

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

SCHEDULE 14A INFORMATION

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)

Payment of Filing Fee (Check the appropriate box)

- No fee required.
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 3. Filing Party:

 4. Date Filed:

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

NOTICE OF ANNUAL MEETING OF STOCKHOLDERS

To Be Held On June 14, 2021

Dear Stockholder:

You are cordially invited to attend the 2021 Annual Meeting of Stockholders of Regulus Therapeutics Inc., a Delaware corporation (the "Company"). The meeting will be held on June 14, 2021 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 increase the number of authorized shares of common stock from 200,000,000 to 400,000,000;
3. To approve, on an advisory basis, the compensation of the Company's named executive officers;
4. 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, 2021; and
5. 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.
6. 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 16, 2021. 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 30, 2021

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, 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 2021 ANNUAL MEETING OF STOCKHOLDERS
To Be Held On June 14, 2021**

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 2021 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 30, 2021.

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 10, 2021.

How do I attend the annual meeting?

The meeting will be held on June 14, 2021 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 16, 2021 will be entitled to vote at the annual meeting. On this record date, there were 74,923,660 shares of common stock outstanding and entitled to vote.

Stockholder of Record: Shares Registered in Your Name

If on April 16, 2021 your shares were registered directly in your name with 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 16, 2021 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 four matters scheduled for a vote:

- Proposal 1: Election of the ten nominees for director named herein;
- Proposal 2: Approval of amendment to our Amended and Restated Certificate of Incorporation to increase the number of authorized shares of common stock from 200,000,000 to 400,000,000;
- Proposal 3: Approval, on an advisory basis, of the compensation of the Company’s named executive officers, as disclosed in this proxy statement;
- Proposal 4: 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, 2021; and
- Proposal 5: Authorization of the adjournment of the Annual Meeting, if necessary, to solicit additional proxies if there are not sufficient votes in favor of the Proposal 2.

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 13, 2021 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 13, 2021 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 16, 2021.

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 or 3, without your instructions, but may vote your shares on Proposals 2, 4 and 5.

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 increase the number of authorized shares of common stock as described in Proposal 2, "For" the approval of the stockholder advisory vote on the compensation of our Named Executive Officers as described in Proposal 3, "For" 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, 2021 as described in Proposal 4, and “For” the authorization to adjourn the Annual Meeting, if necessary, to solicit additional proxies if there are not sufficient votes in favor of the Proposal 2 as described in Proposal 5. 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 (including a director nomination) must be submitted in writing by December 31, 2021 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 14, 2022 and March 16, 2022. You are also advised to review the Company’s Bylaws, which contain additional requirements about advance notice of stockholder proposals and director nominations.

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 and 5 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 Proposals 1, and 3. Proposals 2, 4 and 5 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 on an increase in the authorized shares, must receive “For” votes from the holders of a majority of shares outstanding. Abstentions will have the same effect as “Against” votes.
- To be approved, Proposal 3, regarding the approval on an advisory basis of the compensation paid to 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.
- To be approved, Proposal 4, 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, 2021, 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.
- To be approved, Proposal 5, 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, 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.

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 74,923,660 shares outstanding and entitled to vote. Thus, the holders of 37,461,831 shares 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 2020 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.

<u>Name</u>	<u>Age</u>	<u>Position Held With the Company</u>
Dr. Stelios Papadopoulos	72	Chairman of the Board of Directors
Ms. Kathryn J. Collier	53	Director
Dr. David Baltimore	83	Director
Mr. Joseph P. Hagan	52	Director, President and Chief Executive Officer
Dr. Alice S. Huang	82	Director
Mr. Jake R. Nunn	50	Director
Dr. William H. Rastetter	73	Director
Dr. Hugh Rosen	62	Director
Dr. Simos Simeonidis	51	Director
Ms. Pascale Witz, MBA, MSc	53	Director

Stelios Papadopoulos, Ph.D. Chairman of the Board, has served on our Board of Directors since our conversion to a corporation in January 2009 and as our Chairman 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 Chairman 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 chairman of the board of directors since June 2014. Since August 2020, Dr. Papadopoulos has served as chairman 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 Chairman 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 Chairman 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. Since 2006, Dr. Baltimore has served as President Emeritus and Robert Andrews Millikan Professor of Biology at the California Institute of Technology, 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. with High Honors in Chemistry 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 July 2019, Ms. Collier has served as the vice president for audit services of Sempra Energy, a publicly-traded energy services holding company whose subsidiaries provide electricity, natural gas and value-added products and services. In this position, Ms. Collier oversees the internal audit function for Sempra Energy, 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 Energy. 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 Energy from April 2012 to August 2018. Prior to joining Sempra Energy in 2012, Ms. Collier held several executive positions within global corporate and investment banking at Bank of America Merrill Lynch. Ms. Collier holds a bachelor's degree in accounting from Valparaiso University, Valparaiso, Indiana. 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. 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. 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, 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 the California Institute of Technology ("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 & Development Command and Food & 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., 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 CNS since July 2013 and Addex Therapeutics Ltd., a publicly-held biopharmaceutical company focused on allosteric modulators for neurological disorders since June 2019 and Oventus Medical Ltd., a publicly-held medical device company since February 2020. 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 from December 1986 through November 2003, and as Chairman from May 1996 to November 2003. Upon the merger of IDEC Pharmaceuticals and Biogen in November 2003, Dr. Rastetter served as Executive Chairman of Biogen Idec until the end of 2005. Dr. Rastetter served as chairman 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 chairman until the sale of the publicly held company to Celgene in 2015. Currently, he has served as the chairman of the board of directors of Fate Therapeutics, Inc., a publicly held biotechnology company, since November 2011; chairman 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 chairman from August 2017 to November 2018. Dr. Rastetter served on the board of directors of Cerulean Pharma Inc., a publicly held biotechnology company since January 2014, as its lead independent director from April 2014 to June 2016, and as its chairman from June 2016 until July 2017 when Cerulean and Daré Bioscience Inc. completed a reverse merger and he currently serves as chairman 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 Chairman 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 Chairman of the Committee for Advanced Human Therapeutics of TSRI. Prior to joining The Scripps Research Institute, 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. 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. Since June 2017, Dr. Simeonidis has served as a Partner at Sarissa Capital. Prior to joining Sarissa Capital, he was a Managing Director and Senior Biotechnology Analyst at the Royal Bank of Canada (RBC) in New York from July 2014 to June 2017. Since October 2020, Dr. Simeonidis has also served on the board of Sarissa Capital Acquisition, a publicly-held special acquisition company focused on healthcare. 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 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 BS in Biology from Loyola University Chicago, and his MA, MPhil and PhD degrees in Cellular, Molecular and Biophysical Sciences from Columbia University's College of Physicians & 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 Perkin Elmer, since October 2017, and. 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, Fontainebleau, France and her MS in Biochemistry from the Institut National des Sciences Appliquées (INSA) Lyon, France. She was also a Ph.D. student in Molecular Biology at the Centre National de la Recherche Scientifique, Strasbourg, France. 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 Chairman 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 Chairman of the Board of Directors but is not an officer. We expect and intend the positions of Chairman 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. 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.

As a result of the COVID-19 pandemic, we have and may in the future experience disruptions that could severely impact our business, preclinical studies and clinical trials. Given the evolving nature of the pandemic, our senior management and our Board of Directors are communicating and meeting more frequently to monitor potential business impacts and further strategic planning.

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 2020 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, 2020 for each of the Board committees:

<u>Name</u>	<u>Audit</u>	<u>Compensation</u>	<u>Nominating and Corporate Governance</u>
Dr. David Baltimore			X*
Kathryn J. Collier	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 2020	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 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; 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, Mr. Nunn and Dr. Papadopoulos. The Audit Committee met five 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, 2020 with management of the Company. The Audit Committee has discussed with the independent registered public accounting firm the matters required to be discussed by the applicable requirements of the Public Company Accounting Oversight Board (“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, 2020.

