
**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.
- Fee computed on table below per Exchange Act Rules 14a-6(i)(1) and 0-11.

1. Title of each class of securities to which transaction applies:

2. Aggregate number of securities to which transaction applies:

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

4. Proposed maximum aggregate value of transaction:

5. Total fee paid:

Fee paid previously with preliminary materials.

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

1. Amount Previously Paid:

2. Form, Schedule or Registration Statement No.:

3. Filing Party:

4. Date Filed:

REGULUS THERAPEUTICS INC.

10614 Science Center Drive
San Diego, California 92121

NOTICE OF ANNUAL MEETING OF STOCKHOLDERS

To Be Held On June 2, 2016

Dear Stockholder:

You are cordially invited to attend the 2016 Annual Meeting of Stockholders of Regulus Therapeutics Inc., a Delaware corporation (the "Company"). The meeting will be held on Thursday, June 2, 2016 at 9:00 a.m. local time at the Company's principal executive offices located at 10614 Science Center Drive, San Diego, CA 92121 for the following purposes:

1. To elect the seven nominees for director named herein to serve until the next annual meeting and their successors are duly elected and qualified.
2. To approve an amendment to the Company's Amended and Restated Certificate of Incorporation to permit removal of a member of the Board of Directors with or without cause by a majority vote of stockholders.
3. 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 2016.
4. 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.

The record date for the annual meeting is April 8, 2016. Only stockholders of record at the close of business on that date may vote at the meeting or any adjournment thereof.

Important Notice Regarding the Availability of Proxy Materials for the Stockholders' Meeting to Be Held on June 2, 2016 at 9:00 a.m. local time at the Company's offices located at 10614 Science Center Drive, San Diego, CA 92121.

The proxy statement and annual report to stockholders are available at www.regulusrx.com.

By Order of the Board of Directors



Christopher Aker
Corporate Secretary

San Diego, California
April 22, 2016

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 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.

10614 Science Center Drive
San Diego, California 92121

**PROXY STATEMENT
FOR THE 2016 ANNUAL MEETING OF STOCKHOLDERS**

To be held on June 2, 2016

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 2016 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 was first mailed to our stockholders of record entitled to vote at the annual meeting on April 22, 2016.

How do I attend the annual meeting?

The meeting will be held on Thursday, June 2, 2016 at 9:00 a.m. local time at 10614 Science Center Drive, 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.

Who can vote at the annual meeting?

Only stockholders of record at the close of business on April 8, 2016 will be entitled to vote at the annual meeting. On this record date, there were 52,781,009 shares of common stock outstanding and entitled to vote.

Stockholder of Record: Shares Registered in Your Name

If on April 8, 2016 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 8, 2016 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 a 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 three matters scheduled for a vote:

- Election of the seven nominees for director named herein;
- Approval of an amendment to our Amended and Restated Certificate of Incorporation (“Certificate of Incorporation”) to permit removal of a member of the Board of Directors with or without cause with a majority vote of shareholders; and
- 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 2016.

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 Proposals 2 and 3, 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, by proxy over the telephone, by proxy through the internet, or by proxy using a proxy card that you may request. 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 a proxy card that may be delivered to you at a later time, simply complete, sign and date the proxy card 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 1-800-690-6903 using a touch-tone phone and follow the recorded instructions. You will be asked to provide the company number and control number from the Notice. Your vote must be received by 11:59 p.m. Eastern Time on June 1, 2016 to be counted.
- To vote through the internet, go to www.proxyvote.com to complete an electronic proxy card. You will be asked to provide the company number and control number from the Notice. Your vote must be received by 11:59 p.m. Eastern Time on June 1, 2016 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 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.

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 8, 2016.

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 Proposal 1 or Proposal 2 without your instructions, but may vote your shares on Proposal 3.

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 seven nominees for director, “For” the amendment of our Certificate of Incorporation as provided in Proposal 2 and “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 2016. 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 and Broadridge 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, but Broadridge will be paid its customary fee of approximately \$3,000.00 plus out-of-pocket expenses if it solicits 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 set of proxy materials?

If you receive more than one set of proxy materials, your shares may be registered in more than one name or in different accounts. Please follow the voting instructions on the proxy cards 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

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- You may send a timely written notice that you are revoking your proxy to Regulus Therapeutics Inc.'s Secretary at its principal executive offices. If the mailing date of your revocation notice is prior to May 5, 2016, you should direct your notice to the Company's current principal executive offices located at 3545 John Hopkins Court, Suite 210, San Diego, CA 92121. If the mailing date of your revocation notice is on or after May 5, 2016, you should direct your notice to the Company's new principal executive offices located at 10614 Science Center Drive, San Diego, California 92121.
 - You may attend the annual meeting and vote in person. Simply attending the meeting will not, by itself, revoke your proxy.

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

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

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

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

To be considered for inclusion in the Company's proxy materials for next year's annual meeting of stockholders, your proposal must be submitted in writing by December 23, 2016 to the attention of the Secretary of Regulus Therapeutics Inc. at 10614 Science Center Drive, 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 10614 Science Center Drive, San Diego, California 92121 between February 2, 2017 and March 4, 2017. 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 and 3 and will have the same effect as "Against" votes. Broker non-votes will have no effect and will not be counted towards the vote total for any proposal except Proposal 2. For Proposal 2, broker non-votes will have the same effect as "Against" votes.

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, the election of directors, the seven 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" or "Withheld" will affect the outcome.
- To be approved, Proposal 2, regarding the amendment of our Certificate of Incorporation, must receive "For" votes from the holders of 66 2/3% of shares outstanding and entitled to vote on the record date. Abstentions and broker non-votes will have the same effect as "Against" votes.
- To be approved, Proposal 3, ratifying 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 2016, must receive “For” votes from the holders of a majority of shares present and entitled to vote either in person or represented by proxy. If you mark your proxy to “Abstain” from voting, it will have the same effect as an “Against” vote.

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 outstanding shares entitled to vote are present at the meeting in person or represented by proxy. On the record date, there were 52,781,009 shares outstanding and entitled to vote. Thus, the holders of 26,390,505 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 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.

What proxy materials are available on the internet?

The letter to stockholders, proxy statement, Form 10-K and annual report to stockholders are available at www.regulusrx.com.

PROPOSAL 1

ELECTION OF DIRECTORS

Our Board of Directors currently consists of six directors. There are seven nominees for director this year, consisting of our six incumbent directors, and Hugh Rosen, M.D., Ph.D., who our Nominating and Corporate Governance Committee has nominated for election at the annual meeting but does not currently serve on our Board of Directors. Each director to be elected and qualified will hold office until the next annual meeting of stockholders and until his 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, other than Dr. Rosen. 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 seven nominees receiving the highest number of affirmative votes will be elected. It is the Company’s policy to invite nominees for directors to attend the annual meeting. None of our current directors attended our 2015 Annual Meeting of Stockholders, except for Dr. Grint.

Nominees

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

The Nominating and Corporate Governance Committee seeks to assemble a Board that, as a whole, possesses the appropriate balance of professional and industry knowledge, financial expertise and high-level management experience necessary to oversee and direct the Company’s business. To that end, the Nominating and Corporate Governance Committee has identified and evaluated nominees in the broader context of the

Board's overall composition, with the goal of recruiting members who complement and strengthen the skills of other members and who also exhibit integrity, collegiality, sound business judgment and other qualities that the Nominating and Corporate Governance Committee views as critical to effective functioning of the Board. The brief biographies below include information, as of the date of this proxy statement, regarding the specific and particular experience, qualifications, attributes or skills of each director or nominee that led the Nominating and Corporate Governance Committee to recommend that person as a nominee. However, each of the members of the Nominating and Corporate Governance Committee may have a variety of reasons why he or she believes a particular person would be an appropriate nominee for the Board, and these views may differ from the views of other members.

Name	Age	Position Held With the Company
Dr. Stelios Papadopoulos	67	Chairman of the Board of Directors
Dr. David Baltimore	78	Director
Mr. Mark G. Foletta	55	Director
Dr. Paul C. Grint	58	Director, President and Chief Executive Officer
Dr. William H. Rastetter	68	Director
Dr. Hugh Rosen	57	Nominee for Director
Dr. Douglas E. Williams	58	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. From 2000 to 2011, Dr. Papadopoulos served as a member of the board of directors of Anadys Pharmaceuticals, Inc. prior to its acquisition by F. Hoffman-La Roche, or Roche. Since 2003, Dr. Papadopoulos has 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 M.B.A. 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. Since 1997, Dr. Baltimore has served as a director of Amgen Inc., a publicly-held biotechnology company, and also serves as a director of Immune Design Corp., a privately-held biotechnology company, and as chairman of the board of directors of Calimmune, Inc., a privately-held biotechnology company. 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.

Mark G. Foletta has served on our Board of Directors since January 2013. Since August 2015, Mr. Foletta has served as the interim Chief Financial Officer of Biocept, Inc., a publicly-traded diagnostics company. He previously served as Senior Vice President, Finance and Chief Financial Officer of Amylin Pharmaceuticals, Inc. from March 2006 through Amylin's acquisition by Bristol Myers-Squibb Company in August 2012. Prior to joining Amylin in 2000, Mr. Foletta held a number of management positions with Intermark, Inc. and Triton Group Ltd. and served as an Audit Manager with Ernst & Young. Mr. Foletta served as a director of Anadys Pharmaceuticals, Inc., a publicly-held biopharmaceutical company, from September 2005 through November 2011 (acquired by Roche) and of Ambit Biosciences during 2014 until its acquisition by Daiichi Sankyo. He is currently a member of the Board of Directors and Audit Committee of AMN Healthcare Services, Inc., a publicly-traded health services company, DexCom, Inc., a publicly-held healthcare company, and ViaCyte Inc., a privately-held biotechnology company. Mr. Foletta received a B.A. in Business Economics from the University of California, Santa Barbara. He is a Certified Public Accountant and a member of the Corporate Directors Forum. Our Nominating and Corporate Governance Committee believes that Mr. Foletta's extensive financial and operational experience in the biotechnology industry qualifies him to serve on our Board of Directors.

Paul C. Grint, M.D. has served as our President and Chief Executive Officer and on our Board of Directors since June 2015, and prior to that was our Chief Medical Officer since June 2014. From February 2011 to June 2014, Dr. Grint served as the President of Cerexa, Inc., a wholly owned subsidiary of Forest Laboratories, Inc., a pharmaceutical company, where he was responsible for the oversight of anti-infective product development. Before that, Dr. Grint served as Senior Vice President of Research at Forest Research Institute, Inc., the scientific development subsidiary of Forest Laboratories, Inc., from January 2009 to February 2011, as Chief Medical Officer of Kalypsys, Inc., a biopharmaceutical company, from 2006 to 2008, and as Senior Vice President and Chief Medical Officer of Zephyr Sciences, Inc., a biopharmaceutical company, during 2006. Dr. Grint also previously served in similar executive level positions at Pfizer Inc., IDEC Pharmaceuticals Corporation, and Schering-Plough Corporation. Dr. Grint has served on the board of directors of Synedgen, a privately-held bio-pharmaceutical company, since December 2014 and AmpliPhi Biosciences Corporation, a publicly-held biopharmaceutical company, since November 2014. Dr. Grint also served on the Board of Directors of Illumina, Inc. from April 2005 to May 2013. Dr. Grint received a B.S. in Medical Science from St. Mary's Hospital in London and his medical degree from St. Bartholomew's Hospital Medical College at the University of London. Dr. Grint is a Fellow of the Royal College of Pathologists, a member of numerous professional and medical societies, and the author or co-author of over 50 scientific publications. Our Nominating and Governance Committee believes that Dr. Grint's expertise in clinical development and commercialization of novel therapeutics qualify him to serve on our Board of Directors.

