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 Pursuant to § 240.14a-12

Regulus Therapeutics Inc.

(Name of Registrant as Specified In Its Charter)

Not Applicable
(Name of Person(s) Filing Proxy Statement, if other than the Registrant)

Payment of Filing Fee (Check all boxes that apply)

☒ No fee required.

☐ Fee paid previously with preliminary materials.

☐ Fee computed on table in exhibit required by Item 25(b) per Exchange Act Rules 14a-6(i)(1) and 0-11.

REGULUS THERAPEUTICS INC.
4224 Campus Point Court, Suite 210
San Diego, California 92121

NOTICE OF ANNUAL MEETING OF STOCKHOLDERS

To Be Held On June 9, 2022

Dear Stockholder:

You are cordially invited to attend the 2022 Annual Meeting of Stockholders (the "Annual Meeting") of Regulus Therapeutics Inc., a Delaware corporation (the "Company"). The meeting will be held on June 9, 2022 at 9:00 a.m. local time at the Company's principal executive offices located at 4224 Campus Point Court, Suite 210, San Diego, CA 92121 for the following purposes:

1. To elect the ten nominees for director named herein to serve until the next annual meeting of stockholders and their successors are duly elected and qualified;

2. To approve an amendment to our Amended and Restated Certificate of Incorporation to effect a reverse stock split of our common stock at a ratio in the range of 1-for-5 to 1-for-20, with such ratio to be determined in the discretion of our board of directors and with such reverse stock split to be effected at such time and date, if at all, as determined by our board of directors in its sole discretion (Proposal 2);

3. To approve an amendment to our Amended and Restated Certificate of Incorporation to reduce, if and only if Proposal 2 is both approved and implemented, the number of authorized shares of our common stock to 300,000,000 shares (Proposal 3);

4. To approve, on an advisory basis, the compensation of the Company's named executive officers;

5. To ratify the selection by the Audit Committee of the Board of Directors of Ernst & Young LLP as the independent registered public accounting firm of the Company for its fiscal year ending December 31, 2022;

6. To approve the Regulus Therapeutics Inc. 2022 Employee Stock Purchase Plan (the "2022 ESPP"), pursuant to which 1,291,072 shares of our common stock will be available for sale and issuance to our employees;

7. To approve the authorization to adjournment of the Annual Meeting, if necessary, to solicit additional proxies if there are not sufficient votes in favor of Proposal 2 or Proposal 6; and

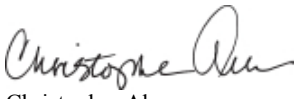
8. To conduct any other business properly brought before the meeting.

These items of business are more fully described in the Proxy Statement accompanying this notice.

In light of the ongoing COVID-19 pandemic and applicable government guidelines, we are planning for the possibility that the annual meeting may be held solely by means of remote communication. If we take this step, we will announce the decision to do so in advance in a press release and details on how to participate will be available at http://ir.regulusrx.com/financial-information/annual-reports as soon as practicable before the annual meeting.

The record date for the annual meeting is April 12, 2022. Only stockholders of record at the close of business on that date may vote at the meeting or any adjournment thereof.

By Order of the Board of Directors



Christopher Aker
Corporate Secretary

San Diego, California
April 27, 2022

You are cordially invited to attend the meeting in person. Whether or not you expect to attend the meeting, please complete, date, sign and return the proxy card that may be mailed to you or vote by telephone or through the internet as instructed in these materials, the proxy card or the Notice of Internet Availability of Proxy Materials, as promptly as possible in order to ensure your representation at the meeting. Even if you have voted by proxy, you may still vote in person if you attend the meeting. 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 meeting, you must obtain a proxy issued in your name from that record holder.

REGULUS THERAPEUTICS INC.
4224 Campus Pointe Court, Suite 210
San Diego, California 92121

PROXY STATEMENT
FOR THE 2022 ANNUAL MEETING OF STOCKHOLDERS
To Be Held On June 9, 2022

QUESTIONS AND ANSWERS ABOUT THESE PROXY MATERIALS AND VOTING

Why did I receive a notice regarding the availability of proxy materials on the internet, rather than a full set of proxy materials?

Pursuant to rules adopted by the Securities and Exchange Commission (the "SEC"), we have elected to provide access to our proxy materials over the internet. Accordingly, we have sent you a Notice of Internet Availability of Proxy Materials (a "Notice") because the Board of Directors (sometimes referred to as the "Board") of Regulus Therapeutics Inc. (sometimes referred to as "we," "us," the "Company" or "Regulus") is soliciting your proxy to vote at our 2022 Annual Meeting of Stockholders, including at any adjournments or postponements of the meeting. All stockholders will have the ability to access the proxy materials on the website referred to in the Notice or request to receive a printed set of the proxy materials. Instructions on how to access the proxy materials over the internet or to request a printed copy may be found in the Notice.

The Notice will be first mailed to our stockholders of record entitled to vote at the annual meeting on April 28, 2022.

Will I receive any other proxy materials by mail?

We may send you a proxy card, along with a second Notice, on or after May 8, 2022.

How do I attend the annual meeting?

The meeting will be held on June 9, 2022 at 9:00 a.m. local time at 4224 Campus Point Court, Suite 210, San Diego, California 92121. Directions to the annual meeting may be found at www.regulusrx.com. Information on how to vote in person at the annual meeting is discussed below.

In light of the ongoing COVID-19 pandemic and applicable government guidelines, we are planning for the possibility that the annual meeting may be held solely by means of remote communication. If we take this step, we will announce the decision to do so in advance in a press release and details on how to participate will be available at http://ir.regulusrx.com/financial-information/annual-reports as soon as practicable before the annual meeting.

Who can vote at the annual meeting?

Only stockholders of record at the close of business on April 12, 2022 will be entitled to vote at the annual meeting. On this record date, there were 145,981,180 shares of common stock outstanding and entitled to vote.

Stockholder of Record: Shares Registered in Your Name

If on April 12, 2022 your shares were registered directly in your name with the Company's transfer agent, Computershare, then you are a stockholder of record. As a stockholder of record, you may vote in person at the meeting or vote by proxy. Whether or not you plan to attend the meeting, we urge you to vote by proxy to ensure your vote is counted.

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

If on April 12, 2022 your shares were held, not in your name, but rather in an account at a brokerage firm, bank, dealer or other similar organization, then you are the beneficial owner of shares held in "street name" and received this Notice from that organization. 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 in person at the meeting unless you request and obtain a valid proxy from your broker or other agent.

What am I voting on?

There are seven matters scheduled for a vote:

- Proposal 1: Election of the ten nominees for director named herein;
- Proposal 2: Approval of an amendment to our Amended and Restated Certificate of Incorporation to effect a reverse stock split of our common stock at a ratio in the range of 1-for-5 to 1-for-20, with such ratio to be determined in the discretion of our board of directors and with such reverse stock split to be effected at such time and date, if at all, as determined by our board of directors in its sole discretion;
- Proposal 3: Approval of an amendment to our Amended and Restated Certificate of Incorporation to reduce, if and only if Proposal 2 is both approved and implemented, the number of authorized shares of our common stock to 300,000,000 shares;
- Proposal 4: Approval, on an advisory basis, of the compensation of the Company's named executive officers, as disclosed in this proxy statement;
- Proposal 5: Ratification of the selection by the Audit Committee of the Board of Directors of Ernst & Young LLP as the independent registered public accounting firm of the Company for its fiscal year ending December 31, 2022;
- Proposal 6: Approval of the 2022 ESPP, pursuant to which 1,291,072 shares of our common stock will be available for sale and issuance to our employees; and
- Proposal 7: Authorization of the adjournment of the Annual Meeting, if necessary, to solicit additional proxies if there are not sufficient votes in favor of Proposal 2 or Proposal 6.

What if another matter is properly brought before the meeting?

The Board of Directors 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, it is the intention of the persons named in the proxy to vote on those matters in accordance with their best judgment.

How do I vote?

You may either vote "For" all the nominees to the Board of Directors or you may "Withhold" your vote for any nominee you specify. For all other matters, you may vote "For" or "Against" or abstain from voting.

The procedures for voting are fairly simple:

Stockholder of Record: Shares Registered in Your Name

If you are a stockholder of record, you may vote in person at the annual meeting, over the telephone, 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 meeting, we urge you to vote by proxy to ensure your vote is counted. You may still attend the meeting and vote in person even if you have already voted by proxy.

- To vote using the proxy card, simply complete, sign and date the proxy card that may be delivered 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.
- To vote over the telephone, dial toll-free 1-800-652-8683 using a touch-tone phone and follow the recorded instructions. You will be asked to provide the company number and control number from the enclosed Notice. Your vote must be received by 11:59 p.m. Eastern Time on June 8, 2022 to be counted.
- To vote through the internet, go to www.investorvote.com/RGLS to complete an electronic proxy card. You will be asked to provide the company number and control number from the enclosed Notice. Your vote must be received by 11:59 p.m. Pacific Time on June 8, 2022 to be counted.
- To vote in person, come to the annual meeting and we will give you a ballot when you arrive.

Beneficial Owner: Shares Registered in the Name of Broker or Bank

If you are a beneficial owner of shares registered in the name of your broker, bank, or other agent, you should have received a Notice containing voting instructions from that organization rather than from Regulus. Simply follow the voting instructions in the Notice to ensure that your vote is counted. To vote in person at the annual meeting, you must obtain a valid proxy from your broker, bank or other agent. Follow the instructions from your broker or bank included with these proxy materials, or contact your broker or bank to request a proxy form.

Internet proxy voting may be provided to allow you to vote your shares online, with procedures designed to ensure the authenticity and correctness of your proxy vote instructions. However, please be aware that you must bear any costs associated with your internet access, such as usage charges from internet access providers and telephone companies.

How many votes do I have?

On each matter to be voted upon, you have one vote for each share of common stock you owned as of April 12, 2022.

What happens if I do not vote?

Stockholder of Record: Shares Registered in Your Name

If you are a stockholder of record and do not vote by completing a proxy card, or by telephone, through the internet, or in person at the annual meeting, your shares will not be voted.

Beneficial Owner: Shares Registered in the Name of Broker or Bank

If you are a beneficial owner and do not instruct your broker, bank, or other agent how to vote your shares, the question of whether your broker or nominee will still be able to vote your shares depends on whether the particular proposal is considered to be a routine matter under applicable rules. Brokers and nominees can use their discretion to vote uninstructed shares with respect to matters that are considered to be routine under applicable rules, but not with respect to non-routine matters. Under applicable rules and interpretations, non-routine matters are matters that may substantially affect the rights or privileges of stockholders, such as mergers, stockholder proposals, elections of directors (even if not contested), executive compensation (including any advisory stockholder votes on executive compensation and on the frequency of stockholder votes on executive compensation), and certain corporate governance proposals, even if management-supported. Accordingly, your broker or nominee may not vote your shares on Proposals 1, 4 or 6, without your instructions, but may vote your shares on Proposals 2, 3, 5 and 7.

What if I return a proxy card or otherwise vote but do not make specific choices?

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 all ten nominees for director named herein, "For" the approval of an amendment to our Amended and Restated Certificate of Incorporation to effect a reverse stock split of our common stock at a ratio in the range of 1-for-5 to 1-for-20, as described in Proposal 2, "For" the approval of an amendment to our Amended and Restated Certificate of Incorporation to reduce, the number of authorized shares of our common stock to 300,000,000 shares, as described in Proposal 3; "For" the approval of the stockholder advisory vote on the compensation of our named executive officers, as described in Proposal 4, "For" the ratification of the selection by the Audit Committee of the Board of Ernst & Young LLP as the independent registered public accounting firm of the Company for its fiscal year ending December 31, 2022, as described in Proposal 5, "For" the approval of the 2022 ESPP, as described in Proposal 6, and "For" the authorization of the adjournment of the Annual Meeting, if necessary, to solicit additional proxies if there are not sufficient votes in favor of Proposal 2 or Proposal 6, as described in Proposal 7. If any other matter is properly presented at the meeting, your proxyholder (one of the individuals named on your proxy card) will vote your shares using his or her best judgment.

Who is paying for this proxy solicitation?

We will pay for 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 may also reimburse brokerage firms, banks and other agents for the cost of forwarding proxy materials to beneficial owners.

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

If you receive more than one Notice, your shares may be registered in more than one name or in different accounts. Please follow the voting instructions on the Notices in the proxy materials 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. You can revoke your proxy at any time before the final vote at the meeting. If you are the record holder of your shares, you may revoke your proxy in any one of the following ways:

- You may submit a properly completed proxy card with a later date.
- You may grant a subsequent proxy by telephone or through the internet.
- You may send a timely written notice that you are revoking your proxy to Regulus Therapeutics Inc.'s Secretary at its principal executive offices located at 4224 Campus Point Court, Suite 210, San Diego, California 92121.
- You may attend the annual meeting and vote in person. Simply attending the meeting will not, by itself, revoke your proxy.

Your most current proxy card or telephone or internet proxy is the one that is counted.

Beneficial Owner: Shares Registered in the Name of Broker or Bank

If your shares are held by your broker or bank as a nominee or agent, you should follow the instructions provided by your broker or bank.

When are stockholder proposals and director nominations due for next year's annual meeting?

To be considered for inclusion in the Company's proxy materials for next year's annual meeting of stockholders, your proposal must be submitted in writing by December 29, 2022 to the attention of the Secretary of Regulus Therapeutics Inc. at 4224 Campus Point Court, Suite 210, San Diego, California 92121. If you wish to submit a proposal (including a director nomination) at the meeting that is not to be included in the Company's proxy materials for next year's annual meeting, your written request must be received by the Secretary for Regulus Therapeutics Inc. at 4224 Campus Point Court, Suite 210, San Diego, California 92121 between February 9, 2023 and March 11, 2023. You are also advised to review the Company's Bylaws, which contain additional requirements about advance notice of stockholder proposals and director nominations. In addition to satisfying the foregoing requirements under the Company's Bylaws, to comply with the universal proxy rules (once effective), stockholders who intend to solicit proxies in support of director nominees other than our Board's nominees must provide notice that sets forth any additional information required by Rule 14a-19 promulgated under the Securities Exchange Act of 1934, as amended, no later than April 10, 2023.

How are votes counted?

Votes will be counted by the inspector of election appointed for the meeting, who will separately count, for the proposal to elect directors, votes "For," "Withhold" and broker non-votes and with respect to the other proposals, votes "For" and "Against," abstentions and, if applicable, broker non-votes. Abstentions will be counted towards the vote total for Proposals 2, 3, 4, 5, 6 and 7 and will have the same effect as "Against" votes. Broker non-votes will be counted for purposes of determining the presence of a quorum and will have no effect for any proposal other than Proposals 2 and 3, for which broker non-votes will have the same effect as "Against" votes. Proposals 2, 3, 5, 6 and 7 are considered routine matters on which a broker, bank or other agent has discretionary authority to vote, so there may not be any broker non-votes in connection with these proposals.

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 or nominee holding the shares as to how to vote on matters deemed to be non-routine under applicable rules, the broker or nominee may not vote the shares. These unvoted shares are counted as "broker non-votes."

How many votes are needed to approve each proposal?

- For Proposal 1, regarding the election of directors, the ten nominees receiving the most "For" votes from the holders of shares present in person or represented by proxy and entitled to vote on the election of directors will be elected. Only votes "For" will affect the outcome. However, if the number of votes "For" any of the ten nominees does not exceed a majority of the total number of votes cast (excluding abstentions and broker non-votes) with respect to such nominee's election (from the holders of votes of shares either present in person or represented by proxy and entitled to vote), such nominee will promptly tender his or her resignation as a director, and the Nominating and Corporate Governance Committee of the Board will make a recommendation to the Board as to whether to accept or reject such director's resignation.
- To be approved, Proposal 2, regarding the approval of an amendment to our Amended and Restated Certificate of Incorporation to effect a reverse stock split of our common stock at a ratio in the range of 1-for-5 to 1-for-20, must receive "For" votes from the holders of a majority of shares outstanding on the record date for the Annual Meeting. Abstentions will have the same effect as "Against" votes. Broker non-votes, if any, will have the same effect as "Against" votes.
- To be approved, Proposal 3, regarding the approval of an amendment to our Amended and Restated Certificate of Incorporation to reduce, the number of authorized shares of our common stock to 300,000,000 shares if and only if Proposal 2 is both approved and implemented, must receive "For"

votes from the holders of a majority of shares outstanding on the record date for the Annual Meeting. Abstentions will have the same effect as "Against" votes. Broker non-votes, if any, will have the same effect as "Against" votes.

- To be approved, Proposal 4, regarding the approval on an advisory basis of the compensation of the Company's named executive officers, must receive "For" votes from the holders of a majority of shares present and entitled to vote either in person or represented by proxy. Abstentions will have the same effect as "Against" votes. Broker non-votes will have no effect.
- To be approved, Proposal 5, regarding the ratification of the selection by the Audit Committee of the Board of Directors of Ernst & Young LLP as the independent registered public accounting firm of the Company for its fiscal year ending December 31, 2022, must receive "For" votes from the holders of a majority of shares present and entitled to vote either in person or represented by proxy. Abstentions will have the same effect as "Against" votes. Broker non-votes, if any, will have no effect.
- To be approved, Proposal 6, regarding the adoption of the 2022 ESPP, pursuant to which 1,291,072 shares of our common stock will be available for sale and issuance to our employees, must receive "For" votes from the holders of a majority of shares present and entitled to vote either in person or represented by proxy. Abstentions will have the same effect as "Against" votes. Broker non-votes will have no effect.
- To be approved, Proposal 7, regarding the authorization to adjourn the Annual Meeting, if necessary, to solicit additional proxies if there are not sufficient votes in favor of Proposal 2 or Proposal 6, must receive "For" votes from the holders of a majority of shares present and entitled to vote either in person or represented by proxy. Abstentions will have the same effect as "Against" votes. Broker non-votes, if any, will have no effect.

What is the quorum requirement?

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 shares outstanding on the record date and entitled to vote are present at the meeting in person or represented by proxy. On the record date, there were 145,981,180 shares outstanding and entitled to vote. Thus, the holders of 72,990,591shares must be present in person or represented by proxy at the 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 meeting. Abstentions and broker non-votes 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.

How can I find out the results of the voting at the annual meeting?

Preliminary voting results will be announced at the annual meeting. In addition, final voting results will be published in a current report on Form 8-K that we expect to file within four business days after the completion of the annual meeting. If final voting results are not available to us in time to file a Form 8-K within four business days after the meeting, we intend to file a Form 8-K to publish preliminary results and, within four business days after the final results are known to us, file an additional Form 8-K to publish the final results.

PROPOSAL 1

ELECTION OF DIRECTORS

Our Board of Directors currently consists of ten directors. There are ten nominees for director this year, consisting of our incumbent directors. Each director to be elected and qualified will hold office until the next annual meeting of stockholders and until his or her successor is elected, or, if sooner, until the director's death, resignation or removal. Each of the nominees listed below is currently a director of the Company who was previously elected by the stockholders. 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. The ten nominees receiving the highest number of affirmative votes will be elected. Pursuant to the Company's Corporate Governance Principles, if the number of votes "For" any of the ten nominees does not exceed a majority of the total number of votes cast (excluding abstentions and broker non-votes) with respect to such nominee's election (from the holders of votes of shares either present in person or represented by proxy and entitled to vote), such nominee will promptly tender his or her resignation as a director, and the Nominating and Corporate Governance Committee of the Board will make a recommendation to the Board as to whether to accept or reject such director's resignation. The Board may accept or reject the resignation in its discretion. Shares represented by executed proxies will be voted, if authority to do so is not withheld, for the election of the ten nominees named below. If any nominee becomes unavailable for election as a result of an unexpected occurrence, your shares may be voted for the election of a substitute nominee proposed by Regulus. Each person nominated for election has agreed to serve if elected. The Company's management has no reason to believe that any nominee will be unable to serve.

It is the Company's policy to invite nominees for directors to attend the annual meeting. None of our current directors attended our 2021 Annual Meeting of Stockholders, except for Mr. Hagan.

Nominees

The following is a brief biography of each nominee for director and a discussion of the specific experience, qualifications, attributes or skills of each nominee that led the Nominating and Corporate Governance Committee to recommend that person as a nominee for director, as of the date of this proxy statement.

The Nominating and Corporate Governance Committee seeks to assemble a Board that, as a whole, possesses the appropriate balance of professional and industry knowledge, financial expertise and high-level management experience necessary to oversee and direct the Company's business. To that end, the Nominating and Corporate Governance Committee has identified and evaluated nominees in the broader context of the Board's overall composition, with the goal of recruiting members who complement and strengthen the skills of other members and who also exhibit integrity, collegiality, sound business judgment and other qualities that the Nominating and Corporate Governance Committee views as critical to effective functioning of the Board. The brief biographies below include information, as of the date of this proxy statement, regarding the specific and particular experience, qualifications, attributes or skills of each director or nominee that led the Nominating and Corporate Governance Committee to recommend that person as a nominee. However, each of the members of the Nominating and Corporate Governance Committee may have a variety of reasons why he or she believes a

particular person would be an appropriate nominee for the Board, and these views may differ from the views of other members.

Name	Age	Position Held With the Company
Dr. Stelios Papadopoulos	73	Chair of the Board of Directors
Ms. Kathryn J. Collier	54	Director
Dr. David Baltimore	84	Director
Mr. Joseph P. Hagan	53	Director, President and Chief Executive Officer
Dr. Alice S. Huang	83	Director
Mr. Jake R. Nunn	51	Director
Dr. William H. Rastetter	74	Director
Dr. Hugh Rosen	62	Director
Dr. Simos Simeonidis	52	Director
Ms. Pascale Witz, MBA, MSc	55	Director

Stelios Papadopoulos, Ph.D. Chair of the Board, has served on our Board of Directors since our conversion to a corporation in January 2009 and as our Chair since June 2013, and prior to that was a director of Regulus Therapeutics LLC since July 2008. Since 1994, Dr. Papadopoulos has served as a director and, since 1998, as Chair of the Board for Exelixis, Inc., a publicly held biotechnology company, which he co-founded. Since July 2008, Dr. Papadopoulos has served as a member of the board of directors of Biogen Inc. (formerly Biogen Idec Inc.), a publicly held biopharmaceutical company, and has served as its Chair of the board of directors since June 2014. Since August 2020, Dr. Papadopoulos has served as Chair of the board of Eucrates Biomedical Acquisition Corp., a special purpose acquisition corporation. From 2003 to 2018, Dr. Papadopoulos served as a member of the board of directors of BG Medicine, Inc., a publicly-held life sciences company. From 2000 to 2006, Dr. Papadopoulos served as Vice Chair with Cowen and Co., LLC, an investment banking firm. From 1987 to 2000, Dr. Papadopoulos served in several positions with PaineWebber, Incorporated, most recently as Chair of PaineWebber Development Corp., a PaineWebber subsidiary focusing on biotechnology. Dr. Papadopoulos holds an M.S. in Physics, a Ph.D. in Biophysics and an MBA in Finance from New York University. Our Nominating and Corporate Governance Committee believes that Dr. Papadopoulos is qualified to serve on our Board of Directors due to his knowledge and expertise regarding the biotechnology and healthcare industries, his broad leadership experience on various boards and his experience with financial matters.

David Baltimore, Ph.D. has served on our Board of Directors since our conversion to a corporation in January 2009, and prior to that was a director of Regulus Therapeutics LLC since November 2007. Dr. Baltimore is currently President Emeritus and Distinguished Professor of Biology at the California Institute of Technology ("Caltech"), and before that from 1997 to 2006, Dr. Baltimore served as President of the California Institute of Technology. From 1968 to 1972, Dr. Baltimore served as an associate professor at the Massachusetts Institute of Technology, and from 1972 to 1997 was a professor at the Massachusetts Institute of Technology. From 1990 to 1994, Dr. Baltimore served as professor at The Rockefeller University where he also served as the President from July 1990 to December 1991. Dr. Baltimore served as a director of Amgen Inc., a publicly held biotechnology company from 1997 to May 2018, and also served as a director of Immune Design Corp., a publicly held biotechnology company, from 1997 until its acquisition by Merck & Co., Inc. in February 2019. In 1975, Dr. Baltimore received the Nobel Prize in Medicine as a co-recipient. Dr. Baltimore holds a Ph.D. in Biology from The Rockefeller University and a B.A. from Swarthmore College. Our Nominating and Corporate Governance Committee believes that Dr. Baltimore is qualified to serve on our Board of Directors due to the many years Dr. Baltimore has spent in scientific academia, which has provided him with a deep understanding of our industry and our activities.

Kathryn J. Collier has served on our Board of Directors since April 2018. Since March 2022, Ms. Collier has served as the Senior Vice President of Corporate Finance for Pattern Energy Group LP, a privately-held renewable energy company. From July 2019 to March 2022, Ms. Collier served as the vice president for audit services of Sempra Energy ("Sempra"), a publicly-traded energy services holding company overseeing the

internal audit function for Sempra, including the Financial Leadership Program and audit oversight of Sempra's operating companies. From March 2019 to July 2019, Ms. Collier served as the chief strategy and origination officer for Sempra LNG, a wholly-owned subsidiary of Sempra. From August 2018 to March 2019, Ms. Collier served as chief financial officer and chief administrative officer for Sempra North America Infrastructure. Ms. Collier also previously served as vice president and treasurer for Sempra from April 2012 to August 2018. Prior to joining Sempra in 2012, Ms. Collier held several executive positions within global corporate and investment banking at Bank of America Merrill Lynch. Ms. Collier holds a B.A. in accounting from Valparaiso University. Our Nominating and Corporate Governance Committee believes that Ms. Collier is qualified to serve on our Board of Directors due to her extensive financial and operational experience, her experience in investment banking and her corporate governance experience with various boards.

Joseph P. Hagan has served as our President and Chief Executive Officer and principal executive officer since May 2017. Mr. Hagan previously served as our Chief Operating Officer, principal financial officer and principal accounting officer from January 2016 to May 2017. From June 2011 through December 2015, Mr. Hagan served as the Executive Vice President, Chief Financial Officer and Chief Business Officer of Orexigen Therapeutics, Inc. ("Orexigen"). From May 2009 to June 2011, Mr. Hagan served as Orexigen's Senior Vice President, Corporate Development, Strategy and Communications. From September 1998 to April 2008, Mr. Hagan served as Managing Director of Amgen Ventures. Prior to starting the Amgen Ventures Fund, Mr. Hagan served as Head of corporate development for Amgen Inc. ("Amgen"). Before joining Amgen, Mr. Hagan spent five years in the bioengineering labs at Genzyme and Advanced Tissue Sciences. Mr. Hagan has served on the board of directors of Zosano Pharma Corp, a publicly-traded biotechnology company, since May 2015 and on the board of Aurinia Pharmaceuticals, Inc., since February 2018. He received an M.B.A. from Northeastern University and a B.S. in Physiology and Neuroscience from the University of California, San Diego. Our Nominating and Corporate Governance Committee believes that Mr. Hagan's expertise in business development, commercialization and financing of public companies qualify him to serve on our Board of Directors.

Alice S. Huang, Ph.D. has served on our Board of Directors since January 2021. Dr. Huang is currently Senior Faculty Associate of Biology and Biological Engineering at Caltech, having joined Caltech in July 1997. Previous to her tenure at Caltech she was Dean for Science and Professor of Biology at New York University, Professor of Microbiology and Molecular Genetics at Harvard Medical School and Director, Laboratories of Infectious Disease at Boston Children's Hospital. She also served as director of Virus-Host Interactions in Cancer for 15 years, a training program at Harvard funded by the National Cancer Institute. Dr. Huang has served on the Board of Trustees of the Keck Graduate Institute since 1998 and has previously served on the Board of Trustees of Waksman Foundation for Microbiology, the Rockefeller Foundation, Public Agenda, Johns Hopkins University, the Health Effects Institute, and the University of Massachusetts. Dr. Huang is serving on the advisory boards of the Institute for Basic Biomedical Sciences at Johns Hopkins University School of Medicine since 2008 as well as the Schlesinger Library at Radcliffe Institute since 2018. She has previously served on the advisory boards of the National Foundation for Infectious Diseases, the US Army Medical Research and Development Command and Food and Drug Administration. She has been a fellow of the American Association of Women in Science since 1978, American Academy of Microbiology since 1982, Academia Sinica in Taiwan since July 1990, and the American Association for the Advancement of Science since 2000, serving as its president from 2010 to 2011. Dr. Huang received her B.A., M.A. and Ph.D. degrees from the Johns Hopkins University. Our Nominating and Corporate Governance Committee believes that Dr. Huang is qualified to serve on our Board of Directors due to the many years she has spent in scientific academia, which has provided her with a deep understanding of our scientific activities.