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, Dr. Rosen, Dr. Huang 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 eight 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, modifying and approving (or if it deems appropriate, making recommendations to the full Board of Directors regarding) our overall compensation strategy and policies;
- reviewing and recommending to our Board of Directors the compensation and other terms of employment of our executive officers;
- reviewing and recommending to our Board of Directors the performance goals and objectives relevant to the compensation of our executive officers and assessing their performance against these goals and objectives;
- reviewing and approving (or if it deems it appropriate, making recommendations to the full Board of Directors regarding) the equity incentive plans, compensation plans and similar programs advisable for us, as well as modifying, amending or terminating 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;
- reviewing and approving (or if it deems it appropriate, making recommendations to the full Board of Directors regarding) the type and amount of compensation to be paid or awarded to our non-employee board members;
- establishing policies for allocating between long-term and currently paid out compensation, between cash and non-cash compensation and the factors used in deciding between the various forms of compensation;
- 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;
- reviewing and assessing the independence of compensation consultants, legal counsel and other advisors as required by Section 10C of the Exchange Act;
- establishing elements of corporate performance for purposes of increasing or decreasing compensation;
- administering our equity incentive plans;
- establishing policies with respect to equity compensation arrangements;
- 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 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
- preparing the compensation committee report as required by SEC rules.

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 2020, 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 program 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. 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 this firm as a compensation consultant 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 awards 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 2020, the subcommittee exercised its authority to grant options and stock awards to purchase an aggregate of 752,750 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 determines any adjustments to his compensation as well as awards to be granted. 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, 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, 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 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.

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.

APPROVAL OF THE INCREASE IN NUMBER OF AUTHORIZED SHARES OF COMMON STOCK PROPOSAL

General

The Board has approved an amendment (the “Authorized Shares Amendment”) to the Company’s Amended and Restated Certificate of Incorporation (the “Certificate of Incorporation”) to increase the number of authorized shares of common stock from 200,000,000 to 400,000,000. The Authorized Shares Amendment will not change the number of authorized shares of preferred stock, which currently consists of 10,000,000 shares of preferred stock.

The additional shares of common stock authorized for issuance by the Authorized Shares Amendment would be a part of the existing class of common stock and, if and when issued, would have the same rights and privileges as the common stock presently issued and outstanding. The full text of the proposed Authorized Shares Amendment is attached to this Proxy Statement as Appendix 1. However, the text of the Authorized Shares Amendment is subject to revision to include such changes as may be required by the Secretary of State of the State of Delaware and as deemed necessary and advisable to effect the Authorized Shares Amendment.

Provided the stockholders approve the Authorized Shares Amendment, the increased number of shares would be authorized for issuance, but would remain unissued until such time as the Board approves a specific issuance of such shares. Other than future issuances under the Company’s equity compensation plans and issuances of up to \$30,000,000 of common stock that may be issued and sold under our common stock sales agreement with H.C. Wainwright & Co., LLC, the Company currently has no plans or arrangements to issue the additional authorized shares of common stock that will result in the event that the Company’s stockholders approve, and the Company implements, the Authorized Shares Amendment.

Adoption of the Authorized Shares Amendment would not affect the rights of the holders of currently outstanding common stock, except for effects incidental to increasing the number of shares of our common stock outstanding, such as dilution of the earnings per share and voting rights of current holders of common stock, to the extent that any additional shares of common stock are ultimately issued out of the increase in authorized shares proposed in the Authorized Shares Amendment.

If the proposed Authorized Shares Amendment is approved by the requisite vote of the stockholders, it will become effective upon the filing of a Certificate of Amendment with the Secretary of State of the State of Delaware. The Board reserves its right to elect not to proceed with and abandon the Authorized Shares Amendment if it determines, in its sole discretion at any time, that this proposal is no longer in the best interests of our stockholders.

If we fail to obtain stockholder approval of this proposal at the Annual Meeting, we intend to continue to seek to obtain stockholder approval at each subsequent annual meeting of stockholders and/or special meetings of stockholders until such approval has been obtained and we will incur the costs associated therewith.

Background

In addition to the 74,923,660 shares of common stock outstanding on April 16, 2021, we have also reserved 62,118,152 shares for issuance upon the exercise of outstanding warrants, 18,538,240 shares for issuance upon the conversion of preferred shares, 9,192,985 shares for issuance upon the exercise of outstanding stock awards and 2,117,878 shares for issuance pursuant to the Company’s equity incentive and employee stock purchase plans, meaning that we presently have 33,109,085 authorized shares available for issuance, which is insufficient to meet our needs in connection with future financings or strategic transactions and properly incentivizing our key personnel.

Purposes and Effects of the Authorized Shares Amendment

The Board is recommending the proposed increase in the authorized number of shares of common stock to provide the Company with appropriate flexibility to issue additional shares in the future on a timely basis if such need arises in connection with potential financings, business combinations or other corporate purposes. Approval of the Authorized Shares Amendment could enable the Company to take advantage of market conditions, the availability of more favorable financing, and opportunities for business combinations and other strategic transactions, without the potential delay and expense associated with convening a special stockholders' meeting.

Our success also depends in part on our continued ability to attract, retain and motivate highly qualified management and key personnel. If this proposal is not approved by our stockholders, the lack of unissued and unreserved authorized shares of common stock to provide future equity incentive opportunities could adversely impact our ability to achieve these goals. In short, if our stockholders do not approve this proposal, we may not be able to access the capital markets, complete corporate collaborations or partnerships, attract, retain and motivate employees, and pursue other business opportunities integral to our growth and success.

The proposed increase in the number of authorized shares of common stock will not, by itself, have an immediate dilutive effect on our current stockholders. However, if this proposal is approved, unless otherwise required by applicable law or stock exchange rules, the Board will be able to issue the additional shares of common stock from time to time in its discretion without further action or authorization by the stockholders. The newly authorized shares of common stock would be issuable for any proper corporate purpose, including capital raising transactions of equity or convertible debt securities, the establishment of collaborations or other strategic agreements, stock splits, stock dividends, issuance under current or future equity incentive plans, future acquisitions, investment opportunities, or for other corporate purposes. The future issuance of additional shares of common stock or securities convertible into our common stock may occur at times or under circumstances that could result in a dilutive effect on the earnings per share, book value per share, voting power and percentage interest of the present holders of our common stock, some of whom have preemptive rights to subscribe for additional shares that we may issue.

Potential Anti-Takeover Effect

An increase in the number of authorized but unissued shares of common stock relative to the number of outstanding shares of common stock may also, under certain circumstances, be construed as having an anti-takeover effect. Although not designed or intended for such purposes, the effect of the Authorized Shares Amendment might be to render more difficult or to discourage a merger, tender offer, proxy contest or change in control of us and the removal of management, which stockholders might otherwise deem favorable. For example, the authority of the Board to issue common stock might be used to create voting impediments or to frustrate an attempt by another person or entity to effect a takeover or otherwise gain control of us because the issuance of additional common stock would dilute the voting power of the common stock then outstanding. Our common stock could also be issued to purchasers who would support the Board in opposing a takeover bid which our board determines not to be in our best interests and those of our stockholders. In addition to the Authorized Shares Amendment, the Certificate of Incorporation and Amended and Restated Bylaws also include other provisions that may have an anti-takeover effect. These provisions, among other things, permit the Board to issue preferred stock with rights senior to those of the common stock without any further vote or action by the stockholders, provide that special meetings of stockholders may only be called by the Board and some of our officers, and do not provide for cumulative voting rights, which could make it more difficult for stockholders to effect certain corporation actions and may delay or discourage a change in control. The Board is not presently aware of any attempt, or contemplated attempt, to acquire control of the Company and the Authorized Shares Amendment is not part of any plan by the Board to recommend or implement a series of anti-takeover measures.