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 serves as the chairman of the board of directors of Fate Therapeutics, Inc., a publicly-held biotechnology company, chairman of the board of directors of Neurocrine Biosciences, Inc., a publicly-held biotechnology company, lead outside director of Cerulean Pharma Inc., a publicly-held biotechnology company and on the board of directors of Grail, Inc., a majority-owned subsidiary of Illumina, Inc.. In addition, he serves as an advisor to Leerink Partners, a healthcare-focused investment bank and on the board of trustees of Caltech. 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. is a nominee to our Board of Directors. Since 2002, Dr. Rosen has been a Professor of Chemical Physiology at The Scripps Research Institute in La Jolla, California where he focuses 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 serves 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 currently serves on the Receptos Scientific Advisory Board. He also serves on the Scientific Advisory Board of ActivX Biosciences Inc., a wholly owned biopharmaceutical subsidiary of Kyorin Pharmaceuticals Co., Ltd. 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.

Douglas E. Williams, Ph.D. has served on our Board of Directors since November 2012. He has served as the Chief Executive Officer and President of Codiak Biosciences, Inc. since November 2015. He served as Executive Vice President of Research and Development at Biogen, a publicly-held biopharmaceutical company, from January 2011 to July 2015. Dr. Williams was the Chief Executive Officer and member of the Board of Directors of ZymoGenetics, Inc., a publicly-held biopharmaceutical company, from January 2009 until November 2010 (acquired by Bristol-Myers Squibb). He also served as President of ZymoGenetics, Inc. from 2007 to 2009 and as Chief Scientific Officer and Executive Vice President from 2004 to 2007. Previously, he was the Chief Scientific Officer and Executive Vice President of Research and Development at Seattle Genetics Inc., a publicly-held biotechnology company, Head of Health and Strategic Development at Genesis Research & Development Corp. Ltd, and Senior Vice President and Washington Site Leader at Amgen Inc., a publicly-held biopharmaceutical company. Dr. Williams also served in a series of scientific and senior leadership positions over a decade at Immunex Corp., a publicly held biopharmaceutical company (acquired by Amgen, Inc.) including Executive Vice President and Chief Technology Officer, Senior Vice President of Discovery Research and Vice President of Research and Development. Before entering the biotechnology industry, Dr. Williams served on the faculty of the Indiana University School of Medicine and the Department of Laboratory Medicine at the Roswell Park Memorial Institute in Buffalo, New York. He holds a Ph.D. in Physiology from the State University of New York at Buffalo, Roswell Park Memorial Institute Division and a B.S. magna cum laude in Biological Sciences from the University of Massachusetts, Lowell. Our Nominating and Corporate Governance Committee believes that Dr. Williams is qualified to serve on our Board of Directors due to his extensive operational and leadership experience in the biotechnology industry.

**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 four directors are independent

directors within the meaning of the applicable NASDAQ listing standards: Dr. Baltimore, Mr. Foletta, Dr. Papadopoulos and Dr. Rastetter. 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, Dr. Grint 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.

MEETINGS OF THE BOARD OF DIRECTORS

The Board of Directors met five times during the last fiscal year and four times in executive session. All directors who served in 2015 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 has three committees: 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, 2015 for each of the Board committees:

Name	Audit	Compensation	Nominating and Corporate Governance
Dr. David Baltimore		X	X*
Dr. Bruce L.A. Carter†	X	X	
Mr. Mark G. Foletta	X*		X
Dr. Stelios Papadopoulos	X		
Dr. William H. Rastetter	X	X*	X
Total meetings in 2015	4	3	2

* Committee Chairperson

† Dr. Carter resigned from our Board of Directors and all Board committees on which he served on November 24, 2015.

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: Mr. Foletta, Dr. Papadopoulos and Dr. Rastetter. 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 each member of our Audit Committee meets the requirements for independence under the NASDAQ listing standards.

Our Board of Directors has determined that Mr. Foletta qualifies as an “audit committee financial expert,” as defined in applicable SEC rules. Our Board of Directors has made a qualitative assessment of Mr. Foletta’s level of knowledge and experience based on a number of factors, including his formal education, his experience as a chief financial officer for a public company and his service as an Audit Manager with Ernst & Young. In addition to the Audit Committee, Mr. Foletta also serves on the audit committee of AMN Healthcare Services and during 2014 served on the Audit Committee of Ambit Biosciences. Our Board of Directors has determined that this simultaneous service does not impair Mr. Foletta’s ability to effectively serve on our Audit Committee.

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, 2015 with management of the Company. The Audit Committee has discussed with the independent registered public accounting firm the matters required to be discussed by Auditing Standard No. 16, *Communications with Audit Committees*, as adopted by the Public Company Accounting Oversight Board (“PCAOB”). 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, 2015.

Mr. Mark G. Foletta (Chair)
Dr. Stelios Papadopoulos
Dr. William H. Rastetter

* 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, 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 two directors: Dr. Baltimore and Dr. Rastetter. 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 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, including:

- establishment of corporate and individual performance objectives relevant to the compensation of the Company's executive officers, directors and other senior management and evaluation of performance in light of these stated objectives;
- review and recommendation to the Board for approval of the compensation and other terms of employment or service, including severance and change-in-control arrangements, of the Company's Chief Executive Officer and the other executive officers and directors; and
- administration of the Company's equity compensation plans, pension and profit-sharing plans, deferred compensation plans and other similar plan and programs.

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 the past fiscal year, 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 Dr. Grint, to which it delegated authority to grant, without any further action required by the Compensation Committee, stock options to employees who are not officers of the Company. The purpose of this delegation of authority is to enhance the flexibility of option administration within the Company and to facilitate the timely grant of options to non-management employees, particularly new employees, within specified limits approved by the Compensation Committee. In particular, the subcommittee may grant options only within pre-approved guidelines and not to any employee who will have a vice president title or higher. Typically, as part of its oversight function, the Committee will review on a regular basis the list of grants made by the subcommittee. During fiscal year 2015, the subcommittee exercised its authority to grant options to purchase an aggregate of 786,000 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 Senior Vice President, Human Capital, including analyses of executive and director compensation paid at other companies identified by the Company's Senior Vice President, Human Capital.

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, Mr. Foletta and Dr. Rastetter. 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 2015. 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.

Section 16(a) Beneficial Ownership Reporting Compliance

Section 16(a) of the Exchange Act requires the Company's directors and executive officers, and persons who own more than ten percent of a registered class of the Company's equity securities, to file with the SEC initial reports of ownership and reports of changes in ownership of common stock and other equity securities of the Company. Officers, directors and greater than ten percent stockholders are required by SEC regulation to furnish the Company with copies of all Section 16(a) forms they file.

To the Company's knowledge, based solely on a review of the copies of such reports furnished to the Company and written representations that no other reports were required, during the fiscal year ended December 31, 2015, all Section 16(a) filing requirements applicable to its officers, directors and greater than ten percent beneficial owners were complied with; except that each of Drs. Baltimore, Papadopoulos, Carter, Grint, Rastetter, Williams and Mr. Foletta failed to timely file one report each, each report covering one transaction.

PROPOSAL 2

APPROVAL OF AMENDMENT TO AMENDED AND RESTATED CERTIFICATE OF INCORPORATION

The Company's Amended and Restated Certificate of Incorporation (the "Certificate of Incorporation") currently provides that neither the Board of Directors nor any individual director may be removed without cause, and that any individual director or directors may be removed with cause by the affirmative vote of the holders of at least 66 2/3% of the voting power of all then-outstanding shares of capital stock of the Company entitled to vote generally at an election of directors, voting together as a single class.

On December 21, 2015, the Delaware Chancery Court issued an opinion in *In re VAALCO Energy, Inc. Stockholder Litigation*, Consol. C.A. No. 11775-VCL, invalidating as a matter of law provisions of the certificate of incorporation and bylaws of VAALCO Energy, Inc., a Delaware corporation that permitted the removal of VAALCO's directors by its stockholders only for cause. The Chancery Court held that, in the absence of a classified board of cumulative voting, VAALCO's "only for-cause" director removal provisions conflict with Section 141(k) of the Delaware General Corporation Law and are therefore invalid.

Section C of Article V of the Certificate of Incorporation contains a similar "only for-cause" director removal provision, and we do not have a classified board of directors or cumulative voting. As such, and in light of the *VAALCO* decision, the Board of Directors is requesting stockholder approval of the amendment and restatement of the Certificate of Incorporation (the "Charter Amendment") to provide that any of our directors or our entire Board of Directors may be removed, with or without cause, by the holders of a majority of the shares then entitled to vote at an election of directors. The Charter Amendment is attached to this proxy statement as Appendix A.

If the Charter Amendment is adopted by our stockholders, it will become effective upon the filing thereof with the Secretary of State of the State of Delaware. If the Charter Amendment is not approved by our stockholders, Section C of Article V of the Certificate of Incorporation will continue to be in conflict with Section 141(k) of the Delaware General Corporation Law.

Section 20 of our Amended and Restated Bylaws (the "Bylaws") also contains a similar "only for-cause" director removal provision. On March 22, 2016, the Board of Directors approved, subject to stockholder approval of the Charter Amendment, the amendment and restatement of the Bylaws in order to provide that, consistent with Section 141(k) of the Delaware General Corporation Law, any of our directors or our entire Board of Directors may be removed, with or without cause, by the holders of a majority of our shares of common stock then entitled to vote at an election of directors. No stockholder approval is being requested nor is required with respect to such amendment and restatement of the Bylaws.

Approval of this Proposal requires the affirmative vote of at least 66 2/3% of the shares of our common stock that are outstanding on the record date for the annual meeting. Abstentions and broker non-votes will be counted toward the tabulation of votes cast on the proposal and will have the same effect as "Against" votes.

Our Board of Directors believes that approval of this Proposal is advisable and in the best interests of our stockholders.

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

PROPOSAL 3

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, 2016 and has further directed that management submit the selection of independent registered public accounting firm for ratification by the stockholders at the annual meeting. Ernst & Young has audited the Company's financial statements since its incorporation in 2009. Representatives of Ernst & Young are expected to be present at the annual meeting. They will have an opportunity to make a statement if they so desire and will be available to respond to appropriate questions.

Neither the Company's Bylaws nor other governing documents or law require stockholder ratification of the selection of Ernst & Young as the Company's independent registered public accounting firm. However, the Audit Committee is submitting the selection of Ernst & Young to the stockholders for ratification as a matter of good corporate practice. If the stockholders fail to ratify the selection, the Audit Committee will reconsider whether or not to retain that firm. Even if the selection is ratified, the Audit Committee in its discretion may direct the appointment of different independent auditors at any time during the year if they determine that such a change would be in the best interests of the Company and its stockholders.

The affirmative vote of the holders of a majority of the shares present in person or represented by proxy and entitled to vote at the annual meeting will be required to ratify the selection of Ernst & Young. Abstentions will be counted toward the tabulation of votes on proposals presented to the stockholders and will have the same effect as negative votes. Broker non-votes (if any) are counted towards a quorum, but are not counted for any purpose in determining whether this matter has been approved.

PRINCIPAL ACCOUNTANT FEES AND SERVICES

The following table represents aggregate fees billed to the Company for the fiscal years ended December 31, 2015 and December 31, 2014, by Ernst & Young LLP, the Company's principal accountant. All fees described below were pre-approved by the Audit Committee.

	Fiscal Year Ended	
	2015	2014
	(in thousands)	
Audit Fees(1)	\$438	\$389
Audit-related Fees	—	—
Tax Fees(2)	101	—
All Other Fees	—	—
Total Fees	\$539	\$389

- (1) Audit fees consist of fees billed 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.
- (2) Tax fees consist of fees billed for professional services by Ernst & Young for analysis of the Company's research credit.

All fees described above were pre-approved by the Audit Committee.

In connection with the audit of each of the 2015 and 2014 financial statements, the Company entered into an engagement agreement 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.

During the fiscal years ended December 31, 2015 and December 31, 2014, none of the total hours expended on the Company's financial audit by Ernst & Young were provided by persons other than Ernst & Young full-time permanent employees.

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 3**

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>
Paul C. Grint, M.D.	57	President and Chief Executive Officer
Joseph "Jay" Hagan	47	Chief Operating Officer

Dr. Grint's biographical information is set forth above under Proposal 1.

Joseph "Jay" Hagan has served as our Chief Operating Officer, principal financial officer and principal accounting officer since January 2016. 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. He received an M.B.A. from Northeastern University and a B.S. in Physiology and Neuroscience from the University of California, San Diego.