Jake R. Nunn has served on our Board of Directors since June 2019. Mr. Nunn is currently a venture advisor at New Enterprise Associates, Inc. ("NEA"), a venture capital firm, where he was a partner from June 2006 until January 2019. Prior to joining NEA, he served as a partner and an analyst for the MPM BioEquities Fund, a life sciences fund at MPM Capital, L.P., a private equity firm. Previously, he was a healthcare research analyst and portfolio manager at Franklin Templeton Investments and an investment banker with Alex Brown & Sons.

Mr. Nunn has served on the board of directors of Trevena, Inc., a publicly-held biotechnology company focused on the central nervous system since July 2013, Addex Therapeutics Ltd., a publicly-held biopharmaceutical company focused on allosteric modulators for neurological disorders since June 2018, Oventus Medical Ltd., a publicly-held medical device company since February 2020 and Hexima Limited, a publicly-held biopharmaceutical company focused on novel anti-fungals since September 2021. Mr. Nunn served on the board of directors of Dermira, Inc., a publicly-held biopharmaceutical company focused on dermatology, from May 2011 until its acquisition by Eli Lilly and Company in February 2020. From 2009 to May 2015, Mr. Nunn served on the board of directors of Hyperion Therapeutics, Inc. and from 2008 to February 2016, Mr. Nunn served on the board of directors of TriVascular Technologies, Inc. Mr. Nunn received his A.B. in economics from Dartmouth College and his M.B.A. from the Stanford Graduate School of Business. He also holds the Chartered Financial Analyst designation and is a member of the CFA Society of San Francisco. Our Nominating and Corporate Governance Committee believes that Mr. Nunn is qualified to serve on our Board of Directors due to his extensive financial experience, his experience in investment banking and his corporate governance experience with various boards.

William H. Rastetter, Ph.D. has served on our Board of Directors since April 2013. From 2006 to February 2013, Dr. Rastetter served as a partner in the venture capital firm, Venrock. He served as Chief Executive Officer of IDEC Pharmaceuticals Corp. ("IDEC Pharmaceuticals") from December 1986 through November 2003, and as Chair from May 1996 to November 2003. Upon the merger of IDEC Pharmaceuticals and Biogen Inc. in November 2003, Dr. Rastetter served as Executive Chair of Biogen Idec until the end of 2005. Dr. Rastetter served as Chair of the board of Illumina, Inc., a publicly held biotechnology company, from 2005 to January 2016 and served on its board of directors from 1998 to January 2016. He was a founder of Receptos, Inc. in 2009 and served as its Chair until the sale of the publicly held company to Celgene Corporation in 2015. Currently, he has served as the Chair of the board of directors of Fate Therapeutics, Inc., a publicly held biotechnology company, since November 2011; Chair of the board of directors of Neurocrine Biosciences, Inc., a publicly held biotechnology company, since May 2011 and on its board of directors since February 2010; on the board of directors of Grail, Inc., a privately-held company, since January 2016, and as its Chair from August 2017 to November 2018. Dr. Rastetter served on the board of directors of Cerulean Pharma Inc. ("Cerulean"), a publicly held biotechnology company since January 2014, as its lead independent director from April 2014 to June 2016, and as its Chair from June 2016 until July 2017 when Cerulean and Daré Bioscience Inc. completed a reverse merger and he currently serves as Chair of the board of the surviving company, Daré Bioscience Inc., a publicly-traded company. In addition, he serves as an advisor to Illumina Ventures. He is the author of numerous scientific papers and patent applications in the fields of organic and bioorganic chemistry, protein and enzyme engineering, and biotechnology. Dr. Rastetter holds an S.B. in Chemistry from the Massachusetts Institute of Technology and received his M.A. and Ph.D. in Chemistry from Harvard University. Our Nominating and Corporate Governance Committee believes that Dr. Rastetter's knowledge and expertise regarding the biotechnology industry and his leadership experience on various biotechnology company boards of directors qualifies him to serve on our Board of Directors.

Hugh Rosen, M.D., Ph.D. has served on our Board of Directors since June 2016. Since April 2017, Dr. Rosen has served as the President and Chair of the Board of Activx Biosciences, Inc., a wholly owned biopharmaceutical subsidiary of Kyorin Pharmaceutical Co., Ltd. From 2002 until March 2017, Dr. Rosen served as a Professor of Chemical Physiology at The Scripps Research Institute ("TSRI") in La Jolla, California where he focused on pursuing his primary interests in lymphocyte trafficking and barrier regulation by signaling lipids, and contributing towards the development of translational infrastructure at TSRI. He also served as Chair of the Committee for Advanced Human Therapeutics of TSRI. Prior to joining TSRI, Dr. Rosen served in various capacities with Merck Research Laboratories most recently serving as Executive Director in Immunology, Rheumatology and Infectious Diseases and Chair of the Worldwide Business Strategy Team for Antibacterials and Antifungals, reporting to the Management Committee. Dr. Rosen was a scientific founder of Receptos, Inc., now a wholly owned biopharmaceutical subsidiary of Celgene Corporation, and of RBNC Therapeutics, Inc. He received his M.D. from the University of Cape Town, South Africa and his Ph.D. in Physiological Sciences from Oxford. Our Nominating and Corporate Governance Committee believes that Dr. Rosen is qualified to serve on

our Board of Directors due to the many years Dr. Rosen has spent in scientific academia as well as the biopharmaceutical industry, which has provided him with a deep understanding of our industry and our activities.

Simos Simeonidis, Ph.D. has served on our Board of Directors since June 2019. Dr. Simeonidis served as a Partner at Sarissa Capital from June 2017 to November 2021. Prior to joining Sarissa Capital, he was a Managing Director and Senior Biotechnology Analyst at the Royal Bank of Canada in New York from July 2014 to June 2017. Dr. Simeonidis spent more than a decade covering the biotechnology sector as an analyst at a number of investment banks, including Cowen and Company, First Albany Capital and Morgan Stanley. In addition to his investment management and financial expertise, Dr. Simeonidis combines both biopharmaceutical industry and biomedical research expertise, having worked at Novartis International AG in Business Development and Strategic Planning, and prior to his corporate career, having served as a faculty member at Harvard Medical School. Dr. Simeonidis received his B.S. in Biology from Loyola University Chicago, and his M.A., MPhil and Ph.D. degrees in Cellular, Molecular and Biophysical Sciences from Columbia University's College of Physicians and Surgeons. He completed his Postdoctoral Fellowship at the laboratory of Professor Tucker Collins at Harvard Medical School and the Brigham and Women's Hospital, where he worked on the transcriptional regulation of gene expression. Dr. Simeonidis also holds an MBA in Healthcare Management at the Wharton School of the University of Pennsylvania. Our Nominating and Corporate Governance Committee believes that Dr. Simeonidis is qualified to serve on our Board of Directors due to his extensive experience in investment banking and as an analyst covering the life sciences industry, his prior employment in the biopharmaceutical industry, and his medical and scientific background.

Pascale Witz, MBA, MSc has served on our Board of Directors since June 2017. Ms. Witz is the founder and since November 2016, the president of PWH Advisors, a consultancy firm advising management at life science companies and investment firms. From September 2015 through May 2016, Ms. Witz served as the Executive Vice President, Diabetes & Cardiovascular for Sanofi, S.A. ("Sanofi"). Prior to that position, Ms. Witz served as the Executive Vice President, Global Divisions and Strategic Development, commencing in July 2013. During her tenure at Sanofi, she launched multiple medicines across three continents, and strengthened the pipeline through licensing and partnerships. From 2009 to 2013, Ms. Witz served as President and CEO of General Electric's ("GE") Pharmaceutical Diagnostics, an integrated Pharmaceutical organization. Ms. Witz joined GE Healthcare in 1996, where she held various positions of increasing responsibilities and lead global businesses based out of the USA, France and the UK. She formerly worked for Becton Dickinson Pharmaceutical Systems from 1991 to 1996. Ms. Witz has served on the board of Fresenius Medical Care AG & Co. KGaA, since May 2016, Horizon Pharma, since August 2017 and PerkinElmer, Inc., since October 2017. Ms. Witz also served on the board of TESARO, Inc., from May 2018 until its acquisition by GlaxoSmithKline plc in January 2019 and from May 2016 to April 2018, served on the board of Savencia SA. Ms. Witz received her MBA from INSEAD and her M.S. in Biochemistry from the Institut National des Sciences Appliquées. She was also a Ph.D. student in Molecular Biology at the Centre National de la Recherche Scientifique. Our Nominating and Corporate Governance Committee believes that Ms. Witz is qualified to serve on our Board of Directors due to her knowledge, expertise and prior employment in the pharmaceutical industry and her experience on other company boards, which has provided her with a deep understanding of our industry and our activities.

THE BOARD OF DIRECTORS RECOMMENDS
A VOTE FOR EACH NAMED NOMINEE

INDEPENDENCE OF THE BOARD OF DIRECTORS

As required under the Nasdaq Stock Market ("Nasdaq") listing standards, a majority of the members of a listed company's Board of Directors must qualify as "independent," as affirmatively determined by the Board of Directors. 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 family members, and the Company, its senior management and its independent auditors, the Board has affirmatively determined that the following nine directors are independent directors within the meaning of the applicable Nasdaq listing standards: Dr. Baltimore, Ms. Collier, Dr. Huang, Mr. Nunn, Dr. Papadopoulos, Dr. Rastetter, Dr. Rosen, Dr. Simeonidis and Ms. Witz. In making this determination, the Board found that none of these directors or nominees for director had a material or other disqualifying relationship with the Company.

BOARD LEADERSHIP STRUCTURE

Our Board of Directors is currently chaired by Stelios Papadopoulos, Ph.D. As a general policy, our Board of Directors believes that separation of the positions of Chair and Chief Executive Officer reinforces the independence of the Board of Directors from management, creates an environment that encourages objective oversight of management's performance and enhances the effectiveness of the Board of Directors as a whole. As such, Mr. Hagan serves as our President and Chief Executive Officer while Dr. Papadopoulos serves as our Chair of the Board of Directors but is not an officer. We expect and intend the positions of Chair of the Board of Directors and Chief Executive Officer to continue to be held by separate individuals in the future.

ROLE OF THE BOARD IN RISK OVERSIGHT

One of the key functions of our Board of Directors is informed oversight of our risk management process. The Board of Directors does not have a standing risk management committee, but rather administers this oversight function directly through the Board of Directors as a whole, as well as through various standing committees of our Board of Directors that address risks inherent in their respective areas of oversight. In particular, our Board of Directors is responsible for monitoring and assessing strategic risk exposure, and our Audit Committee has the responsibility to consider and discuss our major financial risk exposures and the steps our management has taken to monitor and control these exposures, including guidelines and policies to govern the process by which risk assessment and management is undertaken. The Audit Committee also monitors compliance with legal and regulatory requirements, and oversees our cybersecurity risks at least annually. Our Nominating and Corporate Governance Committee monitors the effectiveness of our corporate governance practices, including whether they are successful in preventing illegal or improper liability-creating conduct. Our Compensation Committee assesses and monitors whether any of our compensation policies and programs has the potential to encourage excessive risk-taking.

MEETINGS OF THE BOARD OF DIRECTORS

The Board of Directors met thirteen times during the last fiscal year and four times in executive session. All directors who served in 2021 attended at least 75% of the aggregate number of meetings of the Board and of the committees on which they served, held during the portion of the last fiscal year for which they were directors or committee members, respectively.

INFORMATION REGARDING COMMITTEES OF THE BOARD OF DIRECTORS

The Board maintains an Audit Committee, a Compensation Committee and a Nominating and Corporate Governance Committee. The following table provides membership and meeting information for the year ended December 31, 2021 for each of the Board committees:

Name	Audit	Compensation	Nominating and Corporate Governance
Dr. David Baltimore			X*
Kathryn J. Collier	X*		
Dr. Alice S. Huang		X	
Jake Nunn	X		
Dr. Stelios Papadopoulos	X		X
Dr. William H. Rastetter		X*	
Dr. Hugh Rosen		X	
Dr. Simos Simeonidis			X
Pascale Witz		X	
Total meetings in 2021	5	3	2

* Committee Chairperson

Below is a description of each committee of the Board of Directors. Each of the committees has authority to engage legal counsel or other experts or consultants, as it deems appropriate to carry out its responsibilities. Our Board of Directors has determined that each member of each committee meets the applicable Nasdaq rules and regulations regarding "independence" and that each member is free of any relationship that would impair his or her individual exercise of independent judgment with regard to the Company.

Audit Committee

The Audit Committee of our Board of Directors was established by our Board of Directors in accordance with Section 3(a)(58)(A) of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), to oversee the Company's corporate accounting and financial reporting processes and audits of its financial statements. For this purpose, our Audit Committee performs several functions. Our Audit Committee, among other things, evaluates the performance of and assesses the qualifications of the independent auditors; determines and approves the engagement of the independent auditors; determines whether to retain or terminate the existing independent auditors or to appoint and engage new independent auditors; reviews and approves the retention of the independent auditors to perform any proposed permissible non-audit services; monitors the rotation of partners of the independent auditors on the Company's audit engagement team as required by law; reviews and approves or rejects transactions between the Company and any related persons; confers with management and the independent auditors regarding the effectiveness of internal controls over financial reporting; establishes 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; reviews and discusses with management and the Company's auditors the Company's guidelines and policies with respect to risk assessment and risk management, including cybersecurity risks, and other policies; and meets to review the Company's annual audited financial statements and quarterly financial statements with management and the independent auditor, including a review of the Company's disclosures under "Management's Discussion and Analysis of Financial Condition and Results of Operations."

Our Audit Committee is currently composed of three directors: Ms. Collier (who Chairs the Audit Committee), Mr. Nunn and Dr. Papadopoulos. The Audit Committee met four times during the last fiscal year. Our Board of Directors has adopted a written charter of the Audit Committee that is available to stockholders on

the Company's website at www.regulusrx.com. Our Board of Directors reviews the Nasdaq listing standards definition of independence for Audit Committee members on an annual basis and has determined that all members of our Audit Committee are independent (as independence is currently defined in Rule 5605(c)(2)(A) of the Nasdaq listing standards).

Our Board of Directors has determined that Ms. Collier qualifies as an "audit committee financial expert," as defined in applicable SEC rules. Our Board of Directors has made a qualitative assessment of Ms. Collier's level of knowledge and experience based on a number of factors, including her formal education, her experience in the investment banking industry and as the holder of various positions with responsibility for finance of a subsidiary of a major publicly-traded energy services holding company.

Report of the Audit Committee of the Board of Directors*

The Audit Committee has reviewed and discussed the audited financial statements for the fiscal year ended December 31, 2021 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 ("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 of Directors that the audited financial statements be included in the Company's Annual Report on Form 10-K for the fiscal year ended December 31, 2021.

Ms. Kathryn J. Collier (Chair)
Dr. Stelios Papadopoulos
Mr. Jake Nunn

* This material is not "soliciting material," is not deemed "filed" with the SEC and is not to be incorporated by reference in any filing of the Company under the Exchange Act or the Securities Act of 1933, as amended (the "Securities Act"), whether made before or after the date hereof and irrespective of any general incorporation language in any such filing.

Compensation Committee

The Compensation Committee is currently composed of four directors: Dr. Rastetter (who chairs the Compensation Committee), Dr. Huang, Dr. Rosen and Ms. Witz. The Board of Directors reviews the Nasdaq listing standards definition of independence for Compensation Committee members on an annual basis and has determined that all members of the Company's Compensation Committee are independent (as independence is currently defined in Rule 5605(d)(2)(A of the Nasdaq listing standards). The Compensation Committee met three times during the last fiscal year. The Compensation Committee has adopted a written charter that is available to stockholders on the Company's website at www.regulusrx.com.

The Compensation Committee acts on behalf of the Board to review, adopt and/or recommend for adoption and oversee the Company's compensation strategy, policies, plans and programs. The functions of the Compensation Committee include, among other things:

- reviewing and approving (or if it deems appropriate, making recommendations to the full Board of Directors regarding) our overall compensation strategy and policies, including corporate performance goals and objectives to support and reinforce the Company's long-term strategic goals, relevant to the Company's compensation plans and programs;
- evaluating and approving (or, if it deems appropriate, making recommendations to the full Board of Directors regarding) the compensation plans and programs advisable for the Company, as well as the modification or termination of existing plans and programs;

- evaluating risks associated with our compensation policies and practices and assessing whether risks arising from our compensation policies and practices for our employees are reasonably likely to have a material adverse effect on us;
- establishing policies with respect to equity compensation arrangements, with the objective of appropriately balancing the perceived value of equity compensation and the dilutive and other costs of that compensation to the Company;
- establishing elements of corporate performance for purposes of increasing or decreasing compensation;
- administering our equity incentive plans, including establishing policies on the timing and pricing of equity awards for newly hired employees, promotions and annual grants for executives and non-executive employees and directors;
- establishing policies with respect to votes by our stockholders to approve executive compensation as required by Section 14A of the Exchange Act and determining our recommendations regarding the frequency of advisory votes on executive compensation, as well as reviewing the considering the results of any advisory vote on executive compensation;
- reviewing regional and industry-wide compensation practices and trends to assess the competitiveness of our executive compensation programs and evaluating the effectiveness of our compensation policy and strategy in achieving expected benefits to us;
- reviewing and making recommendations to the full Board of Directors regarding the adequacy of the type and amount of compensation to be paid or awarded to our non-employee board members;
- reviewing and approving (or, if it deems appropriate, making recommendations to the full Board of Directors regarding) the terms of any employment agreements, severance arrangements, change-of-control protections and any other compensatory arrangements (including, without limitation, any material perquisites and any other form of compensation) for the Company's executive officers (other than the Chief Executive Officer of the Company), including reviewing and approving (or, if it deems appropriate, making recommendations to the full Board of Directors regarding) any payments, compensation or other awards under such agreements and arrangements;
- recommending to the full Board of Directors for its approval the terms of any employment agreements, severance arrangements, change-of-control protections and any other compensatory arrangements (including, without limitation, any material perquisites and any other form of compensation) for the Company's Chief Executive Officer;
- reviewing and approving (or, if it deems appropriate, making recommendations to the full Board of Directors regarding) any compensation arrangement for any executive officer involving any subsidiary, special purpose or similar entity;
- considering and, if appropriate, establishing a policy designed to encourage executive officers and directors to acquire and hold a meaningful equity interest in the Company;
- evaluating the efficacy of the Company's compensation policy and strategy in achieving expected benefits to the Company and otherwise furthering the Committee's policies;
- reviewing and assessing the independence of compensation consultants, legal counsel and other advisors as required by Section 10C of the Exchange Act;
- reviewing the adequacy of its charter on a periodic basis;
- reviewing with management and approving our disclosures under the caption "Compensation Discussion and Analysis" in our periodic reports or proxy statements to be filed with the SEC, as applicable; and
- to the extent applicable, preparing the compensation committee report as required by SEC rules.

The Compensation Committee recommends to the full Board of Directors for its approval the compensation and other terms of employment of our Chief Executive Officer and evaluates the Chief Executive Officer's performance in light of relevant performance goals and objectives, taking into account, among other things, the policies of the Compensation Committee and the Chief Executive Officer's performance in fostering a corporate culture that promotes the highest levels of integrity and the highest ethical standards; the Chief Executive Officer's role in developing and executing the Company's long-term strategic plan and conducting the business of the Company in a manner appropriate to enhance long-term stockholder value; achievement of any other corporate performance goals and objectives deemed relevant to the Chief Executive Officer as established by the Board of Directors; and achievement of the Chief Executive Officer's individual performance goals and objectives established by the Compensation Committee.

The Compensation Committee reviews, determines and approves (or, if it deems appropriate, recommends to the full Board of Directors for its approval), the individual and corporate performance goals and objectives of the Company's other officers and determines and approves (or, if it deems appropriate, recommends to the full Board of Directors for its determination and approval) the compensation and other terms of employment of each such executive officer, taking into consideration the executive officer's success in achieving his or her individual performance goals and objectives and the corporate performance goals and objectives deemed relevant to the executive officer as established by the Compensation Committee.

Compensation Committee Processes and Procedures

Typically, the Compensation Committee meets at least twice annually and with greater frequency if necessary. The agenda for each meeting is usually developed by the Chair of the Compensation Committee, in consultation with the Chief Executive Officer. The Compensation Committee meets regularly in executive session. However, from time to time, various members of management and other employees as well as outside advisors or consultants may be invited by the Compensation Committee to make presentations, to provide financial or other background information or advice or to otherwise participate in Compensation Committee meetings. The Chief Executive Officer may not participate in, or be present during, any deliberations or determinations of the Compensation Committee regarding his compensation. The charter of the Compensation Committee grants the Compensation Committee full access to all books, records, facilities and personnel of the Company, as well as authority to obtain, at the expense of the Company, advice and assistance from internal and external legal, accounting or other advisors and consultants and other external resources that the Compensation Committee considers necessary or appropriate in the performance of its duties. In particular, the Compensation Committee has the sole authority to retain compensation consultants to assist in its evaluation of executive and director compensation, including the authority to approve the consultant's reasonable fees and other retention terms.

During fiscal year 2021, the Compensation Committee engaged Aon/Radford as a compensation consultant. The Committee engaged Aon/Radford to provide a competitive assessment of the Company's executive compensation programs compared to executive compensation paid to executives at selected publicly traded peer companies. Following a gap analysis of the peer companies, Aon/Radford made certain recommendations to the Compensation Committee to make modest increases in the level of equity grants to the Company's executive team and to increase annual cash compensation for certain Company executives and Board Committee members who were paid below the median compared to the peer companies. In addition, the Compensation Committee engaged Aon/Radford to assess its non-employee director compensation program as compared to the Company's peer companies. Following that analysis, no changes to cash compensation were recommended but modest increases in the level of equity grants were recommended (and subsequently approved by the full Board of Directors, with such increases to be effective beginning on January 1, 2022). The Compensation Committee analyzed whether the work of Aon/Radford as a compensation consultant raised any conflict of interest, taking into consideration the following factors: (i) the provision of other services to the Company by the compensation consultant; (ii) the amount of fees from the Company paid to the compensation consultant as a percentage of the firm's total revenue; (iii) the policies and procedures of the compensation consultant that are designed to prevent

conflicts of interest; (iv) any business or personal relationship of the compensation consultant or the individual compensation advisors employed by this firm with an executive officer of the Company; (v) any business or personal relationship of the individual compensation advisors with any member of the Compensation Committee; and (vi) any stock of the Company owned by the compensation consultant or the individual compensation advisors employed by this firm. The Compensation Committee concluded, based on its analysis of the above factors, that the work of Aon/Radford and the individual compensation advisors employed by it as compensation consultants to the Company has not created any conflict of interest.

Under its charter, the Compensation Committee may form, and delegate authority to, subcommittees as appropriate. In 2012, the Compensation Committee formed a Non-Management Stock Option Committee, currently composed of Mr. Hagan, to which it delegated authority to grant, without any further action required by the Compensation Committee, stock options to employees who are not officers of the Company. The purpose of this delegation of authority is to enhance the flexibility of option administration within the Company and to facilitate the timely grant of options to non-management employees, particularly new employees, within specified limits approved by the Compensation Committee. In particular, the subcommittee may grant options only within pre-approved guidelines and not to any employee who will have a vice president title or higher. Typically, as part of its oversight function, the Committee will review on a regular basis the list of grants made by the subcommittee. During fiscal year 2021, the subcommittee exercised its authority to grant options to purchase an aggregate of 660,500 shares of the Company's common stock to non-officer employees.

Historically, the Compensation Committee has made most of the significant adjustments to annual compensation, determined bonus and equity awards and established new performance objectives at one or more meetings held during the last quarter of the year. However, the Compensation Committee also considers matters related to individual compensation, such as compensation for new executive hires, as well as high-level strategic issues, such as the efficacy of the Company's compensation strategy, potential modifications to that strategy and new trends, plans or approaches to compensation, at various meetings throughout the year. Generally, the Compensation Committee's process comprises two related elements: the determination of compensation levels and the establishment of performance objectives for the current year.

For executives other than the Chief Executive Officer, the Compensation Committee solicits and considers evaluations and recommendations submitted to the Committee by the Chief Executive Officer. In the case of the Chief Executive Officer, the evaluation of his performance is conducted by the Compensation Committee, which makes recommendations to the full Board of Directors regarding any adjustments to his compensation as well as awards to be granted. In making such recommendations for determining the long-term incentive component of the Chief Executive Officer's compensation, the Compensation Committee shall take into consideration the Company's performance and relative stockholder return, the value of similar incentive awards given to chief executive officers of comparable companies, the awards given to the Company's Chief Executive Officer in past years, other elements of the Chief Executive Officer's compensation including total compensation and such other criteria as the Committee deems advisable.

For all executives and directors as part of its deliberations, the Compensation Committee may review and consider, as appropriate, materials such as financial reports and projections, operational data, tax and accounting information, tally sheets that set forth the total compensation that may become payable to executives in various hypothetical scenarios, executive and director stock ownership information, company stock performance data, analyses of historical executive compensation levels and current Company-wide compensation levels and recommendations of the Company's General Counsel, including analyses of executive and director compensation paid at other companies identified by the Company's General Counsel.

Nominating and Corporate Governance Committee

The Nominating and Corporate Governance Committee of the Board of Directors is responsible for identifying, reviewing and evaluating candidates to serve as directors of the Company (consistent with criteria

approved by the Board), reviewing and evaluating incumbent directors, recommending to the Board for selection candidates for election to the Board of Directors, making recommendations to the Board regarding the membership of the committees of the Board, assessing the performance of the Board, and monitoring the Company's adherence to its Code of Business Conduct and Ethics.

The Nominating and Corporate Governance Committee is composed of three directors: Dr. Baltimore (who Chairs the Nominating and Corporate Governance Committee), Dr. Papadopoulos and Dr. Simeonidis. All members of the Nominating and Corporate Governance Committee are independent (as independence is currently defined in Rule 5605(a)(2) of the Nasdaq listing standards). The Nominating and Corporate Governance Committee met twice during 2020. The Nominating and Corporate Governance Committee has adopted a written charter that is available to stockholders on the Company's website and www.regulusrx.com.

The Nominating and Corporate Governance Committee believes that candidates for director, both individually and collectively, can and do provide the integrity, experience, judgment, commitment (including having sufficient time to devote to the Company and level of participation), skills, diversity and expertise appropriate for the Company. In assessing the directors, both individually and collectively, the Nominating and Corporate Governance Committee may consider the current needs of the Board and the Company to maintain a balance of knowledge, experience and capability in various areas. However, the Nominating and Corporate Governance Committee retains the right to modify these qualifications from time to time. 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 (including diversity of gender, race, national origin and other self-identified diversity characteristics), 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. 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. The Nominating and Corporate Governance Committee then uses its network of contacts to compile a list of potential candidates, but may also engage, if it deems appropriate, a professional search firm. 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 by majority vote. The Nominating and Corporate Governance Committee assesses diversity, including self-identified diversity characteristics, in connection with the annual nomination process as well as in new director searches.

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. Stockholders who wish to recommend individuals for consideration by the Nominating and Corporate Governance Committee to become nominees for election to the Board may do so by delivering a written recommendation to the Nominating and Corporate Governance Committee at the Company's principal executive offices, Attn: Secretary, no later than the 90th day and no earlier than the 120th day prior to the one year anniversary of the preceding year's annual meeting. Submissions must include (1) the name and address of the Company stockholder on whose behalf the submission is made; (2) the number of Company shares that are owned beneficially by such stockholder as of the date of the submission; (3) the full name of the proposed candidate; (4) a description of the proposed candidate's business experience for at least the previous five years; (5) the complete biographical information for the proposed candidate; (6) a description of the proposed candidate's qualifications as a director; and (7) any other information required by the Company Bylaws. The Company may require any proposed nominee to furnish such other

information as it may reasonably require to determine the eligibility of such proposed nominee to serve as an independent director of the Company or that could be material to a reasonable stockholder's understanding of the independence, or lack thereof, of such proposed nominee.

