

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

SCHEDULE 14A

Proxy Statement Pursuant to Section 14(a) of
the Securities Exchange Act of 1934 (Amendment No.)

Filed by the Registrant

Filed by a Party other than the Registrant

Check the appropriate box:

- Preliminary Proxy Statement
- Confidential, for Use of the Commission Only (as permitted by Rule 14a-6(e)(2))**
- Definitive Proxy Statement
- Definitive Additional Materials
- Soliciting Material under §240.14a-12

Entasis Therapeutics Holdings Inc.

(Name of Registrant as Specified In Its Charter)

(Name of Person(s) Filing Proxy Statement, if other than the Registrant)

Payment of Filing Fee (Check the appropriate box):

- No fee required.
- Fee computed on table below per Exchange Act Rules 14a-6(i)(1) and 0-11.

(1) Title of each class of securities to which transaction applies:

(2) Aggregate number of securities to which transaction applies:

(3) Per unit price or other underlying value of transaction computed pursuant to Exchange Act Rule 0-11 (set forth the amount on which the filing fee is calculated and state how it was determined):

(4) Proposed maximum aggregate value of transaction:

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- Fee paid previously with preliminary materials.
- Check box if any part of the fee is offset as provided by Exchange Act Rule 0-11(a)(2) and identify the filing for which the offsetting fee was paid previously. Identify the previous filing by registration statement number, or the Form or Schedule and the date of its filing.

(1) Amount Previously Paid:

(2) Form, Schedule or Registration Statement No.:

(3) Filing Party:

(4) Date Filed:



April 30, 2021

Dear Stockholder:

You are cordially invited to attend the 2021 Annual Meeting of Stockholders, or Annual Meeting, of Entasis Therapeutics Holdings Inc., a Delaware corporation, or Entasis. The Annual Meeting will be held on June 10, 2021 at 9:30 a.m. local time and will be held in a completely virtual format. There will not be a physical location for the Annual Meeting.

Details regarding the business to be conducted at the Annual Meeting are described in the accompanying Notice of Annual Meeting of Stockholders and Proxy Statement.

We have elected to provide access to our proxy materials over the Internet under the U.S. Securities and Exchange Commission's "notice and access" rules. As a result, we are mailing to our stockholders a Notice of Internet Availability of Proxy Materials instead of paper copies of this Proxy Statement and our 2020 Annual Report. The Notice contains instructions on how to access those documents over the Internet. The Notice also contains instructions on how stockholders can receive a paper copy of our proxy materials, including this Proxy Statement, our 2020 Annual Report and a form of proxy card or voting instruction form. We believe that providing our proxy materials over the Internet increases the ability of our stockholders to connect with the information they need, while reducing the environmental impact and cost of our Annual Meeting.

Stockholders of record at the close of business on April 16, 2021 will be entitled to notice of and to vote at the Annual Meeting or at any adjournment or postponement thereof. You may also attend and participate in the Annual Meeting virtually via the internet at www.meetingcenter.io/227937811 using the password ETTX2021 where you will be able to vote electronically and submit questions during the meeting. You will be able to vote electronically and submit questions during the Annual Meeting only if you use your control number, which will be included on your Notice of Internet Availability of Proxy Materials or proxy card (if you received a printed copy of the proxy materials), to log on to the meeting.

Your vote is important. Whether or not you plan to attend the Annual Meeting, we hope you will vote as soon as possible. You may vote over the Internet, by telephone or, if you receive a paper proxy card by mail, by completing and returning the proxy card or voting instruction form mailed to you. Please carefully review the instructions on each of your voting options described in this Proxy Statement, as well as in the notice you received in the mail.

On behalf of the Board of Directors and the employees of Entasis, we thank you for your continued support and look forward to seeing you at the Annual Meeting.

Sincerely,

/s/ MANOUSSOS PERROS, PH.D.

Manoussos Perros, Ph.D.

President and Chief Executive Officer

ENTASIS THERAPEUTICS HOLDINGS INC.
35 Gatehouse Drive
Waltham, Massachusetts 02451

(781) 810-0120

NOTICE OF 2021 ANNUAL MEETING OF STOCKHOLDERS

Date	Thursday, June 10, 2021
Time	9:30 a.m. local time
Virtual Meeting	This meeting will be via webcast only at: www.meetingcenter.io/227937811 using the password ETTX2021. There will not be a physical location for the Annual Meeting.
Purpose	<ol style="list-style-type: none">(1) To elect two Class III directors named in the attached Proxy Statement, to hold office until the 2024 Annual Meeting of Stockholders or until their successors have been duly elected and qualified, or, if sooner, until their death, resignation or removal;(2) To ratify the selection by the Audit Committee of the board of directors of KPMG LLP as our independent registered public accounting firm for the fiscal year ending December 31, 2021;(3) To conduct any other business properly brought before the meeting or any adjournment or postponement thereof. <p>These items of business are more fully described in the Proxy Statement accompanying this Notice.</p>
Record Date	<p>The record date for the Annual Meeting is April 16, 2021. Only stockholders of record at the close of business on that date may vote at the meeting or any adjournment thereof.</p> <p>A list of stockholders entitled to vote at the Annual Meeting will be available for inspection by any stockholder at our executive offices for a period of 10 days prior to the Annual Meeting, and also during the Annual Meeting at www.envisionreports.com/ETTX, until the close of such meeting.</p>
Attendance and Voting	<p>You may attend the Annual Meeting virtually via the internet at www.meetingcenter.io/227937811 using the password ETTX2021. Stockholders may vote and submit questions while attending the Annual Meeting virtually via the internet. You will need the 16-digit control number included on your Notice of Internet Availability of Proxy Materials or proxy card (if you received a paper delivery of proxy materials), to enter the Annual Meeting via the internet. Instructions on how to attend and participate virtually via the internet, including how to demonstrate proof of share ownership, are posted at www.envisionreports.com/ETTX.</p> <p>Whether or not you expect to attend the Annual Meeting, you are strongly encouraged to vote by telephone or through the Internet, or, if you receive a paper proxy card by mail, by completing and returning the proxy card mailed to you, as promptly as possible in order to ensure your representation at the Annual Meeting. Voting instructions are provided in the Notice of Internet Availability of Proxy Materials, or, if you receive a paper proxy card by mail, the instructions are printed on your proxy card and included in the accompanying Proxy Statement. Even if you have voted by proxy, you may still vote over the internet during the Annual Meeting by following the instructions located at www.meetingcenter.io/227937811. Please note, however, that if your shares are held of record by a broker, bank or other nominee and you wish to vote at the Annual Meeting, you must obtain a proxy issued in your name from that agent in order to vote your shares that are held in such agent's name and account.</p>

Your vote is important. Whether or not you plan to attend the Annual Meeting, we hope you will vote as soon as possible. You may vote over the Internet, by telephone or, if you receive a paper proxy card by mail, by completing and returning the proxy card or voting instruction form mailed to you. Please carefully review the instructions on each of your voting options described in this Proxy Statement, as well as in the notice you received in the mail.

IMPORTANT NOTICE REGARDING THE AVAILABILITY OF PROXY MATERIALS FOR THE ANNUAL MEETING TO BE HELD ON JUNE 10, 2021: THE COMPANY'S PROXY MATERIALS AND ANNUAL REPORT ARE AVAILABLE AT www.envisionreports.com/ETTX.

By order of the Board,

/s/ MICHAEL GUTCH, PH.D.

Michael Gutch, Ph.D.,

Secretary

Waltham, Massachusetts

April 30, 2021

The Proxy Materials are being made available on or about April 30, 2021.

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ENTASIS THERAPEUTICS HOLDINGS INC.

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

**PROXY STATEMENT
FOR THE 2021 ANNUAL MEETING OF STOCKHOLDERS
TO BE HELD ON JUNE 10, 2021
AT 9:30 A.M. LOCAL TIME**

QUESTIONS AND ANSWERS ABOUT THESE PROXY MATERIALS AND VOTING

We are providing you with these Proxy Materials (as defined below) because the Board of Entasis Therapeutics Holdings Inc., or the Board, is soliciting your proxy to vote at the 2021 Annual Meeting of Stockholders, or the Annual Meeting, of Entasis Therapeutics Holdings Inc., including at any adjournments or postponements thereof, to be held on Thursday, June 10, 2021 at 9:30 a.m. local time and will be held in a completely virtual format. There will not be a physical location for the Annual Meeting. Please visit the website www.meetingcenter.io/227937811 using the password ETTX2021 and enter your control number to register to attend the Annual Meeting. You are invited to attend the Annual Meeting to vote on the proposals described in this Proxy Statement. However, you do not need to attend the Annual Meeting to vote your shares. Instead, you may simply follow the instructions below to submit your proxy. As used in this Proxy Statement, references to “we,” “us,” “our” and the “Company” refer to Entasis Therapeutics Holdings Inc.

Why did I receive a Notice of Internet Availability of Proxy Materials on the internet instead of a full set of Proxy Materials?

Pursuant to rules adopted by the SEC we have elected to provide access to our Proxy Materials over the Internet. Accordingly, on or about April 30, 2021, we have sent you a Notice of Internet Availability of Proxy Materials, or the Notice of Internet Availability, because the Board is soliciting your proxy to vote at the Annual Meeting, including at any adjournments or postponements of the Annual Meeting. The Notice of 2021 Annual Meeting of Stockholders, or the Notice of Annual Meeting, this Proxy Statement and proxy card or, for shares held in street name (held for your account by a broker, bank or other nominee), voting instruction form, and the Annual Report on Form 10-K for the year ended December 31, 2020, or the Annual Report on Form 10-K, or collectively the Proxy Materials, are available to stockholders on our website at www.envisionreports.com/ETTX. The Notice of Internet Availability will provide instructions as to how stockholders may access and review the Proxy Materials or, alternatively, how to request that a copy of the Proxy Materials, including a proxy card, be sent to them by mail. The Notice of Internet Availability will also provide voting instructions. Please note that website addresses referenced herein are intended to provide inactive, textual references only, and the information on these websites is not incorporated by reference in or considered to be a part of this document.

We intend to mail the Notice of Internet Availability on or about April 30, 2021 to all stockholders of record entitled to vote at the Annual Meeting. The Proxy Materials will be made available to stockholders on our website at www.envisionreports.com/ETTX on the same date.

Will I receive any other Proxy Materials by mail?

You will not receive any additional Proxy Materials via mail unless (1) you request a printed copy of the Proxy Materials in accordance with the instructions set forth in the Notice of Internet Availability or (2) we elect, in our discretion, to send you a proxy card and a second Notice of Internet Availability, which we may send on or after April 30, 2021.

How do I attend the annual meeting?

The meeting will be held on Thursday, June 10, 2021 at 9:30 a.m. local time.

You may attend the Annual Meeting virtually via the internet at www.meetingcenter.io/227937811 using the password ETTX2021. Stockholders may vote and submit questions while attending the Annual Meeting virtually via the internet. You will need the 16-digit control number included on your Notice of Internet Availability of Proxy Materials or proxy card (if you received a paper delivery of proxy materials), to enter the Annual Meeting via the internet. Instructions on how to attend and participate virtually via the internet, including how to demonstrate proof of share ownership, are posted at www.envisionreports.com/ETTX.

When is the record date for the Annual Meeting?

The Board has fixed the record date for the Annual Meeting as of the close of business on April 16, 2021.

Who can vote at the Annual Meeting?

Only stockholders of record at the close of business on April 16, 2021 will be entitled to vote at the Annual Meeting. On this record date, there were a total of 37,310,254 shares of common stock outstanding and entitled to vote.

Stockholder of Record: Shares Registered in Your Name

If on April 16, 2021, your shares were registered directly in your name with our transfer agent, Computershare Trust Company, N.A., then you are a stockholder of record. As a stockholder of record, you may vote at the Annual Meeting, vote by proxy over the telephone or through the internet, or vote by proxy using a proxy card that you may request or that we may elect to deliver at a later time. Whether or not you plan to attend the Annual Meeting, we urge you to vote by proxy to ensure your vote is counted.

