VERTEX PHARMACEUTICALS INC / MA

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UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

SCHEDULE 14A

Proxy Statement Pursuant to Section 14(a) of the Securities Exchange Act of 1934

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Check the appropriate box:

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

Vertex Pharmaceuticals Incorporated

(Name of Registrant as Specified In Its Charter)

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- x No fee required.
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April 30, 2015

DEAR SHAREHOLDERS:

We cordially invite you to attend our 2015 annual meeting of shareholders. We will hold our meeting on Thursday, June 4, 2015, at 9:30 a.m. at our headquarters at 50 Northern Avenue, Boston, Massachusetts.

At this year's meeting, you will be asked to vote on the election of directors, to approve an amendment to our Restated Articles of Organization to increase the number of shares of common stock available for issuance from 300 million to 500 million, to approve an amendment and restatement of our 2013 Stock and Option Plan that, among other things, increases the number of shares authorized for issuance under this plan by 7.8 million shares, to ratify Ernst & Young LLP as our independent registered public accounting firm for 2015, to provide your advisory views on our executive compensation program and to vote on two proposals submitted by shareholders.

Whether or not you attend the meeting in person, we encourage you to vote by completing, signing and returning the enclosed proxy prior to the meeting. Every shareholder vote is important. To ensure your vote is counted at the annual meeting, please vote as promptly as possible.

Thank you for giving these materials your careful consideration.

Sincerely,

Jeffrey M. Leiden, M.D., Ph.D. Chairman, Chief Executive Officer and President

NOTICE OF ANNUAL MEETING OF SHAREHOLDERS

Dear Shareholders:

You are invited to attend Vertex Pharmaceuticals Incorporated's 2015 Annual Meeting of Shareholders. At the meeting, shareholders will vote:

to elect the three director nominees that are set forth in the attached proxy statement to the class of directors whose term will expire in 2018;

to approve an amendment to our Restated Articles of Organization that increases the number of shares of common stock authorized for issuance from 300 million to 500 million;

• to approve an amendment and restatement of our 2013 Stock and Option Plan that, among other things, increases the number of shares authorized for issuance under this plan by 7.8 million shares;

to ratify the selection of Ernst & Young LLP as our independent registered public accounting firm for 2015; to approve our named executive officers' compensation in an advisory vote; and

on two proposals submitted by our shareholders, if properly presented at the meeting.

Shareholders also will transact any other business that may properly come before the annual meeting or any adjournment or postponement of the annual meeting.

MEETING INFORMATION:

Date: June 4, 2015 Time: 9:30 a.m.

Location: 50 Northern Avenue

Boston, Massachusetts 02210

Record Date: You can vote if you were a shareholder of record on April 10, 2015.

Your vote matters. Whether or not you plan to attend the annual meeting, please ensure that your shares are represented by voting, signing, dating and returning your proxy in the enclosed envelope, which requires no postage if mailed in the United States.

By Order of the Board of Directors

Michael J. LaCascia

Secretary April 30, 2015

IMPORTANT NOTICE REGARDING AVAILABILITY OF PROXY MATERIALS. This proxy statement and the enclosed proxy card are first being mailed or furnished to our shareholders on or about May 4, 2015. This proxy statement and our Annual Report on Form 10-K for the year ended December 31, 2014 are available to holders of record of our common stock at www.envisionreports.com/vrtx and to beneficial holders of our common stock at www.edocumentview.com/vrtx.

SUMMARY INFORMATION

To assist you in reviewing the proposals to be acted upon, we call your attention to the following proxy summary. The following description is only a summary. Please review this proxy statement and our Annual Report on Form 10-K for the year ended December 31, 2014, or 2014 Annual Report, in full.

PROXY SUMMARY

Vertex has performed exceptionally well during both the one- and the three-year periods ended December 31, 2014 resulting in a strong shareholder return during these periods. The following charts set forth our stock price and market capitalization for the three years ended December 31, 2014.

