hereof (such registration statement is referred to herein as the “Registration Statement”).

We have reviewed such corporate records, certificates and other documents, and such questions of law, as we have considered necessary or appropriate for the purposes of this opinion. We have assumed that all signatures are genuine, that all documents submitted to us as originals are authentic and that all copies of documents submitted to us conform to the originals.

We have relied as to certain matters on information obtained from public officials, officers of the Company and other sources believed by us to be responsible.

Based upon the foregoing, we are of the opinion that the 2018 Plan Shares and the ESPP Shares have been duly authorized and, when issued in accordance with the terms of the 2018 Plan and the ESPP, respectively, and any individual agreements relating to such Shares, the Shares will be validly issued, fully paid and nonassessable.

We are members of the bar of the District of Columbia. We do not express any opinion herein on any laws other than the General Corporation Law of the State of Delaware and reported judicial decisions interpreting these laws.

We hereby consent to the filing of this opinion as Exhibit 5.1 to the Registration Statement. In giving such consent, we do not thereby admit that we are in the category of persons whose consent is required under Section 7 of the Act.

Very truly yours,

/s/ Covington &amp; Burling LLP

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**Consent of Independent Registered Public Accounting Firm**

The Board of Directors  
Entasis Therapeutics Holdings Inc.:

We consent to the use of our report incorporated by reference herein in the prospectus.

/s/ KPMG LLP

Boston, Massachusetts  
March 23, 2021

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