Vote Required

Approval of this proposal requires the affirmative vote of a majority of the outstanding shares of our common stock. Abstentions will have the same effect as an “against” vote on this proposal. As noted above, we believe that this proposal will be considered a “routine” matter and, as a result, we do not expect there to be any broker non-votes on this proposal. If, however, a broker non-vote occurs (or if your shares are not affirmatively voted in favor of this proposal for any other reason), it will have the same effect as an “against” vote on this proposal.

**THE BOARD OF DIRECTORS RECOMMENDS
A VOTE FOR PROPOSAL 2**

PROPOSAL 3

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 2, and abstentions will have the same effect as “Against” votes.

**THE BOARD OF DIRECTORS RECOMMENDS
A VOTE FOR PROPOSAL 3**

EXECUTION COMPENSATION

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 2020 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, 2020:

- 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, 2020 and December 31, 2019, compensation awarded to, paid to, or earned by, the Named Executive Officers.

<u>Name and Principal Position</u>	<u>Year</u>	<u>Salary (\$)</u>	<u>Stock Options (\$)(1)</u>	<u>Restricted Stock Units (RSUs) (\$)(1)</u>	<u>Non-Equity Incentive Plan Compensation (\$)(2)</u>	<u>All Other Compensation (\$)(3)</u>	<u>Total (\$)</u>
Joseph P. Hagan	2020	551,500	1,507,054	—	264,720	9,860	2,333,134
<i>President & Chief Executive Officer</i>	2019	535,600	540,342	69,079	860,652	8,610	2,014,283
Christopher R. Aker	2020	315,000	351,646	—	132,300	10,172	809,118
<i>SVP & General Counsel</i>	2019	290,000	188,913	23,696	275,500	9,798	787,907
Cris Calsada	2020	315,000	251,176	—	132,300	9,350	707,826
<i>Chief Financial Officer</i>	2019	104,526	151,749	—	45,965	636	302,876

- (1) In accordance with SEC rules, this column reflects the aggregate grant date fair value of the stock awards 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, 2020. These amounts do not reflect the actual economic value that will be realized by the Named Executive Officer upon the vesting of the stock awards, the exercise of the stock options, or the sale of the common stock underlying such stock awards. The grant date fair value of the stock awards granted during 2020 that vest based on performance conditions is reported based on the probable outcome of such performance conditions, as determined in accordance with ASC 718, which is the same as the grant date fair value of such awards at the grant date, assuming that the highest level of performance conditions will be achieved.
- (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.” The 2019 amounts shown for Mr. Hagan and Mr. Aker also include a Board of Directors approved discretionary bonus and retention award paid in recognition of their contributions following our July 2018 corporate restructuring and reduction in workforce and our entry into a private placement financing transaction in May 2019.

- (3) Amounts shown include term life insurance and long-term disability insurance paid by us on behalf of the Named Executive Officers, matching payments made to the NEO's Health Savings Account (if the NEO participated in our high deductible health plan) and matching contributions we paid under the terms of our 401(k) plan. 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 2020 were base salary, annual performance-based 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' 2020 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 2020 compensation decisions was comprised of the following companies:

Alpine Immune Sciences	aTyr Pharma	Caladrius Biosciences	Calithera Biosciences	Capricor Therapeutics
Catalyst Biosciences	Chimerix	Cidara Therapeutics	Conatus Pharmaceuticals	ContraFect
Corvus Pharmaceuticals	Flex Pharma	Infinity Pharmaceuticals	Lineage Cell Therapeutics	Miragen Therapeutics
Otonomy	Protagonist Therapeutics	Sienna Biopharmaceuticals	Sunesis Pharmaceuticals	Synthetic Biologics
Tocagen	TRACON Pharmaceuticals			

The peer group was recommended by Radford and chosen in late-2019 based on the following parameters: biopharmaceutical companies that were pre-commercial and with programs in early clinical development, had market values generally under \$200 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 \$15 million and our headcount was 24 employees.

Base Salary

In December 2019, 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 2019, each executive's prior experience and internal pay equity in order to determine 2020 base salaries of our NEOs.

The Named Executive Officers' 2020 annual base salaries (effective January 1, 2020) and increases from 2019 annual base salaries approved by the Compensation Committee were as follows:

<u>Name</u>	<u>2020 Base Salary (\$)</u>	<u>Increase from 2019 Base Salary (%)</u>
Joseph P. Hagan	551,500	3.0%
Christopher R. Aker	315,000	8.6%
Cris Calsada	315,000	1.6%

Annual Performance-Based Bonus Opportunity

The annual performance-based 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. Except for the Chief Executive Officer whose entire annual bonus depends upon the CPF, 20% of each other NEO's annual bonus is also 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, except our Chief Executive Officer and our other Named Executive Officers do not make recommendations with respect to their own achievement, and 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 2020.

Each Named Executive Officer's target bonus for 2020, represented as a percentage of base salary, or a target bonus percentage, was 50% of base salary, with the exception of Mr. Hagan's target bonus percentage, 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.

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 2020, the CPF goals related primarily to advancing our most promising program, RGLS4326 for the treatment of autosomal dominant polycystic kidney disease (“ADPKD”), while also make some progress on our preclinical pipeline. The specific CPF goals were as follows:

- Complete the RGLS4326 Multiple Ascending Dose (the “MAD”) study in healthy volunteers with top-line data by mid-year 2020;
- Start the RGLS4326 Mechanism of Action (the “MOA”) study by early fourth quarter of 2020;
- Gain alignment or input from FDA on a framework for addressing the requirements for the partial clinical hold;
- Nominate a development candidate for at least one research program by year end 2020;
- Advance a discovery research program to lead identification; and
- Extend our cash runway by providing sufficient cash to complete the Mechanism of Action study.

In December 2020, after careful review, our Board of Directors, upon the recommendation of our Compensation Committee, concluded that we had achieved 80% of our CPF goals, based on the following:

- We initiated the MAD study on time and completed the study despite the challenges of the COVID pandemic;
- We redesigned the MOA study to an adaptive open-label design, saving money, providing optionality based on clinical outcomes and generating additional data for our future interactions with the U.S. Food & Drug Administration concerning this program. While we did not seek to gain alignment from FDA on our remaining clinical hold requirements we did engage key experts to build a robust model based on the new data generated from the additional preclinical work to better address the remaining hold requirements;
- We commenced the MOA study enrolling the first patient in October 2020 and were on track to have the first cohort of the study fully enrolled by January 2021 thereby enabling data at the end of the first quarter of 2021;
- We advanced toward development two candidates from other preclinical programs, although we did not nominate a candidate;
- We commenced new research around possible targets in new therapeutic areas and produced some early promising data; and
- We closed a private financing netting approximately \$18.2 million to fund on our ongoing development programs.

The IPF goals varied by individual and included individual performance contributions towards maintaining a leading position in *microRNA* research, accelerating efforts in *microRNA* 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. Our Chief Executive Officer did not have IPF goals as his bonus is entirely dependent on our CPF goals, because our Chief Executive Officer has a direct impact on, and responsibility for, our corporate performance.