Board Diversity

Board Diversity Matrix (as of April 12, 2022)

Total Number of Directors: 10

	Female	Male	Non-Binary	Did Not Disclose Gender
Directors	3	6	—	1
Number of Directors Who Identify In Any of the Categories Below:				
African-American or Black	—	—	—	—
Alaskan Native, Native American, Native Hawaiian or Pacific Islander	—	—	—	—
Asian	1	—	—	—
Hispanic or Latinx	—	—	—	—
White	2	6	—	—
Two or More Races or Ethnicities	—	—	—	—
LGTBQ+	—	—	—	—
Did Not Disclose Demographic Background	—		—	1

Stockholder Communications with the Board of Directors

The Company's Board has adopted a formal process by which stockholders may communicate with the Board or any of its directors. Stockholders who wish to communicate with the Board may do so by sending written communications addressed to the Secretary of Regulus Therapeutics Inc. at the Company's principal executive offices. Each communication must set forth: the name and address of the Company stockholder on whose behalf the communication is sent; and the number of Company shares that are owned beneficially by such stockholder as of the date of the communication. Each communication will be reviewed by the Company's Secretary to determine whether it is appropriate for presentation to the Board or relevant directors.

Communications determined by the Company's Secretary to be appropriate for presentation to the Board or any relevant directors are submitted to the Board or relevant directors on a periodic basis.

Code of Ethics

The Company has adopted a Code of Business Conduct and Ethics that applies to all directors, officers (including our principal executive officer, principal financial officer and principal accounting officer) and employees. The Code of Business Conduct and Ethics is available on the Company's website at www.regulusrx.com under the Corporate Governance section of our Investor Relations page. If the Company makes any substantive amendments to the Code of Business Conduct and Ethics that applies to our principal executive officer, principal financial officer, principal accounting officer, controller or persons performing similar functions, or grants any waiver from a provision of the Code of Business Conduct and Ethics to any of these specified individuals that is required to be disclosed pursuant to SEC rules and regulations, the Company will promptly disclose the nature of the amendment or waiver on its website.

Hedging Policy

The Company's insider trading and window period policy provides that no officer, director, other employee or consultant of the Company may engage in short sales, transactions in put or call options, hedging transactions or other inherently speculative transactions with respect to the Company's stock at any time. In addition, no officer, director, other employee or consultant of the Company may margin, or make any offer to margin, any of the Company's stock, including without limitation, borrowing against such stock, at any time.

PROPOSAL 2

APPROVAL OF AN AMENDMENT TO OUR AMENDED AND RESTATED CERTIFICATE OF INCORPORATION TO EFFECT A REVERSE STOCK SPLIT OF OUR COMMON STOCK

BACKGROUND

Our Board of Directors has unanimously approved a series of alternate amendments to our Amended and Restated Certificate of Incorporation, which would:

- effect a reverse stock split ("Reverse Stock Split") of all issued and outstanding shares of our common stock, at a ratio ranging from 1-for-5 to 1-for-20, inclusive.

Accordingly, effecting a Reverse Stock Split would reduce the number of outstanding shares of our common stock. The effectiveness of any one of these amendments and the abandonment of the other amendments, or the abandonment of all of these amendments, will be determined by our Board of Directors following the Annual Meeting and prior to the one-year anniversary of the Annual Meeting, or June 9, 2023. Our Board of Directors has recommended that these proposed amendments be presented to our stockholders for approval.

Our stockholders are being asked to approve these proposed amendments pursuant to Proposal 2, and to grant authorization to our Board of Directors to determine, at its option, whether to implement a Reverse Stock Split, including its specific timing and ratio.

Should we receive the required stockholder approvals for Proposal 2, our Board of Directors will have the sole authority to elect, at any time on or prior to the one-year anniversary of the Annual Meeting and without the need for any further action on the part of our stockholders, whether to effect a Reverse Stock Split and the number of whole shares of our common stock, between and including five (5) and twenty (20), that will be combined into one share of our common stock.

Notwithstanding approval of Proposal 2 by our stockholders, our Board of Directors may, at its sole option, abandon the proposed amendments and determine prior to the effectiveness of any filing with the Secretary of State of the State of Delaware not to effect any Reverse Stock Split, as permitted under Section 242(c) of the General Corporation Law of the State of Delaware. If our Board of Directors does not implement a Reverse Stock Split on or prior to the one-year anniversary of the Annual Meeting, stockholder approval would again be required prior to implementing any Reverse Stock Split.

By approving Proposal 2, our stockholders will: (a) approve a series of alternate amendments to our Amended and Restated Certificate of Incorporation pursuant to which any whole number of outstanding shares of common stock between and including five (5) and twenty (20) could be combined into one share of common stock; and (b) authorize our Board of Directors to file only one such amendment, as determined by the Board at its sole option, and to abandon each amendment not selected by the Board. Our Board of Directors may also elect not to undertake any Reverse Stock Split and therefore abandon all amendments.

APPROVAL OF REVERSE STOCK SPLIT OF OUR COMMON STOCK (PROPOSAL 2)

Our Board of Directors has adopted and is recommending that our stockholders approve a series of alternate amendments to our Amended and Restated Certificate of Incorporation to effect a Reverse Stock Split. The text of the proposed form of Certificate of Amendment to our Amended and Restated Certificate of Incorporation, which we refer to as the Certificate of Amendment, is attached hereto as Appendix A.

We are proposing that our Board of Directors have the discretion to select the Reverse Stock Split ratio from within a range between and including 1-for-5 and 1-for-20, rather than proposing that stockholders approve a

specific ratio at this time, in order to give our Board of Directors the flexibility to implement a Reverse Stock Split at a ratio that reflects the Board's then-current assessment of the factors described below under "Criteria to be Used for Determining Whether to Implement the Reverse Stock Split." If the Board decides to implement a Reverse Stock Split, we will file the Certificate of Amendment with the Secretary of State of the State of Delaware and the Reverse Stock Split will be effective when it is filed with the Secretary of State of the State of Delaware, or such later time as is chosen by the Board and set forth in the Certificate of Amendment. Except for adjustments that may result from the treatment of fractional shares as described below, each of our stockholders will hold the same percentage of our outstanding common stock immediately following the Reverse Stock Split as such stockholder holds immediately prior to the Reverse Stock Split.

Reasons for Reverse Stock Split

To maintain our listing on The Nasdaq Capital Market. By potentially increasing our stock price, the Reverse Stock Split would reduce the risk that our common stock could be delisted from The Nasdaq Capital Market. To continue our listing on The Nasdaq Capital Market, we must comply with Nasdaq Marketplace Rules, which requirements include a minimum bid price of $1.00 per share. On August 9, 2021, we were notified by the Nasdaq Listing Qualifications Department that we do not comply with the $1.00 minimum bid price requirement as our common stock had traded below the $1.00 minimum bid price for 30 consecutive business days at that time. We were automatically provided with a 180 calendar day period, ending on February 7, 2022, within which to regain compliance. On January 31, 2022, we requested an additional 180 calendar day period as permitted by the Nasdaq listing rules, ending on August 7, 2022, to regain compliance, which Nasdaq granted. To regain compliance, our common stock must close at or above the $1.00 minimum bid price for at least 10 consecutive business days or more at the discretion of Nasdaq by August 7, 2022. If we do not regain compliance by August 7, 2022, Nasdaq will notify us that our common stock will be subject to delisting. In that event, we may appeal the decision to a Nasdaq Listing Qualifications Panel (the "Panel"). In the event of an appeal, our common stock would remain listed on The Nasdaq Capital Market pending a written decision by the Panel following a hearing. In the event that the Panel determines not to continue our listing and we are delisted from The Nasdaq Capital Market, our common stock may be delisted and trade on the OTC Bulletin Board or other small trading markets, such as the pink sheets.

The Board of Directors has considered the potential harm to us and our stockholders should Nasdaq delist our common stock from The Nasdaq Capital Market. Delisting could adversely affect the liquidity of our common stock since alternatives, such as the OTC Bulletin Board and the pink sheets, are generally considered to be less efficient markets. An investor likely would find it less convenient to sell, or to obtain accurate quotations in seeking to buy, our common stock on an over-the-counter market. Many investors likely would not buy or sell our common stock due to difficulty in accessing over-the-counter markets, policies preventing them from trading in securities not listed on a national exchange or for other reasons. In addition, the delisting of our common stock from The Nasdaq Capital Market would constitute an event of default under our Loan and Security Agreement with Oxford Finance, LLC.

The Board of Directors believes that the proposed Reverse Stock Split is a potentially effective means for us to regain and maintain compliance with the $1.00 minimum bid price requirement and to avoid, or at least mitigate, the likely adverse consequences of our common stock being delisted from The Nasdaq Capital Market by producing the immediate effect of increasing the bid price of our common stock.

To potentially improve the marketability and liquidity of our common stock. Our Board of Directors believes that the increased market price of our common stock expected as a result of implementing a Reverse Stock Split could improve the marketability and liquidity of our common stock and encourage interest and trading in our common stock.

- Stock Price Requirements: We understand that many brokerage houses, institutional investors and funds have internal policies and practices that either prohibit them from investing in low-priced stocks

or tend to discourage individual brokers from recommending low-priced stocks to their customers or by restricting or limiting the ability to purchase such stocks on margin. Additionally, a Reverse Stock Split could help increase analyst and broker interest in our common stock as their internal policies might discourage them from following or recommending companies with low stock prices.

- Stock Price Volatility: Because of the trading volatility often associated with low-priced stocks, many brokerage houses and institutional investors have internal policies and practices that either prohibit them from investing in low-priced stocks or tend to discourage individual brokers from recommending low-priced stocks to their customers. Some of those policies and practices may make the processing of trades in low-priced stocks economically unattractive to brokers.
- Transaction Costs: Investors may be dissuaded from purchasing stocks below certain prices because brokers' commissions, as a percentage of the total transaction value, can be higher for low-priced stocks.

Criteria to be Used for Determining Whether to Implement Reverse Stock Split

In determining whether to implement the Reverse Stock Split and which Reverse Stock Split ratio to implement, if any, following receipt of stockholder approval of Proposal 2, our Board of Directors may consider, among other things, various factors, such as:

- the historical trading price and trading volume of our common stock;
- the then-prevailing trading price and trading volume of our common stock and the expected impact of the Reverse Stock Split on the trading market for our common stock in the short- and long-term;
- our ability to maintain our listing on The Nasdaq Capital Market;
- which Reverse Stock Split ratio would result in the least administrative cost to us;
- prevailing general market and economic conditions; and
- whether and when our Board of Directors desires to have the additional authorized but unissued shares of common stock that will result from the implementation of a Reverse Stock Split available to provide the flexibility to use our common stock for business and/or financial purposes, as well as to accommodate the shares of our common stock to be authorized and reserved for future equity awards.

Certain Risks and Potential Disadvantages Associated with Reverse Stock Split

We cannot assure you that the proposed Reverse Stock Split will increase our stock price for a sustained period and have the desired effect of maintaining compliance with Nasdaq Marketplace Rules. We expect that the Reverse Stock Split will increase the market price of our common stock so that we may be able to regain and maintain compliance with the Nasdaq $1.00 minimum bid price requirement. However, the effect of the Reverse Stock Split upon the market price of our common stock cannot be predicted with any certainty, and the history of similar reverse stock splits for companies in like circumstances is varied, particularly since some investors may view a reverse stock split negatively. It is possible that the per share price of our common stock after the Reverse Stock Split will not rise in proportion to the reduction in the number of shares of our common stock outstanding resulting from the Reverse Stock Split, and the market price per post-Reverse Stock Split share may not exceed or remain in excess of the $1.00 minimum bid price for a sustained period of time, and the Reverse Stock Split may not result in a per share price that would attract brokers and investors who do not trade in lower priced stocks. In addition, although we believe the Reverse Stock Split may enhance the desirability of our common stock to certain potential investors, we cannot assure you that, if implemented, our common stock will be more attractive to institutional and other long-term investors. Even if we implement the Reverse Stock Split, the market price of our common stock may decrease due to factors unrelated to the Reverse Stock Split. In any case, the market price of our common stock may also be based on other factors which may be unrelated to the number of shares outstanding, including our future performance. If the Reverse Stock Split is consummated and the

trading price of the common stock declines, the percentage decline as an absolute number and as a percentage of our overall market capitalization may be greater than would occur in the absence of the Reverse Stock Split. Even if the market price per post-Reverse Stock Split share of our common stock remains in excess of $1.00 per share, we may be delisted due to a failure to meet other continued listing requirements, including Nasdaq requirements related to the minimum number of shares that must be in the public float, the minimum market value of the public float and the minimum number of "round lot" holders.

The proposed Reverse Stock Split may decrease the liquidity of our common stock and result in higher transaction costs. The liquidity of our common stock may be negatively impacted by a Reverse Stock Split, given the reduced number of shares that would be outstanding after the Reverse Stock Split, particularly if the stock price does not increase as a result of the Reverse Stock Split. In addition, if a Reverse Stock Split is implemented, it will increase the number of our stockholders who own "odd lots" of fewer than 100 shares of common stock. Brokerage commission and other costs of transactions in odd lots are generally higher than the costs of transactions of more than 100 shares of common stock. Accordingly, a Reverse Stock Split may not achieve the desired results of increasing marketability and liquidity of our common stock described above.

The effective increase in the authorized number of shares of our common stock as a result of the Reverse Stock Split could have anti-takeover implications. Even if the proposal to amend our Amended and Restated Certificate of Incorporation to reduce the number of authorized shares of our common stock to 300,000,000 is approved by the stockholders and implemented by the Board, the implementation of a Reverse Stock Split will result in an effective increase in the authorized number of shares of our common stock, which could, under certain circumstances, have anti-takeover implications. The additional shares of common stock that would become available for issuance if this Proposal 2 is approved and a Reverse Stock Split is implemented could be used by us to oppose a hostile takeover attempt or to delay or prevent changes in control or our management. For example, without further stockholder approval, the Board could adopt a "poison pill" which would, under certain circumstances related to an acquisition of our securities that is not approved by the Board, give certain holders the right to acquire additional shares of our common stock at a low price. The Board also could strategically sell shares of common stock in a private transaction to purchasers who would oppose a takeover or favor the current Board. Although this Proposal 2 has been prompted by business and financial considerations and not by the threat of any hostile takeover attempt (nor is the Board currently aware of any such attempts directed at us), stockholders should be aware that approval of this Proposal 2 could facilitate future efforts by us to deter or prevent changes in control, including transactions in which the stockholders might otherwise receive a premium for their shares over then current market prices.

Effects of Reverse Stock Split

After the effective date of any Reverse Stock Split that our Board of Directors elects to implement, each stockholder will own a reduced number of shares of common stock. However, any Reverse Stock Split will affect all of our stockholders uniformly and will not affect any stockholder's percentage ownership interests in Regulus, except to the extent that the Reverse Stock Split results in any of our stockholders owning a fractional share as described below. Voting rights and other rights and preferences of the holders of our common stock will not be affected by a Reverse Stock Split (other than as a result of the payment of cash in lieu of fractional shares). For example, a holder of 2% of the voting power of the outstanding shares of our common stock immediately prior to a Reverse Stock Split would continue to hold 2% (assuming there is no impact as a result of the payment of cash in lieu of issuing fractional shares) of the voting power of the outstanding shares of our common stock immediately after such Reverse Stock Split. The number of stockholders of record will not be affected by a Reverse Stock Split (except to the extent that any stockholder holds only a fractional share interest and receives cash for such interest after such Reverse Stock Split).

The principal effects of a Reverse Stock Split will be that:

- depending on the Reverse Stock Split ratio selected by the Board, each five to twenty shares of our common stock owned by a stockholder will be combined into one new share of our common stock;

- no fractional shares of common stock will be issued in connection with any Reverse Stock Split; instead, holders of common stock who would otherwise receive a fractional share of common stock pursuant to the Reverse Stock Split will receive cash in lieu of the fractional share as explained more fully below;
- even if the total number of authorized shares of our common stock is reduced pursuant to the approval of Proposal 3, it will not be reduced proportionally to the Reverse Stock Split and, therefore, the Reverse Stock Split will, result in an effective increase in the authorized number of shares of our common stock;
- based upon the Reverse Stock Split ratio selected by the Board, proportionate adjustments will be made to the per share exercise price and/or the number of shares issuable upon the exercise or vesting of all then outstanding stock options, restricted stock units and warrants (if any), which will result in a proportional decrease in the number of shares of our common stock reserved for issuance upon exercise or vesting of such stock options, restricted stock units and warrants, and, in the case of stock options and warrants, a proportional increase in the exercise price of all such stock options and warrants; and
- the number of shares then reserved for issuance under our equity compensation plans will be reduced proportionately based upon the Reverse Stock Split ratio selected by the Board.

The following table contains approximate information, based on share information as of March 31, 2022, relating to our outstanding common stock based on the proposed Reverse Stock Split ratios (without giving effect to the treatment of fractional shares but giving effect to Proposal 3 to reduce the number of authorized shares of common stock):

Status	Number of Shares of Common Stock Authorized	Number of Shares of Common Stock Issued and Outstanding	Number of Shares of Common Stock Reserved for Future Issuance	Number of Shares of Common Stock Authorized but Unissued and Unreserved
Pre-Reverse Stock Split	400,000,000	145,981,180	138,203,370	115,815,450
Post-Reverse Stock Split 1:5	300,000,000	29,196,236	27,640,674	243,163,090
Post-Reverse Stock Split 1:6	300,000,000	24,330,197	23,033,895	252,635,908
Post-Reverse Stock Split 1:7	300,000,000	20,854,454	19,743,339	259,402,207
Post-Reverse Stock Split 1:8	300,000,000	18,247,648	17,275,421	264,476,931
Post-Reverse Stock Split 1:9	300,000,000	16,220,131	15,355,930	268,423,939
Post-Reverse Stock Split 1:10	300,000,000	14,598,118	13,820,337	271,581,545
Post-Reverse Stock Split 1:11	300,000,000	13,271,016	12,563,943	274,165,041
Post-Reverse Stock Split 1:12	300,000,000	12,165,098	11,516,948	276,317,954
Post-Reverse Stock Split 1:13	300,000,000	11,229,322	10,631,028	278,139,650
Post-Reverse Stock Split 1:14	300,000,000	10,427,227	9,871,669	279,701,104
Post-Reverse Stock Split 1:15	300,000,000	9,732,079	9,213,558	281,054,363
Post-Reverse Stock Split 1:16	300,000,000	9,123,824	8,637,711	282,238,466
Post-Reverse Stock Split 1:17	300,000,000	8,587,128	8,129,610	283,283,262
Post-Reverse Stock Split 1:18	300,000,000	8,110,066	7,677,965	284,211,969
Post-Reverse Stock Split 1:19	300,000,000	7,683,220	7,273,862	285,042,918
Post-Reverse Stock Split 1:20	300,000,000	7,299,059	6,910,169	285,790,773

After the effective date of any Reverse Stock Split that our Board of Directors elects to implement, our common stock would have a new committee on uniform securities identification procedures (CUSIP) number, a number used to identify our common stock.

Our common stock is currently registered under Section 12(b) of the Securities Exchange Act of 1934, as amended (the “Exchange Act”), and we are subject to the periodic reporting and other requirements of the

Exchange Act. The implementation of any proposed Reverse Stock Split will not affect the registration of our common stock under the Exchange Act. Our common stock would continue to be listed on The Nasdaq Capital Market under the symbol "RGLS" immediately following the Reverse Stock Split, although it is likely that Nasdaq would add the letter "D" to the end of the trading symbol for a period of twenty trading days after the effective date of the Reverse Stock Split to indicate that the Reverse Stock Split had occurred.

Effective Date

The proposed Reverse Stock Split would become effective at 5:00 p.m., Eastern Time, on the business day following the filing of a Certificate of Amendment with the office of the Secretary of State of the State of Delaware, or such later date as is chosen by the Board and set forth in the Certificate of Amendment, which date we refer to in this Proposal 2 as the Effective Date. Except as explained below with respect to fractional shares, effective as of 5:00 p.m., Eastern Time, on the Effective Date, shares of common stock issued and outstanding immediately prior thereto will be combined, automatically and without any action on the part of us or our stockholders, into a fewer number of new shares of our common stock in accordance with the Reverse Stock Split ratio determined by our Board within the limits set forth in this Proposal 2.

Cash Payment In Lieu of Fractional Shares

No fractional shares of common stock will be issued as a result of any Reverse Stock Split. Instead, in lieu of any fractional shares to which a stockholder of record would otherwise be entitled as a result of the Reverse Stock Split, Regulus will pay cash (without interest) equal to such fraction multiplied by the average of the closing sales prices of the common stock on The Nasdaq Capital Market during regular trading hours for the five consecutive trading days immediately preceding the Effective Date (with such average closing sales prices being adjusted to give effect to the Reverse Stock Split). After the Reverse Stock Split, a stockholder otherwise entitled to a fractional interest will not have any voting, dividend or other rights with respect to such fractional interest except to receive payment as described above.

As of March 31, 2022, there were thirteen stockholders of record of our common stock. Upon stockholder approval of this Proposal 2, if our Board of Directors elects to implement the proposed Reverse Stock Split, stockholders owning, prior to the Reverse Stock Split, less than the number of whole shares of common stock that will be combined into one share of common stock in the Reverse Stock Split would no longer be stockholders. For example, if a stockholder held 10 shares of common stock immediately prior to the Reverse Stock Split and the Reverse Stock Split ratio selected by the Board was 1-for-15, then such stockholder would cease to be a stockholder of Regulus following the Reverse Stock Split and would not have any voting, dividend or other rights except to receive payment for the fractional share as described above. Based on our stockholders of record as of April 12, 2022, and assuming a Reverse Stock Split ratio of 1-for-15, we expect that cashing out fractional stockholders will reduce the number of stockholders of record by only one record stockholder. In addition, we do not intend for this transaction to be the first step in a series of plans or proposals of a "going private transaction" within the meaning of Rule 13e-3 of the Exchange Act.

Record and Beneficial Stockholders

If this Proposal 2 is approved by our stockholders and our Board of Directors elects to implement a Reverse Stock Split, stockholders of record holding all of their shares of our common stock electronically in book-entry form under the direct registration system for securities will be automatically exchanged by the exchange agent and will receive a transaction statement at their address of record indicating the number of new post-split shares of our common stock they hold after the Reverse Stock Split along with payment in lieu of any fractional shares. Non-registered stockholders holding common stock through a bank, broker or other nominee should note that such banks, brokers or other nominees may have different procedures for processing the Reverse Stock Split and making payment for fractional shares than those that would be put in place by us for registered stockholders. If you hold your shares with such a bank, broker or other nominee and if you have questions in this regard, you are encouraged to contact your nominee.

If this Proposal 2 is approved by our stockholders and our Board of Directors elects to implement a Reverse Stock Split, stockholders of record holding some or all of their shares in certificate form will receive a letter of transmittal from Regulus or its exchange agent, as soon as practicable after the effective date of the Reverse Stock Split. Our transfer agent is expected to act as "exchange agent" for the purpose of implementing the exchange of stock certificates. Holders of pre-Reverse Stock Split shares will be asked to surrender to the exchange agent certificates representing pre-Reverse Stock Split shares in exchange for post-Reverse Stock Split shares and payment in lieu of fractional shares (if any) in accordance with the procedures to be set forth in the letter of transmittal. No new post-Reverse Stock Split share certificates will be issued to a stockholder until such stockholder has surrendered such stockholder's outstanding certificate(s) together with the properly completed and executed letter of transmittal to the exchange agent.

STOCKHOLDERS SHOULD NOT DESTROY ANY PRE-SPLIT STOCK CERTIFICATE AND SHOULD NOT SUBMIT ANY CERTIFICATES UNTIL THEY ARE REQUESTED TO DO SO.

Accounting Consequences

The par value per share of our common stock would remain unchanged at $0.001 per share after any Reverse Stock Split. As a result, on the Effective Date, the stated capital on our balance sheet attributable to the common stock would be reduced proportionally, based on the actual Reverse Stock Split ratio, from its present amount, and the additional paid-in capital account would be credited with the amount by which the stated capital would be reduced. The net income or loss per share of common stock would be increased because there would be fewer shares of common stock outstanding. The Reverse Stock Split would be reflected retroactively in our financial statements. We do not anticipate that any other accounting consequences would arise as a result of any Reverse Stock Split.

No Appraisal Rights

Our stockholders are not entitled to dissenters' or appraisal rights under the General Corporation Law of the State of Delaware with respect to the proposed alternate amendments to our Amended and Restated Certificate of Incorporation to allow for a Reverse Stock Split.

Material U.S. Federal Income Tax Consequences

The following is a summary of the material U.S. federal income tax consequences of a Reverse Stock Split that are generally expected to be applicable to U.S. Holders (as defined below) of our common stock who hold their common shares as capital assets within the meaning of Section 1221 of Internal Revenue Code of 1986, as amended (the "Code") (generally property held for investment). This summary is based on provisions of the Code, applicable Treasury Regulations promulgated thereunder, judicial authority and current administrative rulings and practices as in effect on the date of this proxy statement. Changes to these laws could alter the tax consequences described below, possibly with retroactive effect, which may result in the U.S. federal income tax consequences of the Reverse Stock Split differing substantially from the consequences summarized below. We have not sought and will not seek an opinion of counsel or a ruling from the Internal Revenue Service regarding the federal income tax consequences of a Reverse Stock Split.

This discussion is for general information only and does not purport to consider all aspects of U.S. federal income taxation that might be relevant to a U.S. Holder. This discussion does not address the tax consequences which may apply to stockholders subject to special rules, such as financial institutions, insurance companies, tax-exempt organizations dealers in securities, real estate investment trusts, regulated investment companies, stockholders who hold their pre-reverse split shares through individual retirement or other tax-deferred accounts, stockholders who are not U.S. Holders (as defined below), stockholders who have a functional currency other than the U.S. dollar, partnerships or other entities classified as partnerships or disregarded entities for U.S. federal income tax purposes (or persons holding our common stock through such entities), stockholders who hold

the pre-reverse split shares as part of a straddle, hedge, or conversion transaction, stockholders who hold the pre-reverse split shares as qualified small business stock within the meaning of Section 1202 of the Code or Section 1244 stock for purposes of Section 1244 of the Code, stockholders who acquired their stock in a transaction subject to the gain rollover provisions of Section 1045 of the Code, or stockholders who acquired their pre-reverse split shares pursuant to the exercise of employee stock options or otherwise as compensation.

In addition, this summary does not address: (a) the tax consequences of transactions effectuated before, after or at the same time as the Reverse Stock Split, whether or not they are in connection with the Reverse Stock Split; (b) any U.S. federal non-income tax consequences of the Reverse Stock Split, including estate, gift or other tax consequences; (c) any state, local or non-U.S. tax consequences of the Reverse Stock Split; (d) the alternative minimum tax, the Medicare contribution tax on net investment income, or special tax accounting rules under Section 451(b) of the Code, or (e) tax consequences to holders of options, warrants or similar rights to acquire our common stock. Stockholders are urged to consult their own tax advisors to determine the particular consequences to them.

For purposes of this discussion, a "U.S. Holder" means a beneficial owner of shares of our common stock that is any of the following:

- an individual who is a citizen or resident of the United States or someone treated as a U.S. citizen or resident for U.S. federal income tax purposes;
- a corporation (or other entity treated as a corporation for U.S. federal income tax purposes) created or organized in or under the laws of the United States, any state thereof, or the District of Columbia;
- an estate, the income of which is subject to U.S. federal income taxation regardless of its source; or
- a trust if (i) a U.S. court can exercise primary supervision over the trust's administration and one or more "United States persons" (within the meaning of Section 7701(a)(30) of the Code) are authorized or have the authority to control all substantial decisions of the trust or (ii) it has a valid election in effect under applicable U.S. Treasury Regulations to be treated as a United States person for U.S. federal income tax purposes.