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, 2016 by: (i) each of our directors; (ii) each of our Named Executive Officers as defined below 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 52,774,550 shares of common stock outstanding as of March 31, 2016. 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 within 60 days following March 31, 2016. Unless otherwise indicated, the address for the following stockholders is c/o Regulus Therapeutics Inc., 3545 John Hopkins Court, Suite 210, San Diego, CA 92121.

Beneficial Owner	Beneficial Ownership	
	Number of Shares	Percent of Total
Greater than 5% Stockholders		
FMR LLC(1) 245 Summer Street Boston, Massachusetts 02210	7,851,397	14.9%
Aventisub LLC(2). c/o Sanofi 54, rue La Boétie 75414 Paris – France	5,053,779	9.6%
Alnylam Pharmaceuticals, Inc. 300 Third Street, 3rd Floor Cambridge, MA 02142	4,896,716	9.3%
Wellington Management Group LLP(3) 280 Congress Street Boston, MA 02210	4,213,856	8.0%
AstraZeneca AB(4) SE-431 83 Mölndal Sweden	3,522,000	6.7%
RA Capital Management, LLC(5) 20 Park Plaza, Suite 1200 Boston, Massachusetts 02116	3,482,924	6.6%
Ionis Pharmaceuticals, Inc. 2855 Gazelle Court Carlsbad, CA 92010	2,843,172	5.4%
UBS AG(6) Bahnhofstrasse 45 Zurich, Switzerland	2,609,098	4.9%
Named Executive Officers and Directors		
David Baltimore, Ph.D.(7)	259,825	*
Mark G. Foletta(8)	68,680	*
Paul C. Grint, M.D.(9)	190,705	*
Stelios Papadopoulos, Ph.D.(10)	231,180	*
William H. Rastetter, Ph.D.(11)	158,680	*
Douglas E. Williams, Ph.D.(12)	58,680	*
Kleanthis G. Xanthopoulos, Ph.D.(13)	0	*
Neil W. Gibson, Ph.D.(14)	254,793	*
David L. Szekeres(15)	0	*
All current executive officers and directors as a group (7 persons)(16)	1,232,543	2.3%

* Less than one percent.

- (1) Consists of shares beneficially owned, or that may be deemed to be beneficially owned, by FMR LLC, certain of its subsidiaries and affiliates, and other companies (collectively, the “FMR Reporters”). Does not reflect securities, if any, beneficially owned by certain other companies whose beneficial ownership of securities is disaggregated from that of the FMR Reporters in accordance with Securities and Exchange Commission Release No. 34-39538 (January 12, 1998). Edward C. Johnson 3d is a Director and the Chairman of FMR LLC and Abigail P. Johnson is a Director, the Vice Chairman, the Chief Executive Officer and the President of FMR LLC. Members of the family of Edward C. Johnson 3d, including Abigail P. Johnson, are the predominant owners, directly or through trusts, of Series B voting common shares of FMR LLC, representing 49% of the voting power of FMR LLC. The Johnson family group and all other Series B shareholders have entered into a shareholders’ voting agreement under which all Series B voting common shares will be voted in accordance with the majority vote of Series B voting common shares. Accordingly, through their ownership of voting common shares and the execution of the shareholders’ voting agreement, members of the Johnson family may be deemed, under the Investment Company Act of 1940, to form a controlling group with respect to FMR LLC. Neither FMR LLC nor Edward C. Johnson 3d nor Abigail P. Johnson has the sole power to vote or direct the voting of the shares owned directly by the various investment companies registered under the Investment Company Act (“Fidelity Funds”) advised by Fidelity Management & Research Company (“FMR Co”), a wholly owned subsidiary of FMR LLC, which power resides with the Fidelity Funds’ Boards of Trustees. Fidelity Management & Research Company carries out the voting of the shares under written guidelines established by the Fidelity Funds’ Boards of Trustees.
- (2) Aventisub LLC is a subsidiary of Sanofi. Sanofi has the ability to exercise voting and dispositive power over the shares held by Aventisub LLC.
- (3) Consists of 4,213,856 shares of common stock held by clients of, or investment advisors affiliated with, Wellington Management Group, LLP (“Wellington”). Wellington may be deemed to beneficially own these shares in its, or its affiliated investment advisers’, capacity as investment adviser
- (4) AstraZeneca AB is an indirect wholly owned subsidiary of AstraZeneca PLC. AstraZeneca PLC has the ability to exercise voting and dispositive power over the shares held by AstraZeneca AB.
- (5) Consists of 2,877,679 shares held by RA Capital Healthcare Fund, L.P. (the “Fund”), for which RA Capital Management, LLC (“RA Capital”) serves as the sole general partner, and 605,245 shares held in a separately managed account for which RA Capital serves as investment adviser. RA Capital has shared voting and dispositive power over all of the foregoing shares due its role as sole general partner of the Fund and investment advisor to the separately managed account. Peter Kolchinsky serves as the manager of RA Capital and has shared voting and dispositive power over the shares beneficially owned by RA Capital. Each of Peter Kolchinsky, RA Capital and Fund disclaims beneficial ownership of the shares except to the extent of his or its pecuniary interest therein.
- (6) Consists of 2,609,098 shares held by UBS Asset Management, Inc. for the benefit of the UBS Group.
- (7) Includes 259,825 shares that Dr. Baltimore has the right to acquire from us within 60 days of March 31, 2016 pursuant to the exercise of stock options.
- (8) Includes 58,680 shares that Mr. Foletta has the right to acquire from us within 60 days of March 31, 2016 pursuant to the exercise of stock options.
- (9) Includes 190,705 shares that Dr. Grint has the right to acquire from us within 60 days of March 31, 2016.
- (10) Includes 30,503 shares that Dr. Papadopoulos has the right to acquire from us within 60 days of March 31, 2016 pursuant to the exercise of stock options.
- (11) Includes 58,680 shares that Dr. Rastetter has the right to acquire from us within 60 days of March 31, 2016 pursuant to the exercise of stock options.
- (12) Includes 58,680 shares that Dr. Williams has the right to acquire from us within 60 days of March 31, 2016 pursuant to the exercise of stock options.
- (13) Dr. Xanthopoulos resigned as an executive officer and a director of the Company on June 1, 2015.
- (14) Dr. Gibson resigned as an executive officer of the Company on June 1, 2015.

(15) Mr. Szekeres resigned as an executive officer of the Company on December 3, 2016.

(16) Includes the shares described in notes (7) through (12) and 10,000 shares held by an executive officer not listed in the table above.

EXECUTIVE COMPENSATION

This “Executive Compensation” section describes the compensation decisions for the following individuals, who are our “Named Executive Officers” for the year ended December 31, 2015:

- Paul C. Grint, M.D., our current President and Chief Executive Officer;
- Kleanthis G. Xanthopoulos, Ph.D., our former President and Chief Executive Officer;
- Neil W. Gibson, Ph.D., our former Chief Scientific Officer; and
- David L. Szekeres, our former Chief Business Officer and General Counsel.

Dr. Grint was our only executive officer serving as of December 31, 2015. This section includes certain compensation information for Mr. Hagan, who commenced employment as our Chief Operating Officer in January 2016, to the extent such information may be helpful to an understanding of our executive compensation program.

SUMMARY COMPENSATION TABLE

The following table shows for the fiscal years ended December 31, 2015 and December 31, 2014, compensation awarded to, paid to, or earned by, the Named Executive Officers.

Name and Principal Position	Year	Salary (\$)	Option Awards (\$)(1)	Non-Equity Incentive Plan Compensation (\$)(2)	All Other Compensation (\$)(3)	Total (\$)
Paul C. Grint, M.D.(4) President & Chief Executive Officer	2015	446,532	4,306,175	250,000	4,022	5,006,729
	2014	195,271	2,290,597	82,973	1,851	2,570,692
Kleanthis G. Xanthopoulos, Ph.D.(5) Former President & Chief Executive Officer	2015	267,933	1,752,311(5)	—	1,029,016(5)	3,049,260
	2014	618,000	2,743,355	533,952	7,343	3,902,650
Neil W. Gibson, Ph.D.(6) Former Chief Scientific Officer	2015	185,838	707,985(6)	—	422,369(6)	1,316,192
	2014	360,500	1,070,391	204,404	4,600	1,639,895
David L. Szekeres(7) Former Chief Business Officer & General Counsel	2015	281,494	500,725	—	357,344(7)	1,139,563
	2014	244,724	2,925,341	117,606	4,124	3,291,795

(1) In accordance with SEC rules, this column reflects the aggregate grant date fair value of the option awards granted during 2015 and 2014, as applicable, 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, 2015. These amounts do not reflect the actual economic value that will be realized by the Named Executive Officer upon the vesting of the stock options, the exercise of the stock options, or the sale of the common stock underlying such stock options. The grant date fair value of the option awards granted during 2015 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. Performance-based options granted to Dr. Xanthopoulos, Dr. Gibson and Mr. Szekeres with performance goals that had not been achieved as of the resignation date were cancelled.

- (2) Amounts shown represent performance bonuses earned for 2015 and 2014, which were each paid in a cash lump sum in the first quarter of 2016 and 2015, respectively.
- (3) Amounts shown for all Named Executive Officers in 2015 include term life insurance and long-term disability insurance paid by us on behalf of the Named Executive Officers and matching contributions we paid under the terms of our 401(k) plan. 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 “Perquisites, Health, Welfare and Retirement Benefits.”
- (4) Dr. Grint served as our Chief Medical Officer until his promotion to the position of President and CEO effective June 1, 2015. Dr. Grint’s base salary was increased from \$371,676 to \$500,000 upon such promotion.
- (5) Dr. Xanthopoulos resigned from Regulus effective June 1, 2015. Dr. Xanthopoulos received certain severance benefits in connection with his resignation, as described in more detail below under “Employment Agreements with Named Executive Officers”. The amount shown in the “Option Awards” column for Dr. Xanthopoulos includes the incremental fair value (\$100,366), computed as of the modification date in accordance with ASC 718, of the modification to Dr. Xanthopoulos’ stock options to extend the time in which Dr. Xanthopoulos was permitted to exercise all of his outstanding options, pursuant to the terms of his resignation. The amount shown in the “All Other Compensation” column for Dr. Xanthopoulos includes \$1,023,355 in cash severance payments to Dr. Xanthopoulos pursuant to the terms of his resignation, all of which was paid in June 2015, except for \$477,869 which is being paid in equal monthly installments over the following 12-month period.
- (6) Dr. Gibson resigned from Regulus effective June 30, 2015. Dr. Gibson received certain severance benefits in connection with his resignation, as described in more detail below under “Employment Agreements with Named Executive Officers”. The amount shown in the “Option Awards” column for Dr. Gibson includes the incremental fair value (\$28,501), computed as of the modification date in accordance with ASC 718, of the modification to Dr. Gibson’ stock options to extend the time in which Dr. Gibson was permitted to exercise all of his outstanding options, pursuant to the terms of his resignation. The amount shown in the “All Other Compensation” column for Dr. Gibson includes \$416,754 in cash severance payments to Dr. Gibson pursuant to the terms of his resignation.
- (7) Mr. Szekeres resigned from Regulus effective December 3, 2015. Mr. Szekeres received certain severance benefits in connection with his resignation, as described in more detail below under “Employment Agreements with Named Executive Officers”. The amount shown in the “All Other Compensation” column for Dr. Szekeres includes \$354,271 in cash severance payments to Mr. Szekeres pursuant to the terms of his resignation.

Annual Base Salary

The compensation of our Named Executive Officers is generally determined and approved by our Compensation Committee, who recommends its decisions to our Board of Directors. Our Board of Directors, without members of management present, ultimately ratifies and approves all compensation decisions. On December 2, 2014, our Board of Directors, upon the recommendation of our Compensation Committee, approved the following 2015 annual base salaries for our Named Executive Officers, which became effective on January 1, 2015, with the exception of Dr. Grint whose base salary became effective upon his elevation to President and Chief Executive Officer on June 1, 2015:

Name	2015 base salary (\$)
Paul C. Grint, M.D.	500,000(1)
Kleanthis G. Xanthopoulos, Ph.D	637,158
Neil W. Gibson, Ph.D.	371,676
David L. Szekeres	303,267

- (1) Prior to his promotion to President and CEO on June 1, 2015, Dr. Grint’s base salary was \$371,676.