Share Price

(as of December 31, per share)

Market Capitalization (as of December 31, billions)

Business Performance

Over the last three years we have established a leadership position in treating cystic fibrosis, or CF, which we believe has created a foundation for significant long-term revenue and earnings growth. Children who are born with mutations in their cystic fibrosis transmembrane conductance regulator, or CFTR, gene have diminished or absent function of their CFTR protein, which leads to progressive loss of lung function and early death. In 2012, we received approval to market KALYDECO (ivacaftor), and we currently estimate that more than 3,400 patients with CF worldwide are eligible to receive KALYDECO. The FDA identified KALYDECO as a breakthrough therapy for the CF community, because other existing therapies treat only the symptoms of this genetic disease, while KALYDECO addresses the underlying cause. Our KALYDECO net product revenues increased by 25% in 2014, and we expect KALYDECO net product revenues to further increase in 2015.

While KALYDECO delivers significant benefits to a portion of patients with CF, our vision is to develop additional medicines and combinations of medicines that will enable us to treat more patients with CF and to continue to enhance the clinical benefit that patients with CF receive from our medicines, with the goal of slowing or halting the progression of the disease. In 2014, we completed development of lumacaftor in combination with ivacaftor in patients with CF twelve years of age and older who are homozygous for the F508del mutation in their CFTR gene, which is the most prevalent form of CF. We believe that there are approximately 22,000 patients with CF twelve years of age and older who are homozygous for the F508del mutation in their CFTR gene in North America, Europe and Australia. We expect that this combination regimen will be approved in mid-2015 in the United States and late-2015 in the European Union, and that if we obtain timely approval for, and successfully commercialize this combination therapy, it will serve as the catalyst for revenue growth and profitability.

We have established our leadership position in CF during an exceptionally challenging period, as we exited the field of treatment for hepatitis C virus infection while successfully maintaining our financial strength by managing our operating expenses and securing non-dilutive sources of financing. During this period, we focused our research and development efforts and have advanced a number of programs, including our next-generation CFTR corrector program and programs in oncology and neurology.

SUMMARY INFORMATION (continued)

Our achievements over the last three years have occurred under the leadership of Dr. Jeffrey Leiden and the rest of our executive team. We believe that over the next several years, the leadership of Dr. Leiden and our executive team will be critical to our business as:

In the near term, we seek to:

Obtain approval for and successfully commercialize lumacaftor in combination with ivacaftor;

Develop a broad pipeline of drug candidates, including drug candidates for the treatment of CF and other serious diseases; and

Achieve a revenue and operating expense profile that supports earnings growth.

In the long term, we seek to:

Achieve significant revenues from multiple transformational medicines for serious diseases; and Deliver sustained revenue and earnings growth to shareholders.

Peer Performance

From 2012 through 2014, we had a three-year total shareholder return, or TSR, of 52.9% on an annualized basis. On this basis, we significantly outperformed (i) the peer group, or Peer Group, established by our management development and compensation committee, or MDCC, (ii) the S&P 500 Healthcare Sector Index and (iii) the S&P 500 overall.

The top and bottom dotted lines in the preceding charts indicate the 3-year TSR for the 25th and 75th percentiles, respectively, for companies in each of these groups.

In addition, based on an analysis of our CEO's compensation as compared to that of other CEOs in the Peer Group, we believe that our CEO's compensation is aligned on a relative basis with our performance. For additional information regarding the analysis of our performance against the Peer Group and the alignment of our CEO's compensation with our performance, please see the section "Pay and Performance Alignment" starting on page 46 of this proxy statement. Key 2014 Compensation Decisions

In light of our successes and recognizing the importance of completing our transition into a global biopharmaceutical company capable of delivering revenue and earnings growth, in 2014, our board of directors and MDCC:

Awarded our executive officers annual cash bonuses and equity grants generally at above target levels to reward them for the company's and their individual successes.

120% to 225% of target for cash bonuses; and

50% to 150% of target for annual equity awards.

Amended Dr. Leiden's employment agreement to extend its term through December 2017.