Beneficial Owner: Shares Registered in the Name of a Broker, Bank or Other Nominee

If on April 16, 2021, your shares were held, not in your name, but rather in an account of a broker, bank or other nominee, then you are the beneficial owner of shares held in “street name” and that organization is responsible for delivering the Notice of Internet Availability to you. The organization holding your account is considered to be the stockholder of record for purposes of voting at the Annual Meeting. As a beneficial owner, you have the right to direct your broker or other agent regarding how to vote the shares in your account. You are also invited to attend the Annual Meeting. However, since you are not the stockholder of record, you may not vote your shares at the Annual Meeting unless you request and obtain a valid proxy from your broker or other agent.

What am I voting on?

There are three matters scheduled for a vote:

- Election of two Class III directors to hold office until the 2024 Annual Meeting of Stockholders; and
- Ratification of the selection of KPMG LLP as our independent registered public accounting firm for the fiscal year ending December 31, 2021.

What if another matter is properly brought before the meeting?

The Board knows of no other matters that will be presented for consideration at the Annual Meeting. If any other matters are properly brought before the meeting, proxies will be voted in accordance with the recommendation of the Board or, in the absence of such a recommendation, in accordance with the judgment of the proxy holder.

How do I vote?

If you are a stockholder of record and your shares are registered directly in your name, you may vote:

- *By Internet.* To vote through the internet, go to www.envisionreports.com/ETTX to complete an electronic proxy card. You will be asked to provide the company number and control number from the Notice of Internet Availability. Your Internet vote must be received by 1:00 a.m., Eastern time, on June 10, 2021 to be counted.
- *By Telephone.* Call (800) 652-8683 toll-free from the U.S., U.S. territories and Canada, and follow the instructions on the Notice. You will be asked to provide your control number from the Notice. Your telephone vote must be received by 1:00 a.m., Eastern time, on June 10, 2021 to be counted.
- *By Proxy Card.* Complete and mail the proxy card, which you may have received by mail, and return it promptly in the envelope provided. If you return your signed proxy card to us before the Annual Meeting, we will vote your shares as you direct.
- *Virtually at the Annual Meeting.* Registered holders may vote during the Annual Meeting via the Internet by going to www.meetingcenter.io/227937811, entering in the meeting password ETTX2021, clicking on the “Cast Your Vote” link and entering the control number included on your Notice of Internet Availability of Proxy Materials or, if you received a printed copy of the proxy materials, on your proxy card to be able to vote during the Annual Meeting via the Internet.

If your shares of common stock are held in street name (i.e., held for your account by a broker, bank or other nominee), you should receive a notice containing voting instructions from that organization rather than from us. You should follow the instructions in the notice to ensure your vote is counted. To vote at the Annual Meeting, you must obtain a valid proxy from your broker, bank or other nominee. Follow the instructions from your broker, bank or other nominee or contact your broker, bank or other nominee to request a proxy form.

How many votes do I have?

On each matter to be voted upon, you have one vote for each share of common stock you own as of April 16, 2021.

What are the Board’s recommendations on how to vote my shares?

The Board recommends a vote:

Proposal 1: **FOR** the election of the two Class III director nominees; and

Proposal 2: **FOR** ratification of the selection of KPMG LLP as our independent registered public accounting firm for the fiscal year ending December 31, 2021.

Who is paying for the cost for soliciting proxies?

We will pay the entire cost of soliciting proxies. In addition to these Proxy Materials, our directors and employees may also solicit proxies in person, by telephone, or by other means of communication. Directors and employees will not be paid any additional compensation for soliciting proxies. We will also reimburse brokers, banks, custodians, other nominees and fiduciaries for forwarding these materials to their principals to obtain the authorization for the execution of proxies.

What if I return a proxy card or otherwise vote without giving specific voting instructions?

If you return a signed and dated proxy card or otherwise vote without marking voting selections, your shares will be voted, as applicable, “For” the election of each of the two nominees for director and “For” ratification of the selection of KPMG LLP as our independent registered public accounting firm for the fiscal year ending December 31, 2021.

If I am a beneficial owner of shares held in street name and I do not provide my broker or bank with voting instructions, what happens?

If your shares are held in street name, your broker, bank or other nominee may under certain circumstances vote your shares if you do not instruct your broker, bank or other nominee how to vote your shares. Brokers, banks and other nominees can vote your shares on routine matters, but cannot vote such shares on non-routine matters. The election of directors (Proposal 1) is a non-routine matter. The ratification of the selection of our independent registered public accounting firm for the fiscal year ending December 31, 2021 (Proposal 2) is a routine matter. We encourage you to provide voting instructions to your broker, bank or other nominee. This ensures that your shares will be voted at the Annual Meeting according to your instructions. You should receive directions from your broker, bank or other nominee about how to submit your proxy to them at the time you receive this Proxy Statement.

If you are a beneficial owner of shares held in street name, in order to ensure your shares are voted in the way you would prefer, you must provide voting instructions to your broker, bank or other agent by the deadline provided in the materials you receive from your broker, bank or other agent.

What does it mean if I receive more than one Notice of Internet Availability?

If you receive more than one Notice of Internet Availability, your shares may be registered in more than one name or in different accounts. Please follow the voting instructions on the Notice of Internet Availability to ensure that all of your shares are voted.

Can I change my vote after submitting my proxy?

Stockholder of Record: Shares Registered in Your Name

Yes. If you are the stockholder of record for your shares, you may revoke your proxy at any time before the final vote at the Annual Meeting in one of the following ways:

- by notifying our Secretary in writing at 35 Gatehouse Drive, Waltham, Massachusetts 02451 that you are revoking your proxy;
- by submitting another properly completed proxy with a later date;
- by transmitting a subsequent vote over the Internet or by telephone prior to 1:00 a.m., Eastern time, on June 10, 2021; or
- by attending the Annual Meeting and voting via the Internet at www.meetingcenter.io/227937811 using the password ETTX2021.

Your last vote, whether prior to or at the Annual Meeting, is the vote that we will count.

Beneficial Owner: Shares Registered in the Name of a Broker, Bank or Other Nominee

If your shares are held in street name, you must contact your broker, bank or other nominee for instructions as to how to change your vote. Your attendance at the Annual Meeting does not revoke your proxy. Your last vote, whether prior to or at the Annual Meeting, is the vote that we will count.

How is a quorum reached?

A quorum of stockholders is necessary to hold a valid meeting. A quorum will be present if stockholders holding at least a majority of the outstanding shares entitled to vote are present at the Annual Meeting in person or represented by proxy. On the record date, there were 37,310,254 shares outstanding and entitled to vote. Thus, the holders of 18,655,127 shares must be present in person or represented by proxy at the Annual Meeting to have a quorum.

Your shares will be counted towards the quorum only if you submit a valid proxy (or one is submitted on your behalf by your broker, bank or other nominee) or if you vote in person at the Annual Meeting. Abstentions and broker non-votes, if any, will be counted towards the quorum requirement. If there is no quorum, the holders of a majority of shares present at the meeting in person or represented by proxy may adjourn the meeting to another date.

What are “broker non-votes”?

As discussed above, when a beneficial owner of shares held in street name does not give instructions to the broker, bank or other nominee holding the shares as to how to vote on matters deemed to be “non-routine,” the broker, bank or other nominee cannot vote the shares. These unvoted shares and uninstructed shares for which the broker, bank or other nominee does not elect to exercise discretionary authority over “routine” matters are “broker non-votes.”

What vote is required to approve each proposal and how are votes counted?

The vote required to elect directors and approve each of the matters scheduled for a vote at the Annual Meeting is set forth below:

<u>Proposal</u>	<u>Board Recommendation</u>	<u>Vote Required</u>	<u>Broker Discretionary Voting Allowed?</u>
Proposal 1: Election of two Class III directors	FOR	Plurality of shares present in person or represented by proxy	No
Proposal 2: Ratification of the selection of KPMG LLP as our independent registered public accounting firm for the fiscal year ending December 31, 2021	FOR	Majority of shares present in person or represented by proxy	Yes

Plurality of shares present in person or represented by proxy means that, with respect to Proposal 1, the nominees for director receiving the greatest number of “For” votes, even if less than a majority, will be elected. With respect to Proposal 1, withheld votes and broker non-votes will have no effect on the election of a nominee.

Majority of shares present in person or represented by proxy means that a proposal that receives an affirmative vote of the holders of a majority of the shares present in person or represented by proxy and entitled to vote on the matter will be approved. Abstentions will have the same effect as an “Against” vote. Broker non-votes, if any, will not be counted “For” or “Against” Proposal 1 or Proposal 2 and will have no effect on the outcome of such proposals.

Who counts the votes?

Computershare Trust Company, N.A., or Computershare, has been engaged as our independent agent to tabulate stockholder votes as the Inspector of Elections. If you are a stockholder of record, your executed proxy card should be

returned directly to Computershare for tabulation. If you hold your shares through a broker, bank or other nominee, your broker, bank or other nominee will return one proxy card to Computershare on behalf of all its clients.

How can I find out the results of the voting at the Annual Meeting?

We will announce preliminary voting results at our Annual Meeting. We expect to announce final voting results in a Current Report on Form 8-K filed with the SEC no later than the fourth business day after the Annual Meeting. If final voting results are not available at that time, we will disclose the preliminary results in the Current Report on Form 8-K and, within four business days after the final voting results are known to us, file an amended Current Report on Form 8-K to disclose the final voting results.

When are stockholder proposals due for the 2022 Annual Meeting of Stockholders?

If you wish to submit proposals for inclusion in our proxy statement for the 2022 annual meeting of stockholders, or the 2022 Annual Meeting, we must receive them on or before December 29, 2021. However, if the date of the 2022 Annual Meeting is more than 30 days before or after the first anniversary of the Annual Meeting, the deadline is a reasonable time before we begin to print and send our proxy materials for the 2022 Annual Meeting. Nothing in this paragraph shall require us to include in our proxy statement or proxy card for the 2022 Annual Meeting any stockholder proposal that does not meet the requirements of the SEC in effect at the time. Any such proposal will be subject to Rule 14a-8 of the Securities Exchange Act of 1934, as amended, or the Exchange Act.

If you wish to nominate a director or submit a proposal for presentation at the 2022 Annual Meeting, without including such proposal in next year's proxy statement, you must be a stockholder of record and provide timely notice in writing to our Secretary at c/o Entasis Therapeutics Holdings Inc., 35 Gatehouse Drive, Waltham, Massachusetts 02451. To be timely, we must receive the notice not less than the close of business on the 90th day nor more than the close of business on the 120th day prior to the first anniversary of the Annual Meeting, that is, between February 10, 2022 and March 12, 2022. However, in the event that the date of the 2022 Annual Meeting is more than 30 days before or more than 30 days after such anniversary date, we must receive your notice (a) no earlier than the close of business on the 120th day prior to the 2022 Annual Meeting and (b) no later than the close of business on the later of the 90th day prior to the 2022 Annual Meeting or the close of business on the 10th day following the day on which we first make a public announcement of the date of the 2022 Annual Meeting. Your written notice must contain specific information required in Section 5 of our amended and restated bylaws, or the Bylaws. For additional information about our director nomination requirements, please see our Bylaws.

Who should I call if I have any additional questions?

If you are the stockholder of record for your shares, please call Michael Gutch, Ph.D., our Secretary, at (781) 810-0120. If your shares are held in street name, please contact the telephone number provided on your voting instruction form or contact your broker, bank or other nominee directly.

PROPOSAL 1: ELECTION OF DIRECTORS

General

Our amended and restated certificate of incorporation, or the Certificate of Incorporation, provides for a classified Board consisting of three classes of directors. Each class consists, as nearly as possible, of one-third of the total number of directors, and each class has a three-year term. Vacancies on our Board may be filled only by persons elected by a majority of the remaining directors. A director elected by our Board to fill a vacancy in a class, including vacancies created by an increase in the number of directors, shall serve for the remainder of the full term of that class and until the director's successor is duly elected and qualified.

Our Board currently is composed of six directors with two vacancies. There are two directors whose term of office expires in 2021. Upon the recommendation of the Nominating and Corporate Governance Committee, our Board has nominated David Hastings and Dr. Manoussos Perros, Ph.D., for election as directors at the Annual Meeting, to hold office until the 2024 Annual Meeting of Stockholders. If you elect the nominees listed below, they will hold office until the 2024 Annual Meeting of Stockholders and until their successors have been duly elected and qualified, or, if sooner, until their death, resignation or removal. If you elect the nominees listed below, our Board following the Annual Meeting will be composed of six directors with two vacancies. All nominees have consented to being named in this Proxy Statement and to serve if elected. It is our policy to encourage directors and nominees for director to attend the Annual Meeting.