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 a

80% CPF and IPF as indicated, weighted 80% and 20%, respectively, except for our Chief Executive Officer, whose bonus was weighted 100% on CPF goals:

<u>Name</u>	<u>Target Bonus (\$)</u>	<u>IPF Achievement (%)</u>	<u>Cash Bonus Paid (\$)</u>
Joseph P. Hagan	\$ 330,900	—	\$ 264,720
Christopher Aker(1)	\$ 157,500	100%	\$ 132,300
Cris Calsada(2)	\$ 157,500	100%	\$ 132,300

- (1) Mr. Aker's performance-based bonus was approved based on 80% CPF and 100% IPF in recognition of his roles in procuring additional capital, assisting in the initiation of the RGLS4326 MOA study including contracting with the clinical sites, his operational leadership concerning our response to the COVID pandemic and his role in recruiting additional scientific talent.
- (2) Ms. Calsada's performance-based bonus was approved based on the 80% CPF and 100% 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

Equity incentives are a key component of our executive compensation program that the Compensation Committee believes 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, more recently, RSU stock awards that vest based on continued service.

Stock Awards. In 2020, each of our Named Executive Officers received time-vesting stock options and performance-based stock options in the amounts listed below.

<u>Name</u>	<u>Time-Vesting Stock Options (# of shares)(1)</u>	<u>Performance-Vesting Stock Options (# of shares)(2)</u>
Joseph P. Hagan	900,000	600,000
Christopher R. Aker	210,000	140,000
Cris Calsada	150,000	100,000

- (1) Consists of a stock option granted on January 22, 2020 with a vesting commencement date of January 1, 2020 with an exercise price of \$1.31 per share 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.
- (2) Consists of two equal performance-vesting stock options granted on January 22, 2020 with an exercise price of \$1.31 per share. The options will vest only upon achievement of two specified development goals related to our RGLS4326 program. Upon achievement of each goal, 50% of the options subject to the grant immediately vested with the remaining options 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.

The performance-vesting stock options vest and can be earned only if performance goals key to our future success are achieved (in addition to continued service), thereby further incentivizing our Named Executive Officers to achieve these goals to drive increases in our long-term value for stockholders.

Other Compensation

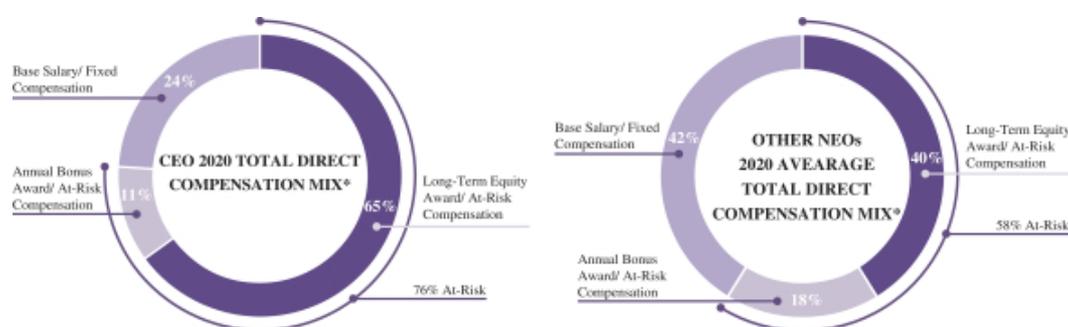
Our Named Executive Officers are eligible to participate in all of our employee benefit plans, including our medical, dental, vision, group life and disability insurance plans, in each case on the same basis as other employees. We also pay the premiums for term life insurance and long-term disability 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 2020 (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 2020, 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.

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 CEO's and other executive officers' compensation is "at-risk", performance-based compensation, in the form of long-term equity awards (including performance-vesting equity awards) and annual cash incentives that are only earned if we achieve measurable corporate metrics. The charts below show the 2020 total reported pay mix of our CEO, 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 2020 cash compensation, consisting of annual base salaries and performance bonus earned, and 2020 equity awards granted, based on such equity incentives' grant date fair value as reported in the "Summary Compensation Table," for each of our NEOs.

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. In December 2015, we 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 of \$415,000 and is eligible to receive an annual performance bonus, with a target bonus amount of 40% of his annual base salary. 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 and have been subsequently increased. In May 2017, Mr. Hagan was appointed as our President and Chief Executive Officer. At that time, his base salary was increased to \$500,000 and his target bonus was increased to 50%. Additionally, Mr. Hagan's employment agreement provides for the grant of stock option awards, which were made in January 2016. Pursuant to Mr. Hagan's employment agreement, all outstanding stock options subject to vesting based on Company performance that are held by Mr. Hagan 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. Hagan remains employed by us as of such date. In 2020, Mr. Hagan's base salary was increased to \$551,500 and his target bonus (which was increased in 2019) remained at 60% of his annual base salary.

If we terminate Mr. Hagan's employment without cause (other than due to his death or complete disability) or if Mr. Hagan 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, Mr. Hagan will receive, subject to receiving an effective release and waiver of claims from him, (1) a lump sum severance payment equal to 12 months of his 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 Mr. Hagan as of such termination or resignation.

If we terminate Mr. Hagan's employment without cause (other than due to his death or complete disability) or if Mr. Hagan 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 Mr. Hagan, subject to receiving an effective release and waiver of claims from him, a lump sum payment equal to the target amount of Mr. Hagan's annual performance bonus for the year of termination or resignation.

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 of \$246,376 and is eligible to receive an annual performance bonus, with a target bonus amount of 50% of his annual base salary. 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 and his base salary has been subsequently increased. 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 2020, Mr. Aker's base salary was increased to \$315,000 and his target bonus remained at 50% of his annual base salary.

If we terminate Mr. Aker's employment without cause (other than due to his death or complete disability) or if Mr. Aker 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, Mr. Aker will receive, subject to receiving an effective release and waiver of claims from him, (1) a lump sum severance payment equal to 12 months of his 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 Mr. Aker as of such termination or resignation.

If we terminate Mr. Aker's employment without cause (other than due to his death or complete disability) or if Mr. Aker 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 Mr. Aker, subject to receiving an effective release and waiver of claims from him, a lump sum payment equal to the target amount of Mr. Aker's annual performance bonus for the year of termination or resignation.

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 of \$310,000 and is eligible to receive an annual performance bonus, with a target bonus amount of 50% of her annual base salary. 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 and her base salary has been subsequently increased. At the time she commenced her employment with us, Ms. Calsada also received an initial stock option grant of 100,000 shares. 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 2020, Ms. Calsada's base salary was increased to \$315,000 and her target bonus remained at 50% of her annual base salary.

If we terminate Ms. Calsada's employment without cause (other than due to her death or complete disability) or if Ms. Calsada 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, Ms. Calsada will receive, subject to receiving an effective release and waiver of claims from her, (1) a lump sum severance payment equal to 12 months of her 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 Ms. Calsada as of such termination or resignation.

If we terminate Ms. Calsada's employment without cause (other than due to her death or complete disability) or if Ms. Calsada 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 Ms. Calsada, subject to receiving an effective release and waiver of claims from her, a lump sum payment equal to the target amount of Ms. Calsada's annual performance bonus for the year of termination or resignation.

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.