Implemented a retention program designed to retain and incentivize our executive officers, including our CEO, during the critical business transition period from 2015-2017. This retention program consisted of one-time

SUMMARY INFORMATION (continued)

performance-contingent restricted stock grants that will be 100% forfeited if we do not achieve positive earnings, as measured by trailing twelve-month EBITDA, and that will not vest for at least three years. This performance measure was selected because we believe it is an objective financial measure that would demonstrate our transition from a research and development organization into an integrated biopharmaceutical company capable of delivering sustained revenue and earnings growth. In addition, we believe that achieving positive EBITDA, which is difficult in the biopharmaceutical industry, has historically been an indicator of strong TSR in future periods.

Shareholder Engagement

Throughout 2014, we continued discussions with a number of our shareholders regarding, among other matters, our executive compensation program, dilution caused by our broad-based equity compensation program and our corporate governance practices. During these discussions we listened to our shareholders' perspectives and gained insight into how we could further align the interests of our company with the interests of our shareholders.

In 2014, our board and MDCC took the following steps to improve our compensation program and governance practices:

Performance-Contingent Equity: Expanded use of performance-contingent equity with our 2014 retention program. Policy Against Tax Gross-Up Payments: Adopted a policy, consistent with our long-term practices, that we will not enter into or amend any agreement to pay 280G exercise tax gross-ups to executives, except to the extent an executive was eligible for this benefit as of the adoption date of this policy. Dr. Leiden's employment agreement does not include a 280G excise tax gross-up provision.

Director Stock Ownership Guidelines: Adopted stock-ownership guidelines for our non-employee directors to complement the CEO and executive stock-ownership guidelines our board of directors had previously adopted. The above changes supplement our pre-existing compensation practices and corporate governance policies, including: Reduced Dilution to Shareholders: Implemented a significant modification to our equity compensation programs that resulted in a 25% decrease in the number of shares we granted under our equity programs in 2014 as compared to 2012 and a decrease in our annual dilution rate from 3.5% to 2.3% over the same period. We expect the dilution rate to decrease further in 2015 as compared to 2014.

Code of Conduct: Establishes ethical standards and code of business conduct for directors and employees.

Board Structure: Two co-lead independent directors to ensure independent board leadership.

Board Independence: Eight of our nine directors are independent.

Change-of-Control: No single-trigger change of control provisions.

Clawback Policy: Permits recoupment of executive compensation for fraud or intentional misconduct.

Anti-Hedging Policy: Prohibits directors and employees from hedging or pledging company securities.

Majority Voting: Requires that director candidate tender resignation to board if candidate does not receive a majority of votes in uncontested election.

Voting Matters

Proposal	Board of Directors Recommendation
Item 1: Election of Directors for Three Year Term Expiring in 2018	FOR all Nominees
Item 2: Approve Charter Amendment to Increase Authorized Common	FOR
Stock	1010
Item 3: Approve Amendment and Restatement of 2013 Stock and Option	1
Plan to Increase Number of Shares Issuable Pursuant to Plan by 7.8	FOR
Million	
Item 4: Ratify Selection of Independent Auditor for 2015	FOR
Item 5: Approve, on an Advisory Basis, Our Named Executive Officer	FOR
Compensation	TOK
Item 6: Shareholder Proposal Regarding Proxy Access	AGAINST
Item 7: Shareholder Proposal Regarding a Report on Specialty Drug	AGAINST
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PROXY STATEMENT

This proxy statement, with the enclosed proxy card, is being furnished to shareholders of Vertex Pharmaceuticals Incorporated in connection with the solicitation by our board of directors of proxies to be voted at our 2015 annual meeting of shareholders and at any postponements or adjournments thereof. The annual meeting will be held on Thursday, June 4, 2015, at 9:30 a.m. at our headquarters, which are located at 50 Northern Avenue, Boston, Massachusetts.

This proxy statement and the enclosed proxy card are first being mailed or otherwise furnished to our shareholders on or about May 4, 2015. Our 2014 Annual Report on Form 10-K and other materials regarding our company are being mailed to the shareholders with this proxy statement, but are not part of the proxy statement.