Information About Our Class III Director Nominees for Election to a Three-Year Term Expiring at the 2024 Annual Meeting of Stockholders

The brief biographies of our Class III director nominees below include information, as of the date of this Proxy Statement, regarding the specific and particular experience, qualifications, attributes or skills that led the Company to believe that each nominee should serve on the Board. There are no family relationships among any of our executive officers or directors. The Board has no reason to believe that any of the nominees would prove unable to serve if elected. There are no arrangements or understandings between us and any director, or nominee for directorship, pursuant to which such person was selected as a director or nominee.

Nominee	Age	Term Expires	Position(s) Held	Director Since
David Hastings	59	2021	Director	2018
Manoussos Perros, Ph.D.	53	2021	President, Chief Executive Officer and Director	2015

David C. Hastings has served as a member of our Board since April 2018. Mr. Hastings has served as the Chief Financial Officer of Arbutus Biopharma Corporation since June 2018. Prior to joining Arbutus, Mr. Hastings served as the Senior Vice President and Chief Financial Officer of Unilife Corporation from February 2015 to June 2017 and as Unilife's Chief Accounting Officer and Treasurer from July 2016 to June 2017. Unilife filed for bankruptcy in April 2017. From October 2003 to October 2014, Mr. Hastings served as Executive Vice President and Chief Financial Officer at Incyte Corporation. Mr. Hastings has served on the board of directors and chairs the audit committee of Scynexis Inc. and VBL Therapeutics Ltd., both publicly held companies, since 2015 and 2018, respectively. Mr. Hastings received his B.A. in Economics from the University of Vermont. We believe that Mr. Hastings is qualified to serve on our Board because of his extensive financial experience, including experience as the chief financial officer of multiple publicly traded companies.

Manoussos Perros, Ph.D., has served as our President, Chief Executive Officer, and a member of our Board since May 2015. Prior to this, Dr. Perros worked for AstraZeneca AB, or AstraZeneca, as vice president and head of its infection research and early development organization from 2010 to 2015 and as site head for its research center in Waltham, Massachusetts from 2012 to 2015. Prior to joining AstraZeneca, Dr. Perros served as director of the Novartis Institute for Tropical Diseases in Singapore, and prior to that, as vice-president and chief scientific officer, antivirals, at Pfizer, Inc. A chemist by training, Dr. Perros conducted his Ph.D. work in Belgium, France and Germany, and was an associate in the Biophysics department at Yale from 1993 to 1995. Dr. Perros received the PhRMA Discoverer's Award

in 2010. We believe that Dr. Perros is qualified to serve on our Board because of his extensive knowledge of our company as President, Chief Executive Officer, his experience at major pharmaceutical companies and his scientific experience and achievements.

Vote Required

Directors are elected by a plurality of the votes of the holders of shares present in person or represented by proxy and entitled to vote on the election of directors. Accordingly, the two nominees receiving the greatest number of “For” votes, even if less than a majority, will be elected. Withheld votes and broker non-votes will have no effect on the election of a nominee. Shares represented by executed proxies will be voted, if authority to do so is not withheld, for the election of the nominees named above. If the nominees become unavailable for election as a result of an unexpected occurrence, your shares will be voted for the election of a substitute nominee proposed by our Board.

Our Recommendation

THE BOARD UNANIMOUSLY RECOMMENDS A VOTE “FOR” EACH OF THE CLASS II DIRECTOR NOMINEES.

Information About Our Continuing Class I and Class II Directors

Set forth below are the names, ages and length of service of the remaining members of our Board whose terms continue beyond the Annual Meeting.

Continuing Directors	Age	Term Expires	Position(s) Held	Director Since
David Meek	57	2022	Chairman of the Board	2019
Heather Preston, M.D.	55	2022	Director	2017
Heather Behanna, Ph.D.	46	2023	Director	2017
Howard Mayer, M.D.	58	2023	Director	2019

The principal occupation, business experience and education of each of our continuing directors are set forth below. Unless otherwise indicated, principal occupations shown for each director have extended for five or more years.

Class I Directors Continuing in Office until the 2022 Annual Meeting of Stockholders

David Meek has served as Chairman of the Board since June 2019. Mr. Meek is an executive biopharma leader with more than 30 years of experience in the biopharma industry, where he has held various global executive positions in major pharmaceutical and biotechnology companies. Most recently, Mr. Meek was president and chief executive officer, director of FerGene, a gene therapy biotech focused on cancer from January 2020 to March 2021. From July 2016 to December 2020, Mr. Meek was chief executive officer and a member of the board of Ipsen Biopharmaceuticals, Inc., a public biopharma company. Prior to joining Ipsen, he was executive vice president and president of the oncology division of Baxalta prior to being acquired by Shire from July 2014 to June 2016. He spent two years as chief commercial officer of Endocyte from August 2012 to July 2014. Mr. Meek also spent eight years at Novartis as a global franchise head from 2005 to 2007, chief executive officer of Novartis Canada from 2007 to 2009, and region head of oncology for northern, central and eastern Europe from 2010 to 2012. He began his biopharma career at Johnson & Johnson and Janssen Pharmaceuticals where he worked from 1989 to 2004, where he held increasingly senior levels of executive roles. Mr. Meek serves as a director for uniQure and Stargazer Pharmaceuticals, a private biotech. Mr. Meek holds a B.A. from the University of Cincinnati. We believe that Mr. Meek is qualified to serve on our Board because of his extensive experience and commercialization expertise within the biopharmaceutical industry as well as his experience as a director of public companies in the biopharmaceutical industry.

Heather Preston, M.D., has served as a member of our Board since August 2017. Dr. Preston has served as a managing partner at Pivotal bioVenture Partners since July 2018 and as a senior advisor to TPG Biotech, a biotechnology venture capital firm, since July 2018. Dr. Preston was previously a partner and managing director at TPG

Biotech from 2005 to July 2018. Prior to joining TPG Biotech, Dr. Preston served for two years as a medical device and biotechnology venture capital investor at J.P. Morgan Partners, LLC, a private equity firm. Prior to that, she was an entrepreneur-in-residence at New Enterprise Associates, a venture capital firm, and was a leader of the pharmaceutical and medical products consulting practice at McKinsey & Co. Dr. Preston is currently serving on the boards of directors of Oxford BioMedica plc, Karuna Therapeutics, Fusion Therapeutics and Akuous Inc., all publicly held companies. Dr. Preston has also served on the board of a number of private companies. Dr. Preston received her M.D. from the University of Oxford and a B.S. in Biochemistry from the University of London. We believe that Dr. Preston is qualified to serve on our Board because of her extensive experience in the biopharmaceutical investment industry and her scientific background.

Class II Directors Continuing in Office until the 2023 Annual Meeting of Stockholders

Heather Behanna, Ph.D., has served as a member of our Board since August 2017. Dr. Behanna is a principal at SR One Capital Management LP, a position she has held since April 2019. From January 2017 to November 2018, she was a principal at Sofinnova Investments, or Sofinnova, focusing on biopharmaceutical investments. Prior to joining Sofinnova, Dr. Behanna was a senior vice president and biotechnology sell-side analyst at Wedbush Securities from August 2014 to December 2016, preceded by a role as an associate at JMP Securities LLC from September 2010 to June 2014. Prior to this, Dr. Behanna worked in early stage drug discovery at the Astellas Research Institute and was also an adjunct professor at the Feinberg School of Medicine at Northwestern University. Dr. Behanna received her Ph.D. in Chemistry from Northwestern University, an M.S. in Organic Chemistry from the Weizmann Institute of Science and her B.S. from Tufts University. We believe that Dr. Behanna is qualified to serve on our Board because of her extensive experience in the biopharmaceutical investment industry and her scientific background.

Howard Mayer, M.D. has served as a member of our Board since August 2019. Dr. Mayer is the executive vice president, head of research and development for Ipsen Biopharmaceuticals, Inc., a position he has held since 2019. Prior to joining Ipsen, Dr. Mayer was most recently senior vice president, chief medical officer and global head of R&D, Neuroscience Division at Shire Pharmaceuticals, or Shire Pharma, from 2018 to 2019 (acquired by Takeda Pharmaceutical Company in 2019). Previously, Dr. Mayer was senior vice president and head of global clinical development at Shire Pharma from 2013 to 2018. In this role, Dr. Mayer was responsible for global clinical development (Phase I-IV) across the hematology, immunology, oncology, genetic diseases, GI/metabolic, neuroscience and ophthalmology therapeutic areas. He was also responsible for clinical development operations, clinical pharmacology, and medical devices. Previously he served as chief medical officer at EMD Serono, a division of Merck KGaA. Prior to that, he held a variety of global roles at Pfizer Inc. over nearly eight years, including head of clinical development and medical affairs for Virology/Infectious Diseases. Prior to joining Pfizer, he served as director of infectious diseases clinical research at Bristol-Myers Squibb for five years. Dr. Mayer obtained his BA from the University of Pennsylvania and his M.D. from Albert Einstein College of Medicine in New York, which was followed by an internship and residency at Mount Sinai Hospital and an Infectious Diseases fellowship at Harvard Medical School. Dr. Mayer serves on the board of Adagio Therapeutics. He also has served on the board of Autism Speaks in New England since 2011. He was honored by PharmaVoice as one of the 100 Most Inspiring People in the Life Sciences Industry in 2011 and 2017. We believe that Dr. Mayer is qualified to serve on our Board because of his extensive experience in the biopharmaceutical industry and his scientific background.

INFORMATION REGARDING THE BOARD AND CORPORATE GOVERNANCE

Board Independence

As required under the Nasdaq Stock Market LLC, or Nasdaq, listing standards, a majority of the members of a listed company's board of directors must qualify as "independent." Under the Nasdaq listing standards, a director is independent only if the board of directors of a company makes an affirmative determination that the director has no material relationship with the company that would impair his or her independence. The Board consults with the Company's counsel to ensure that the Board's determinations are consistent with relevant securities and other laws and regulations regarding the definition of "independent," including those set forth in pertinent listing standards of Nasdaq, as in effect from time to time.

Consistent with these considerations, after review of all relevant identified transactions or relationships between each director, or any of his or her family members, and the Company, its senior management and its independent auditors, our Board has affirmatively determined that all of our current directors, except Dr. Perros, by virtue of his position as our President and Chief Executive Officer, are independent within the meaning of the applicable Nasdaq listing standards. In making these determinations, our Board has determined, upon the recommendation of our Nominating and Corporate Governance Committee, that none of our directors or nominees for director had a material or other disqualifying relationship with the Company. The Board has also determined that each member of our Audit, Compensation and Nominating and Corporate Governance committees satisfies the independence standards for such committees established by the SEC and the Nasdaq listing standards, as applicable.

Leadership Structure and Risk Oversight

The Board is currently chaired by Mr. Meek. Mr. Meek has authority, among other things, to call and preside over Board meetings, including meetings of the independent directors, to set meeting agendas and to determine materials to be distributed to the Board. Accordingly, the Chairman of the Board has substantial ability to shape the work of the Board. The Company believes that separating the positions of Chairman and Chief Executive Officer creates an environment that is more conducive to objective evaluation and oversight of management's performance, increasing management accountability and improving the ability of the Board to monitor whether management's actions are in the best interests of the Company and its stockholders. The Company believes that this separation can enhance the effectiveness of the Board as a whole.

One of the Board's key functions is informed oversight of our risk management process. The Board does not have a standing risk management committee, but rather administers this oversight function directly through the Board as a whole, as well as through its various standing committees that address risks inherent in their respective areas of oversight.

In particular, our Board is responsible for monitoring and assessing strategic risk exposure, including a determination of the nature and level of risk appropriate for the Company.