On February 4, 2016, our Board of Directors, upon recommendation from the Compensation Committee approved the 2016 annual base salary for Dr. Grint, in the amount of \$515,000, which was effective as of January 1, 2016. Our Board of Directors, upon the recommendation of our Compensation Committee, approved a 2016 annual base salary for Mr. Hagan of \$415,000 effective upon Mr. Hagan's commencement of employment on January 4, 2016.

Annual Performance-Based Bonus Opportunity

In addition to base salaries, our Named Executive Officers are eligible to receive annual performance-based cash bonuses, which are designed to provide appropriate incentives to our executives to achieve defined annual corporate goals and to reward our executives for individual achievement towards these goals.

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. There is no designated proportion of the bonus attributed to the CPF and the IPF and there is no maximum bonus percentage or amount established for the Named Executive Officer and, as a result, the bonus amounts vary from year to year based on corporate and individual performance. At the end of the year, our Compensation Committee approves the extent to which we achieved the CPF. The extent to which each individual Named Executive Officer achieves his or her IPF is determined based on our Chief Executive Officer's and management'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 this discretion in awarding the bonuses in 2015.

Pursuant to their employment agreements, each Named Executive Officer had a target bonus for 2015 represented as a percentage of base salary, or a target bonus percentage, which is subject to modification from time to time in the discretion of our Board of Directors. Our Named Executive Officers' target bonus percentages for 2015 were as follows:

<u>Name</u>	<u>Target bonus (%)</u>	<u>Target bonus (\$)</u>
Paul C. Grint, M.D.	50 ⁽¹⁾	250,000
Kleanthis G. Xanthopoulos, Ph.D.	60	382,295
Neil W. Gibson, Ph.D.	35	130,087
David L. Szekeres	35	106,143

(1) Dr. Grint's target bonus percentage was increased from 35% to 50%, effective June 1, 2015 upon his promotion to Chief Executive Officer.

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, but relate generally to achievement of discovery, clinical, regulatory and manufacturing milestones for clinical development candidates, financial factors such as raising or preserving capital and performance against our operating budget and business

development goals related to *micro*RNA therapeutics. 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 2015, the CPF overall goals related to continuing to advance our clinical programs from RG-101 and RG-012, selecting a clinical candidate, completing the year with at least \$100 million in cash, enhancing the leadership team and maintaining a robust culture by retaining the best talent and developing new initiatives. The IPF goals varied by individual and included maintaining a leading position in *micro*RNA research, accelerating efforts in *micro*RNA therapeutic development, supporting our growth with additional capital, licenses and brand recognition, fostering a culture of value creating and building good processes and policies. Our Chief Executive Officer's IPF goals are tied more closely with our CPF goals, as our Chief Executive Officer has a direct impact on our corporate performance.

During 2015, we achieved our key goals under the Clinical Map Initiative to advance our clinical development of RG-101 and RG012, further advanced our *micro*RNA pipeline, concluded the year with over \$100 million in cash and succeeded in limiting our turnover. We also made significant achievements in the development of new initiatives during 2015, including our filing of multiple regulatory documents to initiate clinical trials in RG-101 and RG-012, the establishment of a global supply chain for RG-101, commencement of a collaboration with GSK to investigate RG-101 in combination with a GSK compound, and entry into a lease agreement for new premises which will allow the Company's future growth. In February 2016, our Board of Directors, upon the recommendation of our Compensation Committee, approved a CPF achievement of 100% which our Board believed was appropriate based on our achievements described above. Based on Human Resources' recommendations with respect to each Named Executive Officer, and our Compensation Committee's deliberations with respect to each Named Executive Officer's individual performance against the IPF, in February 2016 our Compensation Committee and Board approved a performance-based bonus in the amount of \$250,000 for Dr. Grint, in recognition of his ability to lead and develop the organization towards progressing our clinical portfolio, exploring different possible combinations of RG-101 with other antivirals and exceeding our year-end cash projections. Our other Named Executive Officers did not receive performance-based bonuses due to their resignations.

For 2016, upon recommendation by the Compensation Committee, the Board of Directors approved a 2016 target bonus for Mr. Hagan of 40% of his annual base salary. Dr. Grint's 2016 target bonus remains the same as his 2015 target bonus.

Long-Term Incentive Compensation

Our long-term, equity-based incentive awards are designed to align the interests of our Named Executive Officers and our other employees, non-employee directors and consultants with the interests of our stockholders. Because vesting is based on continued service, our equity-based incentives also encourage the retention of our Named Executive Officers through the vesting period of the awards.

We use stock options as the primary incentive for long-term compensation to our Named Executive Officers because they are able to profit from stock options only if our stock price increases relative to the stock option's exercise price. We generally provide initial grants in connection with the commencement of employment of our Named Executive Officers and annual retention grants at or shortly following the end of each year.

Prior to 2012, we granted all stock options pursuant to our 2009 Equity Incentive Plan (the "2009 Plan"), the terms of which are described below under "Equity Compensation Plans and Other Benefit Plans—2009 Equity Incentive Plan." All options granted under the 2009 Plan were granted with an exercise price per share equal to no less than the fair market value of our common stock on the date of grant of each award. Since October 2012,

all stock options have been granted pursuant to our 2012 Equity Incentive Plan (the “2012 Plan”) or the 2015 Inducement Plan (“2015 Inducement Plan”), the terms of which are described below under “Equity Compensation Plans and Other Benefits Plans—2012 Equity Incentive Plan” and “Equity Compensation Plans and Other Benefits Plans—2015 Inducement Plan” respectively. All options granted under the 2012 Plan or the 2015 Inducement Plan are granted with an exercise price per share equal to the fair market value of our common stock on the date of grant.

Most of our stock option grants vest over a four-year period and may be granted with an early exercise feature allowing the holder to exercise and receive unvested shares of our stock, so that the employee may exercise and have a greater opportunity for gains on the shares to be taxed at long-term capital gains rates rather than ordinary income rates. Beginning in late 2013, our Compensation Committee also decided to grant options that vest based on our achievement of specific Company goals, which we believe further aligns our Named Executive Officers’ interests with our Company goals and the interests of our stockholders. In addition, our Compensation Committee has approved certain grants of options to our Named Executive Officers containing accelerated vesting provisions upon an involuntary termination (both termination without cause and resignation for good reason) as well as upon certain material change in control transactions. Our Compensation Committee believes these accelerated vesting provisions reflect current market practices, based on the collective knowledge and experiences of our Compensation Committee members (and without reference to specific peer group data), and allow us to attract and retain highly qualified executive officers. In addition, we believe these accelerated vesting provisions will allow our Named Executive Officers to focus on closing a transaction that may be in the best interest of our stockholders even though the transaction may otherwise result in a termination of their employment and, absent such accelerated vesting, a forfeiture of their unvested equity awards. Additional information regarding accelerated vesting provisions for our Named Executive Officers is discussed below under “Employment Agreements with Executive Officers.”

On January 5, 2015, our Compensation Committee granted performance-based stock option awards to purchase 72,625 shares to Dr. Grint, 152,267 shares of common stock to Dr. Xanthopoulos, 62,631 shares to Dr. Gibson, and 46,154 shares to Mr. Szekeres, each of which options were granted with an exercise price of \$16.24 per share. The terms of the options specify that vesting commences only upon achievement, by June 30, 2016, of a future corporate goal that relates to specified outcomes concerning our current and future clinical development plans. The extent to which we achieve each goal will be determined by our Compensation Committee and upon such determination, if the goal is achieved, 50% of the shares attributable to such goal will vest and the remaining shares attributable to the goal shall vest in equal installments on a monthly basis thereafter such that all shares shall be vested within two years of the achievement of the goal, provided that the option holder continues to provide services to us through such dates. Each of Dr. Xanthopoulos, Dr. Gibson and Mr. Szekeres forfeited the foregoing options upon their resignations in 2015.

On June 25, 2015, in connection with his appointment as President and CEO, we granted Dr. Grint an option to purchase 500,000 shares of common stock with an exercise price of \$10.22 per share. Twenty-five percent of the total number of shares subject to the option vested on June 24, 2016, and the remainder will vest in equal monthly installments thereafter for the following three years, provided that Dr. Grint continues to provide services to us through such dates.

On February 4, 2016, we awarded an annual retention grant to Dr. Grint in the form of an option to purchase 265,000 shares of common stock which option has an exercise price of \$6.35 per share. Twenty-five percent of the total number of shares subject to the option vests on January 1, 2017, and the remainder will vest in equal monthly installments thereafter over the following three years, provided that Dr. Grint continues to provide services to us through such dates. In addition, on February 4, 2016, we granted Dr. Grint a performance-based stock option to purchase 130,000 shares of common stock which option also has an exercise price of \$6.35 per share. The option will commence vesting only upon achievement of a future corporate goal that relates to specified outcomes concerning our future clinical development plans and must be achieved by the end of 2016.

On January 4, 2016, in connection with his commencement of employment as our Chief Operating Officer, we granted Mr. Hagan a stock option exercisable for up to 420,000 shares of common stock, 25% of which shares will vest one year after the grant date and the balance of which will vest in equal monthly installments over the following three years, subject to Mr. Hagan's continuous service with us. On January 4, 2016 we also granted Mr. Hagan a performance-based stock option exercisable for up to 122,631 shares of common stock. The stock option will vest upon the achievement of specified performance-based development milestones. Fifty percent of the shares subject to any particular performance-based milestone will vest upon the determination by the Board or Compensation Committee that such milestone has been achieved, and the balance of the shares subject to such milestone will vest in equal monthly installments over the following two years, subject to Mr. Hagan's continuous service with us.

Perquisites, Health, Welfare and Retirement Benefits

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 provide 401(k) matching contributions as discussed in the section below entitled "Equity Compensation Plans and Other Benefit Plans—401(k) Plan."

We do not provide perquisites or personal benefits to our Named Executive Officers. We do, however, 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.

Compensation Committee Interlocks and Insider Participation

As indicated above, the Compensation Committee currently consists of Dr. Baltimore and Dr. Rastetter. No member of the Compensation Committee has ever been an officer or employee of ours. None of our executive officers currently serves, or has served during the last completed fiscal year, on the compensation committee or board of directors of any other entity that has one or more executive officers serving as a member of our Board of Directors or Compensation Committee.

Outstanding Equity Awards at Fiscal Year-End.

The following table shows certain information regarding outstanding equity awards as of December 31, 2015 for the Named Executive Officers.