Outstanding Equity Awards at Fiscal Year-End

The following table shows certain information regarding outstanding equity awards as of December 31, 2020 for the Named Executive Officers:

Name	Grant Date	Number of Securities Underlying Unexercised Stock Options (#) Exercisable	Number of Securities Underlying Unexercised Stock Options (#) Unexercisable	Option Awards ⁽¹⁾			Stock Awards ⁽¹⁾	
				Equity Incentive Plan Awards: Number of Securities Underlying Unexercised Options	Option Exercise Price (\$)	Option Expiration Date	Number of Shares or Units of Stock That Have Not Vested (#)	Market Value of Shares or Units of Stock That Have Not Vested (\$) ⁽²⁾
Joseph P. Hagan	11/12/2018 ⁽³⁾						164,837	31,790
	2/5/2019 ⁽⁴⁾	31,145	33,855		0.95	2/4/2029		
	2/5/2019 ⁽⁵⁾	8,958	1,042		0.95	2/4/2029		
	10/10/2019 ⁽⁴⁾	170,083	416,948		0.64	10/09/2029		
	1/22/2020 ⁽⁴⁾	206,250	675,000		1.31	1/21/2030		
	1/22/2020 ⁽⁷⁾			300,000	1.31	1/21/2030		
	1/22/2020 ⁽⁷⁾			300,000	1.31	1/21/2030		
Christopher R. Aker	11/12/2018 ⁽³⁾						33,698	6,499
	2/5/2019 ⁽⁴⁾	11,979	13,021		0.95	2/4/2029		
	2/5/2019 ⁽⁵⁾	6,718	782		0.95	2/4/2029		
	10/10/2019 ⁽⁴⁾	97,708	237,292		0.64	10/09/2029		
	1/22/2020 ⁽⁴⁾	48,125	161,875		1.31	1/21/2030		
	1/22/2020 ⁽⁷⁾			70,000	1.31	1/21/2030		
	1/22/2020 ⁽⁷⁾			70,000	1.31	1/21/2030		
Cris Calsada	8/30/2019 ⁽⁶⁾	33,333	66,667		0.62	8/29/2029		
	10/10/2019	61,250	148,750		0.64	10/09/2029		
	1/22/2020 ⁽⁴⁾	34,375	115,625		1.31	1/21/2030		
	1/22/2020 ⁽⁷⁾			50,000	1.31	1/21/2030		
	1/22/2020 ⁽⁷⁾			50,000	1.31	1/21/2030		

- (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) Represents the number of unvested RSUs multiplied by the closing stock price as of December 31, 2020.
- (3) Consists of performance-vesting RSUs granted to each Named Executive Officer in the tender offer completed in November 2018, in which eligible options were exchanged for RSUs on a value-for-value basis. The new RSUs that our employees received in the exchange offer can be earned only if performance goals key to our future success are achieved (in addition to continued service). On May 14, 2019, the Board of Directors concluded the Company had met the criteria to commence vesting of the RSUs 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 RSUs subject to the grant immediately vested with the remaining RSUs vesting in quarterly installments over the following 24 months, subject to the recipient's continued service to the Company through each such vesting date. The number of shares underlying outstanding stock options held by each Named Executive Officers as of immediately before the tender offer exchange in November 2018 were as follows: Mr. Hagan: 278,714 shares; Mr. Aker: 62,297.
- (4) 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.

- (5) 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.
- (6) 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.
- (7) 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. 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.

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) 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 2015 Inducement Plan ("2015 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, or ISOs, within the meaning of Section 422 of the Code, nonstatutory stock options, or 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 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.

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 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, which 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 in August 2019. 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.

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.

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, 2020:

<u>Name</u>	<u>Fees Earned or Paid in Cash(\$)(1)</u>	<u>Option Awards (\$)(2)</u>	<u>Total (\$)</u>
David Baltimore, Ph.D.(4)	48,000	15,544(3)	63,544
Kathryn J. Collier(4)	60,000	15,544(3)	75,544
Jake Nunn(4)	50,000	15,544(3)	65,544
Stelios Papadopoulos, Ph.D.(4)	84,000	15,544(3)	99,544
William H. Rastetter, Ph.D.(4)	52,000	15,544(3)	67,544
Hugh Rosen, M.D., Ph.D.(4)	46,000	15,544(3)	61,544
Simos Simeonidis, Ph.D.(4)	0	15,544(3)	15,544
Pascale Witz(4)	46,000	15,544(3)	61,544

- (1) Amounts listed represent cash payments made for Board and Committee service which were earned in 2020. Dr. Simeonidis is required by his employer, Sarissa Capital, to assign his cash payments to Sarissa Capital.
- (2) Amounts listed represent the aggregate grant date fair value amount computed as of the grant date of each option awarded during 2020 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, 2020.
- (3) Represents the annual option grant to purchase 23,350 shares of our common stock granted to each of our non-employee directors serving on June 16, 2020 under our non-employee director compensation policy, as further described below.
- (4) As of December 31, 2020, each director held outstanding options to purchase 58,125 shares.

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. We have a non-employee director compensation policy, or our director compensation policy, that became effective following our initial public offering. Under our director compensation policy, our Compensation Committee determines individual non-employee members of our Board of Directors who will be eligible to receive compensation and who we refer to as our Eligible Directors. All of our non-employee directors were Eligible Directors for 2020 compensation under our director compensation policy. Pursuant to our director compensation policy in effect in 2020, we provide cash compensation in the form of an annual retainer of \$40,000 to each of our Eligible Directors and \$70,000 to our Chairman of the Board. We also pay an additional annual retainer of \$20,000 to the chairman of our Audit Committee, \$10,000 to other independent Eligible Directors who serve on our Audit Committee, \$12,000 to the chairman of our Compensation Committee, \$6,000 to other independent Eligible Directors who serve on our Compensation Committee, \$8,000 to the chairman of our Nominating and Corporate Governance Committee and \$4,000 to other independent 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.

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. The number of options is usually determined in December of the prior year. In addition, the Board of Directors also determines the number of stock options to be awarded to each director re-elected at our next annual stockholder meeting.

In December 2019, 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 2020 and (ii) an annual option grant to each Eligible Director re-elected at our annual meeting of stockholders in 2020 of 23,250 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. All awards granted under our director compensation policy will vest in full upon the closing of a change in control of the Company.

In January 2021, Alice Huang, Ph.D., was appointed to our Board of Directors, and the Compensation Committee determined that Dr. Huang is an Eligible Director under our director compensation policy. Accordingly, in January 2021, following determination of the appropriate number of options by our Board of Directors in December 2020, Dr. Huang was granted an initial option grant to purchase 80,000 shares of our common stock at an exercise price of \$1.55 per share. These options will vest and become exercisable as provided under our director compensation policy.

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 and Other Benefit Plans-2019 Equity Incentive Plan."

PROPOSAL 4

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, 2021 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.

Principal Accounting Fees and Services

The following table represents aggregate fees incurred by the Company for the fiscal years ended December 31, 2020 and December 31, 2019, 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	
	2020	2019
	(in thousands)	
Audit Fees ⁽¹⁾	\$ 305	\$ 359
Audit-related Fees	—	—
Tax Fees	—	—
All Other Fees	104	—
Total Fees	<u>\$ 409</u>	<u>\$ 359</u>

- (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 2020 and 2019 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 4**

PROPOSAL 5

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 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. 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, 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. As noted above, we believe that this proposal will be considered a “routine” matter and, as a result, we do not expect there to be any broker non-votes on this proposal. If, however, your shares are represented at the Annual Meeting and your broker fails to vote your shares on this proposal, it will have the same effect as an “against” vote on this proposal.

**THE BOARD OF DIRECTORS RECOMMENDS
A VOTE FOR PROPOSAL 5**

EXECUTIVE OFFICERS

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

<u>Name</u>	<u>Age</u>	<u>Position Held With the Company</u>
Joseph P. Hagan	52	President and Chief Executive Officer
Christopher Aker	60	Senior Vice President and General Counsel
Cris Calsada	51	Chief Financial Officer
Denis Drygin, Ph.D.	47	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 since February 2011. Prior to joining us, Mr. Aker served as the Senior Director, Administration and Senior Corporate Counsel for Phenomix Corporation, 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., a wholly-owned subsidiary of Pharmacia, until its acquisition by Pfizer. Prior to SUGEN, Mr. Aker was in private practice with various law firms. Mr. Aker received his Bachelor of Arts degree 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. since December 2017. 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., 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 Chief Scientific Officer. Prior to joining Regulus, Dr. Drygin served as Vice President of Research & Development for Pimera Inc., a privately held biopharmaceutical company of which Dr. Drygin is a Founder. Before Pimera, Dr. Drygin was with Cylene Pharmaceuticals, 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.