The Reverse Stock Split should constitute a "recapitalization" for U.S. federal income tax purposes. In general, the federal income tax consequences of a Reverse Stock Split will vary depending upon whether a U.S. Holder receives cash for fractional shares or solely a reduced number of shares of common stock in exchange for their old shares of common stock. We believe that because the Reverse Stock Split is not part of a plan to increase periodically a stockholder's proportionate interest in our assets or earnings and profits, the Reverse Stock Split should have the following federal income tax effects. A U.S. Holder who receives solely a reduced number of shares of common stock will generally not recognize gain or loss in the Reverse Stock Split. A U.S. Holder's aggregate tax basis in the reduced number of shares of common stock should equal the U.S. Holder's aggregate tax basis in its old shares of common stock and such U.S. Holder's holding period in the reduced number of shares will include the holding period in its old shares exchanged. Treasury Regulations provide detailed rules for allocating the tax basis and holding period of the shares of common stock surrendered to the shares of common stock received in a recapitalization pursuant to the Reverse Stock Split. U.S. Holders should consult their tax advisors as to application of the foregoing rules where shares of common stock were acquired at different times or at different prices.

A U.S. Holder who receives cash in lieu of a fractional share as a result of the Reverse Stock Split should generally recognize gain or loss equal to the difference, if any, between the amount of cash received and the stockholder's basis in the fractional share. Such gain or loss will be a capital gain or loss and will be short term if the pre-reverse split shares were held for one year or less and long term if held more than one year. Long-term capital gains of non-corporate U.S. Holders are generally subject to preferential tax rates. There are limitations on the deductibility of capital losses under the Code. A U.S. Holder's aggregate tax basis in the reduced number of shares of common stock should equal the U.S. Holder's aggregate tax basis in its old shares of common stock

decreased by the basis allocated to the fractional share for which such U.S. Holder is entitled to receive cash, and the holding period of the reduced number of shares received will include the holding period of the old shares exchanged.

We will not recognize any gain or loss as a result of the proposed Reverse Stock Split.

Required Vote

Stockholder approval of this Proposal 2 requires a "FOR" vote from at least a majority of the outstanding shares of our common stock on the record date.

THE BOARD OF DIRECTORS RECOMMENDS THAT STOCKHOLDERS VOTE "FOR" THE APPROVAL OF A REVERSE STOCK SPLIT AS SET FORTH IN PROPOSAL 2.

PROPOSAL 3

APPROVAL OF AN AMENDMENT TO OUR AMENDED AND RESTATED CERTIFICATE OF INCORPORATION TO REDUCE THE NUMBER OF AUTHORIZED SHARES OF OUR COMMON STOCK TO 300,000,000 SHARES

Our Board of Directors has adopted and is recommending that our stockholders approve an amendment (the "Authorized Shares Reduction") to our Amended and Restated Certificate of Incorporation to reduce the number of authorized shares of our common stock from 400,000,000 to 300,000,000. The text of the proposed Certificate of Amendment to our Amended and Restated Certificate of Incorporation, which we refer to as the Certificate of Amendment, is attached hereto as Appendix A.

The implementation of this Proposal 3 is expressly conditioned upon the approval and implementation of Proposal 2; if Proposal 2 is not approved and implemented, then this Proposal 3 will not be implemented. Accordingly, if we do not receive the required stockholder approval for Proposal 2 or the Reverse Stock Split is not otherwise implemented on or prior to the date of the one-year anniversary of the date of the Annual Shareholder Meeting, or June 9, 2023, then we will not implement the Authorized Shares Reduction. If we receive the required stockholder approval for Proposal 2 but do not receive the required stockholder approval for Proposal 3, then our Board of Directors will nonetheless retain the ability to implement a Reverse Stock Split and, if so effected, the total number of authorized shares of our common stock would remain unchanged.

Reasons for the Authorized Shares Reduction; Certain Risks

As a matter of Delaware law, the implementation of a Reverse Stock Split does not require a reduction in the total number of authorized shares of our common stock. However, if Proposals 2 and 3 are approved by our stockholders and a Reverse Stock Split is implemented, the authorized number of shares of our common stock would be reduced to 300,000,000 shares. The reduction in the authorized number of shares of common stock will not be proportionate to the Reverse Stock Split ratio, so the practical effect of any Reverse Stock Split and the Authorized Shares Reduction would be to *increase* the number of authorized shares of our common stock.

As described in more detail under "Reasons for Reverse Stock Split" in Proposal 2, our Board of Directors desires to have a sufficient number of unissued and unreserved authorized shares of common stock following the implementation of a Reverse Stock Split to provide us with flexibility with respect to our authorized capital sufficient to execute our business strategy. At the same time, the Authorized Shares Reduction was designed so that we do not have what some stockholders might view as an unreasonably high number of authorized shares of common stock that are unissued or reserved for issuance following the Reverse Stock Split. In this regard, if Proposal 2 is approved but this Proposal 3 is not approved, then the authorized number of shares of our common stock would not be reduced *at all* even if a Reverse Stock Split is implemented; accordingly, our Board of Directors believes that this Proposal 3 is in the best interests of Regulus and our stockholders and strikes the appropriate balance in the event a Reverse Stock Split is implemented. However, the implementation of a Reverse Stock Split and the resulting effective increase in the number of authorized shares of our common stock, could, under certain circumstances, have anti-takeover implications, as described in more detail under "Certain Risks and Potential Disadvantages Associated with the Reverse Stock Split" in Proposal 2. Although we are not proposing a Reverse Stock Split as a result of any threat of a hostile takeover attempt (nor is the Board currently aware of any such attempts directed at us), stockholders should be aware that if Proposal 2 is approved but this Proposal 3 is not approved, the anti-takeover implications associated with any Reverse Stock Split may be enhanced due to the additional number of shares of common stock that could be used by us to deter or prevent changes in control.

Effects of Authorized Shares Reduction

The principal effect of the Authorized Shares Reduction will be that the number of authorized shares of our common stock will be reduced from 400,000,000 to 300,000,000. The Authorized Shares Reduction would not

have any effect on the rights of existing stockholders, and the par value of the common stock would remain unchanged at $0.001 per share.

Effective Date; Conditionality

The proposed Authorized Shares Reduction would become effective at 5:00 p.m., Eastern time, on the business day following the filing of a Certificate of Amendment with the office of the Secretary of State of the State of Delaware, or such later date as is chosen by the Board and set forth in the Certificate of Amendment.

Our Board of Directors intends to proceed with the Authorized Shares Reduction only if and when a Reverse Stock Split is implemented. Accordingly, should we not receive the required stockholder approval for Proposal 2 or the Reverse Stock Split is not otherwise implemented on or prior to the date of the one-year anniversary of the date of the Annual Meeting, or June 9, 2023, then we will not implement the Authorized Shares Reduction even if this Proposal 3 is approved. In this regard, the implementation of Proposal 3 is expressly conditioned upon the approval and implementation of Proposal 2; if Proposal 2 is not approved and implemented, then Proposal 3 will not be implemented. If we receive the required stockholder approval for Proposal 2 but do not receive the required stockholder approval for Proposal 3, then our Board of Directors will nonetheless retain the option to implement a Reverse Stock Split and if so effected, the total number of authorized shares of our common stock would remain unchanged.

Required Vote

Stockholder approval of this Proposal 3 requires a "FOR" vote from at least a majority of the outstanding shares of our common stock on the record date.

THE BOARD OF DIRECTORS RECOMMENDS THAT STOCKHOLDERS VOTE "FOR"
THE APPROVAL OF THE AUTHORIZED SHARE REDUCTION AS SET FORTH IN PROPOSAL 3.

PROPOSAL 4

ADVISORY VOTE ON EXECUTIVE COMPENSATION

At the 2018 Annual Meeting of Stockholders, the stockholders indicated their preference that the Company solicit a non-binding advisory vote on the compensation of the named executive officers, commonly referred to as a "say-on-pay vote," every year. The Board has adopted a policy that is consistent with that preference.

This vote is not intended to address any specific item of compensation, but rather the overall compensation of the Company's named executive officers and the philosophy, policies and practices described in this proxy statement. The compensation of the Company's named executive officers subject to the vote is disclosed in the "Executive Compensation" section, including the compensation tables and the related narrative disclosure, contained in this proxy statement. As discussed in those disclosures, the Company believes that its compensation policies and decisions are focused on pay-for-performance principles and strongly aligned with our stockholders' interests.

Accordingly, the Board is asking the stockholders to indicate their support for the compensation of the Company's named executive officers as described in this proxy statement by casting a non-binding advisory vote "FOR" the following resolution:

"RESOLVED, that the compensation paid to the Company's named executive officers, as disclosed pursuant to Item 402 of Regulation S-K, including the compensation tables and narrative discussion is hereby APPROVED."

Because the vote is advisory, it is not binding on the Board or the Company. Nevertheless, the views expressed by the stockholders, whether through this vote or otherwise, are important to management and the Board and, accordingly, the Board and the Compensation Committee intend to consider the results of this vote in making determinations in the future regarding executive compensation arrangements.

Vote Required

Approval of this proposal requires the vote of the holders of a majority of the shares present in person or represented by proxy and entitled to vote on this matter at the Annual Meeting. Abstentions and broker non-votes will be counted toward a quorum for Proposal 4, and abstentions will have the same effect as "Against" votes.

THE BOARD OF DIRECTORS RECOMMENDS
A VOTE FOR PROPOSAL 4

The Company is a "smaller reporting company" under Item 10 of Regulation S-K promulgated under the Exchange Act, and the following compensation disclosure is intended to comply with the requirements applicable to smaller reporting companies. Although the rules allow the Company to provide less detail about its executive compensation program, the Compensation Committee is committed to providing the information necessary to help stockholders understand its executive compensation-related decisions. Accordingly, this section includes supplemental narratives that describe the 2021 executive compensation program for our Named Executive Officers.

Named Executive Officers. The following individuals are our "Named Executive Officers" or "NEOs" for the year ended December 31, 2021:

- Joseph P. Hagan, our President and Chief Executive Officer;
- Christopher R. Aker, our Senior Vice President and General Counsel; and
- Cris Calsada, our Chief Financial Officer.

Summary Compensation Table

The following table shows, for the fiscal years ended December 31, 2021 and December 31, 2020, compensation awarded to, paid to, or earned by, the Named Executive Officers.

Name and Principal Position	Year	Salary ($)	Option Awards ($)(1)	Non-Equity Incentive Plan Compensation ($)(2)	All Other Compensation ($)(3)	Total ($)
Joseph P. Hagan	2021	567,500	954,000	289,425	11,322	1,822,247
President & Chief Executive Officer	2020	551,500	1,507,054	264,720	9,860	2,333,134
Christopher R. Aker	2021	340,000	286,200	153,000	16,224	795,424
SVP & General Counsel	2020	315,000	351,646	132,300	10,172	809,118
Cris Calsada	2021	324,450	238,500	146,003	10,554	719,507
Chief Financial Officer	2020	315,000	251,176	132,300	9,350	707,826

(1) In accordance with SEC rules, this column reflects the aggregate grant date fair value of stock options granted during the years indicated, computed in accordance with Financial Accounting Standard Board ASC Topic 718 for stock-based compensation transactions, or ASC 718. Assumptions used in the calculation of these amounts are included in Note 10 to the Financial Statements in our Annual Report on Form 10-K for the year ended December 31, 2021. These amounts do not reflect the actual economic value that will be realized by the Named Executive Officer upon the exercise of the stock options, or the sale of the common stock underlying such stock options. Our named executive officers were also granted performance-vesting stock options in 2021 (described below). The grant date fair value of such performance-vesting stock options is reported based on the probable outcome of such performance conditions, as determined in accordance with ASC 718, which we determined to be $0. Assuming that the highest level of performance conditions were to be achieved, the grant date fair value for the performance-vesting stock options granted to our named executive officers would be $636,000 with respect to Mr. Hagan, $190,800 with respect to Mr. Aker and $159,000 with respect to Ms. Calsada.

(2) Amounts shown include annual performance bonuses paid to Mr. Hagan, Mr. Aker and Ms. Calsada, earned for the years indicated. For more information, see below under "Annual Performance-Based Bonus Opportunity."

(3) Amounts shown include term life insurance and long-term disability insurance paid by us on behalf of the Named Executive Officers and matching contributions we paid under the terms of our 401(k) plan. Matching 401(k) contributions paid to our named executive officers were $8,700 with respect to each of

Mr. Hagan, Mr. Aker and Ms. Calsada All of these benefits are provided to the Named Executive Officers on the same terms as provided to all of our regular full-time employees in the United States. For more information regarding these benefits, see below under "Other Compensation."

Narrative Disclosure to Summary Compensation Table

The three principal components of our executive compensation program for our Named Executive Officers in 2021 were base salary, annual performance-based (cash) bonus opportunity and equity compensation. We do not have any formal policies for allocating compensation among salary, performance bonus awards and equity grants, short-term and long-term compensation or among cash and non-cash compensation. Instead, the Compensation Committee uses its judgment to establish a total compensation program for each named executive officer that is a mix of current, short-term and long-term incentive compensation, and cash and non-cash compensation, that it believes appropriate to achieve the goals of our executive compensation program and our corporate objectives. In line with our pay for performance philosophy, we structured a significant portion of our Named Executive Officers' 2021 compensation to be variable, at risk and tied directly to our measurable performance in the form of performance-based bonuses and equity incentives.

The Compensation Committee uses the services of an independent compensation consultant who is retained by, and reports directly to, the Compensation Committee to provide the Compensation Committee with an additional external perspective with respect to its evaluation of relevant market and industry practices. Since 2013, the Compensation Committee has used Radford, an AON Hewitt Company, as a third-party compensation consultant to assist the Compensation Committee in establishing overall compensation levels. Radford conducted analyses and provided advice on, among other things, the appropriate peer group, executive compensation for our executive officers and compensation trends in the life sciences industry.

The peer group of companies used by the Compensation Committee in making 2021 compensation decisions was comprised of the following companies:

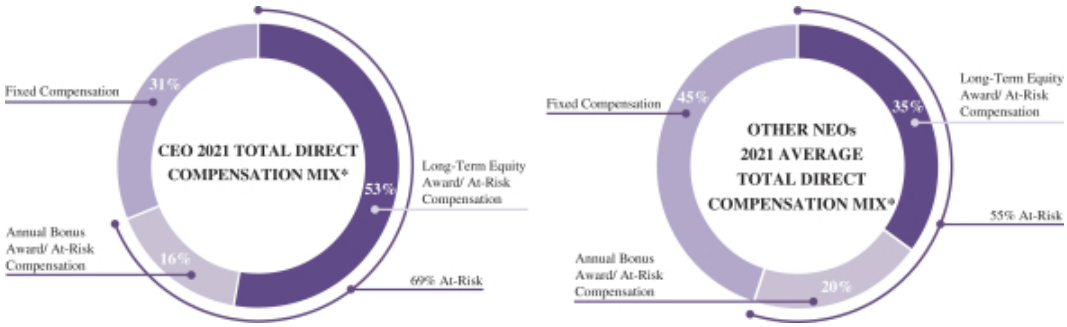
Adial Pharmaceuticals	aTyr Pharma	BioCardia	Caladrius Biosciences	Capricor Therapeutics	Catalyst Biosciences
Cidara Therapeutics	CohBar	ContraFect	Conus Pharmaceuticals	Daré Bioscience	Eledon Pharmaceuticals
Infinity Pharmaceuticals	Lineage Cell Therapies	Metacrine	Otonomy	Pulmatrix	Synlogic
Synthetic Biologics	Tenax Therapeutics	TRACON Pharmaceuticals	Viridian Therapeutics		

The peer group was recommended by Radford and chosen in late-2020 based on the following parameters: biopharmaceutical companies that were pre-commercial and with programs in early clinical development, had market values generally under $300 million and with a preference for companies with headcounts under 100. At the time we choose our peer group companies, our market value was approximately $62 million and our headcount was 24 employees. Based upon changes in our market value from 2019 to 2020, the peer group listed above included several new peer companies.

Pay for Performance/At-Risk Pay

Our executive compensation program is designed to reward achievement of the specific strategic goals that we believe will advance our business strategy and create long-term value for our stockholders. Consistent with our goal of attracting, motivating and retaining a high-caliber executive team, our executive compensation program is designed to pay for performance. We utilize compensation elements that meaningfully align our NEOs' interests with those of our stockholders to create long-term value. As such, a significant portion of our

Chief Executive Officer's and other executive officers' compensation is "at-risk", performance-based compensation, in the form of long-term equity awards (including, from time to time, performance-vesting equity awards) and annual cash incentives that are only earned if we achieve measurable corporate metrics. The charts below show the 2021 total reported pay mix of our Chief Executive Officer, Mr. Hagan, and our other NEOs and the portion of each individual's aggregate reported pay that is tied directly to performance, consisting of annual performance bonus earned and equity incentives awarded (based on such equity incentives' grant date fair value as reported in the "Summary Compensation Table").



* Reflects 2021 cash compensation, consisting of annual base salaries and performance bonus earned, and 2021 equity awards granted, based on such equity incentives' grant date fair value as reported in the "Summary Compensation Table," for each of our NEOs.

Base Salary

In December 2020, the Compensation Committee reviewed the base salaries for our then-current Named Executive Officers, the market data from Radford, our 3% Company-wide corporate merit increase target for base salaries, the scope of each executive's responsibilities for 2020, each executive's prior experience and internal pay equity in order to determine 2021 base salaries of our NEOs. In addition, Mr. Aker's base salary was increased to more closely align with the 25th percentile of base salary for positions similar to that held by Mr. Aker at the Company's peer companies.

The Named Executive Officers' 2021 annual base salaries (effective January 1, 2021) and increases from 2020 annual base salaries approved by the Compensation Committee were as follows:

Name	2021 Base Salary ($)	Increase from 2020 Base Salary (%)
Joseph P. Hagan	567,500	3.0%
Christopher R. Aker	340,000	8.0%
Cris Calsada	324,450	3.0%

Annual Performance-Based Bonus Opportunity

The annual performance-based (cash) bonus each Named Executive Officer is eligible to receive is based on (1) the individual's target bonus, as a percentage of base salary, (2) a Company-based performance factor ("CPF"), and (3) an individual performance factor ("IPF"). The actual performance-based bonus paid, if any, is calculated by taking into consideration the executive officer's annual base salary, target bonus percentage, percentage attainment of the CPF and percentage attainment of the IPF.

Each Named Executive Officer's target bonus for 2021, represented as a percentage of base salary, or a target bonus percentage, was 50% of base salary, with the exception of Mr. Hagan, which was 60% of base salary. The Compensation Committee determined the target bonuses of each of our NEOs, other than our Chief

Executive Officer, should be consistent to promote internal equity and reinforce teamwork across our leadership team.

Except for the Chief Executive Officer whose entire annual bonus depends upon the CPF, 80% of each NEO's annual bonus is dependent upon the CPF, with the remaining 20% annual bonus dependent upon such individual's IPF.

At the end of the year, our Compensation Committee approves the extent to which we achieved the CPF based on achievement of the corporate goals. The extent to which each individual Named Executive Officer achieves his or her IPF is determined based on our Chief Executive Officer's review and recommendation to our Compensation Committee. Our Compensation Committee makes the final decisions with respect to each IPF.

Additionally, our Compensation Committee has the discretion to determine the weighting of each of the goals that comprise the CPF and IPF. Our Compensation Committee may award a bonus in an amount above or below the amount resulting from the calculation described above, based on other factors that our Compensation Committee determines, in its sole discretion, are material to our corporate performance and provide appropriate incentives to our executives; for example, based on events or circumstances that arise after the original CPF and IPF goals are set. Our Compensation Committee did not exercise any such discretion in 2021.

The CPF and IPF goals are determined by our Compensation Committee and communicated to our Named Executive Officers each year, prior to or shortly following the beginning of the year to which they relate. The CPF is composed of several goals that relate to our annual corporate goals and various business accomplishments which vary from time to time depending on our overall strategic objectives. The IPF is composed of factors that relate to each Named Executive Officer's ability to drive his or her own performance and the performance of his or her direct employee reports towards reaching our corporate goals. The proportional emphasis placed on each goal within the CPF and IPF may vary from time to time depending on our overall strategic objectives and our Compensation Committee's subjective determination of which goals have more impact on our performance.

For 2021, the CPF goals related primarily to advancing our most promising program, RGLS4326 for the treatment of autosomal dominant polycystic kidney disease ("ADPKD"), while also making progress on our second generation ADPKD compound, RGLS8429 and our preclinical pipeline. The specific CPF goals were as follows:

- Complete dosing of all cohorts in the RGLS4326 Mechanism of Action study;
- Gain alignment with the Food and Drug Administration ("FDA") concerning the remaining clinical hold requirements for RGLS4326;
- Submit a complete response to the FDA regarding the remaining clinical hold requirements for RGLS4326;
- Position our second generation compound, RGLS8429, to start investigational new drug application ("IND") enabling studies;
- Demonstrate in vivo proof of concept and in vitro proof of concept in specified preclinical programs;
- Establish a research or development partnership with respect to a preclinical program or regional partnership with respect to our ADPKD program; and
- End 2021 with at least six months of cash runway.

In January 2022, after careful review, our Board of Directors, upon the recommendation of our Compensation Committee, concluded that we had achieved 85% of our CPF goals, based on the following:

- Regulus completed the first two cohorts in the RGLS4326 Mechanism of Action study and thereafter terminated before initiation of the third cohort based on the FDA's feedback concerning a possible dose-limiting toxicity thereby saving the company money;

- Regulus completed its assessment of data modeling long term exposure to RGLS4326 as requested by the FDA addressing the remaining clinical hold requirements for RGLS4326. The FDA was in agreement with Regulus' modeling;
- Due to Regulus' decision to cease development of RGLS4326, it did not submit a complete response to the FDA regarding the remaining clinical hold requirements and thus this goal was not achieved;
- Regulus successfully accelerated IND enabling activities for our second generation compound, RGLS8429, enabling the company to request a pre-IND meeting with the FDA and submit the briefing package by the end of 2021;
- Regulus received partial credit for its goal to further preclinical programs as we made much progress but did not complete the goal;
- Regulus did not establish a collaboration or development partnership and thus did not receive credit for this goal; and
- Through the use of its "At the Market" facility and the closing in November of 2021 of a private placement transaction in which the company received $34.6 million, Regulus exceeded its goal of having six months of cash on hand at 2021 year end.

The IPF goals varied by individual and included individual performance contributions towards maintaining a leading position in *micro*RNA research, accelerating efforts in *micro*RNA therapeutic development, supporting our growth with additional capital, fostering a culture of value creation, attracting and retaining key talent and building good processes and policies.

Based on our Chief Executive Officer's recommendations with respect to each other Named Executive Officer, and our Compensation Committee's deliberations with respect to each Named Executive Officer's individual performance against the IPF, our Compensation Committee and Board of Directors approved a performance-based bonus for each of our Named Executive Officers as set forth in the table below based on an 85% CPF achievement and the achievement of IPF as indicated in the table below:

Name	Target Bonus ($)	IPF Achievement (%)	Cash Bonus Paid ($)
Joseph P. Hagan	$ 340,500	—	$ 289,425
Christopher Aker(1)	$ 170,000	110%	$ 153,000
Cris Calsada(2)	$ 162,225	110%	$ 146,003

(1) Mr. Aker's performance-based bonus was approved based on 85% CPF and 110% IPF in recognition of his roles in procuring additional capital, ongoing support of the RGLS4326 Mechanism of Action study, his operational leadership concerning our continuing response to the COVID-19 pandemic and his role in recruiting additional scientific talent.

(2) Ms. Calsada's performance-based bonus was approved based on the 85% CPF and 110% IPF in recognition of her leadership in procuring additional capital, her active management of our research and administrative budgets, and her oversight of financial reporting.

Equity-Based Incentive Awards

The Compensation Committee believes equity incentives motivate executive officers to achieve our business objectives by tying incentives to the appreciation of our common stock and, in the case of performance-vesting awards, measurable performance goals. In the past, we have primarily granted equity awards in the form of stock options that vest based on achievement of specific Company performance goals and/or continued service and we have occasionally also granted restricted stock unit ("RSU") awards, However, no RSU awards were granted in 2021 or outstanding as of December 31, 2021.

Stock Option Awards. In 2021, each of our Named Executive Officers were granted time-vesting stock options and performance-based stock options in the amounts listed below.

Name	Time-Vesting Stock Options (# of shares)(1)	Performance-Vesting Stock Options (# of shares)(2)
Joseph P. Hagan	600,000	400,000
Christopher R. Aker	180,000	120,000
Cris Calsada	150,000	100,000

(1) Consists of stock options granted on February 4, 2021 at an exercise price of $1.59 per share. Such option vests in equal monthly installments over a 48 month period following January 1, 2022, subject to the recipient's continued service to the Company through each such vesting date.

(2) Consists of a performance-vesting stock option granted on February 4, 2021, at an exercise price of $1.59 per share. The shares vest only upon achievement of a specified development goal related to our RGLS4326 program. Upon achievement of the goal, 50% of the shares subject to the award will immediately vest with the remaining shares vesting in equal monthly installments over 24 months of continuous service to the Company. On November 8, 2021, our Compensation Committee determined that the goal would not be met due to the discontinuation of our RGLS4326 program and each such option cancelled.

Other Compensation

Our Named Executive Officers are eligible to participate in all of our employee benefit plans, including our medical, dental, vision, group life and disability insurance plans, in each case on the same basis as other employees. We also pay the premiums for term life insurance and long-term disability for all of our employees, including our Named Executive Officers. None of our Named Executive Officers participate in or have account balances in qualified or non-qualified defined benefit plans sponsored by us. We generally do not provide perquisites or personal benefits to our Named Executive Officers, although we may from time to time provide signing bonuses or other reasonable benefits as our Compensation Committee determines appropriate.

All of our full-time employees in the United States, including our Named Executive Officers, are eligible to participate in our 401(k) plan, which is a retirement savings defined contribution plan established in accordance with Section 401(a) of the Code. Pursuant to our 401(k) plan, employees may elect to defer their eligible compensation into the plan on a pre-tax basis, up to the statutorily prescribed annual limit of $19,500 in 2021 (additional salary deferrals not to exceed $6,500 are available to those employees 50 years of age or older) and to have the amount of this reduction contributed to our 401(k) plan. In 2021, we provided a $0.50 match for every dollar our employees elect to defer up to 6% of their eligible compensation. In general, eligible compensation for purposes of the 401(k) plan includes an employee's wages, salaries, fees for professional services and other amounts received for personal services actually rendered in the course of employment with us to the extent the amounts are includible in gross income, and subject to certain adjustments and exclusions required under the Code. The 401(k) plan currently does not offer the ability to invest in our securities.

Agreements with Named Executive Officers

Employment Agreements. We entered into employment agreements with each of our Named Executive Officers. The agreements provide for at-will employment and for certain base salary, target bonus and severance payments to our Named Executive Officers.

Employment Agreement with Mr. Hagan. We previously entered into an employment agreement with Mr. Hagan, with an effective date of January 1, 2016. Pursuant to his employment agreement, Mr. Hagan is entitled to receive an annual base salary and is eligible to earn an annual performance bonus. Mr. Hagan's base salary and target bonus are subject to periodic review and adjustment from time to time in the discretion of our Board of Directors or the Compensation Committee. In 2021, Mr. Hagan's base salary was increased to $567,500 and his target bonus remained at 60% of his annual base salary.

Employment Agreement with Mr. Aker. In July 2018, we entered into an amended and restated employment agreement with Mr. Aker. Pursuant to his amended and restated employment agreement, Mr. Aker is entitled to receive an annual base salary and is eligible to earn an annual performance bonus. Mr. Aker's base salary and target bonus are subject to periodic review and adjustment from time to time in the discretion of our Board of Directors or the Compensation Committee. Pursuant to Mr. Aker's amended and restated employment agreement, all outstanding stock options subject to vesting based on Company performance that are held by Mr. Aker immediately before a change in control shall become fully vested and exercisable as of immediately before, and contingent upon, the change in control, provided that Mr. Aker remains employed by us as of such date. In 2021, Mr. Aker's base salary was increased to $340,000 and his target bonus remained at 50% of his annual base salary.