Name	Grant Date	Option Awards ⁽¹⁾		Equity Incentive Plan Awards: Number of Securities Underlying Unexercised Options (#)	Option Exercise Price (\$)	Option Expiration Date
		Number of Securities Underlying Unexercised Options (#)	Number of Securities Underlying Unexercised Options (#)			
Dr. Paul C. Grint	06/25/2015 ⁽²⁾	—	500,000	—	10.22	06/24/2025
	01/05/2015 ⁽³⁾	—	—	72,652	16.24	01/04/2025
	12/02/2014 ⁽²⁾	—	50,870	—	17.76	12/01/2024
	06/16/2014 ⁽⁴⁾	46,666	23,334	30,000	7.58	06/15/2024
	06/16/2014 ⁽²⁾	93,750	156,250	—	7.58	06/15/2024
Dr. Kleantis G. Xanthopoulos ⁽⁵⁾		—	—	—		
Dr. Neil W. Gibson ⁽⁶⁾		—	—	—		
David Szekeres ⁽⁷⁾	12/02/2014	81,101	—	—	17.76	03/03/2016 ⁽⁸⁾
	03/26/2014	40,000	—	—	8.51	03/03/2016 ⁽⁸⁾
	02/04/2014	250,000	—	—	8.63	03/03/2016 ⁽⁸⁾

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- (1) All of the options were granted under the 2012 Plan and were granted with a per share exercise price equal to the fair market value of our common stock on the date of grant and become exercisable as they vest. The terms of the 2012 Plan are described below under “Equity Compensation Plans and Other Benefit Plans.” The vesting of the time-based options accelerates upon termination of employment of the Named Executive Officer by us without cause or by the officer for good reason, as described below under “Employment Agreements with Named Executive Officers.”
 - (2) 25% of the shares subject to the option vests on the one year anniversary of the grant date, and 1/48th of the total number of shares subject to the option vests on the first day of each month thereafter, provided that the option holder continues to provide services to us through such dates.
 - (3) The option vests only upon achievement of specified performance goals on or before June 30, 2016 which had not occurred prior to December 31, 2015. Upon achievement of the goal, 50% of the shares subject to the option immediately vests, and 1/24th of the total number of shares subject to the option vests thereafter on the first day of each month, provided that the option holder continues to provide services to us through such dates.
 - (4) The option vests only upon the achievement of specified performance goals, two of which have been achieved. Accordingly, 20,000 shares relating to the first achieved performance goal vested on October 20, 2014 and 833 shares vest on the first day of each month thereafter for 24 months, provided that the option holder continues to provide services to us through such dates. Additionally, 15,000 shares relating to the second achieved performance goal vested on December 16, 2015 and 625 shares will vest on the first day of each month thereafter for 24 months, provided that the option holder continues to provide services to us through such dates. The 30,000 remaining shares are eligible to vest only upon the achievement of a specified performance goal on or before December 31, 2017 and upon achievement of such goal, 15,000 shares will immediately vest, and 625 shares will vest on the first day of each month thereafter for 24 months, provided that the option holder continues to provide services to us through such dates.
 - (5) Dr. Xanthopoulos resigned from the Company effective June 1, 2015. In connection with his resignation, all time-based options were accelerated and exercise of such options was required to be completed by November 30, 2015. Performance-based options with performance goals that had not been achieved as of the resignation date were cancelled. As a result, Dr. Xanthopoulos had no options outstanding as of December 31, 2015.
 - (6) Dr. Gibson resigned from the company effective June 30, 2015. In connection with his resignation, all time-based options were accelerated and exercise of such options was required to be completed by December 28, 2015. Performance-based options with performance goals that had not been achieved as of the resignation date were cancelled. As a result, Dr. Gibson had no options outstanding as of December 31, 2015.
 - (7) Mr. Szekeres resigned effective December 2, 2015. In connection with his resignation, the vesting of all time-based options was accelerated. Performance-based options with performance goals that had not been achieved as of the resignation date were cancelled.
 - (8) Reflects the date by which Mr. Szekeres must exercise his options as a result of his termination, pursuant to our 2012 Plan.

During 2015, we made modifications under ASC 718 to outstanding equity awards of Dr. Xanthopoulos and Dr. Gibson in connection with each of their resignations. The modifications are described above under “Summary Compensation Table” and below under “Employment Agreements with Named Executive Officers.”

Employment Agreements with Named Executive Officers

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 Dr. Grint. In September 2014, we entered into an amended and restated employment agreement with Dr. Grint, which replaced and superseded his previous agreement entered into in June 2014. Pursuant to his employment agreement, Dr. Grint is entitled to an initial annual base salary of \$360,500 (increased most recently to \$500,000) and in 2015 was eligible to receive an annual performance bonus

based on a target amount of 35% (increased most recently to 50%) of his annual base salary. Dr. Grint's base salary and target bonus percentage are subject to modification from time to time in the discretion of our Board of Directors or any authorized committee thereof.

Under the terms of his employment agreement, if we terminate Dr. Grint's employment without cause (other than due to his death or complete disability) or if Dr. Grint 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, we are obligated to pay Dr. Grint, subject to receiving an effective release and waiver of claims from him, (1) a lump sum severance payment equal to 12 months of base salary in effect at the time of termination (ignoring 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 time-based options or other equity incentive awards held by Dr. Grint as of such termination.

If we terminate Dr. Grint's employment without cause (other than due to his death or complete disability) or if Dr. Grint resigns for good reason, in each case during the period beginning one month before and ending 12 months following a change in control, in lieu of the severance payment described above, we are obligated to pay Dr. Grint, subject to receiving an effective release and waiver of claims from him (1) a lump sum severance payment equal to 12 months of his base salary in effect at the time of termination (ignoring any decrease that forms the basis for a resignation for good reason), (2) a lump sum payment equal to the target amount of Dr. Grint's annual performance bonus payable for the year of termination, (3) 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 (4) vesting acceleration of all outstanding time-based options or other equity incentive awards held by Dr. Grint as of such termination.

Employment Agreement with Dr. Xanthopoulos. In September 2014, we entered into an amended and restated employment agreement with Dr. Xanthopoulos, which replaced and superseded his previous employment agreement entered into in June 2012. Pursuant to his employment agreement, Dr. Xanthopoulos was entitled to receive an initial annual base salary (increased most recently to \$637,158) and in 2015 was eligible to receive an annual performance bonus based on a target amount of 60% of his annual base salary. Dr. Xanthopoulos's base salary and target bonus percentage were subject to modification from time to time in the discretion of our Board of Directors or any authorized committee thereof.

In June of 2015, Dr. Xanthopoulos resigned from the Company. In connection with his resignation, and in exchange for our receipt of an effective release and waiver of claims from Dr. Xanthopoulos, Dr. Xanthopoulos received (1) a severance payment equal to 18 months of his base salary in effect at the time of his resignation, (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 18 months and (3) vesting acceleration of all outstanding options held by Dr. Xanthopoulos that were subject to time-based vesting as of the time of his resignation. In addition, the post-termination exercise period of all outstanding options held by Dr. Xanthopoulos was extended to 180 days following the date of his resignation. Half of the total amount of the severance payment described in (1) above was paid in a lump sum payment and half of the total amount of the severance payment will be paid in equal installments over a 12-month period following Dr. Xanthopoulos' resignation.

Employment Agreement with Dr. Gibson. In September 2014, we entered into an amended and restated employment agreement with Dr. Gibson, which replaced and superseded his previous employment agreement entered into in June 2012. Pursuant to his employment agreement, Dr. Gibson was entitled to an initial annual base salary of \$360,500 (increased most recently to \$371,676) and in 2015 was eligible to receive an annual performance bonus based on a target amount of 35% of his annual base salary. Dr. Gibson's base salary and target bonus percentage were subject to modification from time to time in the discretion of our Board of Directors or any authorized committee thereof.

In June of 2015, Dr. Gibson resigned from the Company. In connection with his resignation, and in exchange for our receipt of an effective release and waiver of claims from Dr. Gibson, Dr. Gibson received (1) a

lump-sum severance payment equal to 12 months of his base salary in effect at the time of his resignation, (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 held by Dr. Gibson that were subject to time-based vesting as of the time of his resignation. In addition, the post-termination exercise period of all outstanding options held by Dr. Gibson was extended to 180 days following the date of his resignation.

Employment Agreement with Mr. Szekeres. In September 2014, we entered into an amended and restated employment agreement with Mr. Szekeres, which replaced and superseded his previous agreement entered into in February 2014. Pursuant to his employment agreement, Mr. Szekeres was entitled to an initial annual base salary of \$295,000 (increased most recently to \$303,267) and in 2015 was eligible to receive an annual performance bonus based on a target amount of 35% of his annual base salary. Mr. Szekeres's base salary and target bonus percentage were subject to modification from time to time in the discretion of our Board of Directors or any authorized committee thereof.

In December of 2015, Mr. Szekeres resigned from the Company. In connection with his resignation, and in exchange for our receipt of an effective release and waiver of claims from Mr. Szekeres, Mr. Szekeres received (1) a lump-sum severance payment equal to 12 months of his base salary in effect at the time of his resignation, (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 held by Mr. Szekeres that were subject to time-based vesting as of the time of his resignation.

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. Pursuant to Mr. Hagan's employment agreement, we agreed to pay Mr. Hagan a signing bonus of \$100,000, payable in a lump sum upon Mr. Hagan's commencement of employment with us. All or a portion of the signing bonus is repayable in the event Mr. Hagan is terminated for cause or if he voluntarily resigns without good reason within the first three years of his employment.

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, we will be obligated to pay Mr. Hagan, subject to receiving an effective release and waiver of claims from him, (1) a lump sum severance payment equal to 12 months of his base salary in effect at the time of such termination or resignation (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.

Pursuant to his employment agreement, on January 4, 2016, we granted Mr. Hagan an option to purchase up to 420,000 shares of common stock, 25% of which shares will vest one year after the grant date and the balance of which will vest in equal monthly installments over the following three years, subject to Mr. Hagan's continuous service with us. Pursuant to his employment agreement, on January 4, 2016 we also granted Mr. Hagan a performance-based stock option exercisable for up to 122,631 shares of common stock. The stock

option will vest upon the achievement of specified performance-based development milestones. Fifty percent of the shares subject to any particular performance-based milestone will vest upon the determination by our Board of Directors or Compensation Committee that such milestone has been achieved, and the balance of the shares subject to such milestone will vest in equal monthly installments over the following two years, subject to Mr. Hagan's continuous service with us.

None of the Named Executive Officers' or Mr. Hagan's employment agreements provide for the gross up of any excise taxes imposed by Section 4999 of the Code. If any of the payments under the employment agreements would constitute a "parachute payment" within the meaning of Section 280G of the Code, subject to the excise tax imposed by Section 4999 of the Code, the employment agreements provide for a best-after tax analysis with respect to such payments, under which the executive will receive whichever of the following two alternative forms of payment would result in the executive officer's receipt, on an after-tax basis, of the greater amount of the transaction payment notwithstanding that all or some portion of the transaction payment may be subject to the excise tax: (i) payment in full of the entire amount of the transaction payment, or (ii) payment of only a part of the transaction payment so that the executive receives the largest payment possible without the imposition of the excise tax.

For purposes of the employment agreements, other than during the period beginning one month before and ending 12 months following a change in control, "cause" generally means the executive officer's: (i) commission of any felony or crime involving fraud, dishonesty or moral turpitude under the laws of the United States or any state thereof; (ii) attempted commission of, or participation in, a fraud or act of dishonesty against us; (iii) intentional, material violation of any contract or agreement between the executive officer and us or of any statutory duty owed to us; (iv) unauthorized use or disclosure of our confidential information or trade secrets; or (v) gross misconduct. During the period beginning one month before and ending 12 months following a change in control, "cause" generally means the executive officer's: (I) conviction of any felony or any crime involving fraud, dishonesty or moral turpitude under the laws of the United States or any state thereof; (II) commission of an intentional act of fraud, embezzlement or theft by the executive officer in the course of the executive officer's employment by us; (III) intentional, material violation of any contract or agreement between the executive officer and us (including the employment agreement) or of any statutory duty owed to us which is not remedied within 30 days' written notice from us specifying such failure; (IV) intentional and unauthorized use or disclosure of our confidential information or trade secrets which is materially and demonstrably injurious to us; or (V) gross misconduct.

For purposes of the employment agreements, "good reason" means the occurrence of one or more of the following events (at a time other than within one month before or 12 months following a change in control), subject to the executive providing us with at least 90 days of his intent to terminate for such "good reason" and our failure to remedy the condition within a 30-day cure period (provided, any subsequent proposed voluntary resignation for "good reason" will not be curable): (i) our material breach of the executive officer's employment agreement; (ii) a material reduction of the executive officer's base salary; (ii) a material reduction of the executive officer's authority, duties or responsibilities; or (iii) a relocation of the facility that is the executive officer's principal place of business to a location that requires an increase in the executive officer's one-way driving distance by more than 35 miles. Within one month before or 12 months following a change in control, "good reason" means the occurrence of one of the following without the executive officer's express, written consent: (I) a significant reduction of the executive officer's duties, position or responsibilities (including, without limitation, any negative change in reporting hierarchy involving the executive or the person to whom the executive directly reports, or the executive no longer being a Section 16 reporting officer immediately following the change in control), or the executive officer's removal from such position and responsibilities; (II) our change to the timing associated with long-term incentive awards granted to the executive officer; (III) a reduction by us in the executive officer's (A) base salary or target annual bonus as in effect immediately prior to such reduction, or (B) annual grant date fair value of any long-term incentive awards held by the executive officer relative to the highest fair value award granted to the executive during the three-year period prior to a change in control; (IV) a material reduction by us in the kind or aggregate level of employee benefits to which the executive officer is entitled immediately prior to such reduction with the result that the executive officer's overall benefits package is

significantly reduced; (V) the executive officer is requested to relocate (except for office relocations that would not increase the executive officer's one way commute by more than 35 miles); or (VI) our failure to obtain the assumption of the employment agreement by the acquiror in the change in control transaction.