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, 2021 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 74,689,132 shares of common stock outstanding as of March 31, 2021. 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, 2021. 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 Owner	Beneficial Ownership	
	Number of Shares	Percent of Total
Greater than 5% Stockholders		
Entities affiliated with RS Investments ⁽¹⁾ One Bush Street, Suite 400 San Francisco, CA 94104	14,548,183	18.02%
Entities affiliated with Sarissa Capital Management LP ⁽²⁾ c/o Sarissa Capital Management LP 660 Steamboat Road Greenwich, CT 06830	12,166,942	14.31%
Entities affiliated with New Enterprise Associates, Inc. ⁽³⁾ 1954 Greenspring Dr., Suite 600 Timonium Maryland 21093	6,709,193	9.99%
Entities affiliated with BVF Partners, L.P. ⁽⁴⁾ 1 Sansome Street, 30 th Floor San Francisco, California 94104	6,760,484	9.99%
Point72 Associates LLC ⁽⁵⁾ 72 Cummings Point Road Stamford, Connecticut 06902	5,627,013	7.30%
Altium Growth Fund, LP ⁽⁶⁾ 551 Fifth Avenue, FL 19 New York, New York 10176	4,557,581	5.75%
Entities affiliated with Asymmetry Capital ⁽⁷⁾ One Sansome Street, Suite 1810 San Francisco, CA 94104	3,475,718	4.65%
Named Executive Officers and Directors		
Christopher Aker ⁽⁸⁾	285,708	*
David Baltimore, Ph.D. ⁽⁹⁾	93,416	*
Cris Calsada ⁽¹⁰⁾	189,375	*
Kathryn J. Collier ⁽¹¹⁾	95,231	*
Joseph P. Hagan ⁽¹²⁾	1,261,261	1.69%
Alice S. Huang, Ph.D.	—	—
Jake R. Nunn ⁽¹³⁾	67,812	*
Stelios Papadopoulos, Ph.D. ⁽¹⁴⁾	4,719,355	6.32%
William H. Rastetter, Ph.D. ⁽¹⁵⁾	777,222	1.04%
Hugh Rosen, M.D., Ph.D. ⁽¹⁶⁾	85,529	*
Simos Simeonidis, Ph.D. ⁽¹⁷⁾	67,812	*
Pascale Witz, MBA, MSc ⁽¹⁸⁾	280,177	*
All current executive officers and directors as a group (13 persons) ⁽¹⁹⁾	7,932,898	10.62%

* Less than one percent.

- (1) Consists of an aggregate of 8,519,242 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 (the “RS Funds”). RS Investments as the Investment Advisor to the RS Funds may be deemed to have the shared power to vote or direct the vote of (and the shared power to dispose or direct the disposition of) the shares of our common stock held by the RS Funds. Shares of common stock beneficially owned by the Victory Funds are owned individually and not jointly. By delegation from each Victory Fund and each Victory Fund’s respective Board of Trustees, Victory Capital has the power to dispose of the securities acting through Chris Clark, a member of its investment franchise, RS Investments Growth, and to vote the securities in accordance with its proxy voting policy through its proxy committee, which is composed of seven individuals.
- (2) 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, or Sarissa Offshore, Sarissa Capital Catapult Fund LLC, or Sarissa Catapult, and Sarissa Capital Hawkeye Fund LP, or Sarissa Hawkeye, or, collectively, the Sarissa Funds. Sarissa Capital Management LP, or Sarissa Capital, as the Investment Advisor to the Sarissa Funds may be deemed to have the shared power to vote or direct the vote of (and the shared power to dispose or direct the disposition of) the shares of our common stock held by the Sarissa Funds. By virtue of his positions as the Chief Investment Officer of Sarissa Capital and as the managing member of Sarissa Capital’s general partner and as controlling the ultimate general partner of each of the Sarissa Funds, Alexander J. Denner, Ph.D. may be deemed to have the shared power to vote or direct the vote of (and the shared power to dispose or direct the disposition of) the shares of our common stock by the Sarissa Funds. Each Sarissa Reporting Person disclaims beneficial ownership of all applicable shares except to the extent of their actual pecuniary interest therein.
- (3) Consists of 6,451,057 shares of common stock and 258,136 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. New Enterprise Associates 16, L.P., or NEA 16, is the sole member of GEO, NEA Partners 16, L.P., or NEA Partners 16, is the sole general partner of NEA 16 and NEA 16 GP, LLC, or NEA 16 LLC, is the sole general partner of NEA Partners 16. Peter J. Barris, Forest Baskett, Ali Behbahani, Carmen Chang, Anthony A. Florence, Jr., Mohamad H. Makhzoumi, Joshua Makower, David M. Mott, Scott D. Sandell, Peter W. Sonsini and Paul Walker, or, collectively, the Managers, are the managers of NEA 16 LLC. The persons named herein are referred to individually herein as a NEA Reporting Person and collectively as the NEA Reporting Persons. GEO is the record owner of the GEO Shares. As the sole member of GEO, NEA 16 may be deemed to own beneficially the GEO Shares. As the general partner of NEA 16, NEA Partners 16 may be deemed to own beneficially the GEO Shares. As the sole general partner of NEA Partners 16, NEA 16 LLC may be deemed to own beneficially the GEO Shares. Each of the Managers of NEA 16 LLC may be deemed to own beneficially the GEO Shares. The number of shares beneficially owned by the NEA Reporting Persons in the aggregate is limited by beneficial ownership limitations applicable to the warrants and shares of Class A-1, Class A-2 and Class A-3 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 17,693,822 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 and 2,587,070 shares of common stock issuable upon the conversion of Class A-3 convertible preferred stock held by GEO. Each NEA Reporting Person disclaims beneficial ownership of all applicable shares except to the extent of their actual pecuniary interest therein.