Employment Agreement with Ms. Calsada. In August 2019, we entered into an employment agreement with Ms. Calsada with an effective date of August 30, 2019 upon her commencement of employment as our Chief Financial Officer. Pursuant to her employment agreement, Ms. Calsada is entitled to receive an annual base salary and is eligible to earn an annual performance bonus. Ms. Calsada's base salary and target bonus are subject to periodic review and adjustment from time to time in the discretion of our Board of Directors or the Compensation Committee. Pursuant to Ms. Calsada's employment agreement, all outstanding stock options subject to vesting based on Company performance that are held by Ms. Calsada immediately before a change in control shall become fully vested and exercisable as of immediately before, and contingent upon, the change in control, provided that Ms. Calsada remains employed by us as of such date. In 2021, Ms. Calsada's base salary was increased to $324,450 and her target bonus remained at 50% of her annual base salary.

Change in Control and Severance Benefits

Under the terms of the employment agreements with each of our Named Executive Officers described above, either we or the executive may terminate the executive's employment at any time. Each of our Named Executive Officers is eligible, under the terms of his or her respective employment agreement, to receive, in exchange for a release of claims, severance benefits upon the termination of employment either by us without cause or by the executive for good reason, with additional severance benefits provided in the event the termination is in connection with a change in control.

In addition, the terms of the equity awards granted to our Named Executive Officers are subject to the terms of our equity plans and award agreements thereunder, which includes accelerated vesting provisions upon certain material change in control transactions. We do not provide any excise tax gross-ups on change-in-control benefits.

If we terminate a Named Executive Officer's employment "without cause" (other than due to his/her death or complete disability) or if the Named Executive Officer resigns for "good reason" at any time other than during the period beginning one month before and ending 12 months following a change in control, such Named Executive Officer will receive, subject to our receiving an effective release and waiver of claims, (1) a lump sum severance payment equal to 12 months of the Named Executive Officer's then-current base salary (disregarding any decrease that forms the basis for a resignation for good reason), (2) a lump sum cash amount equal to 229.56% multiplied by the total cost of the projected premiums for group medical, dental and vision insurance for a period of 12 months and (3) vesting acceleration of all outstanding options and other equity incentive awards subject to time-based vesting held by such Named Executive Officer as of such termination or resignation.

If we terminate the Named Executive Officer's employment without cause (other than due to his/her death or complete disability) or if the Named Executive Officer resigns for good reason, in each case during the period beginning one month before and ending 12 months following a change in control, in addition to the severance payment described above, we will also be obligated to pay, subject to receiving an effective release and waiver of claims, a lump sum payment equal to the target amount of the Named Executive Officer's annual performance bonus for the year of termination or resignation.

In addition, and pursuant to each Named Executive Officer's employment agreement, all outstanding stock options subject to vesting based on Company performance that are held by such Named Executive Officer immediately before a change in control shall become fully vested and exercisable as of immediately before, and contingent upon, the change in control, provided that such Named Executive Officer remains employed by us as of such date. These options are described below in the table entitled *Outstanding Equity Awards at Fiscal Year-End.*

Outstanding Equity Awards at Fiscal Year-End

The following table shows certain information regarding outstanding equity awards as of December 31, 2021, for the Named Executive Officers:

			Option Awards(1)				
Name	Grant Date	Vesting Commencement Date	Number of Securities Underlying Unexercised Stock Options (#) Exerciseable	Number of Securities Underlying Unexercised Stock Options (#) Unexerciseable	Equity Incentive Plan Awards: Number of Securities Underlying Unexercised Unearned Options	Option Exercise Price ($)	Option Expiration Date
Joseph P. Hagan	2/5/2019(2)	1/1/2019	47,395	17,605		0.95	2/4/2029
	2/5/2019(3)	5/14/2019	10,000			0.95	2/4/2029
	10/10/2019(2)	10/10/2019	541,666	458,334		0.64	10/09/2029
	1/22/2020(2)	1/1/2020	431,250	468,750		1.31	1/21/2030
	1/22/2020(4)	—			300,000	1.31	1/21/2030
	1/22/2020(4)	—			300,000	1.31	1/21/2030
	2/4/2021(2)	1/1/2021	137,500	462,500		1.59	2/3/2031
Christopher R. Aker	2/5/2019(2)	1/1/2019	18,229	6,771		0.95	2/4/2029
	2/5/2019(3)	5/14/2019	7,500			0.95	2/4/2029
	10/10/2019(2)	10/10/2019	181,458	153,542		0.64	10/09/2029
	1/22/2020(2)	1/1/2020	100,625	109,375		1.31	1/21/2030
	1/22/2020(4)	—			70,000	1.31	1/21/2030
	1/22/2020(4)	—			70,000	1.31	1/21/2030
	2/4/2021(2)	1/1/2021	41,250	138,750		1.59	2/3/2031
Cris Calsada	8/30/2019(5)	8/30/2019	58,333	41,677		0.62	8/29/2029
	10/10/2019(2)	10/10/2020	113,750	96,250		0.64	10/09/2029
	1/22/2020(2)	1/1/2020	71,875	78,125		1.31	1/21/2030
	1/22/2020(4)	—			50,000	1.31	1/21/2030
	1/22/2020(4)	—			50,000	1.31	1/21/2030
	2/4/2021(2)	1/1/2021	34,375	115,625		1.59	2/3/2031

(1) Stock awards granted prior to October 2019 were granted under the 2012 Equity Incentive Plan. Stock awards granted thereafter were granted under the 2019 Equity Incentive Plan. The terms of the 2012 Equity Incentive Plan and 2019 Equity Incentive Plan are described below under "Equity Compensation Plans and Other Benefit Plans."

(2) Consists of stock options vesting in equal monthly installments over a 48 month period, subject to the recipient's continued service to the Company through each such vesting date.

(3) Consists of performance-vesting stock option with an exercise price of $0.95 per share, which only vest upon achievement of a previously-specified performance objective. On May 14, 2019, the Board of Directors concluded the Company had met the criteria to commence vesting of the performance-vesting stock option consisting of a Board-approved transaction which the Board, in its sole discretion, determines is reasonably expected to provide adequate cash runway for achievement of the Company's strategic

objectives. Because of the achievement of the performance objective, 50% of the shares subject to the grant immediately vested with the remaining shares vesting in equal monthly installments over the following 24 months, subject to the recipient's continued service to the Company through each such vesting date.

(4) Consists of performance-vesting stock option with an exercise price of $1.31 per share which only vest upon achievement of a previously-specified performance objective related to (1) our most advanced clinical program and (2) progressing an early preclinical program and in each case only if achieved by December 31, 2024. Upon achievement of the performance objective, 50% of the shares subject to the grant immediately vested with the remaining shares vesting in equal monthly installments over the following 24 months, subject to the recipient's continued service to the Company through each such vesting date.

(5) Consists of a stock option that vests as follows: 25% of the shares subject to the grant vest on the first anniversary of the grant with the remainder vesting in equal monthly installments over a 36 month period, subject to the recipient's continued service to the Company through each such vesting date.

Equity Compensation Plans

From October 2012 until August 2019, all equity awards (other than inducement awards) were granted pursuant to our 2012 Equity Incentive Plan (the "2012 Plan"). Beginning in August 2019, all equity awards (other than inducement awards) have been, and will be granted, pursuant to our 2019 Equity Incentive Plan (the "2019 Plan"). In addition, we may grant inducement awards to new employees under our 2021 Inducement Plan (the "2021 Inducement Plan"). The terms of these plans are described below.

2019 Equity Incentive Plan

The 2019 Plan, which became effective in August 2019, provides for the grant of incentive stock options ("ISOs"), within the meaning of Section 422 of the Code, nonstatutory stock options ("NSOs"), stock appreciation rights, restricted stock awards, restricted stock unit awards, performance-based stock awards, and other forms of equity compensation (collectively, "stock awards"). Additionally, the 2019 Plan provides for the grant of performance cash awards. ISOs may be granted only to employees, subject to certain limitations. All other awards may be granted to employees, including officers, and to non-employee directors and consultants. As of December 31, 2021, under the 2019 Plan, there were outstanding stock options to purchase 8,661,385 shares of our common stock and 400,500 RSUs outstanding.2,164,112 shares of our common stock remained available for the grant of stock awards under the 2019 Plan.

Our Board of Directors, or a duly authorized committee thereof, has the authority to administer the 2019 Plan. Our Board of Directors has delegated its authority to administer the 2019 Plan to our Compensation Committee under the terms of our Compensation Committee's charter. Our Board of Directors or our Compensation Committee may also delegate certain authority to one or more of our officers. Our Board of Directors or its authorized committee is referred to herein as the plan administrator.

Stock options are generally granted with an exercise price equal to the fair market value of our common stock on the date of grant, vest at the rate specified by the plan administrator (often over a four-year period) and may have a term up to a maximum of 10 years. The exercise price for an ISO or NSO generally cannot be less than 100% of the fair market value of our common stock on the date of grant. Unless the terms of an optionee's stock option agreement provides otherwise, if an optionee's service relationship with us, or any of our affiliates, ceases for any reason other than disability, death or cause, the optionee may generally exercise any vested options for a period of three months following the cessation of service. The option term may be extended in the event that exercise of the option following such a termination of service is prohibited by applicable securities laws or our insider trading policy. If an optionee's service relationship with us, or any of our affiliates, ceases due to disability or death, or an optionee dies within a certain period following cessation of service, the optionee or a beneficiary may generally exercise any vested options for a period of 12 months in the event of disability and 18 months in the event of death. In the event of a termination for cause, options generally terminate immediately upon the termination of the individual. In no event may an option be exercised beyond the expiration of its term.

Restricted stock units generally stop vesting upon the holder's termination of service with us and any unvested restricted stock units are forfeited, unless otherwise provided in an agreement with the holder.

Corporate transactions. In the event of certain specified significant corporate transactions (as defined in the 2019 Plan), the plan administrator has the discretion to take any of the following actions with respect to stock awards:

- arrange for the assumption, continuation or substitution of a stock award by a surviving or acquiring entity or parent company;
- arrange for the assignment of any reacquisition or repurchase rights held by us to the surviving or acquiring entity or parent company;
- accelerate the vesting of the stock award and provide for its termination prior to the effective time of the corporate transaction;
- arrange for the lapse of any reacquisition or repurchase right held by us;
- cancel or arrange for the cancellation of the stock award in exchange for such cash consideration, if any, as our Board of Directors may deem appropriate; or
- make a payment equal to the excess of (a) the value of the property the participant would have received upon exercise of the stock award over (b) the exercise price otherwise payable in connection with the stock award.

Change in control. The plan administrator may provide, in an individual award agreement or in any other written agreement between a participant and us, 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 2019 Plan). For example, a stock award may provide for accelerated vesting upon the participant's termination without cause or resignation for good reason in connection with a change in control. In the absence of such a provision, no such acceleration of the stock award will occur.

Repricings. The plan administrator may not: (i) reduce the exercise price of any outstanding options, or (ii) cancel any outstanding options that have an exercise price greater than the current fair market value of the Company's common stock in exchange for cash or other stock awards under the 2019 Plan, unless the stockholders of the Company have approved such an action within twelve months prior to such an event.

Amendment and termination. The Board has the authority to amend, suspend, or terminate the 2019 Plan, provided that such action does not materially impair the existing rights of any participant without such participant's written consent. No ISOs may be granted after the tenth anniversary of the date our Board of Directors adopted the 2019 Plan.

2012 Equity Incentive Plan

The 2012 Plan became effective in connection with our initial public offering in October 2012, and was in effect until the approval by our stockholders of our 2019 Plan. The 2012 Plan provided for the grant of ISOs, NSOs, stock appreciation rights, restricted stock awards, restricted stock unit awards, performance-based stock awards, and other forms of equity compensation, or collectively, stock awards. Additionally, the 2012 Plan provided for the grant of performance cash awards. ISOs were to be granted only to employees, subject to certain limitations. All other awards could be granted to employees, including officers, and to non-employee directors and consultants. As of December 31, 2021, there were outstanding stock options to purchase 8,661,385 shares of our common stock granted under the 2012 Plan.

Our Board of Directors, or a duly authorized committee thereof, administered the 2012 Plan. Our Board of Directors had delegated its authority to administer the 2012 Plan to our Compensation Committee under the terms of our Compensation Committee's charter. Our Board of Directors also delegated certain authority to one or more of our officers. Our Board of Directors or its authorized committee is referred to herein as the plan administrator.

Stock options are generally granted with an exercise price equal to the fair market value of our common stock on the date of grant, vest at the rate specified by the plan administrator (often over a four-year period) and may have a term up to a maximum of 10 years. The exercise price for an ISO or NSO generally cannot be less than 100% of the fair market value of our common stock on the date of grant. Unless the terms of an optionee's stock option agreement provides otherwise, if an optionee's service relationship with us, or any of our affiliates, ceases for any reason other than disability, death or cause, the optionee may generally exercise any vested options for a period of three months following the cessation of service. The option term may be extended in the event that exercise of the option following such a termination of service is prohibited by applicable securities laws or our insider trading policy. If an optionee's service relationship with us, or any of our affiliates, ceases due to disability or death, or an optionee dies within a certain period following cessation of service, the optionee or a beneficiary may generally exercise any vested options for a period of 12 months in the event of disability and 18 months in the event of death. In the event of a termination for cause, options generally terminate immediately upon the termination of the individual. In no event may an option be exercised beyond the expiration of its term. Restricted stock units generally stop vesting upon the holder's termination of service with us and any unvested restricted stock units are forfeited, unless otherwise provided in an agreement with the holder.

Corporate transactions. In the event of certain specified significant corporate transactions (as defined in the 2012 Plan), the plan administrator has the discretion to take any of the following actions with respect to stock awards:

- arrange for the assumption, continuation or substitution of a stock award by a surviving or acquiring entity or parent company;
- arrange for the assignment of any reacquisition or repurchase rights held by us to the surviving or acquiring entity or parent company;
- accelerate the vesting of the stock award and provide for its termination prior to the effective time of the corporate transaction;
- arrange for the lapse of any reacquisition or repurchase right held by us;
- cancel or arrange for the cancellation of the stock award in exchange for such cash consideration, if any, as our Board of Directors may deem appropriate; or
- make a payment equal to the excess of (a) the value of the property the participant would have received upon exercise of the stock award over (b) the exercise price otherwise payable in connection with the stock award.

Change in control. The plan administrator may provide, in an individual award agreement or in any other written agreement between a participant and us, 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 2012 Plan). For example, a stock award may provide for accelerated vesting upon the participant's termination without cause or resignation for good reason in connection with a change in control. In the absence of such a provision, no such acceleration of the stock award will occur.

2021 Inducement Plan

The 2021 Inducement Plan, which was adopted by our Board of Directors in November 2021, provides for the grant of NSOs, stock appreciation rights, restricted stock awards, restricted stock unit awards, performance-based stock and cash awards, and other forms of equity compensation, or collectively, stock awards which may be granted only to persons as a material inducement to their commencement of employment with us, pursuant to Rule 5635(c)(4) of the Nasdaq Listing Rules.

Our Board of Directors, or a duly authorized committee thereof, has the authority to administer the 2021 Inducement Plan. Our Board of Directors has delegated its authority to administer the 2021 Inducement Plan to

our Compensation Committee under the terms of our Compensation Committee's charter. Grants under the 2021 Inducement Plan must be approved by the Compensation Committee (comprised of independent directors) or a majority of our independent directors (as defined in Rule 5605(a)(2) of the Nasdaq Listing Rules) in order to comply with the exemption from the stockholder approval requirement for "inducement grants" provided under Rule 5635(c)(4) of the Nasdaq Listing Rules. The terms of the Inducement Plan and awards granted thereunder are generally the same as the terms of our 2019 Plan as it relates to similar awards granted under our 2019 Plan.

As of December 31, 2021, under the 2021 Inducement Plan, there were outstanding stock options to purchase 200,000 shares of our common stock. 1,800,000 shares of our common stock remained available for the grant of stock awards under the 2021 Inducement Plan.

2012 Employee Stock Purchase Plan

Additional long-term equity incentives are provided through the 2012 Employee Stock Purchase Plan (the "ESPP"), which became effective in connection with our initial public offering in October 2012. The ESPP is intended to qualify as an "employee stock purchase plan" within the meaning of Section 423 of the Code. Our Board of Directors has delegated its authority to administer the ESPP to our Compensation Committee. Under the ESPP, generally all of our regular employees (including our Named Executive Officers during their employment with us) may participate and may contribute, normally through payroll deductions, up to 15% of their earnings for the purchase of our common stock. The ESPP is implemented through a series of offerings of purchase rights to eligible employees. Under the ESPP, we may specify offerings with a duration of not more than six months, and may specify shorter purchase periods within each offering. Each offering will have one or more purchase dates on which our common stock will be purchased for employees participating in the offering. Unless otherwise determined by our Compensation Committee, shares are purchased for accounts of employees participating in the ESPP at a price per share equal to the lower of (a) 85% of the fair market value of our common stock on the first date of an offering or (b) 85% of the fair market value of our common stock on the date of purchase.

DIRECTOR COMPENSATION

The following table shows certain information with respect to the compensation of all non-employee directors of the Company for the fiscal year ended December 31, 2021:

Name	Fees Earned or Paid in Cash($)(1)	Option Awards ($)(2)(3)(4)	Total ($)
David Baltimore, Ph.D.	48,000	30,444	78,444
Kathryn J. Collier	60,000	30,444	90,444
Alice S. Huang, Ph.D.	42,946	122,654(5)	165,600
Jake Nunn	50,000	30,444	80,444
Stelios Papadopoulos, Ph.D.	84,000	30,444	144,444
William H. Rastetter, Ph.D.	52,000	30,444	82,444
Hugh Rosen, M.D., Ph.D.	46,000	30,444	76,444
Simos Simeonidis, Ph.D.	11,000	30,444	41,444
Pascale Witz	46,000	30,444	76,444

(1) Amounts listed represent cash payments made for Board and Committee service which were earned in 2021. Dr. Simeonidis was required by his employer, Sarissa Capital, to assign his cash payments to Sarissa Capital through the third quarter of 2021.

(2) Amounts listed represent the aggregate grant date fair value amount computed as of the grant date of each option awarded during 2021 in accordance with ASC 718. Assumptions used in the calculation of these amounts are included in Note 10 to the Financial Statements in our Annual Report on Form 10-K for the year ended December 31, 2021.

(3) Represents the annual option grant to purchase 40,000 shares of our common stock granted to each of our non-employee directors serving on June 17, 2021 under our non-employee director compensation policy, as further described below. Such option was granted on June 17, 2021, at an exercise price of $0.99 and a fair value per share of $0.7611.

(4) As of December 31, 2021, each director held outstanding options to purchase 109,750 shares with the exception of Dr. Huang who held 120,000 shares.

(5) Represents the sum of (i) the new director grant for Dr. Huang, who was appointed to our Board of Directors effective as of January 26, 2021 of 80,000 shares of our common stock granted on January 26, 2021 at an exercise price of $1.55 per share and a fair value per share of $1.15 plus (ii) the annual option grant to purchase 40,000 shares of our common stock granted to each of our non-employee directors serving as described above in footnote 3.

We maintain a non-employee director compensation policy (our "director compensation policy"), that became effective following our initial public offering. Under our non-employee director compensation policy as in effect for the year ended December 31, 2021, we provide cash compensation in the form of an annual retainer of $40,000 to each of our non-employee directors (our "Eligible Directors") other than the chair of the Board, to whom we provide a $70,000 cash retainer. We also pay an additional annual retainer of $20,000 to the chair of our Audit Committee, $10,000 to other Eligible Directors who serve on our Audit Committee, $12,000 to the chair of our Compensation Committee, $6,000 to other Eligible Directors who serve on our Compensation Committee, $8,000 to the chair of our Nominating and Corporate Governance Committee and $4,000 to other Eligible Directors who serve on our Nominating and Corporate Governance Committee. We have reimbursed and will continue to reimburse our non-employee directors for travel, lodging and other reasonable expenses incurred in attending meetings of our Board of Directors and committees of our Board of Directors.

Directors who are also employees do not receive cash or equity compensation for service on our Board of Directors in addition to the compensation payable for their service as our employees.

Pursuant to our director compensation policy, each Eligible Director who is first elected to our Board of Directors is granted an option to purchase shares of the Company's common stock on the date of his or her initial election to our Board of Directors.

In December 2020, the Board of Directors, upon the recommendation of the Compensation Committee, approved (i) an initial option grant of shares to any new Eligible Directors appointed to the Board in 2021 of 80,000 shares and (ii) an annual option grant to each Eligible Director re-elected at our annual meeting of stockholders in 2021 of 40,000 shares.

Each initial option granted to such Eligible Directors described above will vest and become exercisable with respect to one-third of the shares subject to the option on the first anniversary of the date of grant and the balance of the shares will vest and become exercisable in a series of 24 equal monthly installments thereafter, such that the option is fully vested on the third anniversary of the date of grant, subject to the Eligible Director continuing to provide services to us through such dates. Each annual option granted to such Eligible Directors described above will vest and become exercisable in 12 equal monthly installments such that the option will be fully vested on the first anniversary of the date of grant, or as of the date of the next annual meeting of the Company's stockholders, whichever occurs first and subject to the Eligible Director continuing to provide services to us through such dates. The term of each option granted to an Eligible Director is 10 years and, in general, may remain exercisable with respect to the then-vested shares for up to 12 months following the termination of such Eligible Director's continuous service. All awards granted under our director compensation policy will vest in full upon the closing of a change in control of the Company.

The options granted to our non-employee directors are granted under our 2019 Plan, the terms of which are described in more detail above under "Equity Compensation Plans—2019 Equity Incentive Plan."

PROPOSAL 5

RATIFICATION OF SELECTION OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

The Audit Committee has selected Ernst & Young LLP as the Company's independent registered public accounting firm for the fiscal year ending December 31, 2022 and has further directed that management submit the selection of independent registered public accounting firm for ratification by the stockholders at the annual meeting. Ernst & Young has audited the Company's financial statements since its incorporation in 2009. Representatives of Ernst & Young are expected to be present at the annual meeting. They will have an opportunity to make a statement if they so desire and will be available to respond to appropriate questions.

Neither the Company's Bylaws nor other governing documents or law require stockholder ratification of the selection of Ernst & Young as the Company's independent registered public accounting firm. However, the Audit Committee is submitting the selection of Ernst & Young 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.

The affirmative vote of the holders of a majority of the shares present in person or represented by proxy and entitled to vote at the annual meeting will be required to ratify the selection of Ernst & Young. Abstentions will be counted toward the tabulation of votes on proposals presented to the stockholders and will have the same effect as negative votes. Broker non-votes, if any, will have no effect.

Principal Accounting Fees and Services

The following table represents aggregate fees incurred by the Company for the fiscal years ended December 31, 2021 and December 31, 2020, by Ernst & Young LLP ("Ernst & Young"), the Company's principal accountant. All fees described below were pre-approved by the Audit Committee.

	Fiscal Year Ended	
	2021	2020
	(in thousands)	
Audit Fees(1)	$ 395	$ 305
Audit-related Fees	—	—
Tax Fees	—	—
All Other Fees	60	104
Total Fees	$ 455	$ 409

(1) Audit fees consist of fees incurred for professional services by Ernst & Young for audit and quarterly review of our financial statements and review of our registration statements on Form S-3 and Form S-8, and related services that are normally provided in connection with statutory and regulatory filings or engagements.

In connection with the audit of each of the 2021 and 2020 financial statements, the Company entered into engagement agreements with Ernst & Young, which sets forth the terms by which Ernst & Young will perform audit services for the Company. Such agreements are subject to alternative dispute resolution procedures.

Pre-Approval Policies and Procedures

The Audit Committee must pre-approve the audit and non-audit services rendered by the Company's independent registered public accounting firm.

THE BOARD OF DIRECTORS RECOMMENDS
A VOTE FOR PROPOSAL 5

PROPOSAL 6

APPROVAL OF THE 2022 EMPLOYEE STOCK PURCHASE PLAN

Our Board of Directors is asking our stockholders to approve the Regulus Therapeutics Inc. 2022 Employee Stock Purchase Plan (the "2022 ESPP"), at the Annual Meeting. The 2022 ESPP was approved by our Board on March 2, 2022, subject to approval by our stockholders.

Approval of the 2022 ESPP will allow us to provide our employees with the opportunity to acquire an ownership interest in the Company through their participation in the 2022 ESPP, thereby encouraging them to remain in our service and more closely aligning their interests with those of our stockholders.

We do not maintain any other employee stock purchase plans, except the Regulus Therapeutics Inc. 2012 Employee Stock Purchase Plan (the "2012 ESPP"). The 2012 ESPP will be terminated effective as of the approval of the 2022 ESPP by our stockholders (provided that any ongoing offerings under the 2012 ESPP as of such approval date will continue).

If this Proposal 6 is approved by our stockholders, the maximum number of shares of our common stock that may be issued under the 2022 ESPP (subject to adjustment for certain changes in our capitalization) will be 1,291,072 shares, which is the sum of (i) 291,072 shares of common stock that were available for issuance under the 2012 ESPP as of April 12, 2022 plus (ii) 1,000,000 new shares of common stock.

In addition, if this Proposal 6 is approved by our stockholders, the number of shares of common stock reserved for issuance under the 2022 ESPP will automatically increase on January 1 of each calendar year, beginning on January 1, 2023, and continuing through (and including) January 1, 2032, 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) 500,000 shares; provided that prior to the first day of any such calendar year, the 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 2022 ESPP terminate without having been exercised, the shares of common stock not purchased under such purchase rights will again become available for issuance under the 2022 ESPP.

As of April 12, 2022, a total of 145,981,180 shares of our common stock were outstanding. The 2022 ESPP became effective upon the date it was adopted by our Board, but no purchase rights may be exercised under the 2022 ESPP unless this Proposal 6 is approved by our stockholders.

Description of the 2022 Employee Stock Purchase Plan

The material features of the 2022 ESPP are described below. The following description of the 2022 ESPP is a summary only and is qualified in its entirety by reference to the complete text of the 2022 ESPP. Stockholders are urged to read the actual text of the 2022 ESPP in its entirety, which is attached to this Proxy Statement as Appendix B.

Purpose

The purpose of the 2022 ESPP is to provide a means by which our employees may be given an opportunity to purchase shares of our common stock, to assist us in retaining the services of our employees, to secure and retain the services of new employees and to provide incentives for such persons to exert maximum efforts for our success.

The 2022 ESPP permits us to grant purchase rights that are intended to qualify as options issued under an "employee stock purchase plan" (as defined in Section 423(b) of the Internal Revenue Code of 1986, as amended, or the Code) (under the "423 Component" of the 2022 ESPP), as well as purchase rights that are not intended to so qualify (under the "Non-423 Component" of the 2022 ESPP).

Administration

Our Compensation Committee will administer the 2022 ESPP, unless otherwise determined by our Board. Our Board also retains concurrent authority to administer the 2022 ESPP. Our Compensation Committee will also have the power to delegate to a subcommittee any of the administrative powers our Compensation Committee is authorized to exercise under the 2022 ESPP, and in such case, our Compensation Committee retains the authority to concurrently administer the 2022 ESPP with any such subcommittee. Our Compensation Committee, our Board and any such subcommittee are each considered to be a Plan Administrator for purposes of this Proposal 6. The Plan Administrator has the final power to construe and interpret both the 2022 ESPP and the rights granted under it. The Plan Administrator has the power, subject to the provisions of the 2022 ESPP, to determine how and when rights to purchase our common stock will be granted, the provisions of each offering of such rights (which need not be identical), and whether employees of any of our parent or subsidiary companies will be eligible to participate in the 2022 ESPP.

Stock Subject to 2022 ESPP

Subject to adjustment for certain changes in our capitalization, the maximum number of shares of our common stock that may be issued under the 2022 ESPP will be 1,291,072 shares, which is the sum of (i) 291,072 shares of common stock that were available for issuance under the 2012 ESPP as of April 12, 2022 plus (ii) 1,000,000 new shares of common stock. In addition, the number of shares of common stock reserved for issuance under the 2022 ESPP will automatically increase on January 1 of each calendar year, beginning on January 1, 2023, and continuing through (and including) January 1, 2032, 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) 500,000 shares; provided that prior to the first day of any such calendar year, the Board may determine that such increase will be less than the amount set forth in clauses (i) and (ii). If any rights granted under the 2022 ESPP terminate without being exercised in full, the shares of common stock not purchased under such rights will again become available for issuance under the 2022 ESPP. The shares of common stock purchasable under the 2022 ESPP will be shares of authorized but unissued or reacquired common stock, including shares repurchased by us on the open market.