For purposes of the employment agreements, "change in control" generally means one or more of the following events (i) the acquisition of more than 50% of our combined voting power other than by Alnylam or Ionis (formerly Isis) (although this exception does not apply to Mr. Hagan's employment agreement); (ii) a consummation of a merger, consolidation or similar transaction in which our stockholders cease to own outstanding voting securities representing more than 50% of the voting power of the parent or the surviving entity immediately following the merger; or (iii) a consummated sale, lease, exclusive license or other disposition of all or substantially all of our consolidated assets (other than to an entity of which more than 50% of the voting power is owned immediately following such disposition by our stockholders).

Compensation Recovery Policies

The Board of Directors and the Compensation Committee have not determined whether they would attempt to recover bonuses from our executive officers if the performance objectives that led to the bonus determination were to be restated, or found not to have been met to the extent originally believed by the Board of Directors or the Compensation Committee. However, as a public company subject to the provisions of Section 304 of the Sarbanes-Oxley Act of 2002, if we are required as a result of misconduct to restate our financial results due to our material noncompliance with any financial reporting requirements under the federal securities laws, our Chief Executive Officer and our principal financial officer may be legally required to reimburse us for any bonus or other incentive-based or equity-based compensation they receive. In addition, we will comply with the requirements of the Dodd-Frank Wall Street Reform and Consumer Protection Act and will adopt a compensation recovery policy once final regulations on the subject have been adopted.

Equity Compensation Plans and Other Benefits Plans

2009 Equity Incentive Plan.

Our Board of Directors adopted and our stockholders approved the 2009 Plan in January 2009 for eligible employees, directors and consultants. The terms of the stock option agreements, including vesting requirements, were determined by our Board of Directors, subject to the provisions of the 2009 Plan. Options granted under the 2009 Plan generally vest over four years and are exercisable after they have been granted and up to ten years from the date of grant. The exercise price of the incentive stock options must equal at least 100% of the fair market value of our common stock on the date of grant. Following our initial public offering in October 2012, no additional awards have been or will be granted under the 2009 Plan, and all awards granted under the 2009 Plan that are repurchased, forfeited, expire or are cancelled become available for grant under the 2012 Plan in accordance with its terms. However, all stock options granted under the 2009 Plan prior to our initial public offering continue to be governed by the terms of the 2009 Plan.

2012 Equity Incentive Plan.

The 2012 Plan, which became effective in connection with our initial public offering in October 2012, 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 2012 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 2012 Plan. Our Board of Directors has 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 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.

Initially, the aggregate number of shares of our common stock that may be issued pursuant to stock awards under the 2012 Plan was the sum of (i) 1,500,000 shares, plus (ii) the 731,781 shares reserved for issuance under our 2009 Plan at the time our 2012 Plan became effective, plus (iii) any shares subject to stock options or other stock awards granted under our 2009 Plan that would have otherwise returned to our 2009 Plan (such as upon the expiration or termination of a stock award prior to vesting). Additionally, the number of shares of our common stock reserved for issuance under our 2012 Plan automatically increases on January 1 of each calendar year, beginning on January 1, 2013 and continuing through and including January 1, 2022, by 4% of the total number of shares of our capital stock outstanding on December 31 of the preceding calendar year, or a lesser number of shares determined by our Board of Directors. The maximum number of shares that may be issued upon the exercise of ISOs under our 2012 Plan is 3,000,000 shares. As of December 31, 2015, there were 1,549,163 shares available for future grants under the 2012 Plan. On January 1, 2016, pursuant to the terms of the 2012 Plan, the number of shares available for issuance under the 2012 Plan automatically increased by 2,106,770 shares.

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.

Unless the plan administrator provides otherwise, options generally are not transferable except by will, the laws of descent and distribution, or pursuant to a domestic relations order. An optionee may designate a beneficiary, however, who may exercise the option following the optionee's death.

Corporate transactions. In the event of certain specified significant corporate transactions, 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.

Under the 2012 Plan, a corporate transaction is generally the consummation of (i) a sale or other disposition of all or substantially all of our consolidated assets, (ii) a sale or other disposition of at least 90% of our outstanding securities, (iii) a merger, consolidation or similar transaction following which we are not the surviving corporation, or (iv) a merger, consolidation or similar transaction following which we are the surviving corporation but the shares of our common stock outstanding immediately prior to such transaction are converted or exchanged into other property by virtue of the transaction.

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. 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. Under the 2012 Plan, a change in control is generally (i) the acquisition by a person or entity of more than 50% of our combined voting power other than by merger, consolidation or similar transaction; (ii) a consummated merger, consolidation or similar transaction immediately after which our stockholders cease to own more than 50% of the combined voting power of the surviving entity; (iii) a consummated sale, lease or exclusive license or other disposition of all or substantially of our consolidated assets; or (iv) individuals who were Board members on the date the 2012 Plan was adopted (the "Incumbent Board") cease to constitute a majority of the Board, provided that if the appointment, election or nomination of any new Board member was approved by a majority of the members of the Incumbent Board then still in office, such new member will be considered to be a member of the Incumbent Board.

2015 Inducement Plan.

The 2015 Inducement Plan, which was adopted by our Board of Directors in July of 2015, provides for the grant of NSOs, which may be granted only to persons as a material inducement to their commencement of employment with us, pursuant to Rule 5635(c)(4) of the NASDAQ Listing Rules.

Our Board of Directors, or a duly authorized committee thereof, has the authority to administer the 2015 Inducement Plan. Our Board of Directors has delegated its authority to administer the 2015 Inducement Plan to our Compensation Committee under the terms of our Compensation Committee's charter. Grants under the 2015 Inducement Plan must be approved by the Compensation Committee (comprised of independent directors) or a majority of our independent directors (as defined in Rule 5605(a)(2) of the NASDAQ Listing Rules) in order to comply with the exemption from the stockholder approval requirement for "inducement grants" provided under Rule 5635(c)(4) of the NASDAQ Listing Rules.

Initially, the aggregate number of shares of our common stock that may be issued pursuant to NSOs under the 2015 Inducement Plan was 1,000,000 shares. As of December 31, 2015, there were 958,052 shares available for future grants under the 2015 Inducement Plan. The terms of Inducement Plan and NSOs granted thereunder are generally the same as the terms of our 2012 Plan as it relates to NSOs granted under our 2012 Plan.

2012 Employee Stock Purchase Plan.

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

dates on which our common stock will be purchased for employees participating in the offering. Unless otherwise determined by our Compensation Committee, shares are purchased for accounts of employees participating in the ESPP at a price per share equal to the lower of (a) 85% of the fair market value of our common stock on the first date of an offering or (b) 85% of the fair market value of our common stock on the date of purchase. As of December 31, 2015, there were 1,260,136 shares available for future issuance under the ESPP. On January 1, 2016, pursuant to the terms of the ESPP, the number of shares available for issuance under the ESPP automatically increased by 500,000 shares.

401(k) Plan.

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 \$18,000 in 2015 (additional salary deferrals not to exceed \$6,000 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. We provide a \$0.25 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.

Potential Payments Upon Termination or Change in Control

Dr. Grint eligible to receive severance and change in control benefits under the terms of his employment agreement, and each of Dr. Xanthopoulos, Dr. Gibson and Mr. Szekeres received severance payments in connection with their resignations, each as described above under "—Employment Agreements with Named Executive Officers." Additionally, stock options granted to Dr. Grint are subject to the change in control provisions set forth in the 2012 Plan as further described above under "—Equity Compensation Plans and Other Benefit Plans."

Equity Compensation Plan Information

The following table provides information as of December 31, 2015, with respect to shares of our common stock that may be issued under our existing equity compensation plans:

<u>Plan Category</u>	<u>(a)</u>	<u>(b)</u>	<u>(c)</u>
	Number of securities to be issued upon exercise of outstanding options, warrant and rights	Weighted-average exercise price of outstanding options, warrant and rights	Number of securities remaining available for future issuance under equity compensation plans (excluding securities reflected in column (a))
Equity compensation plans approved by stockholders:			
2009 Equity Incentive Plan	387,566 ⁽¹⁾	\$ 1.21	—
2012 Equity Incentive Plan	4,696,153 ⁽¹⁾	\$ 9.56	1,549,163
2012 Employee Stock Purchase Plan	—	\$ —	1,260,136
Equity compensation plans not approved by stockholders:			
2015 Inducement Plan	41,948 ⁽¹⁾	\$ 6.89	958,052

(1) All shares issuable upon exercise of options.

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, 2015:

Name	Fees Earned or Paid in		Total (\$)
	Cash (\$)	Option Awards (\$) ⁽¹⁾	
David Baltimore, Ph.D.	44,500	117,477 ⁽²⁾	161,977
Bruce L.A. Carter, Ph.D. ⁽³⁾	42,274	117,477 ⁽²⁾	159,751
Mark Foletta	54,500	117,477 ⁽²⁾	171,977
Stelios Papadopoulos, Ph.D.	65,000	117,477 ⁽²⁾	182,477
B. Lynne Parshall ⁽⁴⁾	—	—	—
William H. Rastetter, Ph.D.	40,261	117,477 ⁽²⁾	157,738
Douglas E. Williams, Ph.D.	32,000	117,477 ⁽²⁾	149,577

- (1) Amounts listed represent the aggregate grant date fair value amount computed as of the grant date of each option awarded during 2015 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, 2015. Our directors will only realize compensation to the extent the trading price of our common stock is greater than the exercise price of such stock options.
- (2) Represents the annual option grant to purchase 17,500 shares of our common stock granted to each of our non-employee directors serving on June 10, 2015 under our director compensation policy. As of December 31, 2015, the aggregate number of shares subject to each non-employee director's outstanding option awards was as follows: Dr. Baltimore, 287,500 shares; Dr. Carter, 47,847 shares; Mr. Foletta, 82,500 shares; Dr. Papadopoulos, 54,323 shares; Ms. Parshall, zero shares; Dr. Rastetter, 82,500 shares; and Dr. Williams, 82,500 shares. None of our non-employee directors held unvested stock awards other than stock options as of December 31, 2015.
- (3) Dr. Carter resigned from the Board of Directors effective November 24, 2015. The annual option grant made to Dr. Carter on June 10, 2015 was cancelled in connection with his resignation from the Board of Directors.
- (4) Ms. Parshall completed her service with the Board of Directors as of our annual meeting on June 10, 2015 and therefore has not served on the Board since that date and did not receive the annual option grant on June 10, 2015.

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. In addition, our non-employee directors who are affiliated with our founding stockholders, Alnylam and Ionis (formerly Isis), do not receive cash or equity compensation for service on our Board of Directors.

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. For 2015, our Compensation Committee determined that our Eligible Directors would be non-employee members of our Board of Directors who were not beneficial owners of five percent or more of our stock. Accordingly, during 2015, the Eligible Directors that received cash and/or equity compensation under the director compensation policy were Dr. Baltimore, Dr. Carter, Mr. Foletta, Dr. Papadopoulos, Dr. Rastetter and Dr. Williams.

Pursuant to our director compensation policy in effect in 2015, we provide cash compensation in the form of an annual retainer of \$32,000 to each of our Eligible Directors and \$60,000 to our Chairman of the Board. We also pay an additional annual retainer of \$20,000 to the chairman of our Audit Committee, \$5,000 to other independent Eligible Directors who serve on our Audit Committee, \$10,000 to the chairman of our Compensation Committee,

\$5,000 to other independent Eligible Directors who serve on our Compensation Committee, \$7,500 to the chairman of our Nominating and Corporate Governance Committee and \$2,500 to other independent Eligible Directors who serve on our Nominating and Corporate Governance Committee.

During 2015, the Compensation Committee engaged Aon/Radford to provide a competitive assessment of the Company's director compensation program compared to director compensation paid to directors at selected publicly-traded peer companies. Following an analysis of the peer companies, our Board of Directors revised the director compensation policy for 2016. During 2016, we will 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.