Our Audit Committee has the responsibility to consider and discuss with management and the auditors, as appropriate, the Company's guidelines and policies with respect to financial risk management and financial risk assessment, including the Company's major financial risk exposures and the steps taken by management to monitor and control these exposures. In addition, the Audit Committee considers management risks relating to data privacy, technology and information security, including cybersecurity, and back-up of information systems and the steps the Company has taken to monitor and control such exposures as well as overseeing the performance of our internal audit function. Our Compensation Committee assesses and monitors whether any of our compensation policies and programs has the potential to encourage excessive risk-taking, including risks related to executive compensation and overall compensation and benefit strategies, plans, arrangements, practices and policies. Our Nominating and Corporate Governance Committee monitors the effectiveness of our Corporate Governance Guidelines, including whether they are successful in preventing illegal or improper liability-creating conduct. The Nominating and Corporate Governance Committee also oversees and reviews with management the Company's major legal compliance risk exposures and the steps management has taken to monitor or mitigate such exposures, including the Company's procedures and any related policies with respect to risk assessment and risk management. It is the responsibility of the committee chairs to report findings regarding material risk exposures to the Board as quickly as possible. In connection with its reviews of the operations and corporate functions of our company, our Board evaluates the primary risks associated with those operations and corporate functions. In addition, our Board reviews the risks associated with our Company's business strategies periodically throughout the year as part of its consideration of undertaking any such business strategies. While the Board and its committees oversee risk management strategy, management is responsible for implementing and supervising day-to-day risk management processes and reporting to the Board and its committees on such matters.

Board Meetings and Annual Meeting Attendance

Our Board held 13 meetings during the fiscal year ended December 31, 2020. During 2020, each of the incumbent directors attended at least 80% of the total of the meetings of the Board and the meetings of the committees of

the Board on which he or she served (in each case, which were held during the period for which he or she was a director and/or a member of the applicable committee). It is our policy to encourage our directors to attend the Annual Meeting. We anticipate that a majority of the members of the Board will attend the Annual Meeting. In 2020, all serving directors attended the 2020 Annual Meeting of Stockholders.

As required under applicable Nasdaq listing standards, during 2020, the Company's independent, non-employee directors met in eight regularly scheduled executive sessions at which only independent directors were present.

Board Committees

Our Board has three standing committees: the Audit Committee, the Compensation Committee and the Nominating and Corporate Governance Committee. The following table provides membership and meeting information for the year ended December 31, 2020 for each committee:

Name	Audit Committee	Compensation Committee	Nominating and Corporate Governance Committee
Heather Behanna, Ph.D.	X	X	
David C. Hastings†	X*		X
Heather Preston, M.D.	X		
David Meek			X*
Howard Mayer, M.D.		X*	
Total meetings in 2020	4	4	1

† Financial Expert

* Committee Chair

Below is a description of each committee of the Board. Each of the committees has authority to engage legal counsel or other experts or consultants, as it deems appropriate to carry out its responsibilities. The Board has determined that each member of each committee meets the applicable Nasdaq rules and regulations regarding "independence" and each member is free of any relationship that would impair his or her individual exercise of independent judgment with regard to the Company. Each of the committees operates pursuant to a written charter and each committee reviews and assesses the adequacy of its charter and submits its charter to the Board for approval. The charters are all available at www.entasistx.com/corporate-governance/documents-charters. The inclusion of our website address here and elsewhere in this Proxy Statement does not include or incorporate by reference the information on our website into this Proxy Statement.

Audit Committee

The Audit Committee of the Board is responsible for, among other things:

- evaluating the performance of and assessing the qualifications of the independent registered public accounting firm;
- determining whether to retain or terminate the existing independent registered public accounting firm or to appoint and engage new independent registered public accounting firms;
- determining and approving the engagement of the independent registered public accounting firm;
- determining and approving the engagement of the independent registered public accounting firm to perform any proposed permissible non-audit services;

- monitoring the rotation of partners of the independent registered public accounting firm on the Company's audit engagement team as required by applicable laws and rules;
- conferring with management and the independent registered public accounting firm, as appropriate, regarding the scope, adequacy and effectiveness of internal control over financial reporting and disclosure controls and procedures;
- reviewing and discussing with management risks relating to data privacy, technology and information security, including cybersecurity, and back-up of information systems and the steps the Company has taken to monitor and control such exposures as well as overseeing the performance of the Company's internal audit function;
- establishing procedures, as required under applicable law, for the receipt, retention and treatment of complaints received by the Company regarding accounting, internal accounting controls or auditing matters and the confidential and anonymous submission by employees of concerns regarding questionable accounting or auditing matters; and
- reviewing the Company's annual audited financial statements, quarterly financial statements and disclosures under "Management's Discussion and Analysis of Financial Condition and Results of Operations" and "Risk Factors" in the Company's filings to be filed with the SEC with management and the independent registered public accounting firm, as appropriate.

The current members of our Audit Committee are Mr. Hastings, Dr. Behanna and Dr. Preston with Mr. Hastings serving as chairperson. Our Board has determined that each of the members of our Audit Committee satisfies the requirements for independence and financial literacy under the rules and regulations of Nasdaq and the SEC. Our Board has determined that Mr. Hastings is an "audit committee financial expert" within the meaning of the SEC regulations and applicable listing standards of Nasdaq. During the fiscal year ended December 31, 2020, the Audit Committee met four times.

Compensation Committee

The Compensation Committee is responsible for, among other things:

- reviewing and approving, or reviewing and recommending to the Board for approval, annual corporate goals and objectives relevant to the compensation of our Chief Executive Officer;
- evaluating the performance of our Chief Executive Officer in light of such corporate goals and objectives and determining or recommending to the Board the compensation of our Chief Executive Officer, without the Chief Executive Officer's presence or participation;
- reviewing and approving or recommending to the Board the compensation of our other executive officers and certain other members of senior management, as appropriate;
- reviewing and recommending to the Board the compensation of our directors;
- appointing, compensating and overseeing the work of any compensation consultant, legal counsel or other advisor retained by the Compensation Committee;
- conducting the independence assessment outlined in Nasdaq rules with respect to any compensation consultant, legal counsel or other advisor retained by the Compensation Committee; and
- administering our equity compensation plans, pension and profit-sharing plans, deferred compensation plans and other similar plan and programs.

The current members of our Compensation Committee are Dr. Behanna and Dr. Mayer, with Dr. Mayer serving as chairperson. Our Board has determined that each of the members of our Compensation Committee are independent within the meaning of the independent director requirements of Nasdaq. Our Board has also determined that the composition of our Compensation Committee meets the requirements for independence under, and the functioning of our Compensation Committee complies with, any applicable requirements of Nasdaq and SEC rules and regulations. During the fiscal year ended December 31, 2020, the Compensation Committee met four times.

Compensation Committee Processes and Procedures

The Compensation Committee acts on behalf of the Board to review, modify (as needed) and approve, or review and recommend, as applicable, the overall compensation strategy and policies for the Company. The Committee may form and delegate authority to subcommittees as appropriate.

The Compensation Committee has the authority to obtain, at our expense, advice and assistance from compensation consultants and internal and external legal, accounting or other advisers and other external resources that the Compensation Committee considers necessary or appropriate in the performance of its duties. The Compensation Committee has direct responsibility for the oversight of the work of any consultants or advisers engaged for the purpose of advising the Compensation Committee. In particular, the Compensation Committee has sole authority to retain compensation consultants to assist in its evaluation of executive and director compensation, including authority to approve the consultant's reasonable fees and other retention terms. During the past fiscal year, the Compensation Committee engaged Willis Towers Watson US LLC, or WTW, as a compensation consultant.

Specifically, the Compensation Committee engaged WTW to:

- provide market data, peer group analysis; and
- conduct an executive compensation assessment analyzing the current cash and equity compensation of our executive officers and directors against compensation for similarly situated executives at our peer group.

Independent Compensation Consultant Evaluation

The Compensation Committee may select, or receive advice from, a compensation consultant, legal counsel or other adviser to the Compensation Committee, other than in-house legal counsel and certain other types of advisers, only after assessing the independence of such person in accordance with SEC and Nasdaq requirements that bear upon the adviser's independence. The Compensation Committee has assessed WTW's independence and determined that there was no conflict of interest resulting from retaining WTW for this engagement.

Nominating and Corporate Governance Committee

The Nominating and Corporate Governance Committee is responsible for, among other things:

- identifying, reviewing and evaluating candidates to serve as directors of the Company (consistent with criteria approved by the Board);
- reviewing, evaluating and considering the recommendation for nomination of incumbent directors for re-election to the Board, as well as monitoring the size of the Board;
- recommending to the Board the persons to be nominated for election as directors and to each of the committees of the Board;
- assessing the performance of management and the Board and each of the committees of the Board; and

- reviewing and recommending any appropriate changes to the Company's Corporate Governance Guidelines.

The current members of our Nominating and Corporate Governance Committee are Mr. Hastings and Mr. Meek, with Mr. Meek serving as chair. Our Board has determined that each of the members of our Nominating and Corporate Governance Committee are independent within the meaning of the independent director requirements of Nasdaq. During the fiscal year ended December 31, 2020, the Nominating and Corporate Governance Committee met one time.

Identifying and Evaluating Nominees for Directors

In recommending candidates for election to the Board at the annual meeting of stockholders, or any special meeting of stockholders, the independent members of the Nominating and Corporate Governance Committee believe that candidates for director should have certain minimum qualifications, including the ability to read and understand basic financial statements, understand the Company's industry and having the highest personal integrity and ethics. The Nominating and Corporate Governance Committee also intends to consider such factors as (i) possessing relevant expertise upon which to be able to offer advice and guidance to management, (ii) having sufficient time to devote to the affairs of the Company, (iii) demonstrating excellence in his or her field, (iv) having the ability to exercise sound business judgment, (v) having experience as a board member or executive officer of another publicly held company, (vi) having a diverse personal background, perspective and experience and (vii) having the commitment to rigorously represent the long-term interests of our stockholders. Candidates for director nominees are reviewed in the context of the current composition of the Board, the operating requirements of the Company and the long-term interests of stockholders. In conducting this assessment, the Nominating and Corporate Governance Committee typically considers diversity, age, skills and such other factors as it deems appropriate, given the current needs of the Board and the Company, to maintain a balance of knowledge, experience and capability.

In the case of incumbent directors whose terms of office are set to expire, the Nominating and Corporate Governance Committee reviews these directors' overall service to the Company during their terms, including the number of meetings attended, level of participation, quality of performance and any other relationships and transactions that might impair the directors' independence. The Nominating and Corporate Governance Committee will take into account the results of the Board's self-evaluation, conducted periodically on a group and individual basis. In the case of new director candidates, the Nominating and Corporate Governance Committee also determines whether the nominee is independent for Nasdaq purposes, which determination is based upon applicable Nasdaq listing standards, applicable SEC rules and regulations and the advice of counsel, if necessary. Generally, our Nominating and Corporate Governance Committee identifies candidates for director nominees in consultation with management, using search firms or other advisors, through the recommendations submitted by stockholders or through such other methods as the Nominating and Corporate Governance Committee deems to be helpful to identify candidates. The Nominating and Corporate Governance Committee conducts any appropriate and necessary inquiries into the backgrounds and qualifications of possible candidates after considering the function and needs of the Board. The Nominating and Corporate Governance Committee meets to discuss and consider the candidates' qualifications and then selects a nominee for recommendation to the Board. The Nominating and Corporate Governance Committee may gather information about the candidates through interviews, questionnaires, background checks or any other means that the Nominating and Corporate Governance Committee deems to be appropriate in the evaluation process. We have no formal policy regarding board diversity. Our Nominating and Corporate Governance Committee's priority in selecting board members is identification of persons who will further the interests of our company through his or her established record of professional accomplishment, the ability to contribute positively to the collaborative culture among board members, and professional and personal experiences and expertise relevant to our growth strategy.

As described above, the Nominating and Corporate Governance Committee will consider director candidates recommended by stockholders. The Nominating and Corporate Governance Committee does not intend to alter the manner in which it evaluates candidates, including the minimum criteria set forth above, based on whether or not the candidate was recommended by a stockholder. For more information regarding how a stockholder can recommend individuals for consideration by the Nominating and Corporate Governance Committee to become nominees for election

to the Board, please see the section titled “Questions and Answers About These Proxy Materials - When are stockholder proposals due for the 2022 Annual Meeting of Stockholders?”

Code of Business Conduct and Ethics

We have adopted a Code of Business Conduct and Ethics that applies to all officers, directors and employees. The Code of Business Conduct and Ethics is available on our website at www.entasistx.com/corporate-governance/documents-charters. If we make any substantive amendments to the Code of Business Conduct and Ethics or grant any waiver from a provision of the Code to any executive officer or director, we will promptly disclose the nature of the amendment or waiver on our website.