Offerings

The 2022 ESPP will be implemented by offerings of rights to purchase our common stock to all eligible employees. The Plan Administrator will determine the duration of each offering period, provided that in no event may an offering period exceed 27 months. The Plan Administrator may establish separate offerings which vary in terms (although not inconsistent with the provisions of the 2022 ESPP or the requirements of applicable laws). Each offering period will have one or more purchase dates, as determined by the Plan Administrator prior to the commencement of the offering period. The Plan Administrator has the authority to alter the terms of an offering prior to the commencement of the offering period, including the duration of subsequent offering periods. When an eligible employee elects to join an offering period, he or she is granted a right to purchase shares of our common stock on each purchase date within the offering period. On the purchase date, all contributions collected from the participant are automatically applied to the purchase of our common stock, subject to certain limitations (which are described further below under “Eligibility”).

The Plan Administrator has the discretion to structure an offering so that if the fair market value of our common stock on the first trading day of a new purchase period within the offering period is less than or equal to the fair market value of our common stock on the first day of the offering period, then that offering will terminate immediately as of that first trading day, and the participants in such terminated offering will be automatically enrolled in a new offering beginning on the first trading day of such new purchase period.

Eligibility

Any individual who is employed by us (or by any of our parent or subsidiary companies if such company is designated by the Plan Administrator as eligible to participate in the 2022 ESPP) may participate in offerings

under the 2022 ESPP, provided that such individual has been employed by us (or our parent or subsidiary, if applicable) for such continuous period preceding the first day of the offering period as the Plan Administrator may require (except as the Plan Administrator may provide with respect to newly eligible employees as may be permitted or required by applicable law), but in no event may the required period of continuous employment be equal to or greater than two years. In addition, the Plan Administrator (unless prohibited by law) may provide that an employee will not be eligible to be granted purchase rights under the 2022 ESPP unless such employee is customarily employed for more than 20 hours per week and more than five months per calendar year. The Plan Administrator (unless prohibited by law) may also provide in any offering that certain of our employees who are "highly compensated" as defined in the Code are not eligible to participate in the 2022 ESPP. Furthermore, in the case of any offering under the Non-423 Component of the 2022 ESPP, an eligible employee may be excluded from participation in the 2022 ESPP if the Plan Administrator has determined that the participation of such eligible employee is not advisable or practical for any reason.

No employee will be eligible to participate in the 2022 ESPP if, immediately after the grant of purchase rights, the employee would own, directly or indirectly, stock possessing 5% or more of the total combined voting power or value of all classes of our stock or of any of our parent or subsidiary companies, including any stock which such employee may purchase under all outstanding purchase rights and options. In addition, no employee may purchase more than $25,000 worth of our common stock (determined based on the fair market value of the shares at the time such rights are granted) under all our employee stock purchase plans and any employee stock purchase plans of our parent or subsidiary companies for each calendar year during which such rights are outstanding.

As of April 12, 2022, we had approximately 23 employees who would be eligible to participate in offerings under the 2022 ESPP.

Participation in the 2022 ESPP

An eligible employee may enroll in the 2022 ESPP by delivering to us, within the time specified in the offering, an enrollment form authorizing contributions which may not exceed the maximum amount specified by the Plan Administrator (but which in no event may exceed 15% of such employee's earnings (as determined by the Plan Administrator with respect to each offering) during the offering period). Each participant will be granted a separate purchase right for each offering in which he or she participates. Unless an employee's participation is discontinued, his or her purchase right will be exercised automatically at the end of each purchase period at the applicable purchase price.

Purchase Price

The purchase price per share at which shares of our common stock are acquired pursuant to purchase rights on each purchase date during an offering period will not be less than the lower of (i) 85% of the fair market value of a share of our common stock on the first day of the offering period or (ii) 85% of the fair market value of a share of our common stock on the applicable purchase date.

As of April 12, 2022, the closing price of our common stock as reported on the Nasdaq Global Capital Market was $0.24 per share.

Payment of Purchase Price; Contributions

The purchase of shares during an offering period generally will be funded by a participant's payroll deductions accumulated during the offering period. If specifically provided in an offering, in addition to or instead of making contributions by payroll deductions, a participant may make contributions by cash, check or such other payment method specified by the Plan Administrator. A participant may change his or her rate of contributions, if and as permitted in the offering. All contributions made for a participant are credited to his or

her account under the 2022 ESPP and deposited with our general funds, except where applicable law requires that contributions be deposited with a third party. Unless otherwise specified in the offering or as required by applicable law, we will have no obligation to pay interest on contributions.

Purchase Limits

In connection with each offering made under the 2022 ESPP, the Plan Administrator may specify (i) a maximum number of shares of our common stock that may be purchased by any participant on any purchase date during such offering, (ii) a maximum aggregate number of shares of our common stock that may be purchased by all participants pursuant to such offering and/or (iii) a maximum aggregate number of shares of our common stock that may be purchased by all participants on any purchase date under such offering. If the aggregate number of shares of our common stock issuable upon exercise of purchase rights granted under the offering would exceed any such maximum aggregate number, in the absence of any action by then the Plan Administrator otherwise, a pro rata allocation of available shares of our common stock will be made in as nearly a uniform manner as will be practicable and equitable.

Withdrawal

Participants may withdraw from a given offering by delivering a withdrawal form to us and terminating their contributions. Such withdrawal may be elected at any time prior to the end of an offering, except as otherwise provided by the Plan Administrator. Upon such withdrawal, such employee's right to participate in that offering will terminate, and we will distribute as soon as practicable to the employee his or her accumulated but unused contributions without interest. However, an employee's withdrawal from an offering does not affect such employee's eligibility to participate in subsequent offerings under the 2022 ESPP.

Termination of Eligibility

Unless otherwise required by applicable law, a participant's outstanding purchase rights under any offering under the 2022 ESPP will terminate immediately if the participant either (i) is no longer employed by us or any of our parent or subsidiary companies (subject to any post-employment participation period required by law) or (ii) is otherwise no longer eligible to participate. In such event, we will distribute as soon as practicable to such individual his or her accumulated but unused contributions without interest.

Restrictions on Transfer

Rights granted under the 2022 ESPP are not transferable except by will, by the laws of descent and distribution, or if permitted by us, by a beneficiary designation. During a participant's lifetime, such rights may only be exercised by the participant.

Changes in Capitalization

In the event of certain changes in our capitalization, the Plan Administrator will appropriately and proportionately adjust: (i) the class(es) and maximum number of securities subject to the 2022 ESPP; (ii) the class(es) and number of securities subject to, and the purchase price applicable to outstanding purchase rights; (iii) the class(es) and number of securities that are the subject of any purchase limits under each ongoing offering and (iv) the class(es) and maximum number of securities by which the share reserve is to increase automatically each year.

Effect of Certain Corporate Transactions

In the event of a corporate transaction (as defined in the 2022 ESPP and described below), (i) any surviving or acquiring corporation (or its parent company) may assume or continue outstanding purchase rights granted

under the 2022 ESPP or may substitute similar rights (including a right to acquire the same consideration paid to the stockholders in the corporate transaction) for such outstanding purchase rights, or (ii) if any surviving or acquiring corporation (or its parent company) does not assume or continue such purchase rights or does not substitute similar rights for such purchase rights, then the participants' accumulated contributions will be used to purchase shares of our common stock within ten business days prior to the corporate transaction under such outstanding purchase rights, and such purchase rights will terminate immediately after such purchase.

For purposes of the 2022 ESPP, a corporate transaction generally will be deemed to occur in the event of the consummation of: (i) a sale or other disposition of all or substantially all of our consolidated assets; (ii) a sale or other disposition of more than 50% of our outstanding securities; (iii) a merger, consolidation or similar transaction following which we are not the surviving corporation; or (iv) a merger, consolidation or similar transaction following which we are the surviving corporation but the shares of our common stock outstanding immediately prior to such transaction are converted or exchanged into other property by virtue of such transaction.

Duration, Amendment, Suspension and Termination

The Plan Administrator may amend, suspend or terminate the 2022 ESPP at any time. However, except in regard to certain capitalization adjustments, any such amendment must be approved by our stockholders if such approval is required by applicable law or listing requirements.

Any outstanding purchase rights granted before an amendment, suspension or termination of the 2022 ESPP will not be materially impaired by any such amendment, suspension or termination, except (i) with the consent of the employee to whom such purchase rights were granted, (ii) as necessary to comply with applicable laws, listing requirements or governmental regulations (including Section 423 of the Code), or (iii) as necessary to obtain or maintain favorable tax, listing or regulatory treatment.

Notwithstanding anything in the 2022 ESPP or any offering to the contrary, the Plan Administrator will be entitled to: (i) establish the exchange ratio applicable to amounts withheld in a currency other than U.S. dollars; (ii) permit contributions in excess of the amount designated by a participant in order to adjust for mistakes in the processing of properly completed contribution elections; (iii) establish reasonable waiting and adjustment periods and/or accounting and crediting procedures to ensure that amounts applied toward the purchase of our common stock for each participant properly correspond with amounts withheld from the participant's contributions; (iv) amend such purchase rights or clarify any ambiguities regarding the terms of any offering to enable such purchase rights to qualify under and/or comply with Section 423 of the Code with respect to the 423 Component of the 2022 ESPP; and (v) establish other limitations or procedures as the Plan Administrator determines in its sole discretion advisable that are consistent with the 2022 ESPP. Any such actions by the Plan Administrator will not be considered to alter or impair any purchase rights granted under an offering as they are part of the initial terms of each offering and the purchase rights granted under each offering.

U.S. Federal Income Tax Consequences

The following is a summary of the principal United States federal income tax consequences to participants and us with respect to participation in the 2022 ESPP. This summary is not intended to be exhaustive and does not discuss the income tax laws of any local, state or foreign jurisdiction in which a participant may reside. The information is based upon current federal income tax rules and therefore is subject to change when those rules change. Because the tax consequences to any participant may depend on his or her particular situation, each participant should consult the participant's tax adviser regarding the federal, state, local, and other tax consequences of the grant or exercise of a purchase right or the sale or other disposition of common stock acquired under the 2022 ESPP. The 2022 ESPP is not qualified under the provisions of Section 401(a) of the Code and is not subject to any of the provisions of the Employee Retirement Income Security Act of 1974, as amended. Our ability to realize the benefit of any tax deductions described below depends on our generation of taxable income as well as the requirement of reasonableness and the satisfaction of our tax reporting obligations.

423 Component

Rights granted under the 423 Component of the 2022 ESPP are intended to qualify for favorable federal income tax treatment associated with rights granted under an employee stock purchase plan which qualifies under the provisions of Section 423 of the Code.

A participant will be taxed on amounts withheld for the purchase of shares of our common stock as if such amounts were actually received. Otherwise, under the 423 Component, no income will be taxable to a participant as a result of the granting or exercise of a purchase right until a sale or other disposition of the acquired shares. The taxation upon such sale or disposition will depend upon the holding period of the acquired shares.

Under the 423 Component, if the shares are sold or otherwise disposed of more than two years after the beginning of the offering period and more than one year after the shares are transferred to the participant, then the lesser of the following will be treated as ordinary income: (i) the excess of the fair market value of the shares at the time of such sale or disposition over the purchase price; or (ii) the excess of the fair market value of the shares as of the beginning of the offering period over the purchase price (determined as of the beginning of the offering period). Any further gain or any loss will be taxed as a long-term capital gain or loss.

Under the 423 Component, if the shares are sold or otherwise disposed of before the expiration of either of the holding periods described above, then the excess of the fair market value of the shares on the purchase date over the purchase price will be treated as ordinary income at the time of such sale or disposition. The balance of any gain will be treated as capital gain. Even if the shares are later sold or otherwise disposed of for less than its fair market value on the purchase date, the same amount of ordinary income is attributed to the participant, and a capital loss is recognized equal to the difference between the sales price and the fair market value of the shares on such purchase date. Any capital gain or loss will be short-term or long-term, depending on how long the shares have been held.

There are no federal income tax consequences to us by reason of the grant or exercise of rights under the 423 Component. We are entitled to a deduction to the extent amounts are taxed as ordinary income to a participant for shares sold or otherwise disposed of before the expiration of the holding periods described above (subject to the requirement of reasonableness and the satisfaction of tax reporting obligations).

Non-423 Component

Under the Non-423 Component, the excess of the fair market value of the shares on the purchase date over the purchase price will be treated as ordinary income at the time of such purchase. The amount of such ordinary income will be added to the participant's basis in the shares, and any additional gain or resulting loss recognized on the disposition of the shares after such basis adjustment will be a capital gain or loss. Any capital gain or loss will be short-term or long-term, depending on how long the shares have been held.

Under the Non-423 Component, we are entitled to a deduction in the year of purchase equal to the amount of ordinary income realized by a participant as a result of such purchase (subject to the requirement of reasonableness and the satisfaction of tax reporting obligations).

New Plan Benefits under 2022 ESPP

Participation in the 2022 ESPP is voluntary and each eligible employee will make his or her own decision regarding whether and to what extent to participate in the ESPP. As of April 12, 2022, no shares of our common stock have been purchased under the 2022 ESPP, and no shares of our common stock may be purchased under the 2022 ESPP unless this Proposal 6 is approved by our stockholders. In addition, the Plan Administrator has not granted any purchase rights under the 2022 ESPP that are conditioned on stockholder approval of this Proposal 6. Accordingly, the benefits or amounts that will be received by or allocated to our individual executive

officers or other employees or groups of officers or other employees under the 2022 ESPP, as well as the benefits or amounts that would have been received by or allocated to our executive officers and other employees for fiscal year 2021 if the ESPP had been in effect, are not determinable. Our non-employee directors are not eligible to participate in the 2022 ESPP.

Vote Required

Approval of this proposal requires the vote of the holders of a majority of the shares present in person or represented by proxy and entitled to vote on this matter at the Annual Meeting. Abstentions will be counted toward a quorum for Proposal 6, and will have the same effect as "Against" votes. Broker non-votes will have no effect.

THE BOARD OF DIRECTORS RECOMMENDS
A VOTE FOR PROPOSAL 6

PROPOSAL 7

APPROVAL OF AN ADJOURNMENT OF THE ANNUAL MEETING, IF NECESSARY, TO SOLICIT ADDITIONAL PROXIES

General

If the Annual Meeting is convened and a quorum is present, but there are not sufficient votes to approve Proposal 2 or Proposal 6, or if there are insufficient votes to constitute a quorum, our proxy holders may move to adjourn the Annual Meeting at that time in order to enable the Board to solicit additional proxies.

In this proposal, we are asking our stockholders to authorize the holder of any proxy solicited by the Board to vote in favor of adjourning the Annual Meeting to another time and place, if necessary or appropriate (as determined in good faith by the Board), to solicit additional proxies in the event there are not sufficient votes to approve Proposal 2 or Proposal 6. If our stockholders approve this proposal, we could adjourn the Annual Meeting and any adjourned or postponed session of the Annual Meeting and use the additional time to solicit additional proxies, including the solicitation of proxies from our stockholders that have previously voted. Among other things, approval of this proposal could mean that, even if we had received proxies representing a sufficient number of votes to defeat Proposal 2 or Proposal 6, we could adjourn the Annual Meeting without a vote on such proposal and seek to convince our stockholders to change their votes in favor of such proposal.

If it is necessary or appropriate (as determined in good faith by the Board) to adjourn the Annual Meeting, no notice of the adjourned meeting is required to be given to our stockholders, other than an announcement at the Annual Meeting of the time and place to which the Annual Meeting is adjourned, so long as the meeting is adjourned for 30 days or less and no new record date is fixed for the adjourned meeting. At the adjourned meeting, we may transact any business which might have been transacted at the original meeting.

Vote Required

Approval of this proposal requires the affirmative vote of a majority of the shares represented at the Annual Meeting. Abstentions will have the same effect as an “against” vote on this proposal. Broker non-votes, if any, will have no effect.

THE BOARD OF DIRECTORS RECOMMENDS
A VOTE FOR PROPOSAL 7

EXECUTIVE OFFICERS

The following table sets forth our current executive officers, their ages, and the positions held by each such person with the Company:

Name	Age	Position Held With the Company
Joseph P. Hagan	53	President and Chief Executive Officer
Christopher Aker	61	Senior Vice President and General Counsel
Cris Calsada	52	Chief Financial Officer
Denis Drygin, Ph.D.	49	Chief Scientific Officer

Mr. Hagan's biographical information is set forth above under Proposal 1.

Christopher Aker has served as our Senior Vice President and General Counsel since January 2019, and before that served as our Senior Director, Legal Affairs from February 2011 to January 2019. Prior to joining us, Mr. Aker served as the Senior Director, Administration and Senior Corporate Counsel for Phenomix Corporation ("Phenomix"), a privately-held biopharmaceutical company, and was responsible for operational and legal oversight. Prior to Phenomix, Mr. Aker was Senior Corporate Counsel at SUGEN, Inc. ("SUGEN"), a wholly-owned subsidiary of Pharmacia, until its acquisition by Pfizer Inc. Prior to SUGEN, Mr. Aker was in private practice with various law firms. Mr. Aker received his B.A. in International Relations from the University of California, Davis and his J.D. from Santa Clara University.

Cris Calsada joined Regulus in August 2019 and currently serves as our Chief Financial Officer. Prior to joining us, she served as Chief Financial Officer for Sanifit Therapeutics, S.A. ("Sanifit") from December 2017 to August 2019. Prior to her employment with Sanifit, Ms. Calsada was self-employed as a finance consultant to various life sciences companies. From 2004 until its acquisition in 2015, she served in positions of increasing responsibility with Ambrx, Inc. ("Ambrx"), most recently serving as its Chief Operating Officer and Vice President of Finance. Prior to Ambrx, she worked for Sony Online Entertainment as its Executive Director of Finance and Controller. Earlier in her career, she practiced as a certified public accountant. Ms. Calsada received a B.S. in Business Administration with emphasis in Accounting from San Diego State University and an M.B.A. from the University of Southern California Marshall School of Business.

Denis Drygin, Ph.D. joined Regulus in August 2020 and currently serves as our Chief Scientific Officer. Prior to joining Regulus, from April 2013 Dr. Drygin served as Vice President of Research & Development for Pimera Inc. ("Pimera"), a privately held biopharmaceutical company of which Dr. Drygin is a Founder. Before Pimera, from May 2005 Dr. Drygin was with Cylene Pharmaceuticals, Inc., most recently serving as Vice President of Biology. Dr. Drygin led discovery and/or development of multiple therapeutics including first selective inhibitor of CK2 kinase Silmitasertib (CX-4945), first selective inhibitor of RNA Polymerase I transcription (Pol I) CX-5461, as well as second generation Pol I inhibitor PMR-116. Dr. Drygin received a B.S. and M.S. in Chemistry from Moscow State University, an M.S. and Ph.D. in Molecular and Cellular Biology from University of Massachusetts at Amherst and Post-Doctoral training in Pharmacology and Toxicology from Ionis Pharmaceuticals Inc.

SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT

The following table sets forth certain information regarding the ownership of the Company's common stock as of March 31, 2022 by: (i) each of our directors; (ii) each of our Named Executive Officers as defined above under the heading "Executive Compensation"; (iii) each person known by us to beneficially own more than 5% of our common stock and (iv) all of our current executive officers and directors as a group.

Beneficial ownership is determined in accordance with the rules of the SEC and includes voting and investment power with respect to the securities. This table is based upon information supplied by officers, directors and principal stockholders and Schedules 13D and 13G filed with the SEC. Except as indicated by footnote, and subject to applicable community property laws, we believe the persons named in the table have sole voting and investment power with respect to all shares of common stock shown as beneficially owned by them.

Percentage of beneficial ownership is based on 145,981,180 shares of common stock outstanding as of March 31, 2022. The number of shares of common stock used to calculate the percentage ownership of each listed person includes the shares of common stock underlying options held by such persons that are exercisable, or restricted stock units which will vest, within 60 days following March 31, 2022. Unless otherwise indicated, the address for the persons and entities listed in the table below is c/o Regulus Therapeutics Inc., 4224 Campus Point Court, Suite 210, San Diego, CA 92121.

	Beneficial Ownership	
Beneficial Owner	**Number of Shares**	**Percent of Total**
Greater than 5% Stockholders		
Federated Hermes Kaufmann Funds(1)	29,050,755	19.90%
4000 Ericsson Drive Warrendale, PA 15086		
Entities affiliated with New Enterprise Associates, Inc.(2)	14,614,285	9.99%
1954 Greenspring Dr., Suite 600 Timonium Maryland 21093		
Entities affiliated with Sarissa Capital Management LP(3)	12,166,942	7.78%
c/o Sarissa Capital Management LP 660 Steamboat Road Greenwich, CT 06830		
Entities affiliated with BVF Partners, L.P.(4)	11,431,027	7.26%
1 Sansome Street, 30th Floor San Francisco, California 94104		
Entities affiliated with RS Investments(5)	8,262,472	5.44%
One Bush Street, Suite 400 San Francisco, CA 94104		
Named Executive Officers and Directors		
Christopher Aker(6)	508,394	*
David Baltimore, Ph.D. (7)	132,020	*
Cris Calsada(8)	381,875	*
Kathryn J. Collier(9)	133,835	*
Joseph P. Hagan(10)	2,124,142	1.46%
Alice S. Huang, Ph.D.(11)	72,221	*
Jake R. Nunn(12)	106,416	*
Stelios Papadopoulos, Ph.D.(13)	6,980,181	4.78%
William H. Rastetter, Ph.D.(14)	815,826	*
Hugh Rosen, M.D., Ph.D. (15)	124,133	*
Simos Simeonidis, Ph.D. (16)	106,416	*
Pascale Witz, MBA, MSc(17)	318,787	*
All current executive officers and directors as a group (13 persons)(18)	12,108,829	8.29%

* Less than one percent.

(1) Consists of an aggregate of 29,048,265 shares of common stock and 2,490 shares of common stock issuable upon the conversion of our Class A-4 convertible preferred stock held collectively by (i) Federated Hermes

Kaufmann Small Cap Fund, a portfolio of Federated Hermes Equity Funds, (ii) Federated Hermes Kaufmann Fund, a portfolio of Federated Hermes Equity Funds, and (iii) Federated Hermes Kaufmann Fund II, a portfolio of Federated Hermes Insurance Series, and, collectively, the Federated Hermes Kaufmann Funds. The number of shares beneficially owned by the Federated Hermes Kaufmann Funds in the aggregate is limited by beneficial ownership limitations applicable to shares of Class A-4 convertible preferred stock held by the Federated Hermes Kaufmann Funds, which limit the number of shares the Federated Hermes Kaufmann Funds can beneficially own to a maximum of 19.90% of our outstanding common stock. As a result of such limitations, the number of shares beneficially owned does not include up to an aggregate of 26,504,800 shares of common stock issuable upon the conversion of our Class A-4 convertible preferred stock held by the Federated Hermes Kaufmann Funds.

(2) Consists of 14,451,147 shares of common stock and 163,138 shares of common stock issuable upon the exercise of warrants to purchase common stock, collectively, the GEO Shares, held by Growth Equity Opportunities Fund V, LLC, or GEO. The number of shares beneficially owned by GEO in the aggregate is limited by beneficial ownership limitations applicable to the warrants and shares of Class A-1, Class A-2, Class A-3 and Class A-4 convertible preferred stock held by GEO, which limit the number of shares the NEA Reporting Persons can beneficially own to a maximum of 9.99% of our outstanding common stock. As a result of such limitations, the number of shares beneficially owned does not include up to an aggregate of 17,788,820 shares of common stock issuable upon the exercise of warrants and 2,567,000 shares of common stock issuable upon the conversion of our Class A-1 convertible preferred stock, 9,009,000 shares of common stock issuable upon the conversion of Class A-2 convertible preferred stock, 2,587,070 shares of common stock issuable upon the conversion of Class A-3 convertible preferred stock and 10,749,910 shares of common stock issuable upon the conversion of our Class A-4 convertible preferred stock held by GEO.

(3) Consists of an aggregate of 1,851,851 shares of common stock, 6,083,471 shares of common stock issuable upon the exercise of warrants to purchase common stock and 4,231,620 shares of common stock issuable upon the conversion of Class A-2 convertible preferred stock held collectively by Sarissa Capital Offshore Master Fund LP, Sarissa Capital Catapult Fund LLC, and Sarissa Capital Hawkeye Fund LP.

(4) Consists of an aggregate of 11,431,027 shares of common stock issuable upon the exercise of warrants to purchase common stock held collectively by (i) Biotechnology Value Fund, LP, (ii) Biotechnology Value Fund II, LP, (iii) Biotechnology Value Trading Fund OS, L.P. and (v) MSI BVF SPV, L.L.C.

(5) Consists of an aggregate of 2,233,531 shares of common stock and 6,028,941 shares of common stock issuable upon the exercise of warrants to purchase common stock held collectively by USAA Science & Technology Fund and Victory RS Science and Technology Fund, a Series of Victory Portfolios.

(6) Consists of 41,207 shares of common stock held by Mr. Aker and 467,187 shares of common stock that Mr. Aker has the right to acquire from us within 60 days of March 31, 2022 pursuant to the exercise of stock options.

(7) Consists of 25,604 shares of common stock held by Dr. Baltimore and 106,416 shares of common stock that Dr. Baltimore has the right to acquire from us within 60 days of March 31, 2022 pursuant to the exercise of stock options.

(8) Consists of 381,875 shares of common stock that Ms. Calsada has the right to acquire from us within 60 days of March 31, 2022 pursuant to the exercise of stock options.

(9) Consists of 27,419 shares of common stock held by Ms. Collier and 106,416 shares of common stock that Ms. Collier has the right to acquire from us within 60 days of March 31, 2022 pursuant to the exercise of stock options.

(10) Consists of (i) 417,006 shares of common stock held by Joseph P. Hagan and 1,568,332 shares of common stock that Mr. Hagan has the right to acquire from us within 60 days of March 31, 2022 pursuant to the exercise of stock options and (ii) 138,804 shares of common stock issuable upon the exercise of warrants held by Pacific Premier Trust Custodian FBO Joseph Hagan IRA, or Pacific Premier. Mr. Hagan is the economic beneficiary and may be deemed to be the beneficial owner of the shares held by Pacific Premier.

(11) Consists of 72,221 shares of common stock that Dr. Huang has the right to acquire from us within 60 days of March 31, 2022 pursuant to the exercise of stock options.

(12) Consists of 106,416 shares of common stock that Mr. Nunn has the right to acquire from us within 60 days of March 31, 2022 pursuant to the exercise of stock options.

(13) Consists of 5,061,929 shares of common stock, 1,811,836 shares of common stock issuable upon the exercise of warrants to purchase common stock and 106,416 shares of common stock that Dr. Papadopoulos has the right to acquire from us within 60 days of March 31, 2022 pursuant to the exercise of stock options.

(14) Consists of 390,581 shares of common stock, 318,829 shares of common stock issuable upon the exercise of warrants to purchase common stock, and 106,416 shares of common stock that Dr. Rastetter has the right to acquire from us within 60 days of March 31, 2022 pursuant to the exercise of stock options held by The Rastetter Family Trust, or the Rastetter Trust. Dr. Rastetter is trustee of the Rastetter Trust and may be deemed to be the beneficial owner of the shares held by the Rastetter trust.

(15) Consists of 17,717 shares of common stock held by Dr. Rosen and 106,416 shares of common stock that Dr. Rosen has the right to acquire from us within 60 days of March 31, 2022 pursuant to the exercise of stock options.

(16) Consists of 106,416 shares of common stock that Dr. Simeonidis has the right to acquire from us within 60 days of March 31, 2022 pursuant to the exercise of stock options.