- (4) Consists of an aggregate of 5,988,932 shares of common stock and 771,552 shares of common stock issuable upon the exercise of warrants to purchase common stock held collectively by (i) Biotechnology Value Fund, LP, or BVF, (ii) Biotechnology Value Fund II, LP, or BVF II, (iii) Biotechnology Value Trading Fund OS, L.P., or BVFOS, and (v) MSI BVF SPV, L.L.C., or MSI, and, collectively, the BVF Investment Entities. BVF Partners L.P., or BVF Partners, is the general partner of BVF, BVF II and BVFOS and the investment advisor of MSI and may be deemed to beneficially own the shares held by the BVF Investment Entities. BVF, Inc., as the general partner of BVF Partners, may be deemed to beneficially own the shares beneficially owned by BVF Partners. Mark Lampert, as a director and officer of BVF Inc., may be deemed to beneficially own the shares beneficially owned by BVF, Inc. The number of shares beneficially owned by BVF Partners in the aggregate is limited by beneficial ownership limitations applicable to the exercise of warrants held by the BVF Investment Entities, which limit the number of shares BVF Partners can beneficially own after the exercise of warrants and conversion of shares of convertible preferred stock 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 10,659,475 shares of common stock issuable upon the exercise of warrants held by the BVF Investment Entities.
- (5) Consists of an aggregate of 3,215,436 shares of common stock and 2,411,577 shares of common stock issuable upon the exercise of warrants to purchase common stock held by Point72 Associates, LLC, or Point72 Associates. Point72 Asset Management, L.P. maintains investment and voting power with respect to the securities held by certain investment funds it manages, including Point72 Associates. Point72 Capital Advisors, Inc. is the general partner of Point72 Asset Management, L.P. Mr. Steven A. Cohen controls each of Point72 Associates and Point72 Asset Management, L.P. and Point72 Capital Advisors, Inc and may be deemed to beneficially own the shares held of record by Point72 Associates. By reason of the provisions of Rule 13d-3 of the Exchange Act, each of Point72 Asset Management, L.P., Point72 Capital Advisors, Inc., and Mr. Cohen may be deemed to beneficially own the securities held of record by Point72 Associates reflected herein. Each of Point72 Asset Management, L.P., Point72 Capital Advisors, Inc., and Mr. Cohen disclaims beneficial ownership of any such securities.
- (6) Consists of 4,557,581 shares of common stock issuable upon the exercise of warrants to purchase common stock held by Altium Growth Fund, LP, or Altium Growth. Altium Capital Management, LP is the investment adviser of, and may be deemed to beneficially own securities owned by, Altium Growth. Altium Growth GP, LLC is the general partner of, and may be deemed to beneficially own securities owned by, Altium Growth. Each of Altium Capital Management, LP and Altium Growth GP, LLC, or, together, Altium, shares voting and disposal power over the shares.
- (7) Consists of an aggregate of 3,475,718 shares of common stock held collectively by Atom Master Fund LP, Asymmetry Global Healthcare Fund, L.P. Portland House Partners, Preclude Opportunity Fun and Asymmetry Global Healthcare (Master) Fund, Ltd., the Asymmetry Funds. Asymmetry Capital Management, LP, or Asymmetry Management, as the Sub-Advisor to Atom, Portland and Prelude, may be deemed to have the shared power to dispose or direct the disposition of the shares of our common stock held by Atom, Portland and Prelude and the shared power to vote or direct the vote of the shares held by Prelude. Craig Fischer, as General Counsel and Chief Compliance Officer of Atom, has power to vote or direct the vote of (and the shared power to dispose or direct the disposition of) the shares of our common stock held by Atom. Tim Collins, as President of Portland, has power to vote or direct the vote of (and the shared power to dispose or direct the disposition of) the shares of our common stock held by Portland. Chris Zellner, as COO of Asymmetry Management, Asymmetry Global and Asymmetry Master, has shared power to dispose or direct the disposition of the shares held by the Asymmetry Funds and shared power to vote or direct the vote of the shares held by Asymmetry Global, Prelude and Asymmetry Master.
- (8) Consists of 41,207 shares of common stock held by Mr. Aker and 242,094 shares that Mr. Aker has the right to acquire from us within 60 days of March 31, 2021 pursuant to the exercise of stock options and 2,407 shares that Mr. Aker will acquire upon the vesting of RSUs.
- (9) Consists of 25,604 shares of common stock held by Dr. Baltimore and 67,812 shares that Dr. Baltimore has the right to acquire from us within 60 days of March 31, 2021 pursuant to the exercise of stock options.
- (10) Consists of 189,375 shares that Ms. Calsada has the right to acquire from us within 60 days of March 31, 2021 pursuant to the exercise of stock options.

- (11) Consists of 27,419 shares of common stock held by Ms. Collier and 67,812 shares that Ms. Collier has the right to acquire from us within 60 days of March 31, 2021 pursuant to the exercise of stock options.
- (12) Consists of (i) 241,084 shares of common stock held by Joseph P. Hagan and 805,523 shares that Mr. Hagan has the right to acquire from us within 60 days of March 31, 2021 pursuant to the exercise of stock options and 11,774 shares that Mr. Hagan will acquire upon the vesting of RSUs, and (ii) 138,804 shares of common stock issuable upon the exercise of warrants and 75,850 shares of common stock upon the conversion of Class A-2 preferred stock to purchase common stock 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.
- (13) Consists of 67,812 shares of common stock that Mr. Nunn has the right to acquire from us within 60 days of March 31, 2021 pursuant to the exercise of stock options.
- (14) Consists of 2,839,707 shares of common stock and 1,811,836 shares of common stock issuable upon the exercise of warrants to purchase common stock and 67,812 shares that Dr. Papadopoulos has the right to acquire from us within 60 days of March 31, 2021 pursuant to the exercise of stock options.
- (15) Consists of 390,581 shares of common stock and 318,829 shares of common stock issuable upon the exercise of warrants to purchase common stock, and 67,812 shares that Dr. Rastetter has the right to acquire from us within 60 days of March 31, 2021 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.
- (16) Consists of 17,717 shares of common stock held by Dr. Rosen and 67,812 shares that Dr. Rosen has the right to acquire from us within 60 days of March 31, 2021 pursuant to the exercise of stock options.
- (17) Consists of 67,812 shares of common stock that Dr. Simeonidis has the right to acquire from us within 60 days of March 31, 2021 pursuant to the exercise of stock options.
- (18) 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 upon the conversion of Class A-2 preferred stock held by Pascale Witz and 67,812 shares of common stock that Ms. Witz has the right to acquire from us within 60 days of March 31, 2021 pursuant to the exercise of stock options.
- (19) Includes all shares described in notes (8) through (18) above. Also, represents 10,000 shares of common stock that one other executive officer has the right to acquire from us within 60 days of March 31, 2021 pursuant to the exercise of stock options.

Equity Compensation Plan Information

The following table provides information as of December 31, 2020, with respect to shares of our common stock that may be issued under our existing equity compensation plans:

<u>Plan Category</u>	(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	912 ⁽¹⁾	\$ 31.34	—
2012 Equity Incentive Plan	67,723 ⁽²⁾	\$ 14.89	—
2019 Equity Incentive Plan	6,608,684 ⁽¹⁾	\$ 0.96	868,432
2012 Employee Stock Purchase Plan	—	—	187,689
Equity compensation plans not approved by stockholders:			
None			

(1) All shares issuable upon exercise of options.

(2) Consists of 33,422 shares issuable upon exercise of options and 34,301 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, 2019 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 May 3, 2019, we entered into a Securities Purchase Agreement (the “Purchase Agreement”) with certain institutional and other accredited investors (the “Purchasers”), 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, in up to two closings (collectively, the “Private Placement”).

In May 2019, we completed the initial closing of the Private Placement (the “Initial Closing”) pursuant to which we sold and issued (i) 9,730,534 shares of common stock and accompanying warrants to purchase up to an aggregate of 9,730,534 shares of common stock at a combined purchase price of \$1.205 per share, and (ii) 415,898 shares of non-voting Class A-1 convertible preferred stock, in lieu of shares of common stock, at a price of \$10.80 per share, and accompanying warrants to purchase an aggregate of 4,158,980 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-1 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 \$1.08 per share, subject to proportional adjustments in the event of stock splits or combinations or similar events. In December 2019, following our announcement of our plan to recommence our Phase 1 MAD study of RGLS4326 in the first quarter of 2020, we completed a second and final closing under the Purchase Agreement (the “Milestone Closing”), pursuant to which we sold and issued (i) 3,288,390 shares of non-voting Class A-2 convertible preferred stock, in lieu of shares of common stock, at a price of \$6.66 per share, and accompanying warrants to purchase an aggregate of 32,883,900 shares of common stock at a price of \$0.125 for each share of common stock underlying such warrants. Each share of the non-voting Class A-2 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 \$0.666 per share, pursuant to proportional adjustments in the event of stock splits or combinations or similar events.

