

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

**FORM S-1**

**REGISTRATION STATEMENT  
UNDER  
THE SECURITIES ACT OF 1933**

**Entasis Therapeutics Holdings Inc.**

(Exact name of registrant as specified in its charter)

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

**2834**  
(Primary Standard Industrial Classification Code Number)

**82-4592913**  
(I.R.S. Employer Identification No.)

**35 Gatehouse Drive  
Waltham, MA 02451  
(781) 810-0120**

(Address, including zip code, and telephone number, including area code, of registrant's principal executive offices)

**Manoussos Perros, Ph.D.  
Chief Executive Officer  
Entasis Therapeutics Holdings Inc.  
35 Gatehouse Drive  
Waltham, MA 02451  
(781) 810-0120**

(Name, address, including zip code, and telephone number, including area code, of agent for service)

**Copies to:**

**Christian E. Plaza  
Brent B. Siler  
Brian F. Leaf  
Jaime L. Chase**  
Cooley LLP  
1299 Pennsylvania Avenue, NW, Suite 700  
Washington, DC 20004-2400  
(202) 842-7800

**Lisa Firenze  
Steven D. Singer**  
Wilmer Cutler Pickering Hale and Dorr LLP  
7 World Trade Center  
250 Greenwich Street  
New York, NY 10007  
(212) 230-8800

**Approximate date of commencement of proposed sale to the public: As soon as practicable after this Registration Statement becomes effective.**

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 of 1933, 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, please check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.  (333-226920)

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, 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. (Check one):

Large accelerated filer

Accelerated filer

Non-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.

**CALCULATION OF REGISTRATION FEE**

Title of Securities to be Registered	Amount to be Registered(1)	Proposed Maximum Offering Price Per Share(2)(3)	Proposed Maximum Aggregate Offering Price(3)	Amount of Registration Fee(3)
Common stock, par value \$0.001 per share	676,471	\$ 15.00	\$ 10,147,065	\$ 1,263.31

- (1) Represents only the number of shares being registered pursuant to this Registration Statement, which includes 88,236 shares that the underwriters have the option to purchase to cover over-allotments and are in addition to the 5,073,529 shares that were registered pursuant to the Registrant's Registration Statement on Form S-1 (File No. 333-226920), which included 661,764 shares that the underwriters have the option to purchase to cover over-allotments.
- (2) Based on the public offering price.
- (3) The registration fee is calculated in accordance with Rule 457(a) under the Securities Act of 1933, as amended, based on the proposed maximum aggregate offering price. The registrant previously registered securities at an aggregate offering price not to exceed \$91,323,522 on a Registration Statement on Form S-1 (File No. 333-226920), which was declared effective by the Securities and Exchange Commission on September 25, 2018. In accordance with Rule 462(b) under the Securities Act, an additional amount of securities having a proposed maximum aggregate offering price of \$10,147,065 is hereby registered, which includes shares issuable upon the exercise of the underwriters' option to purchase additional shares.

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**The Registration Statement shall become effective upon filing in accordance with Rule 462(b) promulgated under the Securities Act of 1933, as amended.**

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**EXPLANATORY NOTE AND  
INCORPORATION OF CERTAIN INFORMATION BY REFERENCE**

This Registration Statement (the “*Registration Statement*”) is being filed with the Securities and Exchange Commission (the “*Commission*”) with respect to the registration of additional shares of common stock, par value \$0.001 per share, of Entasis Therapeutics Holdings Inc. (the “*Registrant*”), pursuant to Rule 462(b) under the Securities Act of 1933, as amended (the “*Securities Act*”). This Registration Statement incorporates by reference the contents of, including all amendments and exhibits thereto, the Registration Statement on Form S-1, as amended (File No. 333-226920) (the “*Prior Registration Statement*”), which the Commission declared effective on September 25, 2018, and is being filed solely for the purpose of increasing the number of shares to be offered in the public offering by 676,471 shares, including 88,236 shares that may be sold pursuant to the underwriters’ option to purchase additional shares. The additional shares that are being registered for 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.

**EXHIBIT INDEX**

<b>Exhibit Number</b>	<b>Description</b>
5.1	<a href="#"><u>Opinion of Cooley LLP as to legality.</u></a>
23.1	<a href="#"><u>Consent of KPMG LLP, independent registered public accounting firm.</u></a>
23.2	<a href="#"><u>Consent of Cooley LLP (included in Exhibit 5.1).</u></a>
24.1	<a href="#"><u>Power of Attorney (included on the signature page of the Registration Statement on Form S-1 (File No. 333-226920), filed with the Commission on August 17, 2018 and incorporated herein by reference).</u></a>

## SIGNATURES

Pursuant to the requirements of the Securities Act, 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 the 25<sup>th</sup> day of September, 2018.

ENTASIS THERAPEUTICS HOLDINGS INC.