Corporate Governance Guidelines

The Board has adopted Corporate Governance Guidelines to assure that the Board will have the necessary authority and practices in place to review and evaluate our business operations as needed and to make decisions that are independent of our management. The Corporate Governance Guidelines are also intended to align the interests of directors and management with those of our stockholders. The Corporate Governance Guidelines set forth the practices the Board intends to follow with respect to, among other things, board composition and selection including diversity, board meetings and involvement of senior management, Chief Executive Officer performance evaluation and succession planning, and board committees and compensation. The Corporate Governance Guidelines are available on our website at www.entasistx.com/corporate-governance/documents-charters.

Stockholder Communications with Our Board

The Board has adopted a formal process by which stockholders may communicate with the Board or any of its directors. Should stockholders wish to communicate with the Board or any specified individual directors, such correspondence should be sent to the attention of the Company’s Secretary at 35 Gatehouse Dr., Waltham, Massachusetts 02451. The Secretary will forward the communication to the Board members.

PROPOSAL 2: RATIFICATION OF THE SELECTION OF THE INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

The Audit Committee has selected KPMG LLP as our independent registered public accounting firm for the fiscal year ending December 31, 2021 and has further directed that management submit the selection of its independent registered public accounting firm for ratification by the stockholders at the Annual Meeting. KPMG LLP has audited the Company’s financial statements since 2017. A representative of KPMG LLP is expected to be present at the Annual Meeting with the opportunity to make a statement if he or she desires and to respond to appropriate questions.

Our organizational documents do not require that the stockholders ratify the selection of KPMG LLP as our independent registered public accounting firm. However, the Audit Committee is submitting the selection of KPMG LLP to the stockholders for ratification as a matter of good corporate practice. If the stockholders fail to ratify the selection, the Audit Committee will reconsider whether or not to retain that firm. Even if the selection is ratified, the Audit Committee in its discretion may direct the appointment of different independent auditors at any time during the year if they determine that such a change would be in the best interests of the Company and its stockholders.

Vote Required

The affirmative vote of the holders of a majority of the shares present in person or represented by proxy and entitled to vote on the matter at the annual will be required to ratify the selection of KPMG LLP. Abstentions will have the same effect as an “Against” vote for Proposal 2. Broker non-votes, if any, will not be counted “For” or “Against” Proposal 2, and will have no effect on the outcome of this proposal.

Independent Registered Public Accounting Firm Fees

The following is a summary and description of fees incurred by KPMG LLP for the fiscal years ended December 31, 2020 and 2019, by KPMG LLP, our independent registered public accounting firm. All fees described below were pre-approved by the Audit Committee.

	Fiscal Year Ended	
	2020	2019
Audit Fees ⁽¹⁾	\$ 576,335	\$ 560,325
Audit-related fees	—	—
Tax fees ⁽²⁾	32,712	50,670
All other fees ⁽³⁾	2,730	1,780
Total Fees	<u>\$ 611,777</u>	<u>\$ 612,775</u>

- (1) Audit fees for 2020 consist of fees for our quarterly reviews, audit of our annual financial statements and work on registration statements and PIPE financings. Audit fees for 2019 consist of fees for our quarterly reviews, audit of our annual financial statements and work on registration statements.
- (2) Tax fees consist of tax consultation and compliance services.
- (3) All other fees consist of subscription to KPMG's accounting research online service.

Pre-Approval Policies and Procedures

Our Audit Committee pre-approves all audit and non-audit services provided by KPMG LLP before it is engaged by us to render non-audit services to ensure that the provision of these services does not impair the auditor's independence. These services may include audit-related services, tax services and other non-audit services.

The pre-approval requirement set forth above does not apply with respect to non-audit services if:

- all such services do not, in the aggregate, amount to more than 5% of the total fees paid by us to KPMG LLP during the fiscal year in which the services are provided;
- such services were not recognized as non-audit services at the time of the relevant engagement; and
- such services are promptly brought to the attention of and approved by the Audit Committee (or its delegate) prior to the completion of the annual audit.

The Audit Committee elected to delegate pre-approval authority to the chairperson of the Audit Committee to approve any one or more individual permitted non-audit services for which estimated fees do not exceed \$75,000 as well as adjustments to any estimated pre-approval fee thresholds up to \$50,000 for any individual non-audit service. Any non-audit services that would exceed such limits should be pre-approved by the full Audit Committee. The chairperson shall report any pre-approval granted at the next scheduled meeting of the Audit Committee.

Our Recommendation

THE BOARD UNANIMOUSLY RECOMMENDS A VOTE "FOR" THE RATIFICATION OF THE SELECTION OF KPMG LLP AS OUR INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM FOR THE FISCAL YEAR ENDING DECEMBER 31, 2021.

Audit Committee Report

The material in this report is not deemed to be “soliciting material,” or to be “filed” with the SEC or subject to the SEC’s proxy rules or the liabilities of Section 18 of the Exchange Act and the material is not deemed to be incorporated by reference in any prior or subsequent filing of the Company under the Securities Act of 1933, as amended, or the Securities Act, or the Exchange Act, except to the extent the Company specifically incorporates the material by reference therein.

The Audit Committee has reviewed and discussed the audited financial statements for the fiscal year ended December 31, 2020 with management of the Company. The Audit Committee has discussed with the independent registered public accounting firm the matters required to be discussed by the applicable requirements of the Public Company Accounting Oversight Board, or the PCAOB, and the SEC. The Audit Committee has also received the written disclosures and the letter from the independent registered public accounting firm required by applicable requirements of the PCAOB regarding the independent accountants’ communications with the Audit Committee concerning independence, and has discussed with the independent registered public accounting firm the accounting firm’s independence. Based on the foregoing, the Audit Committee has recommended to the Board that the audited financial statements be included in the Company’s Annual Report on Form 10-K for the fiscal year ended December 31, 2020.

Entasis Therapeutics Holdings Inc.
Audit Committee

David C. Hastings, Chairman
Heather Behanna, Ph.D.
Heather Preston, M.D.

EXECUTIVE OFFICERS

The following table sets forth information regarding our executive officers as of April 30, 2021:

Name	Age	Position(s)
Manoussos Perros, Ph.D.	53	President, Chief Executive Officer and Director
Michael Gutch, Ph.D.	55	Chief Financial Officer and Chief Business Officer
David Altarac, M.D.	60	Chief Medical Officer
John Mueller, Ph.D.	61	Chief Development Officer
Ruben Tommasi, Ph.D.	55	Chief Scientific Officer
Matthew Ronsheim	49	Chief Pharmaceutical Sciences and Manufacturing Officer
Elizabeth Keiley	55	General Counsel

Manoussos Perros, Ph.D. Biographical information for Dr. Perros is included above with the director biographies under the caption “Information About Our Continuing Directors.”

Michael Gutch, Ph.D., has served as our chief financial officer and chief business officer since April 2017. From January 2014 to March 2017, he served as executive director of corporate development and head of equities at AstraZeneca. Dr. Gutch served as managing director, MedImmune Ventures, the corporate venture capital arm of AstraZeneca, from September 2011 to December 2013. Prior to that, Dr. Gutch served as investment director of HIG BioVentures at the investment firm HIG Capital and as a principal of Lilly Ventures, the corporate venture arm of Eli Lilly & Company. He has served on the board of directors of Albireo Pharma, Inc. since 2016. Dr. Gutch received his MBA in Finance from Indiana University and a Ph.D. in Molecular Pathology from SUNY Stony Brook. He received his B.S. degrees in Biology and Chemistry from Alfred University.

David Altarac, M.D., has served as our chief medical officer since November 2019. From July 2015 to April 2019, Dr. Altarac was a senior vice president and head of global regulatory affairs, global drug safety and R&D quality and compliance at Shire Inc., or Shire. Prior to joining Shire, Dr. Altarac was vice president, regulatory affairs at NeoStem Inc., a biopharmaceutical company developing novel, cell-based, individualized therapeutics from July 2013 to June 2015. Dr. Altarac holds an M.D. degree from New York Medical College, a Master of Public Administration (M.P.A.) degree from New York University, and a B.A. in Chemistry from the State University of New York at Binghamton, New York. Dr. Altarac completed his Internal Medicine residency and Infectious Diseases fellowship at Beth Israel Medical Center in New York. Dr. Altarac has held multiple academic, hospital and post graduate teaching appointments during his career and has authored/coauthored numerous scientific publications.

John Mueller, Ph.D., has served as our chief development officer since May 2015. Prior to this, Dr. Mueller served as senior project director at AstraZeneca from June 2011 to May 2015, where he led a global multidisciplinary team to advance zoliflodacin into a Phase 2 clinical trial. Prior to that, Dr. Mueller worked at Pfizer, Inc. and Alexion Pharmaceuticals, Inc. Dr. Mueller received his Ph.D. in Microbiology and Immunology from the Albany Medical College, and subsequently conducted post-doctoral studies at the Tufts Medical School as a National Institutes of Health fellow where he completed his bacterial genetics research training.

Ruben Tommasi, Ph.D., has served as our chief scientific officer since May 2015. Prior to this, Dr. Tommasi served as executive director of chemistry of the infection innovative medicines unit at AstraZeneca from May 2011 to May 2015. Before that, he led the infection chemistry unit at Novartis Institutes for Biomedical Research from December 2006 to April 2011. Prior to that, Dr. Tommasi worked at Novartis International AG. Dr. Tommasi received both his Ph.D. in Organic Chemistry and his B.S. degree in Chemistry from the State University of New York, Albany.

Matthew Ronsheim, Ph.D., has served as our Chief Pharmaceutical Sciences and Manufacturing Officer since September 2020. Prior to joining Entasis, from June 2016 to August 2019, Dr. Ronsheim served as executive director and head of chemistry manufacturing and controls at Enanta Pharmaceuticals Inc. Prior to that, from October 2014 to June 2016, he served as director project leadership and global pharmaceutical commercialization at Cubist Pharmaceuticals LLC, which was acquired by Merck & Company in December 2014. Before joining Cubist/Merck, Dr. Ronsheim held various leadership roles at Forest Laboratories from 2004 to 2014, including director and head of

chemical development. Dr. Ronsheim earned his B.S. in Chemistry from Southern Connecticut State University and a Ph.D. in Synthetic Organic Chemistry from the University of New Hampshire.

Elizabeth Keiley has served as our general counsel since April 2019. Prior to this from 2012 to 2019, Ms. Keiley served in a variety of positions at Oxford Immunotec Global PLC, or Oxford Immunotec, a publicly traded global diagnostics company, including most recently serving as senior vice president and general counsel. Prior to joining Oxford Immunotec, Ms. Keiley was assistant general counsel of Zimmer, Inc., a subsidiary of Zimmer Holdings, Inc., an orthopedic device manufacturer. Prior to working at Zimmer, Ms. Keiley was a trial lawyer and partner with Wildman, Harrold, Allen & Dixon in Chicago, Illinois. Ms. Keiley received her B.S. and B.A. degrees in Psychology and Philosophy, respectively, from Boston College and her J.D. from Loyola University School of Law.