The participants in the 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-1 convertible preferred stock and warrants to purchase common stock issued to these related parties in the Initial Closing and Class A-2 convertible preferred stock and warrants issued to these related parties in the Milestone Closing of the Private Placement. The aggregate shares and warrants set forth below reflect the number issued at the time of the Initial Closing and the Milestone Closing and do not reflect any subsequent conversions:

<u>Name of Related Person</u>	<u>Common Stock Issued in the Initial Closing</u>	<u>Warrants Issued in the Initial Closing</u>	<u>Class A-1 Convertible Preferred Stock Issued in the Initial Closing</u>	<u>Class A-2 Convertible Preferred Stock Issued in the Milestone Closing</u>	<u>Warrants Issued in the Milestone Closing</u>	<u>Aggregate Purchase Price of Common Stock, Warrants and Preferred Stock Purchased in the Private Placement</u>
Entities affiliated with New Enterprise Associates, Inc.	1,136,704	3,703,704	256,700	900,900	9,009,000	\$ 11,589,087.72
Entities affiliated with BVF Partners, L.P.	1,000,592	2,592,572	159,198	630,628	6,306,280	\$ 8,112,356.33
Entities affiliated with Sarissa Capital Management LP (1)	1,851,851	1,851,851	—	423,162	4,231,620	\$ 5,578,701.75
Altium Growth Fund, LP	1,327,801	1,327,801	—	322,978	3,229,780	\$ 4,154,759.79
Entities affiliated with EcoR1 Capital, LLC	1,111,110	1,111,110	—	253,897	2,538,970	\$ 3,347,220.08
Samsara BioCapital, L.P.	1,111,111	1,111,111	—	253,897	2,538,970	\$ 3,347,221.29
Stelios Papadopoulos, Ph.D. <i>Chairman of the Board</i>	370,370	370,370	—	84,632	846,320	\$ 1,115,739.63
Joseph P. Hagan(2) <i>President, Chief Executive Officer and Director</i>	33,194	33,194	—	7,585	75,850	\$ 99,996.93
William H. Rastetter(2) <i>Director</i>	92,889	92,889	—	22,594	225,940	\$ 290,653.39
Pascale Witz <i>Director</i>	29,630	29,630	—	6,770	67,700	\$ 89,259.17

(1) Dr. Simeonidis, a director of the Company, is a partner at Sarissa Capital Management.

(2) Securities purchased or to be purchased through an affiliated investment entity.

On December 1, 2020, we entered into a Securities Purchase Agreement (the “Purchase Agreement”) with certain institutional and other accredited investors (the “Purchasers”), 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, in up to two closings (collectively, the “Private Placement”).

In December 2020, we completed the initial closing of the 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 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 Initial Closing	Aggregate Purchase Price of Common Stock, Warrants and Preferred Stock Purchased in the Private Placement
Entities affiliated with New Enterprise Associates, Inc.	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. <i>Chairman of the Board</i>	793,528	595,146	—	\$ 574,395.24
Joseph P. Hagan ⁽¹⁾ <i>President, Chief Executive Officer and Director</i>	39,680	29,760	—	\$ 28,722.37

(1) Securities purchased or to be purchased through an affiliated investment entity.

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. We have received approximately \$16.8 million in upfront payments, payment for program-related materials and interim enrollment milestones. We are also eligible to receive a \$30.0 million development milestone payment.

In September 2014, we entered into an agreement with Sanofi-Aventis Deutschland GmbH (“Sanofi Deutschland”), a contract manufacturing subsidiary of Sanofi, for the manufacture of certain drug substance requirements and other services to support our preclinical and clinical activities associated with the RG-012 program. Pursuant to this agreement, we may engage Sanofi Deutschland from time-to-time to manufacture RG-012 drug product on our behalf. To date, we have engaged Sanofi Deutschland to manufacture multiple cGMP batches of RG-012 and to perform stability testing and related activities at a cost of \$1,831,992. These activities were ongoing during 2018 and in 2019 we paid Sanofi \$45,000 for activities completed in 2018. Pursuant to the assignment of the RG-012 program to Sanofi, we do not expect to incur any further material charges related to Sanofi Deutschland’s activities.

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 30, 2021

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, 2020 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., a corporation organized and existing under and by virtue of the General Corporation Law of the State of Delaware (the "**Company**"), does hereby certify:

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 General Corporation Law of the State of Delaware (the "**DGCL**"), adopted resolutions approving and deeming advisable an amendment to the Company's Amended and Restated Certificate of Incorporation (the "**Restated Certificate**"), as follows:

Paragraph A of Article IV of the Restated Certificate 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 410,000,000 shares. 400,000,000 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 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.

FIFTH: This Certificate of Amendment shall become effective on _____, 2021 at 4:00 p.m. Eastern Time.

IN WITNESS WHEREOF, Regulus Therapeutics Inc. has caused this Certificate of Amendment to be signed by its President and Chief Executive Officer on _____, 2021.

Regulus Therapeutics Inc.

By: _____
Joseph Hagan
President and Chief Executive Officer



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., local time, on June 13, 2021.

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

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 and 5.

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.
- 04 - Alice S. Huang, Ph.D
- 07 - William H. Rastetter, Ph.D.
- 10 - Pascale Witz, MBA, MSc

- 02 - Kathryn J. Collier
- 05 - Jake R. Nunn
- 08 - Hugh Rosen, M.D., Ph.D.

- 03 - Joseph P. Hagan
- 06 - Stelios Papadopoulos, Ph.D.
- 09 - Simos Simeonidis, Ph.D.

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
<input type="checkbox"/>									

- | | | | | | | | | | | | | | | | |
|---|---|--------------------------|--------------------------|--------------------------|---|--|--------------------------|---|---|------------|----------------|----------------|--------------------------|--------------------------|--------------------------|
| <p>2. Approval of an amendment to our Amended and Restated Certificate of Incorporation to increase the number of authorized shares of common stock from 200,000,000 to 400,000,000;</p> | <table border="0"> <tr> <td>For</td><td>Against</td><td>Abstain</td> </tr> <tr> <td><input type="checkbox"/></td><td><input type="checkbox"/></td><td><input type="checkbox"/></td> </tr> </table> | For | Against | Abstain | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <p>3. To approve, on an advisory basis, the compensation of the Company’s named executive officers;</p> | <table border="0"> <tr> <td>For</td><td>Against</td><td>Abstain</td> </tr> <tr> <td><input type="checkbox"/></td><td><input type="checkbox"/></td><td><input type="checkbox"/></td> </tr> </table> | For | Against | Abstain | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| For | Against | Abstain | | | | | | | | | | | | | |
| <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | | | | | | | | | | | | | |
| For | Against | Abstain | | | | | | | | | | | | | |
| <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | | | | | | | | | | | | | |
| <p>4. 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, 2021.</p> | <table border="0"> <tr> <td><input type="checkbox"/></td><td><input type="checkbox"/></td><td><input type="checkbox"/></td> </tr> </table> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <p>5. Authorization of the adjournment of the Annual Meeting, if necessary, to solicit additional proxies if there are not sufficient votes in favor of the Proposal 2.</p> | <table border="0"> <tr> <td><input type="checkbox"/></td><td><input type="checkbox"/></td><td><input type="checkbox"/></td> </tr> </table> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | | | | | | |
| <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | | | | | | | | | | | | | |
| <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | | | | | | | | | | | | | |

REGULUS THERAPEUTICS INC.

2021 Annual Meeting of
Regulus Therapeutics Inc. Stockholders
June 14, 2021 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.**

	<p>Small steps make an impact.</p> <p>Help the environment by consenting to receive electronic delivery, sign up at www.investorvote.com/RGLS</p>	
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IF VOTING BY MAIL, SIGN, DETACH AND RETURN THE BOTTOM PORTION IN THE ENCLOSED ENVELOPE.

Proxy - Regulus Therapeutics Inc.



Notice of 2021 Annual Meeting of Stockholders

Proxy Solicited by Board of Directors for Annual Meeting – June 14, 2021

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 14, 2021 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 and 5, 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.

/ /

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C Non-Voting Items

Change of Address – Please print new address below.

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Comments – Please print your comments below.

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Meeting Attendance

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