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

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

Name	Title	Date
<u>  /s/ MANOUSSOS PERROS  </u> Manoussos Perros, Ph.D.	President, Chief Executive Officer and Director ( <i>Principal Executive Officer</i> )	September 25, 2018
<u>  /s/ MICHAEL GUTCH  </u> Michael Gutch, Ph.D.	Chief Financial Officer and Chief Business Officer ( <i>Principal Financial Officer and Principal Accounting Officer</i> )	September 25, 2018
<u>  *  </u> Nicholas Galakatos, Ph.D.	Director	September 25, 2018
<u>  *  </u> Heather Behanna, Ph.D.	Director	September 25, 2018
<u>  *  </u> David C. Hastings	Director	September 25, 2018
<u>  *  </u> Gregory Norden	Director	September 25, 2018
<u>  *  </u> Heather Preston, M.D.	Director	September 25, 2018
<u>  *  </u> Andrew J. Staples	Director	September 25, 2018
<u>  *  </u> James N. Topper, M.D., Ph.D.	Director	September 25, 2018

\*By:   /s/ MICHAEL GUTCH    
Michael Gutch  
*Attorney-in-Fact*



Brent B. Siler  
T: +1 202 728 7040  
bsiler@cooley.com

September 25, 2018

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

Ladies and Gentlemen:

You have requested our opinion, as counsel to Entasis Therapeutics Holdings Inc., a Delaware corporation (the "**Company**"), in connection with the filing by the Company of a Registration Statement on Form S-1 (the "**Registration Statement**") with the Securities and Exchange Commission pursuant to Rule 462(b) of Regulation C promulgated under the Securities Act of 1933, as amended, relating to an underwritten public offering of an aggregate of 676,471 shares of the Company's common stock, par value \$0.001 (the "**Shares**"), including up to 88,236 Shares that may be sold pursuant to the exercise of an option to purchase additional shares. The Registration Statement incorporates by reference the Registration Statement on Form S-1 (No. 333-226920), which was declared effective on September 25, 2018 (the "**Prior Registration Statement**"), including the prospectus which forms a part of the Prior Registration Statement (the "**Prospectus**").

In connection with this opinion, we have examined and relied upon (a) the Registration Statement, the Prior Registration Statement and the Prospectus, (b) the Company's Amended and Restated Certificate of Incorporation and Bylaws, each as currently in effect, (c) the Company's Amended and Restated Certificate of Incorporation, filed as Exhibit 3.2 to the Registration Statement, which is to be in effect immediately following the closing of the offering contemplated by the Registration Statement, and the Company's Amended and Restated Bylaws, filed as Exhibit 3.4 to the Registration Statement, which is to be in effect immediately prior to the closing of the offering contemplated by the Registration Statement 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 undertaken no independent verification with respect to such matters. We have assumed the genuineness and authenticity of all documents submitted to us as originals, and the conformity to originals of all documents submitted to us as copies and the due execution and delivery of all documents where due execution and delivery are a prerequisite to the effectiveness thereof. 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 against payment therefor as described in the Registration Statement and the Prospectus, will be validly issued, fully paid and non-assessable.

Cooley LLP 1299 Pennsylvania Avenue, NW, Suite 700 Washington DC 20004-2400  
t: (202) 842-7800 f: (202) 842-7899 cooley.com

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We consent to the reference to our firm under the caption "Legal Matters" in the Prospectus included in the Registration Statement and to the filing of this opinion as an exhibit to the Registration Statement.

Sincerely,

Cooley LLP

By: /s/ Brent B. Siler  
Brent B. Siler

Cooley LLP 1299 Pennsylvania Avenue, NW, Suite 700 Washington DC 20004-2400  
t: (202) 842-7800 f: (202) 842-7899 cooley.com

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**Consent of Independent Registered Public Accounting Firm**

The Board of Directors  
Entasis Therapeutics Holdings Inc.:

We consent to the incorporation by reference in this Registration Statement on Form S-1 filed pursuant to Rule 462(b) of the Securities Act of 1933, as amended, of our report dated March 23, 2018, except as to the reverse stock split described in note 2, which is as of September 17, 2018, with respect to the consolidated balance sheets of Entasis Therapeutics Limited (the Company) as of December 31, 2016 and 2017, and the related consolidated statements of operations, redeemable convertible preference shares and shareholders' deficit, and cash flows for the years then ended, and the related notes (collectively, the consolidated financial statements) included in the Registration Statement on Form S-1 (333-226920), as amended, and to the reference to our firm under the heading "Experts" in the prospectus included in such Registration Statement. Our report contains an explanatory paragraph that states that the Company has incurred recurring losses and negative cash flows from operations that raise substantial doubt about its ability to continue as a going concern. The consolidated financial statements do not include any adjustments that might result from the outcome of this uncertainty.

/s/ KPMG LLP

Cambridge, Massachusetts  
September 25, 2018

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