Under our director compensation policy in effect during 2015, each Eligible Director who was first elected to our Board of Directors was granted an option to purchase 30,000 shares of the Company's common stock on the date of his or her initial election to our Board of Directors. In addition, on the date of each annual meeting of the Company's stockholders, each Eligible Director was eligible to receive an option to purchase 17,500 shares of common stock. Such initial and annual options had an exercise price per share equal to the fair market value of the common stock on the date of grant.

Each initial option and annual 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 one year 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. The term of each option granted to an Eligible Director is 10 years.

Following the revision of the director compensation policy adopted by the Board in 2016, each Eligible Director who is first elected to our Board of Directors will be 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 valued at \$300,000 as determined by the Black Scholes method on the date of grant. In addition, on the date of each annual meeting of the Company's stockholders, each Eligible Director will be eligible to receive an option to purchase shares of common stock valued at \$150,000 as determined by the Black Scholes method on the date of grant. Such initial and annual options will have an exercise price per share equal to the fair market value of the common stock on the date of grant.

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 twelve equal monthly installment 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 options are granted under our 2012 Plan, the terms of which are described in more detail above under "Equity Compensation Plans and Other Benefit Plans—2012 Equity Incentive Plan."

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.” For purposes of our policy only, 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 \$120,000.

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, 2015, with respect to which we were a party, will be a party, or otherwise benefited, in which:

- the amounts involved exceeded or will exceed \$120,000; 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.

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 or her family members, and the Company, its senior management and its independent auditors, the Board has affirmatively determined that the following four directors are independent directors within the meaning of the applicable NASDAQ listing standards: Dr. Baltimore, Mr. Foletta, Dr. Papadopoulos and Dr. Rastetter. 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.

Alliance and Collaboration Agreements

Biogen

In August 2014, we and Biogen (formerly “Biogen Idec”) entered into a collaboration and license agreement to collaborate on *microRNA* biomarkers for multiple sclerosis, and simultaneously terminated our previous collaboration and license agreement entered into on August 2012. Doug Williams, Ph.D., one of our directors, was the Executive Vice President of Research and Development of Biogen. Pursuant to the terms of the August 2014 collaboration and license agreement, we received an upfront payment from Biogen of \$2.0 million. In January 2015, May 2015, and September 2015, we earned research milestone payments under the August 2014 collaboration and license agreement of \$0.1 million, \$0.3 million and \$0.3 million, respectively. The parties have completed their obligations under the agreement. Dr. Williams has an indirect interest in these transactions as a result of his stock ownership in Biogen.

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. Under the terms of the restated agreement, we have agreed to collaborate with Sanofi to develop and commercialize licensed compounds targeting four *microRNA* alliance targets initially focused in the field of fibrosis and have granted Sanofi an exclusive license to develop and commercialize products under the alliance. Under the terms of our extended alliance, Sanofi has opt-in rights to our miR-21 preclinical fibrosis program targeting miR-21 for the treatment of Alport Syndrome, our preclinical program targeting miR-21 for oncology indications, and our preclinical programs targeting miR-221/222 for oncology indications, each of which is to be led by us. If Sanofi chooses to exercise its option on any of these programs, Sanofi will reimburse us for a significant portion of our preclinical and clinical development costs and will also pay us an option exercise fee for any such program, provided that \$1.25 million of the \$2.5 million upfront option fee paid to us by Sanofi in connection with the June 2013 option agreement will be creditable against such option exercise fee. We are eligible to receive milestone payments of up to \$101.8 million for proof-of-concept option exercise fees (net of \$1.25 million creditable, as noted above), \$15.0 million for clinical milestones and up to \$300.0 million for regulatory and commercial milestones. In addition, we are entitled to receive royalties based on a percentage of net sales of any products from the miR-21 and miR-221/222 programs which, in the case of sales in the United States, will be in the middle of the 10 to 20% range, and, in the case of sales outside of the United States, will range from the low end to the middle of the 10 to 20% range, depending upon the volume of sales. If we exercise our option to co-promote a product, we will continue to be eligible to receive royalties on net sales of each product in the United States at the same rate, unless we elect to share a portion of Sanofi’s profits from sales of such product in the United States in lieu of royalties.

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.

Ionis Pharmaceuticals, Inc. and Alnylam Pharmaceuticals, Inc.

In January 2009, we amended our amended and restated license and collaboration agreement with Alnylam and Ionis (formerly Isis) which are each greater than 5% stockholders of the Company. In addition, B. Lynne Parshall, one of our former directors who completed her Board service with us in 2015, is an executive officer of Ionis. Under the agreement, we acquired an exclusive, royalty-bearing, worldwide license, with rights to sublicense, to patent rights owned or licensed by Alnylam and Ionis to develop, manufacture and commercialize products covered by the licensed patent rights for use in *micro*RNA compounds which are *micro*RNA antagonists and *micro*RNA therapeutics containing these compounds. In addition, we have certain rights to miR-mimics. Under the agreement, we granted to both Alnylam and Ionis a license to practice our intellectual property developed by us to the extent that it is useful specifically to Alnylam’s RNAi programs or Ionis’s single-stranded oligonucleotide programs, but not including *micro*RNA compounds or therapeutics that are the subject of our exclusive licenses from Alnylam and Ionis. If an election is made by either Alnylam or Ionis (but not both) to opt-in, such party will pay us a one-time fixed payment, the amount of which will depend on whether the first or the second opt-in option was exercised, with a higher amount due if the first opt-in option was exercised. Clinical and regulatory milestones are also payable to us in the event the opt-in election is exercised. Such milestones total \$64.0 million in the aggregate if the election is made during the first opt-in period or \$15.7 million in the aggregate if the election is made at the second opt-in period. Tiered royalties are payable to us as a percentage of net sales on all products commercialized by the opt-in party. These royalties range from the low to middle single digits depending upon the volume of sales. The opt-in party is also entitled to sublicense the development program to a third party. In such a case, we are also entitled to receive a percentage of the sublicense income received by the opt-in party. The percentage payable depends upon the point at which the opt-in party sublicenses the program and ranges from the low end of the 10 to 20% range to the high end of the 40 to 50% range. The opt-in party is only required to pay the higher of the clinical and regulatory milestones or the sublicense income received in any calendar quarter. The opt-in party is also responsible for all third party payments due under other agreements as a result of the development. In the event both Alnylam and Ionis elect to opt-in during either opt-in period, the parties have agreed to work together to amend the development plan to continue development of the project, including funding of such project and assignment of roles and responsibilities. In the event we or one of our strategic alliance partners continues with the development of a program, each of Alnylam and Ionis are entitled to royalties as a percentage of net sales. For products that we independently commercialize, these royalties will be in the low single digits. For products commercialized by a third-party collaborator, the royalties will be either the same percentage of net sales as described above or, if the sublicense does not provide a specified level of royalties to us or upon our election, a percentage of the sublicense income received by us from the strategic alliance partner and a modified royalty. The modified royalty would be based upon the lower of the single digit percentage discussed above or one third of the royalty received by us after payments made by us to third parties for development, manufacture and commercialization activities under other agreements. In addition, if we sublicense rights to a collaborator, we will be required to pay to each of Alnylam and Ionis a percentage of our sublicense income in the mid-single digits. We are also responsible for payments due to third parties under other agreements as a result of our development activities, including payments owed by Alnylam and/or Ionis under their agreements. Under the October 2011 amendment, Alnylam and Ionis granted us the right to research *micro*RNA mimics under the licensed intellectual property of Alnylam and Ionis. In the event we develop a miR-mimic, we must first obtain approval from Alnylam and/or Ionis, as applicable, and such approval is subject to the consent of applicable third parties, if any. No additional consideration will be owed by us to Alnylam or Ionis for granting approval. We have the right to sublicense our research rights. We granted to both Alnylam and Ionis a fully paid up, worldwide and exclusive license to any intellectual property developed by us and useful to their

research programs and which are not *micro*RNA antagonists or approved miR-mimics. In August 2013, we entered into a further amendment to the agreement. Under the terms of the August 2013 amendment, the parties agreed to our use of certain Alnylam-controlled intellectual property concerning the use and manufacture of GalNAc conjugates (“GalNAc Process Technology”) on a non-exclusive basis. We will generally not be permitted to sublicense or otherwise transfer the GalNAc Process Technology and other Alnylam licensed intellectual property rights relating to GalNAc conjugate technology without the prior written consent of Alnylam, subject to certain limited exceptions for sublicenses to third party collaboration partners. There were no financial terms related to the amendment.

In February 2015, we entered into a letter agreement with Alnylam pursuant to which we and Alnylam agreed to the financial terms for certain technology acquired by Alnylam within the licensed patent rights under the foregoing amended and restated license and collaboration agreement (the “additional patent rights”). In addition to any royalties payable by us to Alnylam pursuant to the terms of the amended and restated collaboration agreement, we agreed to pay Alnylam an additional low single-digit royalty on net sales of certain products utilizing the additional patent rights, with the exact royalty percentage payable being dependent on the total amount of net sales during the calendar year. We also agreed to pay Alnylam milestone payments on certain products utilizing the additional patent rights of up to \$33.0 million per product upon the achievement of certain regulatory milestone events.

Ms. Parshall has an indirect interest in these transactions as a result of her stock ownership in Ionis. Ms. Parshall’s beneficial stock ownership in Ionis is disclosed from time to time in Ionis’s public filings with the SEC.

AstraZeneca

In August 2012, we entered into a collaboration and license agreement with AstraZeneca AB, or AstraZeneca, which became a greater than 5% stockholder of our Company following the agreement date. Under the terms of the agreement, we agreed to collaborate with AstraZeneca to identify, research and develop licensed compounds targeting three *micro*RNA alliance targets in the fields of cardiovascular diseases, metabolic diseases and oncology and granted to AstraZeneca an exclusive, worldwide license to thereafter develop, manufacture and commercialize lead compounds designated by AstraZeneca in the course of the collaboration activities against the *micro*RNA alliance targets for all human therapeutic uses. We are responsible for discovery, optimization and development of anti-miR product candidates in each program until the acceptance of an IND or the end of the research term, which extends until the fourth anniversary of the date of the agreement, and may be extended upon mutual written agreement. Following the earlier to occur of the acceptance of an IND in a major market or the end of the research term, AstraZeneca will assume all costs, responsibilities and obligations for further development, manufacture and commercialization of alliance product candidates. We received an upfront payment of \$3.0 million and a subsequent milestone payments in 2015 of \$12.5 million. In addition, if all three targets are successfully developed and commercialized through pre-agreed sales targets, we could receive additional milestone payments up to \$485.5 million in the aggregate, including a preclinical milestone of up to \$2.5 million upon selection of a lead compound for an oncology product, up to \$113.0 million for clinical milestones and up to \$370.0 million for commercialization milestones. In addition, we are entitled to receive royalties based on a percentage of net sales which will range from the mid-single digits to the low end of 10 to 20%, depending upon the product and the volume of sales, which royalties may be reduced in certain, limited circumstances.

In January 2015, we entered into a letter agreement with AstraZeneca to amend the collaboration and license agreement. Under the terms of the letter agreement, we have agreed to perform additional miR-103/107 program research and development activities related to RG-125. AstraZeneca has agreed to fund 50% of the costs for additional activities, as outlined in the letter agreement. In accordance with the collaboration and license agreement, AstraZeneca funded 100% of the costs for product manufacturing activities outlined in the letter agreement necessary to support a Phase I clinical study. As of December 31, 2015, our obligations under the letter agreement were substantially complete.

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 to those stockholders. 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 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 or set of annual meeting materials, please notify your broker or Regulus Therapeutics Inc. Direct your written request to Regulus Therapeutics Inc., Attn: Director of Investor Relations, 3545 John Hopkins Court, Suite 210, San Diego, CA 92121. If the mailing date of your request is on or after May 5, 2016, you should direct your request to the Company's new principal executive offices located at 10614 Science Center Drive, San Diego, California 92121, or contact our Director of Investor Relations at Regulus Therapeutics Inc. by telephone at (858) 202-6300. Stockholders who currently receive multiple Notices 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

A handwritten signature in black ink that reads "Christopher Aker". The signature is written in a cursive style with a large, prominent initial "C".