EXECUTIVE OFFICER AND DIRECTOR COMPENSATION

Executive Officer Compensation

Summary Compensation Table

The following information is furnished for our named executive officers, or Named Executive Officers, for 2020:

- Manoussos Perros, Ph.D., our President and Chief Executive Officer;
- David Altarac, M.D., our Chief Medical Officer
- John Mueller, Ph.D., our Chief Development Officer

Name and Principal Position	Year	Salary (\$)	Option Awards \$(1)	Non-Equity Incentive Plan Compensation \$(2)	All Other Compensation \$(3)	Total (\$)
Manoussos Perros, Ph.D.	2020	536,600	491,811	254,885	143,361	1,426,657
President and Chief Executive Officer	2019	494,900	479,526	247,450	9,090	1,230,966
David Altarac, M.D.	2020	440,000	169,590	147,840	10,448	767,878
Chief Medical Officer	2019(4)	—	—	—	—	—
John Mueller, Ph.D.	2020	383,500	169,590	123,487	77,561	754,138
Chief Development Officer	2019(4)	—	—	—	—	—

- (1) The amounts shown for option awards represent the grant date fair value for option awards determined in accordance with Accounting Standards Codification, or ASC, Topic 718, Compensation—Stock Compensation. Assumptions used in the calculation of these amounts are included in Note 11 – Stock-Based Compensation Expense to our Notes to Consolidated Financial Statements in our Annual Report on Form 10-K, except that we assumed that the executive will perform the requisite service for the award to vest in full. These amounts do not reflect the actual economic value that will be realized by the Named Executive Officer upon the vesting of the stock options, the exercise of the stock options or the sale of the common stock underlying such stock options.
- (2) The amounts shown for non-equity incentive plan compensation represent amounts earned for the fiscal years presented, whether or not actually paid during such year. This column reflects amounts earned based on the achievement of company and individual performance goals and other factors deemed relevant by the Board and compensation committee. For 2020, the compensation committee determined that each Named Executive Officer was entitled to 95% of his target bonus.
- (3) This amount includes: (a) for Dr. Perros: \$8,550 of matching contributions made by us to his 401(k) plan account, \$661 in life insurance premiums paid by us, and \$134,150 related to a retention bonus paid during 2020; (b) for Dr. Altarac: \$8,550 of matching contributions made by us to his 401(k) plan account and \$1,898

in life insurance premiums paid by us; and (c) for Dr. Mueller, \$8,550 of matching contributions made by us to his 401(k) plan account, \$1,898 in life insurance premiums paid by us, and \$67,113 related to a retention bonus paid during 2020.

- (4) Amounts do not require disclosure as Dr. Altarac and Dr. Mueller were not Named Executive Officers in 2019.

Outstanding Equity Awards at 2020 Fiscal Year-End

The following table provides information regarding equity awards held by the Named Executive Officers that were outstanding as of December 31, 2020:

Name	Grant Date	Option Awards		Option Exercise Price (\$)	Option Expiration Date
		Number of Securities Underlying Unexercised Options (#) Exercisable	Number of Securities Underlying Unexercised Options (#) Unexercisable		
Manoussos Perros, Ph.D.	08/11/2015	87,462	— (1)	4.98	08/11/2025
	10/21/2016	69,970	— (2)	3.74	10/21/2026
	11/22/2017	152,510	30,503 (3)	3.11	11/22/2027
	05/01/2018	124,968	41,655 (4)	6.85	04/30/2028
	09/25/2018	44,830	34,868 (5)	15.00	09/24/2028
	01/18/2019	59,177	64,323 (6)	5.66	01/17/2029
	01/23/2020	—	145,000 (7)	4.94	01/22/2030
David Altarac, M.D.	11/04/2019	32,500	87,500 (8)	5.70	11/03/2029
	01/23/2020	—	50,000 (7)	4.94	01/22/2030
John Mueller, Ph. D.	08/11/2015	22,816	— (1)	4.98	08/11/2025
	10/21/2016	18,253	— (2)	3.74	10/21/2026
	11/22/2017	20,910	4,182 (3)	3.11	11/22/2027
	05/01/2018	12,669	4,223 (4)	6.85	04/30/2028
	09/25/2018	4,087	3,178 (5)	15.00	09/24/2028
	01/18/2019	27,073	29,427 (6)	5.66	01/17/2029
	01/23/2020	—	50,000 (7)	4.94	01/22/2030

- (1) Of the shares underlying the option, 25% vested on May 13, 2016, and the remaining shares vest in 36 equal monthly installments thereafter, subject to the officer's continued service through each vesting date. The option is subject to accelerated vesting upon a qualifying termination of the executive's employment with us, as described under "—Potential Payments and Benefits upon Termination or Change of Control."
- (2) Of the shares underlying the option, 25% vested on March 29, 2017, and the remaining shares vest in 36 equal monthly installments thereafter, subject to the officer's continued service through each vesting date.
- (3) Of the shares underlying the option, 25% vested on August 25, 2018, and the remaining shares vest in 36 equal monthly installments thereafter, subject to the officer's continued service through each vesting date.
- (4) Of the shares underlying the option, 25% vested on December 6, 2018, and the remaining shares vest in 36 equal monthly installments thereafter, subject to the officer's continued service through each vesting date.
- (5) Of the shares underlying the option, 25% vested on September 25, 2019, and the remaining shares vest in 36 equal monthly installments thereafter, subject to the officer's continued service through each vesting date.
- (6) Of the shares underlying the option, 25% vested on January 1, 2020, and the remaining shares vest in 36 equal monthly installments thereafter, subject to the officer's continued service through each vesting date.

- (7) Of the shares underlying the option, 25% vested on January 1, 2021, and the remaining shares vest in 36 equal monthly installments thereafter, subject to the officer's continued service through each vesting date.
- (8) Of the shares underlying the option, 25% vested on November 4, 2020, and the remaining shares vest in 36 equal monthly installments thereafter, subject to the officer's continued service through each vesting date.

Employment Arrangements

Below are descriptions of our employment agreements and arrangements with our Named Executive Officers. The agreements generally provide for at-will employment without any specific term and set forth the Named Executive Officers' initial base salary, eligibility for employee benefits and severance benefits upon a qualifying termination of employment or change in control of our company. Furthermore, each of our Named Executive Officers has executed a form of our standard proprietary information and inventions assignment agreement. The key terms of the employment agreements with our Named Executive Officers, including potential payments upon termination or change in control, are described below.

Agreement with Dr. Perros

We have an employment agreement with Manoussos Perros, our president and Chief Executive Officer, which became effective on September 25, 2018, and which sets forth the revised terms of Dr. Perros' employment with us. Pursuant to his employment agreement, Dr. Perros is eligible to receive an annual performance bonus with a target of 45% of his then-current base salary, as determined by our Board, and reimbursement for expenses. Dr. Perros' current base salary is \$552,698. His employment agreement does not have a specified term and his employment may be terminated by us or by Dr. Perros at any time, with or without cause. Dr. Perros is additionally eligible for certain severance and change in control benefits pursuant to his employment agreement, the terms of which are described below under "—Potential Payments and Benefits upon Termination or Change of Control."

Agreement with Dr. Altarac

Effective November 4, 2019, we entered into an employment agreement with David Altarac, M.D., our chief medical officer, which set forth the terms of Dr. Altarac's employment with us. Pursuant to his employment agreement, Dr. Altarac is eligible to receive an annual performance bonus with a target of 35% of his then-current base salary, as determined by our Board, and reimbursement for expenses. Dr. Altarac's current base salary is \$453,200. His employment agreement does not have a specified term and his employment may be terminated by us or by Dr. Altarac at any time, with or without cause. Dr. Altarac is additionally eligible for certain severance and change in control benefits pursuant to his employment agreement, the terms of which are described below under "—Potential Payments and Benefits upon Termination or Change of Control."

Agreement with Dr. Mueller

We have an employment agreement with John Mueller, Ph.D., our chief development officer, which became effective on September 25, 2018, and which sets forth the revised terms of Dr. Mueller's employment with us. Pursuant to his employment agreement, Dr. Mueller is eligible to receive an annual performance bonus with a target of 35% of his then-current base salary, as determined by our Board, and reimbursement for expenses. Dr. Mueller's current base salary is \$383,500. His employment agreement does not have a specified term and his employment may be terminated by us or by Dr. Mueller at any time, with or without cause. Dr. Mueller is additionally eligible for certain severance and change in control benefits pursuant to his employment agreement, the terms of which are described below under "—Potential Payments and Benefits upon Termination or Change of Control."

Potential Payments and Benefits upon Termination or Change of Control

Each of the employment agreements with our Named Executive Officers provides that if we terminate the employment of the Named Executive Officer for any reason other than for cause, or if such executive officer resigns his position with us for good reason, he would be eligible to receive the following severance benefits:

- 12 (or in the case of Dr. Perros, 18) months of his then-current base salary, paid in installments on our regular payroll dates following his termination date; and
- provided the executive officer is participating in our group health insurance as of the date of termination and timely elects to continue receiving coverage, we will continue to pay premiums necessary to continue the executive officer and executive officer's covered dependents' health insurance coverage in effect on the termination date for the lesser of:
 - 12 (or in the case of Dr. Perros, 18) months;
 - the date on which he becomes eligible for health insurance coverage in connection with new employment or self-employment; or
 - the date he ceases to be eligible for continuation coverage for any reason, including plan termination.

Alternatively, if such termination or resignation occurs on or within 18 months after a change of control (as defined therein), the Named Executive Officer is instead eligible for:

- a lump-sum payment equal to 12 (or in the case of Dr. Perros, 18) months of his then-current base salary;
- a lump-sum payment equal to one (or in the case of Dr. Perros, one and one half) times his target bonus for the year in which his employment terminates;
- provided the executive officer is eligible for and timely elects to continue receiving group health insurance, we will continue to pay premiums necessary to continue the executive officer and executive officer's covered dependents' health insurance coverage in effect on the termination date for the lesser of:
 - 12 (or in the case of Dr. Perros, 18) months;
 - the date on which he becomes eligible for health insurance coverage in connection with new employment or self-employment; or
 - the date he ceases to be eligible for continuation coverage for any reason, including plan termination; and
- acceleration of vesting of the entire unvested portion of the outstanding stock options and other stock awards held by the executive officer as of immediately prior to the change in control termination date to the extent such awards are subject to time-based vesting requirements.

Each employment agreement provides that the Named Executive Officer's death (or disability subject to applicable state and federal law) terminates the employment relationship and executive officer's legal representatives will not receive severance benefits. Payment of any of the above-described severance benefits is conditioned on the executive officer's delivery and non-revocation of a severance and release of claims agreement, which will include a general release of claims in our favor, within the time period provided in such agreement, which will be no later than 60 days after such executive officer's termination.

For purposes of the employment agreements:

- “cause” generally means (i) a material breach of the employment agreement or any other written agreement between the executive officer and us; (ii) gross negligence or gross misconduct in the performance of the executive officer’s duties; (iii) the commission of any act or omission constituting dishonesty or fraud that is injurious to us or any affiliate thereof; (iv) any conduct which constitutes a felony under applicable law; (v) conduct by the executive officer which demonstrates gross unfitness to serve; (vi) failure to attempt in good faith to implement a clear, reasonable and legal directive of our Board (or CEO in case of Dr. Altarac or Dr. Mueller) or any board committee; or (vii) breach of a fiduciary duty.
- “good reason” means the occurrence, without the named executive officer’s consent, of any of the following events: (i) any material diminution of the executive officer’s authority, duties or responsibilities; (ii) a material (greater than 10%) reduction by us of the executive officer’s base salary except in the case of across-the-board salary reductions based on our financial performance similarly affecting all or substantially all of our similarly-situated employees; (iii) a relocation of the executive officer’s place of employment to a location in excess of 50 miles from our current principal place of employment; or (iv) any material breach of the employment agreement by us; provided, however, that it will only be deemed good reason if (1) we have not previously notified the executive officer of our intention to terminate his employment; (2) we have been given written notice from the executive officer within 90 days following the first occurrence of a condition that the executive officer considers to constitute good reason (with such notice including a description of the condition); (3) we fail to remedy such condition within 30 days following such written notice; and (4) the executive officer resigns from employment with us effective not later than 30 days after the end of our cure period. Notwithstanding the foregoing, any actions taken by us to accommodate a disability of the executive officer or pursuant to the Family and Medical Leave Act or an applicable state leave law will not be a good reason for purposes of the employment agreement.

Health and Welfare Benefits

All of our current Named Executive Officers are eligible to participate in our employee benefit plans, including our medical, dental and vision insurance plans, in each case on the same basis as all of our other employees.

Long-Term Incentives

2018 Equity Incentive Plan and Amended and Restated Stock Incentive Plan

Our board of directors adopted and our stockholders approved the 2018 Plan in September 2018 for the purpose of attracting and retaining our directors, executive officers and other key employees, consultants and service providers, and to stimulate their efforts toward our continued success, long-term growth and profitability. The 2018 Plan became effective on September 25, 2018 and was amended on June 10, 2020. Our 2018 Plan provides for the grant of stock options qualifying as incentive stock options, or ISOs, within the meaning of Section 422 of the Internal Revenue Code of 1986, as amended, or the Code, to our employees and our parent and subsidiary corporations’ employees, and for the grant of nonstatutory stock options, restricted stock awards, restricted stock unit awards, stock appreciation rights, performance stock awards and other forms of stock compensation to our employees, consultants and directors. Our 2018 Plan also provides for the grant of performance based awards to our employees, consultants and directors. We also maintain the Amended and Restated Stock Incentive Plan, or the 2015 Plan, which has been terminated and under which no future awards will be granted, but under which outstanding awards have been granted. These awards will continue to be governed by the terms of the 2015 Plan.