(17) Consists of 47,341 shares of common stock, 97,330 shares of common stock issuable upon the exercise of warrants to purchase common stock, 67,700 shares of common stock issuable upon the conversion of Class A-2 preferred stock held by Pascale Witz and 106,416 shares of common stock that Ms. Witz has the right to acquire from us within 60 days of March 31, 2022 pursuant to the exercise of stock options.

(18) Includes all shares described in notes (6) through (17) above. Also, represents 100,000 shares of common stock and 204,583 shares of common stock that one other executive officer has the right to acquire from us within 60 days of March 31, 2022 pursuant to the exercise of stock options.

Equity Compensation Plan Information

The following table provides information as of December 31, 2021, with respect to shares of our common stock that may be issued under our existing equity compensation plans:

Plan Category	(a) Number of securities to be issued upon exercise of outstanding options, awards, warrants and rights	(b) Weighted-average exercise price of outstanding options, awards, warrants and rights	(c) Number of securities remaining available for future issuance under equity compensation plans (excluding securities reflected in column (a))
Equity compensation plans approved by stockholders:			
2009 Equity Incentive Plan	864(1)	$ 31.92	—
2012 Equity Incentive Plan	164,713(1)	$ 6.66	—
2019 Equity Incentive Plan	8,696,308(2)	$ 1.07	2,164,112
2012 Employee Stock Purchase Plan	—	—	259,402
Equity compensation plans not approved by stockholders:			
2021 Inducement Plan	200,000(1)	$ 0.36	1,800,000

(1) All shares issuable upon exercise of options.

(2) Consists of 8,295,808 shares issuable upon exercise of options and 400,500 shares issuable upon settlement of restricted stock units.

TRANSACTIONS WITH RELATED PERSONS

We have adopted a written related-person transactions policy that sets forth our policies and procedures regarding the identification, review, consideration, approval and oversight of "related-person transactions." A "related-person transaction" is a past, present or future 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 the lesser of $120,000 or 1% of the average of our total assets at year-end of the last two completed fiscal years.

Transactions involving compensation for services provided to us by an employee, consultant or director are not considered related-person transactions under this policy. A "related person," as determined since the beginning of our last fiscal year, is any executive officer, director or a holder of more than five percent of our common stock, including any of their immediate family members and any entity owned or controlled by such persons.

The policy imposes an affirmative duty upon each director and executive officer to identify any transaction involving them, their affiliates or immediate family members that may be considered a related party transaction before such person engages in the transaction. Under the policy, where a transaction has been identified as a related-person transaction, management must present information regarding the proposed related-person transaction to our audit committee (or, where review by our audit committee would be inappropriate, to another independent body of our board of directors) for review. The presentation must include a description of, among other things, the material facts, the direct and indirect interests of the related persons, the benefits of the transaction to us and whether any alternative transactions are available. In considering related-person transactions, our audit committee or other independent body of our board of directors takes into account the relevant available facts and circumstances including, but not limited to:

- the risks, costs and benefits to us of the transaction;
- the impact on a director's independence in the event the related person is a director, immediate family member of a director or an entity with which a director is affiliated;
- the terms of the transaction;
- the availability of other sources for comparable services or products; and
- the terms available to or from, as the case may be, unrelated third parties or to or from our employees generally.

In the event a director has an interest in the proposed transaction, the director must recuse himself or herself from the deliberations and approval. Our policy requires that, in reviewing a related party transaction, our audit committee must consider, in light of known circumstances, and determine in the good faith exercise of its discretion whether the transaction is in, or is not inconsistent with, the best interests of us and our stockholders.

We describe below transactions and series of similar transactions, since January 1, 2020 with respect to which we were a party, will be a party, or otherwise benefited, in which:

- the amounts involved exceeded or will exceed the lesser of $120,000 or 1% of the average of our total assets at year end of the last two completed fiscal years; and
- a director, executive officer, holder of more than 5% of our common stock or any member of their immediate family had or will have a direct or indirect material interest.

We also describe below certain other transactions with our directors, executive officers and stockholders. We believe that 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 would be paid or received, as applicable, in arm's-length transactions.

Private Placement Financing Transaction

On December 1, 2020, we entered into a Securities Purchase Agreement (the "2020 Purchase Agreement") with certain institutional and other accredited investors, pursuant to which we agreed to sell and issue shares of common stock, shares of our newly designated non-voting convertible preferred stock, and warrants to purchase common stock (the "2020 Private Placement").

In December 2020, we completed the closing of the 2020 Private Placement (the "2020 Closing") pursuant to which we sold and issued (i) 24,341,607 shares of common stock and accompanying warrants to purchase up to an aggregate of 18,256,204 shares of common stock at a combined purchase price of $0.7464 per share (the combined purchase price for officers and directors of the Company was $0.7551), and (ii) 272,970 shares of non-voting Class A-3 convertible preferred stock, in lieu of shares of common stock, at a price of $6.22 per share, and accompanying warrants to purchase an aggregate of 2,047,276 shares of common stock at a price of $0.125 for each share of common stock underlying such warrants. Each share of non-voting Class A-3 convertible preferred stock is convertible into 10 shares of common stock, subject to certain beneficial ownership conversion limitations. The warrants are exercisable for a period of five years following the date of issuance and have an exercise price of $0.7464 per share, subject to proportional adjustments in the event of stock splits or combinations or similar events.

The participants in the 2020 Private Placement included the following executive officers, directors and holders of more than five percent of our common stock or entities affiliated with them. The following table sets forth the aggregate number of shares of common stock, Class A-3 convertible preferred stock and warrants to purchase common stock issued to these related parties in the 2020 Closing. The aggregate shares and warrants set forth below reflect the number issued at the time of the 2020 Closing and do not reflect any subsequent conversions:

Name of Related Person	Common Stock Issued in the 2020 Closing	Warrants Issued in the 2020 Closing	Class A-3 Convertible Preferred Stock Issued in the 2020 Closing	Aggregate Purchase Price of Common Stock, Warrants and Preferred Stock Purchased in the Private Placement
Entities affiliated with New Enterprise Associates, Inc.(1)	4,398,602	5,239,254	258,707	$ 4,999,994.73
Entities affiliated with BVF Partners, L.P.	3,233,577	2,532,155	14,263	$ 2,416,520.13
Stelios Papadopoulos, Ph.D.				
Chair of the Board	793,528	595,146	—	$ 574,395.24
Joseph P. Hagan(2)				
President, Chief Executive Officer and Director	39,680	29,760	—	$ 28,722.37

(1) Jake R. Nunn, a member of our Board of Directors is currently a venture advisor at NEA.
(2) Securities purchased or to be purchased through an affiliated investment entity.

On November 24, 2021, we entered into a Securities Purchase Agreement (the "2021 Purchase Agreement") with certain institutional and other accredited investors, pursuant to which we agreed to sell and issue shares of common stock and shares of our newly designated non-voting convertible preferred stock (the "2021 Private Placement").

In November 2021, we completed the closing of the 2021 Private Placement (the "2021 Closing") pursuant to which we sold and issued (i) 58,923,352 shares of common stock at a purchase price of $0.36 per share, and (ii) 3,725,720 shares of non-voting Class A-4 convertible preferred stock, in lieu of shares of common stock, at a price of $3.60 per share. Each share of non-voting Class A-4 convertible preferred stock is convertible into 10 shares of common stock, subject to certain beneficial ownership conversion limitations.

The participants in the 2021 Private Placement included the following executive officers, directors and holders of more than five percent of our common stock or entities affiliated with them. The following table sets forth the aggregate number of shares of common stock, Class A-4 convertible preferred stock and warrants to purchase common stock issued to these related parties in the 2021 Closing. The aggregate shares and warrants set forth below reflect the number issued at the time of the 2021 Closing and do not reflect any subsequent conversions:

Name of Related Person	Common Stock Issued in the 2021 Closing	Class A-4 Convertible Preferred Stock Issued in the 2021 Closing	Aggregate Purchase Price of Common Stock and Preferred Stock Purchased in the Private Placement
Federated Hermes Kaufmann Funds	29,048,265	2,650,729	$ 10,411,200.00
Entities affiliated with New Enterprise Associates, Inc.(1)	8,000,090	1,074,991	$ 6,750,000.00
Stelios Papadopoulos, Ph.D.			
Chair of the Board	2,222,222	—	$ 799,999.92

(1) Jake R. Nunn, a member of our Board of Directors is currently a venture advisor at NEA.

Alliance and Collaboration Agreements

Sanofi

In February 2014, we amended and restated our 2012 amended and restated license and collaboration agreement with Sanofi, a greater than 5% stockholder of the Company, extending our strategic alliance with Sanofi. Aventisub LLC (formerly Aventis Holdings Inc.) concurrently made a $10.0 million investment in our common stock at a purchase price of $7.67 per share, representing the average of the daily volume weighted average price per share of our common stock during the 30 trading days ending on the date immediately preceding the date of the investment. In November 2018, we entered into an amendment to the 2014 Sanofi Amendment with Sanofi to modify the parties' rights and obligations with respect to our miR-21 programs, including our RG-012 program (the "2018 Sanofi Amendment"). Under the terms of the 2018 Sanofi Amendment, we have granted Sanofi a worldwide, royalty-free, fee-bearing, exclusive license, with the right to grant sublicenses, under our know-how and patents to develop and commercialize miR-21 compounds and products for all indications, including Alport Syndrome. Sanofi will control and will assume all responsibilities and obligations for developing and commercializing each of our miR-21 programs, including our obligations regarding the administration and expense of clinical trials and all other costs, including in-license royalties and other in-license payments, related to our miR-21 programs. Under the terms of the 2018 Sanofi Amendment, we have assigned to Sanofi certain agreements and all materials directed to miR-21 or to any miR-21 compound or product and are required to provide reasonable technical assistance to Sanofi for a period of 24 months after the date of the 2018 Sanofi Amendment. Under the terms of the 2018 Sanofi Amendment, we are eligible to receive approximately $6.8 million in upfront payments for the license and for miR-21 program-related materials (collectively, the "Upfront Amendment Payments"). We are also eligible to receive up to $40.0 million in development milestone payments. In addition, Sanofi has agreed to reimburse us for certain out-of-pocket transition activities and assume our upstream license royalty obligations. We and Sanofi also agreed to a general release of claims against each other for any claims that arose at any time prior to the date of the 2018 Sanofi Amendment, or that thereafter could arise based on anything that occurred prior to the date of the 2018 Sanofi Amendment. In November 2018, we received $2.5 million of the approximately $6.8 million in Upfront Amendment Payments under the 2018 Sanofi Amendment. In March 2019, we received $1.8 million in payment of materials purchased by Sanofi from us related to the RG-012 program. In October 2020 we received an additional $5 million milestone related to an interim enrollment milestone, an additional $4 million milestone upon the completion of the transfer and verification of additional RG-012 development program materials and an additional $1 million payment in exchange for the transfer of such materials. We have received approximately

$21.8 million in upfront payments, payment for program-related materials and interim enrollment milestones. We are also eligible to receive a $25.0 million development milestone payment.

Indemnification Agreements

We have entered into separate indemnification agreements with our directors and executive officers, in addition to the indemnification provided for in our bylaws. These agreements, among other things, require us to indemnify our directors and executive officers for certain expenses, including attorneys' fees, judgments, fines and settlement amounts incurred by a director or executive officer in any action or proceeding arising out of his or her services as one of our directors or executive officers or any other company or enterprise to which the person provides services at our request. We believe that these indemnification agreements, together with the provisions in our bylaws, are necessary to attract and retain qualified persons as directors and officers.

HOUSEHOLDING OF PROXY MATERIALS

The SEC has adopted rules that permit companies and intermediaries (e.g., brokers) to satisfy the delivery requirements for Notices of Internet Availability of Proxy Materials or other annual meeting materials with respect to two or more stockholders sharing the same address by delivering a single Notice of Internet Availability of Proxy Materials or other annual meeting materials. This process, which is commonly referred to as "householding," potentially means extra convenience for stockholders and cost savings for companies.

This year, a number of brokers with account holders who are Regulus Therapeutics Inc. stockholders will be "householding" the Company's proxy materials. 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. Once you have received notice from your broker that they will be "householding" communications to your address, "householding" will continue until you are notified otherwise or until you revoke your consent. If, at any time, you no longer wish to participate in "householding" and would prefer to receive a separate Notice of Internet Availability of Proxy Materials, please notify your broker or Regulus Therapeutics Inc. Direct your written request to Regulus Therapeutics Inc., Attn: Corporate Secretary, 4224 Campus Point Court, Suite 210, San Diego, California 92121, or contact our Corporate Secretary at Regulus Therapeutics Inc. by telephone at (858) 202-6300. 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 of Directors 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, it is the intention of the persons named in the proxy to vote on such matters in accordance with their best judgment.

By Order of the Board of Directors

Christopher Aker
Senior Vice President, General Counsel and Secretary

April 27, 2022

A copy of the Company's Annual Report to the Securities and Exchange Commission on Form 10-K for the fiscal year ended December 31, 2021 is available without charge upon written request to: Corporate Secretary, Regulus Therapeutics Inc., 4224 Campus Point Court, Suite 210, San Diego, California 92121.

APPENDIX A

CERTIFICATE OF AMENDMENT OF THE
AMENDED AND RESTATED CERTIFICATE OF INCORPORATION
OF
REGULUS THERAPEUTICS INC.

REGULUS THERAPEUTICS INC. (the "***Company***"), a corporation organized and existing under and by virtue of the General Corporation Law of the State of Delaware (the "***DGCL***"), does hereby certify that:

FIRST: The name of the Company is Regulus Therapeutics Inc.

SECOND: The date on which the Company's original Certificate of Incorporation was filed with the Secretary of State of the State of Delaware is January 2, 2009.

THIRD: The Board of Directors of the Company (the "***Board***"), acting in accordance with the provisions of Sections 141 and 242 of the DGCL, adopted resolutions amending the Company's Amended and Restated Certificate of Incorporation, as amended (the "***Certificate of Incorporation***"), as follows:

Effective as of the effective time of 5:00 p.m., Eastern Time, on [DATE][1] (the "***Effective Time***"), each [five (5), six (6), seven (7), eight (8), nine (9), ten (10). . .twenty (20)][2] shares of the Company's Common Stock, par value $0.001 per share ("***Common Stock***"), issued and outstanding immediately prior to the Effective Time shall, automatically and without any action on the part of the Company or the respective holders thereof, be combined into one (1) share of Common Stock without increasing or decreasing the par value of each share of Common Stock (the "***Reverse Split***"); provided, however, no fractional shares of Common Stock shall be issued as a result of the Reverse Split and, in lieu thereof, upon receipt after the Effective Time by the exchange agent selected by the Company of a properly completed and duly executed transmittal letter and, where shares are held in certificated form, the surrender of the stock certificate(s) formerly representing shares of pre-Reverse Split Common Stock, any stockholder who would otherwise be entitled to a fractional share of post-Reverse Split Common Stock as a result of the Reverse Split, following the Effective Time (after taking into account all fractional shares of post-Reverse Split Common Stock otherwise issuable to such stockholder), shall be entitled to receive a cash payment (without interest) equal to the fractional share of post-Reverse Split Common Stock to which such stockholder would otherwise be entitled multiplied by the average of the closing sales prices of a share of the Company's Common Stock (as adjusted to give effect to the Reverse Split) on The Nasdaq Stock Market during regular trading hours for the five (5) consecutive trading days immediately preceding the date this Certificate of Amendment is filed with the Secretary of State of the State of Delaware. Each stock certificate that, immediately prior to the Effective Time, represented shares of pre-Reverse Split Common Stock shall, from and after the Effective Time, automatically and without any action on the part of the Company or the respective holders thereof, represent that number of whole shares of post-Reverse Split Common Stock into which the shares of pre-Reverse Split Common Stock represented by such certificate shall have been combined (as well as the right to receive cash in lieu of any fractional shares of post-Reverse Split Common Stock as set forth above; provided, however, that each holder of record of a certificate that represented shares of pre-Reverse Split

1 Insert next business day after filing with the Secretary of State of the State of Delaware.

2 These amendments approve the combination of any whole number of shares of the Company's Common Stock between and including five (5) and twenty (20) into one (1) share of the Company's Common Stock. By these amendments, the stockholders would approve each of the alternate amendments proposed by the Company's Board of Directors. If the reverse stock split proposal is approved by stockholders, the Certificate of Amendment filed with the Secretary of State of the State of Delaware will include only that reverse stock split ratio determined by the Company's Board of Directors to be in the best interests of the Company and its stockholders. The other amendments will be abandoned pursuant to Section 242(c) of the General Corporation Law of the State of Delaware. The Company's Board of Directors may also elect not to effect any reverse stock split, in which case all proposed alternate amendments will be abandoned.

Common Stock shall receive, upon surrender of such certificate, a new certificate representing the number of whole shares of post-Reverse Split Common Stock into which the shares of pre-Reverse Split Common Stock represented by such certificate shall have been combined pursuant to the Reverse Split, as well as any cash in lieu of fractional shares of post-Reverse Split Common Stock to which such holder may be entitled as set forth above. The Reverse Split shall be effected on a record holder-by-record holder basis, such that any fractional shares of post-Reverse Split Common Stock resulting from the Reverse Split and held by a single record holder shall be aggregated.

Paragraph A of Article IV of the Certificate of Incorporation is hereby amended and restated to read in its entirety as follows:

"A. The Company is authorized to issue two classes of stock to be designated, respectively, "Common Stock" and "Preferred Stock." The total number of shares which the Company is authorized to issue is 310,000,000 shares. 300,000,000 shares shall be Common Stock, each having a par value of $0.001. 10,000,000 shares shall be Preferred Stock, each having a par value of $0.001."

FOURTH: The foregoing amendment to the Certificate of Incorporation was duly approved by the Board.

FIFTH: Thereafter, pursuant to a resolution of the Board, this Certificate of Amendment was submitted to the stockholders of the Company for their approval, and was duly adopted in accordance with the provisions of Section 242 of the DGCL.

SIXTH: This amendment to the Certificate of Incorporation shall be effective on and as of the effective time of 5:00 p.m., Eastern Time, on [DATE][3].

[SIGNATURE PAGE FOLLOWS]

3 Insert next business day after filing with the Secretary of State of the State of Delaware.

IN WITNESS WHEREOF, Regulus Therapeutics Inc. has caused this Certificate of Amendment to be executed by its President and Chief Executive Officer as of [ ], 2022.

By: _____
Joseph Hagan
President and Chief Executive

APPENDIX B

REGULUS THERAPEUTICS INC.

2022 EMPLOYEE STOCK PURCHASE PLAN

ADOPTED BY THE BOARD OF DIRECTORS: MARCH 2, 2022
APPROVED BY THE STOCKHOLDERS: [JUNE 9, 2022]

1. GENERAL; PURPOSE.

(a) The Plan is adopted by the Company as the successor to and replacement of the Regulus Therapeutics Inc. 2012 Employee Stock Purchase Plan (the "***Prior Plan***"). Effective as of the approval of the Plan by the stockholders of the Company (the "***Effective Date***"), the Prior Plan shall be terminated. Notwithstanding the foregoing, ongoing Offerings under the Prior Plan on the Effective Date will continue.

(b) The Plan provides a means by which Eligible Employees of the Company and certain designated Related Corporations may be given an opportunity to purchase shares of Common Stock. The Plan permits the Company to grant a series of Purchase Rights to Eligible Employees under an Employee Stock Purchase Plan. In addition, the Plan permits the Company to grant a series of Purchase Rights to Eligible Employees that do not meet the requirements of an Employee Stock Purchase Plan.

(c) The Plan includes two components: a 423 Component and a Non-423 Component. The Company intends (but makes no undertaking or representation to maintain) the 423 Component to qualify as an Employee Stock Purchase Plan. The provisions of the 423 Component, accordingly, will be construed in a manner that is consistent with the requirements of Section 423 of the Code. Except as otherwise provided in the Plan or determined by the Board, the Non-423 Component will operate and be administered in the same manner as the 423 Component.

(d) The Company, by means of the Plan, seeks to retain the services of such Employees, to secure and retain the services of new Employees and to provide incentives for such persons to exert maximum efforts for the success of the Company and its Related Corporations.

2. ADMINISTRATION.

(a) The Board or the Committee will administer the Plan. References herein to the Board shall be deemed to refer to the Committee except where context dictates otherwise.

(b) The Board will have the power, subject to, and within the limitations of, the express provisions of the Plan:

(i) To determine how and when Purchase Rights will be granted and the provisions of each Offering (which need not be identical).

(ii) To designate from time to time (A) which Related Corporations of the Company will be eligible to participate in the Plan, (B) whether such Related Corporations will participate in the 423 Component or the Non-423 Component, and (C) to the extent that the Company makes separate Offerings under the 423 Component, in which Offering the Related Corporations in the 423 Component will participate.

(iii) To construe and interpret the Plan and Purchase Rights, and to establish, amend and revoke rules and regulations for its administration. The Board, in the exercise of this power, may correct any defect, omission or inconsistency in the Plan, in a manner and to the extent it deems necessary or expedient to make the Plan fully effective.

(iv) To settle all controversies regarding the Plan and Purchase Rights granted under the Plan.

(v) To suspend or terminate the Plan at any time as provided in Section 12.

(vi) To amend the Plan at any time as provided in Section 12.

(vii) Generally, to exercise such powers and to perform such acts as it deems necessary or expedient to promote the best interests of the Company and its Related Corporations and to carry out the intent that the Plan be treated as an Employee Stock Purchase Plan with respect to the 423 Component.

(viii) To adopt such rules, procedures and sub-plans as are necessary or appropriate to permit or facilitate participation in the Plan by Employees who are foreign nationals or employed or located outside the United States. Without limiting the generality of, and consistent with, the foregoing, the Board specifically is authorized to adopt rules, procedures, and sub-plans regarding, without limitation, eligibility to participate in the Plan, the definition of eligible "earnings," handling and making of Contributions, establishment of bank or trust accounts to hold Contributions, payment of interest, conversion of local currency, obligations to pay payroll tax, determination of beneficiary designation requirements, withholding procedures and handling of share issuances, any of which may vary according to applicable requirements, and which, if applicable to a Related Corporation designated for participation in the Non-423 Component, do not have to comply with the requirements of Section 423 of the Code.

(c) The Board may delegate some or all of the administration of the Plan to a Committee or Committees. If administration is delegated to a Committee, the Committee will have, in connection with the administration of the Plan, the powers theretofore possessed by the Board that have been delegated to the Committee, including the power to delegate to a subcommittee any of the administrative powers the Committee is authorized to exercise (and references in this Plan and any Offering Document to the Board will thereafter be to the Committee or subcommittee), subject, however, to such resolutions, not inconsistent with the provisions of the Plan, as may be adopted from time to time by the Board. The Board may retain the authority to concurrently administer the Plan with the Committee and may, at any time, revest in the Board some or all of the powers previously delegated. Whether or not the Board has delegated administration of the Plan to a Committee, the Board will have the final power to determine all questions of policy and expediency that may arise in the administration of the Plan.

(d) All determinations, interpretations and constructions made by the Board in good faith will not be subject to review by any person and will be final, binding and conclusive on all persons.

3. SHARES OF COMMON STOCK SUBJECT TO THE PLAN.

(a) Subject to the provisions of Section 11(a) relating to Capitalization Adjustments, the maximum number of shares of Common Stock that may be issued under the Plan will not exceed 1,291,072 shares of Common Stock, which is the sum of (i) 291,072 shares that were available under the Prior Plan as of March 2, 2022 and (ii) an additional 1,000,000 shares that were approved by our stockholders at the 2022 Annual Meeting of Stockholders, plus the number of shares of Common Stock that are automatically added on January 1st of each year for a period of up to ten years, commencing on the first January 1 following the Effective Date and ending on (and including) January 1, 2032, in an amount equal to the lesser of (i) 1% of the total number of shares of Common Stock outstanding on December 31st of the preceding calendar year, and (ii) 500,000 shares of Common Stock. Notwithstanding the foregoing, the Board may act prior to the first day of any calendar year to provide that there will be no January 1st increase in the share reserve for such calendar year or that the increase in the share reserve for such calendar year will be a lesser number of shares of Common Stock than would otherwise occur pursuant to the preceding sentence. For the avoidance of doubt, up to the maximum number of shares of Common Stock reserved under this Section 3(a) may be used to satisfy purchases of Common Stock under the 423 Component and any remaining portion of such maximum number of shares may be used to satisfy purchases of Common Stock under the Non-423 Component.

(b) If any Purchase Right granted under the Plan terminates without having been exercised in full, the shares of Common Stock not purchased under such Purchase Right will again become available for issuance under the Plan.

(c) The stock purchasable under the Plan will be shares of authorized but unissued or reacquired Common Stock, including shares repurchased by the Company on the open market.

4. GRANT OF PURCHASE RIGHTS; OFFERING.

(a) The Board may from time to time grant or provide for the grant of Purchase Rights to Eligible Employees under an Offering (consisting of one or more Purchase Periods) on an Offering Date or Offering Dates selected by the Board. Each Offering will be in such form and will contain such terms and conditions as the Board will deem appropriate, and, with respect to the 423 Component, will comply with the requirement of Section 423(b)(5) of the Code that all Employees granted Purchase Rights will have the same rights and privileges. The terms and conditions of an Offering shall be incorporated by reference into the Plan and treated as part of the Plan. The provisions of separate Offerings need not be identical, but each Offering will include (through incorporation of the provisions of this Plan by reference in the document comprising the Offering or otherwise) the period during which the Offering will be effective, which period will not exceed 27 months beginning with the Offering Date, and the substance of the provisions contained in Sections 5 through 8, inclusive.

(b) If a Participant has more than one Purchase Right outstanding under the Plan, unless he or she otherwise indicates in forms delivered to the Company: (i) each form will apply to all of his or her Purchase Rights under the Plan, and (ii) a Purchase Right with a lower exercise price (or an earlier-granted Purchase Right, if different Purchase Rights have identical exercise prices) will be exercised to the fullest possible extent before a Purchase Right with a higher exercise price (or a later-granted Purchase Right if different Purchase Rights have identical exercise prices) will be exercised.

(c) The Board will have the discretion to structure an Offering so that if the Fair Market Value of a share of Common Stock on the first Trading Day of a new Purchase Period within that Offering is less than or equal to the Fair Market Value of a share of Common Stock on the Offering Date for that Offering, then (i) that Offering will terminate immediately as of that first Trading Day, and (ii) the Participants in such terminated Offering will be automatically enrolled in a new Offering beginning on the first Trading Day of such new Purchase Period.

5. ELIGIBILITY.

(a) Purchase Rights may be granted only to Employees of the Company or, as the Board may designate in accordance with Section 2(b), to Employees of a Related Corporation. Except as provided in Section 5(b) or as required by Applicable Law, an Employee will not be eligible to be granted Purchase Rights unless, on the Offering Date, the Employee has been in the employ of the Company or the Related Corporation, as the case may be, for such continuous period preceding such Offering Date as the Board may require, but in no event will the required period of continuous employment be equal to or greater than two years. In addition, the Board may (unless prohibited by law) provide that no Employee will be eligible to be granted Purchase Rights under the Plan unless, on the Offering Date, such Employee's customary employment with the Company or the Related Corporation is more than 20 hours per week and more than five months per calendar year or such other criteria as the Board may determine consistent with Section 423 of the Code with respect to the 423 Component. The Board may also exclude from participation in the Plan or any Offering Employees who are "highly compensated employees" (within the meaning of Section 423(b)(4)(D) of the Code) of the Company or a Related Corporation or a subset of such highly compensated employees.

(b) The Board may provide that each person who, during the course of an Offering, first becomes an Eligible Employee will, on a date or dates specified in the Offering which coincides with the day on which such

person becomes an Eligible Employee or which occurs thereafter, receive a Purchase Right under that Offering, which Purchase Right will thereafter be deemed to be a part of that Offering. Such Purchase Right will have the same characteristics as any Purchase Rights originally granted under that Offering, as described herein, except that:

(i) the date on which such Purchase Right is granted will be the "Offering Date" of such Purchase Right for all purposes, including determination of the exercise price of such Purchase Right;

(ii) the period of the Offering with respect to such Purchase Right will begin on its Offering Date and end coincident with the end of such Offering; and

(iii) the Board may provide that if such person first becomes an Eligible Employee within a specified period of time before the end of the Offering, he or she will not receive any Purchase Right under that Offering.