Christopher Aker
Vice President, Legal Affairs and Secretary

April 22, 2016

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, 2015 is available without charge upon written request to: Corporate Secretary, Regulus Therapeutics Inc., 3545 John Hopkins Court, Suite 210, San Diego, CA 92121. If the mailing date of your request is on or after May 5, 2016, you should direct your request to the Company's new principal executive offices located at 10614 Science Center Drive, San Diego, California 92121.

APPENDIX A
AMENDED AND RESTATED
CERTIFICATE OF INCORPORATION OF
REGULUS THERAPEUTICS INC.

Regulus Therapeutics Inc., a corporation organized and existing under the laws of the State of Delaware, hereby certifies as follows:

FIRST: The name of this corporation is Regulus Therapeutics Inc.

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

THIRD: The Certificate of Incorporation of said corporation shall be amended and restated to read in full as follows:

I.

The name of this corporation is Regulus Therapeutics Inc. (the "**Company**").

II.

The address of the registered office of the Company in the State of Delaware is 1209 Orange Street, City of Wilmington, County of New Castle, Delaware, 19801 and the name of the registered agent of the Company in the State of Delaware at such address is The Corporation Trust Company.

III.

The purpose of the Company is to engage in any lawful act or activity for which a corporation may be organized under the Delaware General Corporation Law (the "**DGCL**").

IV.

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 210,000,000 shares. 200,000,000 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.

B. The Preferred Stock may be issued from time to time in one or more series. The Board of Directors of the Company (the "**Board of Directors**") is hereby expressly authorized to provide for the issue of any or all of the unissued and undesignated shares of the Preferred Stock in one or more series, and to fix the number of shares and to determine or alter for each such series, such voting powers, full or limited, or no voting powers, and such designation, preferences, and relative, participating, optional, or other rights and such qualifications, limitations, or restrictions thereof, as shall be stated and expressed in the resolution or resolutions adopted by the Board of Directors providing for the issuance of such shares and as may be permitted by the DGCL. The Board of Directors is also expressly authorized to increase or decrease the number of shares of any series subsequent to the issuance of shares of that series, but not below the number of shares of such series then outstanding. In case the number of shares of any series shall be decreased in accordance with the foregoing sentence, the shares constituting such decrease shall resume the status that they had prior to the adoption of the resolution originally

fixing the number of shares of such series. The number of authorized shares of Preferred Stock may be increased or decreased (but not below the number of shares thereof then outstanding) by the affirmative vote of the holders of a majority of the voting power of the stock of the Company entitled to vote thereon, without a separate vote of the holders of the Preferred Stock, or of any series thereof, unless a vote of any such holders is required pursuant to the terms of any certificate of designation filed with respect to any series of Preferred Stock.

C. Each outstanding share of Common Stock shall entitle the holder thereof to one vote on each matter properly submitted to the stockholders of the Company for their vote; provided, however, that, except as otherwise required by law, holders of Common Stock shall not be entitled to vote on any amendment to this Amended and Restated Certificate of Incorporation (this "*Certificate of Incorporation*") (including any certificate of designation filed with respect to any series of Preferred Stock) that relates solely to the terms of one or more outstanding series of Preferred Stock if the holders of such affected series of Preferred Stock are entitled, either separately or together as a class with the holders of one or more other series of Preferred Stock, to vote thereon by law or pursuant to this Certificate of Incorporation (including any certificate of designation filed with respect to any series of Preferred Stock).

V.

For the management of the business and for the conduct of the affairs of the Company, and in further definition, limitation and regulation of the powers of the Company, of its directors and of its stockholders or any class thereof, as the case may be, it is further provided that:

A. The management of the business and the conduct of the affairs of the Company shall be vested in its Board of Directors. The number of directors that shall constitute the Board of Directors shall be fixed exclusively by resolutions adopted by a majority of the authorized number of directors constituting the Board of Directors.

B. Subject to the rights of the holders of any series of Preferred Stock to elect additional directors under specified circumstances, the directors shall be elected at each annual meeting of stockholders to hold office until the next annual meeting. Each director shall hold office either until the expiration of the term for which elected or appointed and until a successor has been elected and qualified, or until such director's earlier death, resignation or removal. No decrease in the number of directors constituting the Board of Directors shall shorten the term of any incumbent director.

C. Subject to the rights of any series of Preferred Stock that may be designated from time to time to elect additional directors under specified circumstances, and subject to any limitation imposed by law, any individual director or directors may be removed with or without cause by the affirmative vote of the holders of a majority of the voting power of all then-outstanding shares of capital stock of the Company entitled to vote generally at an election of directors, voting together as a single class.

D. Subject to the rights of the holders of any series of Preferred Stock that may be designated from time to time, any vacancies on the Board of Directors resulting from death, resignation, disqualification, removal or other causes and any newly created directorships resulting from any increase in the number of directors, shall, unless the Board of Directors determines by resolution that any such vacancies or newly created directorships shall be filled by the stockholders, except as otherwise provided by law, be filled only by the affirmative vote of a majority of the directors then in office, even though less than a quorum of the Board of Directors, and not by the stockholders. Any director elected in accordance with the preceding sentence shall hold office for the remainder of the full term of the director for which the vacancy was created or occurred and until such director's successor shall have been elected and qualified.

E. Subject to the rights of the holders of any series of Preferred Stock that may be designated from time to time, the Board of Directors is expressly empowered to adopt, amend or repeal the Amended and Restated

Bylaws of the Company (the “*Bylaws*”). Any adoption, amendment or repeal of the Bylaws by the Board of Directors shall require the approval of a majority of the authorized number of directors. The stockholders shall also have power to adopt, amend or repeal the Bylaws, subject to any restrictions which may be set forth in this Certificate of Incorporation (including any certificate of designation that may be filed from time to time); provided, however, that, in addition to any vote of the holders of any class or series of stock of the Company required by law or by this Certificate of Incorporation, such action by stockholders shall require the affirmative vote of the holders of at least 66 2/3% of the voting power of all of the then-outstanding shares of the capital stock of the Company entitled to vote generally at an election of directors, voting together as a single class.

F. The directors of the Company need not be elected by written ballot unless the Bylaws so provide.

G. No action shall be taken by the stockholders of the Company except at an annual or special meeting of stockholders called in accordance with the Bylaws. No action shall be taken by the stockholders of the Company by written consent or electronic transmission.

H. Advance notice of stockholder nominations for the election of directors and of business to be brought by stockholders before any meeting of the stockholders of the Company shall be given in the manner provided in the Bylaws.

VI.

A. The liability of a director of the Company for monetary damages shall be eliminated to the fullest extent under applicable law. If the DGCL is amended to authorize corporate action further eliminating or limiting the personal liability of directors, then the liability of a director of the Company shall be eliminated to the fullest extent permitted by the DGCL, as so amended.

B. Any repeal or modification of this Article VI shall be prospective and shall not affect the rights under this Article VI in effect at the time of the alleged occurrence of any act or omission to act giving rise to liability or indemnification.

VII.

A. The Company reserves the right to amend, alter, change or repeal any provision contained in this Certificate of Incorporation, in the manner now or hereafter prescribed by statute, except as provided in Section B of this Article VII, and all rights conferred upon the stockholders herein are granted subject to this reservation.

B. Notwithstanding any other provisions of this Certificate of Incorporation or any provision of law which might otherwise permit a lesser vote or no vote, but in addition to any affirmative vote of the holders of any particular class or series of the Company required by law or by this Certificate of Incorporation or any certificate of designation filed with respect to a series of Preferred Stock that may be designated from time to time, subject to the rights of the holders of any series of Preferred Stock, the affirmative vote of the holders of at least 66 2/3% of the voting power of all of the then-outstanding shares of capital stock of the Company entitled to vote generally at an election of directors, voting together as a single class, shall be required to alter, amend or repeal Articles V, VI or VII of this Certificate of Incorporation.

* * * *

FOURTH: This Amended and Restated Certificate of Incorporation has been duly adopted and approved by the Board of Directors.

FIFTH: This Amended and Restated Certificate of Incorporation has been duly adopted and approved by the stockholders in accordance with sections 211, 242 and 245 of the DGCL.

IN WITNESS WHEREOF, Regulus Therapeutics Inc. has caused this Amended and Restated Certificate of Incorporation to be signed by its President and Chief Executive Officer this day of , 2016.

REGULUS THERAPEUTICS INC.

PAUL C. GRINT, M.D.

President and Chief Executive Officer

REGULUS THERAPEUTICS INC.
10614 SCIENCE CENTER DRIVE
SAN DIEGO, CA 92121

VOTE BY INTERNET - www.proxyvote.com

Use the Internet to transmit your voting instructions and for electronic delivery of information up until 11:59 P.M. Eastern Time the day before the cut-off date or meeting date. Have your proxy card in hand when you access the web site and follow the instructions to obtain your records and to create an electronic voting instruction form.

ELECTRONIC DELIVERY OF FUTURE PROXY MATERIALS

If you would like to reduce the costs incurred by our company in mailing proxy materials, you can consent to receiving all future proxy statements, proxy cards and annual reports electronically via e-mail or the Internet. To sign up for electronic delivery, please follow the instructions above to vote using the Internet and, when prompted, indicate that you agree to receive or access proxy materials electronically in future years.

VOTE BY PHONE - 1-800-690-6903

Use any touch-tone telephone to transmit your voting instructions up until 11:59 P.M. Eastern Time the day before the cut-off date or meeting date. Have your proxy card in hand when you call and then follow the instructions.

VOTE BY MAIL

Mark, sign and date your proxy card and return it in the postage-paid envelope we have provided or return it to Vote Processing, c/o Broadridge, 51 Mercedes Way, Edgewood, NY 11717.

TO VOTE, MARK BLOCKS BELOW IN BLUE OR BLACK INK AS FOLLOWS:

E09481-P75965

KEEP THIS PORTION FOR YOUR RECORDS

DETACH AND RETURN THIS PORTION ONLY

THIS PROXY CARD IS VALID ONLY WHEN SIGNED AND DATED.

REGULUS THERAPEUTICS INC.		For All	Withhold All	For All Except	To withhold authority to vote for any individual nominee(s), mark "For All Except" and write the number(s) of the nominee(s) on the line below.
The Board of Directors recommends you vote FOR the following:					
1. Election of Directors	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	_____	
Nominees:					
01) David Baltimore, Ph.D.		05) William Rastetter, Ph.D.			
02) Mark Foletta		06) Hugh Rosen, M.D., Ph.D.			
03) Paul Grint, M.D.		07) Douglas Williams, Ph.D.			
04) Stelios Papadopoulos, Ph.D.					
The Board of Directors recommends you vote FOR proposals 2 and 3.					For
					Against
					Abstain
2. Approval of Amendment to the Company's Amended and Restated Certificate of Incorporation to permit removal of a member of the Board of Directors with or without cause by majority vote of stockholders.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>		
3. Ratification of the selection of Ernst & Young LLP as the independent registered public accounting firm of the company for the year ending December 31, 2016.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>		
NOTE: Such other business as may properly come before the meeting or any adjournment thereof.					
Please sign exactly as your name(s) appear(s) hereon. When signing as attorney, executor, administrator, or other fiduciary, please give full title as such. Joint owners should each sign personally. All holders must sign. If a corporation or partnership, please sign in full corporate or partnership name by authorized officer.					
_____ Signature [PLEASE SIGN WITHIN BOX]		_____ Date	_____ Signature (Joint Owners)		_____ Date

Important Notice Regarding the Availability of Proxy Materials for the Annual Meeting:
The Proxy Statement, 2015 Annual Report to Stockholders and Form 10-K are available at www.proxyvote.com.

E09482-P75965

REGULUS THERAPEUTICS INC.
Annual Meeting of Stockholders
June 2, 2016 9:00 AM PDT
This proxy is solicited by the Board of Directors

The undersigned hereby appoint(s) Paul Grint, M.D. 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 2, 2016 at the company's offices located at 10614 Science Center Drive, 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 under Proposal 1, FOR Proposal 2, FOR Proposal 3 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