As of April 1, 2021, we had 1,333,657 shares of common stock reserved for issuance pursuant to the 2018 Plan. The number of shares of our common stock reserved for issuance under our 2018 Plan automatically increases on January 1 of each year, for a period of 10 years, through January 1, 2028, by 4% of the total number of shares of our common stock outstanding on December 31 of the preceding calendar year, or a lesser number of shares as may be determined by our Board. The maximum number of shares that may be issued pursuant to the exercise of ISOs under the 2018 Plan is 7,500,000.

The administrator may provide, in an individual award agreement or in any other written agreement between us and the participant, that the stock award will be subject to additional acceleration of vesting and exercisability in the event of a change in control (as defined in the 2018 Plan). In the absence of such a provision, no such acceleration of the stock award will occur in the event of a change in control. See “Equity Compensation Plan Information” for further information.

2018 Employee Stock Purchase Plan

Our board of directors adopted and our stockholders approved the 2018 Employee Stock Purchase Plan, or the ESPP, in September 2018. The ESPP became effective on September 25, 2018. The purpose of the ESPP is to secure the services of new employees, to retain the services of existing employees and to provide incentives for such individuals to exert maximum efforts toward our success and that of our affiliates. The ESPP is intended to qualify as an “employee stock purchase plan” within the meaning of Section 423 of the Code. The ESPP authorizes the issuance of 140,000 shares of our common stock pursuant to purchase rights granted to our employees or to employees of any of our designated affiliates. The number of shares of our common stock reserved for issuance will automatically increase on January 1 of each calendar year, from January 1, 2019 through January 1, 2028, by the lesser of (i) 1% of the total number of shares of our common stock outstanding on December 31 of the preceding calendar year, and (ii) 250,000 shares; provided, that prior to the date of any such increase, our Board may determine that such increase will be less than the amount set forth in clauses (i) and (ii). If purchase rights granted under the ESPP terminate without having been exercised in full, the shares of our common stock not purchased under such purchase rights will again become available for issuance under the ESPP. See “Equity Compensation Plan Information” for further information.

401(k) Plan

We maintain a defined contribution retirement plan that provides eligible U.S. employees with an opportunity to save for retirement on a tax advantaged basis. Eligible employees may defer eligible compensation on a pre-tax basis, up to the statutorily prescribed annual limits on contributions under the Code. Contributions are allocated to each participant’s individual account and are then invested in selected investment alternatives according to the participants’ directions. Employees are immediately and fully vested in their contributions. The 401(k) plan is intended to be qualified under Section 401(a) of the Code with the 401(k) plan’s related trust intended to be tax exempt under Section 501(a) of the Code. As a tax-qualified retirement plan, contributions to the 401(k) plan and earnings on those contributions are not taxable to the employees until distributed from the 401(k) plan. Pursuant to our 401(k) plan, during 2020, we made 50% matching contributions on up to 6% of an employee’s eligible compensation.

Director Compensation

Cash and Equity Compensation

We maintain a non-employee director compensation policy that is intended to provide a total compensation package that enables us to attract and retain qualified and experienced individuals to serve as directors and to align our

directors' interests with those of our stockholders. Effective as of January 1, 2020, the Board amended the non-employee director compensation policy, or the Amended Policy, such that:

- the annual base retainer is \$40,000, with the exception of the non-executive chairperson, who receives \$90,000;
- each member of our Audit, Compensation and Nominating and Corporate Governance Committees receives an additional annual retainer of \$9,000, \$7,500 and \$4,250, respectively; and
- each chairperson of our Audit, Compensation and Nominating and Corporate Governance Committees receives an additional annual retainer of \$18,000, \$15,000 and \$8,500, respectively, in lieu of the member annual retainer.

Retainers are payable in arrears in four equal quarterly installments on the last day of each quarter, provided that the amount of such payment was prorated for any portion of such quarter that the director was not serving on the Board or the applicable committee.

In addition, pursuant to the Amended Policy, each non-employee director elected to the Board receives an initial one-time option to purchase 22,000 shares of our common stock. The shares subject to each such stock option will vest monthly over a three-year period, subject to the director's continued service as a director.

Further, on the date of each annual meeting of stockholders, each non-employee director that continues to serve as a non-employee member on the Board will receive an option to purchase 11,000 shares of our common stock. The shares subject to each such stock option will vest in equal monthly installments over the 12 months following the date of grant, provided that the grant will in any case be fully vested on the date of the next annual meeting of stockholders, subject to the director's continued service on the Board through the date of such meeting. The exercise price of these options will equal the fair market value of our common stock on the date of grant.

For 2021, upon the recommendation of the Compensation Committee and in an effort to more closely align non-executive director compensation to that of the Company's peers, the Board agreed to change the annual option award for 2021 to an award of 22,000 restricted stock units, which have a grant date of April 1, 2021 and will vest in full on the one-year anniversary of grant. The Compensation Committee and the Board believe that this one-time award will further align the non-executive directors' interests with that of the Company's stockholders while also providing a greater retentive effect during the next 12 months, which are likely to be significant given the expectation of topline data readout in the second half of 2021.

Director Compensation

The following table sets forth information regarding the compensation earned for service on the Board by our non-employee directors during the year ended December 31, 2020. The compensation for Dr. Perros as a Named Executive Officer is set forth above under "—Summary Compensation Table."

Name	Fees Earned or Paid in Cash (\$)	Option Awards⁽¹⁾⁽²⁾ (\$)	Total (\$)
David Meek	96,621	21,470	118,091
Nicholas Galakatos, Ph.D.	16,122 ⁽³⁾	—	16,122
Heather Behanna, Ph.D.	56,500	21,470	77,970
David C. Hastings	60,371	21,470	81,841
Gregory Norden	26,207 ⁽⁴⁾	—	26,207
Heather Preston, M.D.	49,000	— ⁽⁵⁾	49,000
Howard Mayer, M.D.	51,683	21,470	73,153

- (1) The amounts reported in this column reflect the aggregate grant date fair value of the option awards granted to our directors as computed in accordance with FASB ASC Topic 718. See Note 11 – Stock-Based Compensation Expense of Notes to Consolidated Financial Statements in our Annual Report on Form 10-K for a discussion of assumptions made us in determining the aggregate grant date fair value of our option awards. Note that the amounts reported in this column reflect the accounting cost for these stock options and do not reflect the actual economic value that may be realized by the directors upon the vesting of the stock options, the exercise of the stock options or the sale of the common stock underlying such stock options.
- (2) The following table provides information regarding the aggregate number of equity awards granted to our existing non-employee directors that were outstanding as of December 31, 2020:

Name	Option Awards Outstanding at Year-End (#)
David Meek	33,500
Heather Behanna, Ph.D.	33,500
David C. Hastings	45,560
Howard Mayer, M.D.	26,000

- (3) Dr. Galakatos resigned as a member of our Board effective May 1, 2020.
- (4) Mr. Norden did not stand for re-election at the 2020 Annual meeting and therefore, his term of office expired on June 10, 2020.
- (5) Dr. Preston has elected not to receive the initial or annual option awards granted to non-employee directors under the Amended Policy.

EQUITY COMPENSATION PLAN INFORMATION

The following table provides certain information with respect to all of our equity compensation plans in effect as of December 31, 2020.

Plan Category	Number of securities to be issued upon exercise of outstanding options, warrants and rights (#)	Weighted-average exercise price of outstanding options, warrants and rights (\$)	Number of securities remaining available for future issuance under equity compensation plans (excluding securities reflected in column (a)) (#)
Equity compensation plans approved by security holders:			
Amended and Restated Stock Incentive Plan	1,032,999	\$ 4.69	— (1)
2018 Equity Incentive Plan	2,474,805 (4)	\$ 6.02	359,416 (2)
2018 Employee Stock Purchase Plan	—	—	404,163 (3)
Equity compensation plans not approved by security holders	—	—	—
Total	3,507,804		763,579

- (1) No further grants were made under our 2015 Plan after the completion of our initial public offering on September 28, 2018.
- (2) The number of shares of common stock reserved for issuance under the 2018 Plan will automatically increase on January 1 of each year, beginning on January 1, 2019 and continuing through and including January 1, 2028, by 4% of the total number of shares of our common stock outstanding on December 31 of the preceding calendar year, or a lesser number of shares determined by our Board. Pursuant to the terms of the 2018 Plan, an

additional 1,465,494 shares were added to the number of available shares effective January 1, 2021, which are not included in the table above.

- (3) The number of shares of common stock reserved for issuance under the ESPP will automatically increase on January 1 of each year, beginning on January 1, 2019 and continuing through and including January 1, 2028, by the lesser of (i) 1% of the total number of shares of our common stock outstanding on December 31 of the preceding calendar year, (ii) 250,000 shares or (iii) such lesser number of shares determined by our Board. Pursuant to the terms of the ESPP, an additional 250,000 shares were added to the number of available shares effective January 1, 2021, which are not included in the table above.
- (4) The number of securities to be issued consists of 2,079,705 options outstanding and 395,100 RSUs outstanding.

TRANSACTIONS WITH RELATED PERSONS

Policies and Procedures Regarding Transactions with Related Parties

We have adopted a written Related Person Transactions Policy that sets forth our policies and procedures regarding the identification, review, consideration and approval or ratification of “related-persons transactions.” For purposes of our policy only, a “related-person transaction” is a transaction, arrangement or relationship (or any series of similar transactions, arrangements or relationships) in which we and any “related person” are participants involving an amount that exceeds or will exceed \$120,000 or, during such time as we qualify as a “smaller reporting company,” the lesser of (1) \$120,000 or (2) 1% of the average of our total assets for the last two completed fiscal years, and in which any related person had or will have a direct or indirect material interest. Transactions involving compensation for services provided to us as an employee, director, consultant or similar capacity by a related person are not covered by this policy. A “related person” is any executive officer, director or a holder of more than 5% of our capital stock, including any of their immediate family members, and any entity owned or controlled by such persons.

Certain Related-Party Transactions

Below are our related-party transactions since January 1, 2010 to which we were a party or will be a party, other than compensation, termination and change of control arrangements with our Named Executive Officers and directors, which are described where required under the sections entitled “Executive Officer and Director Compensation—Employment Arrangements” and “Director Compensation—Cash and Equity Compensation.”

We believe the terms obtained or consideration that we paid or received, as applicable, in connection with the transactions described below were comparable to terms available or the amounts that we would pay or receive, as applicable, in arm’s-length transactions with unrelated third parties.

Pharmaron Beijing Co., Ltd. (China)

We currently contract with Pharmaron Beijing Co., Ltd. (China), or Pharmaron, to provide various medicinal chemistry research, manufacturing development and clinical services related to our ongoing product candidates. We began utilizing Pharmaron as a service provider prior to our spin-off in 2015. In 2019, the Senior Vice President of Strategic Partnerships at Pharmaron, or the Pharmaron Executive, began sharing a household with the Company’s Chief Executive Officer, and as a result we now consider the agreements between us and Pharmaron to be related-party transactions. The Pharmaron Executive is responsible for overseeing client relationships, but is not directly involved in our agreements with Pharmaron, and neither Dr. Perros nor the Pharmaron Executive have participated or will participate in the negotiation or the approval of the ongoing services provided thereunder. In 2019 and 2020, we paid Pharmaron approximately \$5.3 million and \$4.0 million, respectively, for services rendered pursuant to multiple agreements, and since our spin-out in 2015, have paid Pharmaron approximately \$24.2 million for services rendered.

Registration Rights Agreements

We are party to a Registration Rights Agreement, dated September 14, 2018, with Clarus Lifesciences III, L.P., Frazier Life Sciences VIII, LP., Novo Holdings A/S, Pivotal bioVenture Partners Fund I, L.P., TPG Biotechnology Partners V, L.P., Sofinnova Venture Partners IX, L.P., AstraZeneca, Eventide Gilead Fund and Eventide Healthcare & Life Sciences Fund. This agreement provides that these holders are entitled to certain registration rights, including the right to demand that we file a registration statement or request that their shares be covered by a registration statement that we otherwise file. The registration rights will terminate upon the earliest of (1) the closing of a deemed liquidation event, as defined in our Certificate of Incorporation, as currently in effect, (2) with respect to each stockholder, the date when such stockholder can sell all of its registrable shares without limitation during a three-month period without registration pursuant to Rule 144 of the Securities Act or another similar exemption under the Securities Act and (3) five years after the completion of our initial public offering.