(c) No Employee will be eligible for the grant of any Purchase Rights if, immediately after any such Purchase Rights are granted, such Employee owns stock possessing five percent or more of the total combined voting power or value of all classes of stock of the Company or of any Related Corporation. For purposes of this Section 5(c), the rules of Section 424(d) of the Code will apply in determining the stock ownership of any Employee, and stock which such Employee may purchase under all outstanding Purchase Rights and options will be treated as stock owned by such Employee.

(d) As specified by Section 423(b)(8) of the Code, an Eligible Employee may be granted Purchase Rights only if such Purchase Rights, together with any other rights granted under all Employee Stock Purchase Plans of the Company and any Related Corporations, do not permit such Eligible Employee's rights to purchase stock of the Company or any Related Corporation to accrue at a rate which, when aggregated, exceeds US $25,000 of Fair Market Value of such stock (determined at the time such rights are granted, and which, with respect to the Plan, will be determined as of their respective Offering Dates) for each calendar year in which such rights are outstanding at any time.

(e) Officers of the Company and any designated Related Corporation, if they are otherwise Eligible Employees, will be eligible to participate in Offerings under the Plan. Notwithstanding the foregoing, the Board may (unless prohibited by law) provide in an Offering that Employees who are highly compensated Employees within the meaning of Section 423(b)(4)(D) of the Code will not be eligible to participate.

(f) Notwithstanding anything in this Section 5 to the contrary, in the case of an Offering under the Non-423 Component, an Eligible Employee (or group of Eligible Employees) may be excluded from participation in the Plan or an Offering if the Board has determined, in its sole discretion, that participation of such Eligible Employee(s) is not advisable or practical for any reason.

6. PURCHASE RIGHTS; PURCHASE PRICE.

(a) On each Offering Date, each Eligible Employee, pursuant to an Offering made under the Plan, will be granted a Purchase Right to purchase up to that number of shares of Common Stock purchasable either with a percentage or with a maximum dollar amount, as designated by the Board, but in either case not exceeding 15% of such Employee's earnings (as defined by the Board in each Offering) during the period that begins on the Offering Date (or such later date as the Board determines for a particular Offering) and ends on the date stated in the Offering, which date will be no later than the end of the Offering.

(b) The Board will establish one or more Purchase Dates during an Offering on which Purchase Rights granted for that Offering will be exercised and shares of Common Stock will be purchased in accordance with such Offering.

(c) In connection with each Offering made under the Plan, the Board may specify (i) a maximum number of shares of Common Stock that may be purchased by any Participant on any Purchase Date during such Offering, (ii) a maximum aggregate number of shares of Common Stock that may be purchased by all Participants pursuant to such Offering and/or (iii) a maximum aggregate number of shares of Common Stock that may be purchased by all Participants on any Purchase Date under the Offering. If the aggregate purchase of shares of Common Stock issuable upon exercise of Purchase Rights granted under the Offering would exceed any such maximum aggregate number, then, in the absence of any Board action otherwise, a pro rata (based on each Participant's accumulated Contributions) allocation of the shares of Common Stock (rounded down to the nearest whole share) available will be made in as nearly a uniform manner as will be practicable and equitable.

(d) The purchase price of shares of Common Stock acquired pursuant to Purchase Rights will be not less than the lesser of:

(i) an amount equal to 85% of the Fair Market Value of the shares of Common Stock on the Offering Date; or

(ii) an amount equal to 85% of the Fair Market Value of the shares of Common Stock on the applicable Purchase Date.

7. PARTICIPATION; WITHDRAWAL; TERMINATION.

(a) An Eligible Employee may elect to participate in an Offering and authorize payroll deductions as the means of making Contributions by completing and delivering to the Company, within the time specified in the Offering, an enrollment form provided by the Company. The enrollment form will specify the amount of Contributions not to exceed the maximum amount specified by the Board. Each Participant's Contributions will be credited to a bookkeeping account for such Participant under the Plan and will be deposited with the general funds of the Company except where Applicable Law requires that Contributions be deposited with a third party. If permitted in the Offering, a Participant may begin such Contributions with the first payroll occurring on or after the Offering Date (or, in the case of a payroll date that occurs after the end of the prior Offering but before the Offering Date of the next new Offering, Contributions from such payroll will be included in the new Offering). If permitted in the Offering, a Participant may thereafter reduce (including to zero) or increase his or her Contributions. If required under Applicable Law or if specifically provided in the Offering, in addition to or instead of making Contributions by payroll deductions, a Participant may make Contributions through the payment by cash, check or wire transfer prior to a Purchase Date.

(b) During an Offering, a Participant may cease making Contributions and withdraw from the Offering by delivering to the Company a withdrawal form provided by the Company. The Company may impose a deadline before a Purchase Date for withdrawing. Upon such withdrawal, such Participant's Purchase Right in that Offering will immediately terminate and the Company will distribute as soon as practicable to such Participant all of his or her accumulated but unused Contributions and such Participant's Purchase Right in that Offering shall thereupon terminate. A Participant's withdrawal from that Offering will have no effect upon his or her eligibility to participate in any other Offerings under the Plan, but such Participant will be required to deliver a new enrollment form to participate in subsequent Offerings.

(c) Unless otherwise required by Applicable Law, Purchase Rights granted pursuant to any Offering under the Plan will terminate immediately if the Participant either (i) is no longer an Employee for any reason or for no reason (subject to any post-employment participation period required by law) or (ii) is otherwise no longer eligible to participate. The Company will distribute as soon as practicable to such individual all of his or her accumulated but unused Contributions.

(d) Unless otherwise determined by the Board, a Participant whose employment transfers or whose employment terminates with an immediate rehire (with no break in service) by or between the Company and a

Related Corporation that has been designated for participation in the Plan will not be treated as having terminated employment for purposes of participating in the Plan or an Offering; however, if a Participant transfers from an Offering under the 423 Component to an Offering under the Non-423 Component, the exercise of the Participant's Purchase Right will be qualified under the 423 Component only to the extent such exercise complies with Section 423 of the Code. If a Participant transfers from an Offering under the Non-423 Component to an Offering under the 423 Component, the exercise of the Purchase Right will remain non-qualified under the Non-423 Component. The Board may establish different and additional rules governing transfers between separate Offerings within the 423 Component and between Offerings under the 423 Component and Offerings under the Non-423 Component.

(e) During a Participant's lifetime, Purchase Rights will be exercisable only by such Participant. Purchase Rights are not transferable by a Participant, except by will, by the laws of descent and distribution, or, if permitted by the Company, by a beneficiary designation as described in Section 10.

(f) Unless otherwise specified in the Offering or as required by Applicable Law, the Company will have no obligation to pay interest on Contributions.

8. EXERCISE OF PURCHASE RIGHTS.

(a) On each Purchase Date, each Participant's accumulated Contributions will be applied to the purchase of shares of Common Stock, up to the maximum number of shares of Common Stock permitted by the Plan and the applicable Offering, at the purchase price specified in the Offering. No fractional shares will be issued unless specifically provided for in the Offering.

(b) Unless otherwise provided in the Offering, if any amount of accumulated Contributions remains in a Participant's account after the purchase of shares of Common Stock on the final Purchase Date of an Offering, then such remaining amount will not roll over to the next Offering and will instead be distributed in full to such Participant after the final Purchase Date of such Offering without interest (unless otherwise required by Applicable Law).

(c) No Purchase Rights may be exercised to any extent unless the shares of Common Stock to be issued upon such exercise under the Plan are covered by an effective registration statement pursuant to the Securities Act and the Plan is in material compliance with all applicable U.S. federal and state, foreign and other securities, exchange control and other laws applicable to the Plan. If on a Purchase Date the shares of Common Stock are not so registered or the Plan is not in such compliance, no Purchase Rights will be exercised on such Purchase Date, and the Purchase Date will be delayed until the shares of Common Stock are subject to such an effective registration statement and the Plan is in material compliance, except that the Purchase Date will in no event be more than 27 months from the Offering Date. If, on the Purchase Date, as delayed to the maximum extent permissible, the shares of Common Stock are not registered and the Plan is not in material compliance with all Applicable Laws, as determined by the Company in its sole discretion, no Purchase Rights will be exercised and all accumulated but unused Contributions will be distributed to the Participants without interest (unless the payment of interest is otherwise required by Applicable Law).

9. COVENANTS OF THE COMPANY.

The Company will seek to obtain from each U.S. federal or state, foreign or other regulatory commission or agency having jurisdiction over the Plan such authority as may be required to grant Purchase Rights and issue and sell shares of Common Stock thereunder unless the Company determines, in its sole discretion, that doing so would cause the Company to incur costs that are unreasonable. If, after commercially reasonable efforts, the Company is unable to obtain the authority that counsel for the Company deems necessary for the grant of Purchase Rights or the lawful issuance and sale of Common Stock under the Plan, and at a commercially reasonable cost, the Company will be relieved from any liability for failure to grant Purchase Rights and/or to issue and sell Common Stock upon exercise of such Purchase Rights.

10. DESIGNATION OF BENEFICIARY.

(a) The Company may, but is not obligated to, permit a Participant to submit a form designating a beneficiary who will receive any shares of Common Stock and/or Contributions from the Participant's account under the Plan if the Participant dies before such shares and/or Contributions are delivered to the Participant. The Company may, but is not obligated to, permit the Participant to change such designation of beneficiary. Any such designation and/or change must be on a form approved by the Company.

(b) If a Participant dies, and in the absence of a valid beneficiary designation, the Company will deliver any shares of Common Stock and/or Contributions to the executor or administrator of the estate of the Participant. If no executor or administrator has been appointed (to the knowledge of the Company), the Company, in its sole discretion, may deliver such shares of Common Stock and/or Contributions, without interest (unless the payment of interest is otherwise required by Applicable Law), to the Participant's spouse, dependents or relatives, or if no spouse, dependent or relative is known to the Company, then to such other person as the Company may designate.

11. ADJUSTMENTS UPON CHANGES IN COMMON STOCK; CORPORATE TRANSACTIONS.

(a) In the event of a Capitalization Adjustment, the Board will appropriately and proportionately adjust: (i) the class(es) and maximum number of securities subject to the Plan pursuant to Section 3(a), (ii) the class(es) and maximum number of securities by which the share reserve is to increase automatically each year pursuant to Section 3(a), (iii) the class(es) and number of securities subject to, and the purchase price applicable to outstanding Offerings and Purchase Rights, and (iv) the class(es) and number of securities that are the subject of the purchase limits under each ongoing Offering. The Board will make these adjustments, and its determination will be final, binding and conclusive.

(b) In the event of a Corporate Transaction, then: (i) any surviving corporation or acquiring corporation (or the surviving or acquiring corporation's parent company) may assume or continue outstanding Purchase Rights or may substitute similar rights (including a right to acquire the same consideration paid to the stockholders in the Corporate Transaction) for outstanding Purchase Rights, or (ii) if any surviving or acquiring corporation (or its parent company) does not assume or continue such Purchase Rights or does not substitute similar rights for such Purchase Rights, then the Participants' accumulated Contributions will be used to purchase shares of Common Stock (rounded down to the nearest whole share) within ten business days prior to the Corporate Transaction under the outstanding Purchase Rights, and the Purchase Rights will terminate immediately after such purchase.

12. AMENDMENT, TERMINATION OR SUSPENSION OF THE PLAN.

(a) The Board may amend the Plan at any time in any respect the Board deems necessary or advisable. However, except as provided in Section 11(a) relating to Capitalization Adjustments, stockholder approval will be required for any amendment of the Plan for which stockholder approval is required by Applicable Law.

(b) The Board may suspend or terminate the Plan at any time. No Purchase Rights may be granted under the Plan while the Plan is suspended or after it is terminated.

Any benefits, privileges, entitlements and obligations under any outstanding Purchase Rights granted before an amendment, suspension or termination of the Plan will not be materially impaired by any such amendment, suspension or termination except (i) with the consent of the person to whom such Purchase Rights were granted, (ii) as necessary to comply with any laws, listing requirements, or governmental regulations (including, without limitation, the provisions of Section 423 of the Code and the regulations and other interpretive guidance issued thereunder relating to Employee Stock Purchase Plans) including without limitation any such regulations or other guidance that may be issued or amended after the date the Plan is adopted by the Board, or (iii) as necessary to

obtain or maintain favorable tax, listing, or regulatory treatment. To be clear, the Board may amend outstanding Purchase Rights without a Participant's consent if such amendment is necessary to ensure that the Purchase Right and/or the Plan complies with the requirements of Section 423 of the Code with respect to the 423 Component or with respect to other Applicable Laws. Notwithstanding anything in the Plan or any Offering Document to the contrary, the Board will be entitled to: (i) establish the exchange ratio applicable to amounts withheld in a currency other than U.S. dollars; (ii) permit Contributions in excess of the amount designated by a Participant in order to adjust for mistakes in the Company's processing of properly completed Contribution elections; (iii) establish reasonable waiting and adjustment periods and/or accounting and crediting procedures to ensure that amounts applied toward the purchase of Common Stock for each Participant properly correspond with amounts withheld from the Participant's Contributions; (iv) amend any outstanding Purchase Rights or clarify any ambiguities regarding the terms of any Offering to enable the Purchase Rights to qualify under and/or comply with Section 423 of the Code with respect to the 423 Component; and (v) establish other limitations or procedures as the Board determines in its sole discretion advisable that are consistent with the Plan. The actions of the Board pursuant to this paragraph will not be considered to alter or impair any Purchase Rights granted under an Offering as they are part of the initial terms of each Offering and the Purchase Rights granted under each Offering.

13. TAX QUALIFICATION; TAX WITHHOLDING.

(a) Although the Company may endeavor to (i) qualify a Purchase Right for special tax treatment under the laws of the United States or jurisdictions outside of the United States or (ii) avoid adverse tax treatment, the Company makes no representation to that effect and expressly disavows any covenant to maintain special or to avoid unfavorable tax treatment, notwithstanding anything to the contrary in this Plan. The Company will be unconstrained in its corporate activities without regard to the potential negative tax impact on Participants.

(b) Each Participant will make arrangements, satisfactory to the Company and any applicable Related Corporation, to enable the Company or the Related Corporation to fulfill any withholding obligation for Tax-Related Items. Without limitation to the foregoing, in the Company's sole discretion and subject to Applicable Law, such withholding obligation may be satsified in whole or in part by (i) withholding from the Participant's salary or any other cash payment due to the Participant from the Company or a Related Corporation; (ii) withholding from the proceeds of the sale of shares of Common Stock acquired under the Plan, either through a voluntary sale or a mandatory sale arranged by the Company; or (iii) any other method deemed acceptable by the Board.

14. EFFECTIVE DATE OF PLAN.

The Plan will become effective on the date the Plan is approved by the stockholders of the Company. No Purchase Rights will be exercised unless and until the Plan has been approved by the stockholders of the Company, which approval must be within 12 months before or after the date the Plan is adopted (or if required under Section 12(a) above, materially amended) by the Board.

15. MISCELLANEOUS PROVISIONS.

(a) Proceeds from the sale of shares of Common Stock pursuant to Purchase Rights will constitute general funds of the Company.

(b) A Participant will not be deemed to be the holder of, or to have any of the rights of a holder with respect to, shares of Common Stock subject to Purchase Rights unless and until the Participant's shares of Common Stock acquired upon exercise of Purchase Rights are recorded in the books of the Company (or its transfer agent).

(c) The Plan and Offering do not constitute an employment contract. Nothing in the Plan or in the Offering will in any way alter the at will nature of a Participant's employment, if applicable, or be deemed to create in any way whatsoever any obligation on the part of any Participant to continue in the employ of the Company or a

Related Corporation, or on the part of the Company or a Related Corporation to continue the employment of a Participant.

(d) The provisions of the Plan will be governed by the laws of the State of Delaware without resort to that state's conflicts of laws rules.

(e) If any particular provision of the Plan is found to be invalid or otherwise unenforceable, such provision will not affect the other provisions of the Plan, but the Plan will be construed in all respects as if such invalid provision were omitted.

(f) If any provision of the Plan does not comply with Applicable Law, such provision shall be construed in such a manner as to comply with Applicable Law.

16. DEFINITIONS.

As used in the Plan, the following definitions will apply to the capitalized terms indicated below:

(a) "***423 Component***" means the part of the Plan, which excludes the Non-423 Component, pursuant to which Purchase Rights that satisfy the requirements for an Employee Stock Purchase Plan may be granted to Eligible Employees.

(b) "***Applicable Law***" means shall mean any applicable securities, federal, state, foreign, material local or municipal or other law, statute, constitution, principle of common law, resolution, ordinance, code, edict, decree, rule, listing rule, regulation, judicial decision, ruling or requirement issued, enacted, adopted, promulgated, implemented or otherwise put into effect by or under the authority of any Governmental Body (or under the authority of the Nasdaq Stock Market or the Financial Industry Regulatory Authority).

(c) "***Board***" means the Board of Directors of the Company.

(d) "***Capitalization Adjustment***" means any change that is made in, or other events that occur with respect to, the Common Stock subject to the Plan or subject to any Purchase Right after the date the Plan is adopted by the Board without the receipt of consideration by the Company through merger, consolidation, reorganization, recapitalization, reincorporation, stock dividend, dividend in property other than cash, large nonrecurring cash dividend, stock split, liquidating dividend, combination of shares, exchange of shares, change in corporate structure or other similar equity restructuring transaction, as that term is used in Financial Accounting Standards Board Accounting Standards Codification Topic 718 (or any successor thereto). Notwithstanding the foregoing, the conversion of any convertible securities of the Company will not be treated as a Capitalization Adjustment.

(e) "***Code***" means the U.S. Internal Revenue Code of 1986, as amended, including any applicable regulations and guidance thereunder.

(f) "***Committee***" means a committee of one or more members of the Board to whom authority has been delegated by the Board in accordance with Section 2(c).

(g) "***Common Stock***" means the common stock of the Company.

(h) "***Company***" means Regulus Therapeutics Inc., a Delaware corporation.

(i) "***Contributions***" means the payroll deductions and other additional payments specifically provided for in the Offering that a Participant contributes to fund the exercise of a Purchase Right. A Participant may make additional payments into his or her account if specifically provided for in the Offering, and then only if the Participant has not already had the maximum permitted amount withheld during the Offering through payroll deductions.

(j) "***Corporate Transaction***" means the consummation, in a single transaction or in a series of related transactions, of any one or more of the following events:

(i) a sale or other disposition of all or substantially all, as determined by the Board in its sole discretion, of the consolidated assets of the Company and its subsidiaries;

(ii) a sale or other disposition of at least 50% of the outstanding securities of the Company;

(iii) a merger, consolidation or similar transaction following which the Company is not the surviving corporation; or

(iv) a merger, consolidation or similar transaction following which the Company is the surviving corporation but the shares of Common Stock outstanding immediately preceding the merger, consolidation or similar transaction are converted or exchanged by virtue of the merger, consolidation or similar transaction into other property, whether in the form of securities, cash or otherwise.

(k) "***Director***" means a member of the Board.

(l) "***Eligible Employee***" means an Employee who meets the requirements set forth in the document(s) governing the Offering for eligibility to participate in the Offering, provided that such Employee also meets the requirements for eligibility to participate set forth in the Plan.

(m) "***Employee***" means any person, including an Officer or Director, who is "employed" for purposes of Section 423(b)(4) of the Code by the Company or a Related Corporation. However, service solely as a Director, or payment of a fee for such services, will not cause a Director to be considered an "Employee" for purposes of the Plan.

(n) "***Employee Stock Purchase Plan***" means a plan that grants Purchase Rights intended to be options issued under an "employee stock purchase plan," as that term is defined in Section 423(b) of the Code.

(o) "***Exchange Act***" means the U.S. Securities Exchange Act of 1934, as amended and the rules and regulations promulgated thereunder.

(p) "***Fair Market Value***" means, as of any date, the value of the Common Stock determined as follows:

(i) If the Common Stock is listed on any established stock exchange or traded on any established market, the Fair Market Value of a share of Common Stock will be the closing sales price for such stock as quoted on such exchange or market (or the exchange or market with the greatest volume of trading in the Common Stock) on the date of determination, as reported in such source as the Board deems reliable. Unless otherwise provided by the Board, if there is no closing sales price for the Common Stock on the date of determination, then the Fair Market Value will be the closing sales price on the last preceding date for which such quotation exists.

(ii) In the absence of such markets for the Common Stock, the Fair Market Value will be determined by the Board in good faith in compliance with Applicable Laws and regulations and in a manner that complies with Sections 409A of the Code.

(q) "***Governmental Body***" means any: (a) nation, state, commonwealth, province, territory, county, municipality, district or other jurisdiction of any nature; (b) federal, state, local, municipal, foreign or other government; (c) governmental or regulatory body, or quasi-governmental body of any nature (including any governmental division, department, administrative agency or bureau, commission, authority, instrumentality, official, ministry, fund, foundation, center, organization, unit, body or entity and any court or other tribunal, and for the avoidance of doubt, any tax authority) or other body exercising similar powers or authority; or (d) self-regulatory organization (including the Nasdaq Stock Market and the Financial Industry Regulatory Authority).

(r) "Non-423 Component" means the part of the Plan, which excludes the 423 Component, pursuant to which Purchase Rights that are not intended to satisfy the requirements for an Employee Stock Purchase Plan may be granted to Eligible Employees.

(s) "***Offering***" means the grant to Eligible Employees of Purchase Rights, with the exercise of those Purchase Rights automatically occurring at the end of one or more Purchase Periods. The terms and conditions of an Offering will generally be set forth in the "***Offering Document***" approved by the Board for that Offering.

(t) "***Offering Date***" means a date selected by the Board for an Offering to commence.

(u) "***Officer***" means a person who is an officer of the Company or a Related Corporation within the meaning of Section 16 of the Exchange Act.

(v) "***Participant***" means an Eligible Employee who holds an outstanding Purchase Right.

(w) "***Plan***" means this Regulus Therapeutics Inc. 2022 Employee Stock Purchase Plan, as amended from time to time, including both the 423 Component and the Non-423 Component.

(x) "***Purchase Date***" means one or more dates during an Offering selected by the Board on which Purchase Rights will be exercised and on which purchases of shares of Common Stock will be carried out in accordance with such Offering.

(y) "***Purchase Period***" means a period of time specified within an Offering, generally beginning on the Offering Date or on the first Trading Day following a Purchase Date, and ending on a Purchase Date. An Offering may consist of one or more Purchase Periods.

(z) "***Purchase Right***" means an option to purchase shares of Common Stock granted pursuant to the Plan.

(aa) "***Related Corporation***" means any "parent corporation" or "subsidiary corporation" of the Company whether now or subsequently established, as those terms are defined in Sections 424(e) and (f), respectively, of the Code.

(bb) "***Securities Act***" means the U.S. Securities Act of 1933, as amended.

(cc) "***Tax-Related Items***" means any income tax, social insurance, payroll tax, fringe benefit tax, payment on account or other tax-related items arising out of or in relation to a Participant's participation in the Plan, including, but not limited to, the exercise of a Purchase Right and the receipt of shares of Common Stock or the sale or other disposition of shares of Common Stock acquired under the Plan.

(dd) "***Trading Day***" means any day on which the exchange(s) or market(s) on which shares of Common Stock are listed, including but not limited to the NYSE, Nasdaq Global Select Market, the Nasdaq Global Market, the Nasdaq Capital Market or any successors thereto, is open for trading.

REGULUS

VOTE

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Your vote matters – here's how to vote!

You may vote online or by phone instead of mailing this card.

Votes submitted electronically must be received by 11:59 p.m., ET, on June 8, 2022.

Online
Go to **www.investorvote.com/RGLS** or scan the QR code – login details are located in the shaded bar below.

Phone
Call toll free 1-800-652-VOTE (8683) within the USA, US territories and Canada

Save paper, time and money!
Sign up for electronic delivery at www.investorvote.com/RGLS

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

1234 5678 9012 345

▼ 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 all the nominees listed in Proposal 1, and FOR Proposals 2, 3, 4, 5, 6 and 7.

1. To elect the ten nominees for director named herein to serve until the next annual meeting of stockholders and their successors are duly elected and qualified;

01 - David Baltimore, Ph.D.	02 - Kathryn J. Collier	03 - Joseph P. Hagan
04 - Alice S. Huang, Ph.D	05 - Jake R. Nunn	06 - Stelios Papadopoulos, Ph.D.
07 - William H. Rastetter, Ph.D.	08 - Hugh Rosen, M.D., Ph.D.	09 - Simos Simeonidis, Ph.D.
10 - Pascale Witz, MBA, MSc		

☐ **Mark here to vote FOR all nominees** ☐ **Mark here to WITHHOLD vote from all nominees**

☐ **For All EXCEPT** - To withhold a vote for one or more nominees, mark the box to the left and the corresponding numbered box(es) to the right.

01	02	03	04	05	06	07	08	09	10
☐	☐	☐	☐	☐	☐	☐	☐	☐	☐

	For	Against	Abstain
2. To approve an amendment to our Amended and Restated Certificate of Incorporation to effect a reverse stock split of our common stock at a ratio in the range of 1-for-5 to 1-for-20, with such ratio to be determined in the discretion of our board of directors and with such reverse stock split to be effected at such time and date, if at all, as determined by our board of directors in its sole discretion.	☐	☐	☐
3. To approve an amendment to our Amended and Restated Certificate of Incorporation to reduce, if and only if Proposal 2 is both approved and implemented, the number of authorized shares of our common stock to 300,000,000 shares.	☐	☐	☐
4. To approve, on an advisory basis, the compensation of the Company's named executive officers.	☐	☐	☐
5. To ratify the selection by the Audit Committee of the Board of Directors of Ernst & Young LLP as the independent registered public accounting firm of the Company for its fiscal year ending December 31, 2022.	☐	☐	☐
6. To approve the Regulus Therapeutics Inc. 2022 Employee Stock Purchase Plan pursuant to which 1,291,072 shares of our common stock will be available for sale and issuance to our employees.	☐	☐	☐
7. To approve the authorization to adjournment of the Annual Meeting, if necessary, to solicit additional proxies if there are not sufficient votes in favor of Proposal 2 or Proposal 6.	☐	☐	☐

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REGULUS THERAPEUTICS INC.

2022 Annual Meeting of
Regulus Therapeutics Inc. Stockholders
June 9, 2022 9:00 A.M. PDT

Important Notice Regarding the Availability of Proxy Materials for the Annual Meeting:
The Proxy Statement and Form 10-K are available at www.edocumentview.com/RGLS.

Small steps make an impact.
Help the environment by consenting to receive electronic delivery, sign up at www.investorvote.com/RGLS

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

Proxy – Regulus Therapeutics Inc.

Notice of 2022 Annual Meeting of Stockholders

Proxy Solicited by Board of Directors for Annual Meeting – June 9, 2022

The undersigned hereby appoint(s) Joseph P. Hagan and Christopher Aker and each of them, with power to act without the other and with power of substitution, as proxies and attorneys-in-fact and hereby authorizes them to represent and vote, as provided on the other side, all the shares of Regulus Therapeutics Inc. Common Stock which the undersigned is entitled to vote and, in their discretion, to vote upon such other business as may properly come before the Annual Meeting of Stockholders of the Company to be held June 9, 2022 at the company's offices located at 4224 Campus Point Court, Suite 210, San Diego, CA 92121, with all powers which the undersigned would possess if present at the Meeting.

This proxy, when properly executed, will be voted in the manner directed herein. If no direction is made but the card is signed, this proxy card will be voted FOR the election of all nominees listed in Proposal 1, and FOR Proposals 2, 3, 4, 5, 6 and 7, and in the discretion of the proxies with respect to such other business as may properly come before the meeting.

Continued and to be signed on reverse side

B Authorized Signatures – This section must be completed for your vote to be counted. – Date and Sign Below

Please sign exactly as name(s) appears hereon. Joint owners should each sign. When signing as attorney, executor, administrator, corporate officer, trustee, guardian, or custodian, please give 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.

C Non-Voting Items

Change of Address – Please print new address below.

Comments – Please print your comments below.

Meeting Attendance
Mark box to the right if you plan to attend the Annual Meeting. ☐