We are party to a Registration Rights Agreement, dated April 22, 2020, with Innoviva, Inc., or Innoviva, pursuant to which, among other things, we agreed to prepare and file with the SEC a registration statement with respect to resales of the shares of common stock and the warrants purchased by Innoviva. The registration statement was filed with the SEC on August 6, 2020, and declared effective by the SEC on August 14, 2020.

We are party to a Registration Rights Agreement, dated September 1, 2020, with certain investors, including Innoviva, Inc. Pursuant to the agreement, we agreed to prepare and file a registration statement with the SEC for purposes of registering the resale of the shares of common stock, shares of common stock issuable upon exercise of the warrants held by Innoviva, the warrants and any shares of common stock issued as a dividend or other distribution with respect to the shares or shares of common stock issuable upon exercise of the warrants held by Innoviva. The registration statement was filed with the SEC on October 5, 2020, and declared effective by the SEC on October 13, 2020.

Lease Agreement

In May 2015, our U.S. subsidiary, Entasis Therapeutics Inc., entered into a lease agreement with AstraZeneca Pharmaceuticals LP, an affiliate of AstraZeneca, which was amended effective February 2, 2018. Under the terms of the lease, as amended, we lease a total of 20,062 square feet of office, research and development and laboratory facility space in Waltham, Massachusetts. The lease expires on December 31, 2022. During the years ended December 31, 2019 and December 31, 2020, we paid rent of \$0.6 million and \$0.7 million, respectively, under the lease agreement.

SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT

The following table sets forth certain information known to us regarding the beneficial ownership of our common stock as of April 1, 2021 by: (i) each of our Named Executive Officers; (ii) each of our directors (including nominees); (iii) all of our executive officers, directors and director nominees as a group; and (iv) each person or entity, or group of affiliated persons or entities, known by us to beneficially own more than 5% of our outstanding common stock.

Information with respect to beneficial ownership is based on information furnished to us by each director, executive officer or stockholder who holds more than 5% of our outstanding common stock, and Schedules 13G or 13D filed with the SEC, as the case may be. Beneficial ownership is determined according to the rules of the SEC and generally means that a person has beneficial ownership of a security if he or she possesses sole or shared voting or investment power of that security, and includes options and warrants that are currently exercisable within 60 days of April 1, 2021. Options to purchase shares of our common stock that are exercisable within 60 days of April 1, 2021, are deemed to be beneficially owned by the persons holding these options for the purpose of computing percentage ownership of that person, but are not treated as outstanding for the purpose of computing any other person's ownership percentage. Except as indicated in the footnotes below, each of the beneficial owners named in the table below has, to our knowledge, sole voting and investment power with respect to all shares of common stock listed as beneficially owned by him or her, except for shares owned jointly with that person's spouse.

We have based our calculation of beneficial ownership on 37,310,254 shares of our common stock outstanding as of April 1, 2021. Unless otherwise indicated, the address for each of the stockholders in the table below is c/o Entasis Therapeutics Holdings Inc., 35 Gatehouse Drive, Waltham, Massachusetts 02451.

	Number of Shares Beneficially Owned (#)	Percent of Shares Beneficially Owned (%)
Greater than 5% Stockholders:		
Innoviva, Inc. ⁽¹⁾	37,345,794	66.7 %
AstraZeneca AB ⁽²⁾	2,164,855	5.8
Directors, Director Nominee and Named Executive Officers:		
Manoussos Perros, Ph.D. ⁽³⁾	644,837	1.7
David Altarac, M.D. ⁽⁴⁾	61,667	*
John Mueller, Ph.D. ⁽⁵⁾	133,490	*
Heather Behanna, Ph.D. ⁽⁶⁾	32,583	*
David C. Hastings ⁽⁷⁾	41,628	*
Heather Preston, M.D. ⁽⁸⁾	1,180,178	3.1
David Meek ⁽⁹⁾	27,166	*
Howard Mayer, M.D. ⁽¹⁰⁾	18,833	*
All current executive officers, directors and director nominees as a group (12 persons)	2,522,358	6.5

* Represents beneficial ownership of less than 1%.

- (1) Based solely on Schedule 13D/A filed by Innoviva, Inc. on September 1, 2020. This amount consists of 18,672,897 shares that are held directly, as well as warrants to purchase up to 18,672,897 shares of common stock that are exercisable within 60 days of April 1, 2021. The principal business address of Innoviva is 1350 Old Bayshore Highway, Suite 400, Burlingame, California, 94010.
- (2) Based solely on a Schedule 13D/A filed by AstraZeneca PLC on October 12, 2018. 2,164,855 represents shares directly held by AstraZeneca, a wholly owned subsidiary of AstraZeneca PLC. AstraZeneca PLC and AstraZeneca may each be deemed to have sole voting and dispositive power over the shares. The principal business address of AstraZeneca is SE-151, 85 Sodertalje, Sweden.
- (3) Consists of 644,837 shares of common stock issuable upon the exercise of outstanding options exercisable within 60 days of April 1, 2021.
- (4) Consists of 61,667 shares of common stock issuable upon the exercise of outstanding options exercisable within 60 days of April 1, 2021.
- (5) Consists of 133,490 shares of common stock issuable upon the exercise of outstanding options exercisable within 60 days of April 1, 2021.
- (6) Consists of 32,583 shares of common stock issuable upon the exercise of outstanding options exercisable within 60 days of April 1, 2021.
- (7) Consists of 41,628 shares of common stock issuable upon the exercise of outstanding options exercisable within 60 days of April 1, 2021.
- (8) Dr. Preston is a managing partner of Investment Advisor, which is the investment advisor to Pivotal, and is managing partner of Pivotal bioVenture Partners Investment Advisor, LLC, which is the U.S. sub-advisor to the Investment Advisor. Therefore, Dr. Preston may be deemed to beneficially own the shares held by Pivotal. The principal address of Pivotal bioVenture Partners Fund I, L.P. is 1700 Owens Street, Suite 595, San Francisco, CA 94158.

- (9) Consists of 27,166 shares of common stock issuable upon the exercise of outstanding options exercisable within 60 days of April 1, 2021.
- (10) Consists of 18,833 shares of common stock issuable upon the exercise of outstanding options exercisable within 60 days of April 1, 2021.

HOUSEHOLDING OF PROXY MATERIALS

The Company has adopted a procedure approved by the SEC called “householding.” Under this procedure, beneficial shareholders who have the same address and last name and will receive only one copy of the Company’s Notices of Internet Availability of Proxy Materials or other Annual Meeting materials unless one or more of these shareholders notifies the Company that they wish to continue receiving individual copies. This procedure is designed for convenience for stockholders and cost savings for companies.

A single Notice of Internet Availability of Proxy Materials will be delivered to multiple stockholders sharing an address unless contrary instructions have been received from the affected stockholders. Your consent to householding is perpetual unless you revoke it. You may revoke your consent at any time by contacting your broker or the Company (in writing or orally) to Entasis Therapeutics Holdings Inc., 35 Gatehouse Drive, Waltham, Massachusetts 02451, Attn: Michael Gutch, Ph.D., Secretary, or contact Dr. Gutch at (781) 810-0120. You will be removed from the householding program, after which you will receive an individual copy of the proxy materials promptly.

Stockholders who currently receive multiple copies of the Notices of Internet Availability of Proxy Materials at their addresses and would like to request “householding” of their communications should contact their brokers.

OTHER MATTERS

The Board knows of no business to be brought before the 2021 Annual Meeting which is not referred to in the accompanying Notice of Annual Meeting. Should any such matters be presented, the persons named in the proxy shall have the authority to take such action in regard to such matters as in their judgment seems advisable. If you hold shares through a broker, bank or other nominee as described above, they will not be able to vote your shares on any other business that comes before the Annual Meeting unless they receive instructions from you with respect to such matter.

ANNUAL REPORT ON FORM 10-K

A copy of our Annual Report on Form 10-K for the fiscal year ended December 31, 2020 is available without charge upon written request to: Entasis Therapeutics Holdings Inc., 35 Gatehouse Drive, Waltham, Massachusetts 02451, Attn: Michael Gutch, Ph.D., Secretary.

By Order of the Board of Directors

/s/ MICHAEL GUTCH, PH.D.

Michael Gutch, Ph.D.

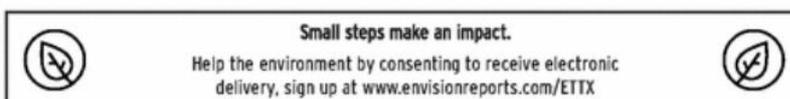
Secretary

April 30, 2021

The 2021 Annual Meeting of Stockholders of Entasis Therapeutics Holdings, Inc. will be held on Thursday, June 10, 2021, 9:30 a.m. EDT, virtually via the internet at www.meetingcenter.io/227937811.

To access the virtual meeting, you must have the information that is printed in the shaded bar located on the reverse side of this form.

The password for this meeting is – ETTX2021.



▼ IF VOTING BY MAIL, SIGN, DETACH AND RETURN THE BOTTOM PORTION IN THE ENCLOSED ENVELOPE. ▼

Proxy – Entasis Therapeutics Holdings Inc.



Notice of 2021 Annual Meeting of Stockholders

Proxy Solicited by Board of Directors for Annual Meeting – June 10, 2021

Manoussos Perros, Ph.D. and Michael Gutch, Ph.D., or any of them, each with the power of substitution, are hereby authorized to represent and vote the shares of the undersigned, with all the powers which the undersigned would possess if present, at the Annual Meeting of Stockholders of Entasis Therapeutics Holdings Inc. to be held virtually on June 10, 2021 or at any postponement or adjournment thereof.

This proxy, when properly executed, will be voted as directed. If no such directions are indicated, the Proxies will have authority to vote FOR all the nominees listed in Proposal 1 and FOR Proposal 2. In their discretion, the Proxies are authorized to vote upon such other business as may properly come before the meeting.

(Items to be voted appear on reverse side.)

C Non-Voting Items

Change of Address – Please print new address below.

Comments – Please print your comments below.





Using a **black ink** pen, mark your votes with an X as shown in this example. Please do not write outside the designated areas.



Annual Meeting Proxy Card

▼ IF VOTING BY MAIL, SIGN, DETACH AND RETURN THE BOTTOM PORTION IN THE ENCLOSED ENVELOPE. ▼

A Proposals – The Board of Directors recommends a vote FOR the nominees listed and FOR Proposal 2.

1. Election of two Class III directors:

	For	Withhold
01 - David Hastings	<input type="checkbox"/>	<input type="checkbox"/>
	For	Withhold
02 - Manoussos Perros, Ph.D	<input type="checkbox"/>	<input type="checkbox"/>



2. Ratification of the selection of KPMG LLP as our independent registered public accounting firm for the fiscal year ending December 31, 2021.

For	Against	Abstain
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

B Authorized Signatures – This section must be completed for your vote to count. Please date and sign below.

Please sign exactly as name(s) appears herein. Joint owners should each sign. When signing as attorney, executor, administrator, corporate officer, trustee, guardian or custodian, please give full title. If the signer is a corporation, partnership or other entity, please sign full entity name by authorized officer, giving full title.

Date (mm/dd/yyyy) – Please print date below.

Signature 1 – Please keep signature within the box.

Signature 2 – Please keep signature within the box.



1UPX 501322



▼ IF VOTING BY MAIL, SIGN, DETACH AND RETURN THE BOTTOM PORTION IN THE ENCLOSED ENVELOPE. ▼

Proxy – Entasis Therapeutics Holdings Inc.

Notice of 2021 Annual Meeting of Stockholders

Proxy Solicited by Board of Directors for Annual Meeting – June 10, 2021

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This proxy, when properly executed, will be voted as directed. If no such directions are indicated, the Proxies will have authority to vote FOR all the nominees listed in Proposal 1 and FOR Proposal 2. In their discretion, the Proxies are authorized to vote upon such other business as may properly come before the meeting.

(Items to be voted appear on reverse side.)