FREQUENTLY ASKED QUESTIONS REGARDING THE ANNUAL MEETING

WHAT IS THE PURPOSE OF THE ANNUAL MEETING?

At the annual meeting, shareholders will act upon the matters outlined in the Notice of Annual Meeting of Shareholders. These include:

The election of directors;

- The approval of an amendment to our Restated Articles of Organization, which increases the number of authorized shares of common stock from 300,000,000 to 500,000,000;
- The approval of an amendment and restatement of our 2013 Stock and Option Plan, that, among other things, increases the number of shares authorized for issuance under this plan by 7.8 million shares;
- The ratification of the appointment of Ernst & Young LLP as our independent registered public accounting firm;
- •The approval, on an advisory basis, of the compensation program for our named executive officers;
- A shareholder proposal regarding a proxy access by-law, if properly presented at the meeting; and
- A shareholder proposal requesting a report on specialty drug prices, if properly presented at the meeting.

Management and representatives of Ernst & Young LLP are expected to attend the annual meeting and be available to respond to questions from shareholders.

WHAT IS A PROXY?

It is your legal designation of another person to vote the stock you own in the manner you direct. That other person is called a proxy. If you designate someone as your proxy in a written document, that document also is called a proxy or a proxy card. We have designated Jeffrey M. Leiden, Ian F. Smith and Michael J. LaCascia to serve as proxies at the annual meeting.

WHAT IS A PROXY STATEMENT?

It is a document that provides certain information about a company and matters to be voted upon at a meeting of shareholders. The SEC and other applicable law requires us to give you, as a shareholder, the information in this proxy statement and certain other information when we are soliciting your vote.

WHAT IS THE DIFFERENCE BETWEEN A SHAREHOLDER OF RECORD AND A SHAREHOLDER WHO HOLDS STOCK IN STREET NAME?

Shareholders of Record. If your shares are registered in your name with our transfer agent, Computershare, you are a shareholder of record with respect to those shares, and these proxy materials were sent directly to you by Computershare.

Street Name Holders. If you hold your shares in an account at a bank or broker, then you are the beneficial owner of shares held in "street name." The proxy materials were forwarded to you by your bank or broker, who is considered the shareholder of record for purposes of voting at the annual meeting. As a beneficial owner, you have the right to direct your bank or broker how to vote the shares held in your account.

HOW MANY SHARES MUST BE REPRESENTED IN ORDER TO HOLD THE ANNUAL MEETING?

In order for us to conduct the annual meeting, holders of a majority of the shares entitled to vote as of the close of business on the record date must be present in person or by proxy. This constitutes a quorum. If you are a shareholder of record, your shares are counted as present if you properly return a proxy card or voting instruction form by mail or if you attend the annual meeting and vote in person. If you are the beneficial owner of shares held in "street name," you must follow the instructions of your bank or broker in order to direct them how to vote the shares held in your account. Abstentions and broker non-votes will be counted as present for purposes of establishing a quorum. If a quorum is not present, we will adjourn the annual meeting until a quorum is obtained.

HOW CAN I VOTE AT THE ANNUAL MEETING IF I OWN SHARES IN STREET NAME?

If you are a street name holder, you may not vote your shares at the annual meeting unless you obtain a legal proxy from your bank or broker. A legal proxy is a bank's or broker's authorization for you to vote the shares it holds in its name on your behalf.

WHAT IS THE RECORD DATE AND WHAT DOES IT MEAN?

The record date for the annual meeting is April 10, 2015 and was established by our board of directors. On the record date, there were 243,613,313 shares of our common stock entitled to vote. Owners of record of common stock at the close of business on the record date are entitled to:

receive notice of the annual meeting; and

FREQUENTLY ASKED QUESTIONS REGARDING THE ANNUAL MEETING (continued)

vote at the annual meeting and any adjournment or postponement of the annual meeting.

IF I SUBMIT A PROXY, MAY I LATER REVOKE IT AND/OR CHANGE MY VOTE?

Shareholders may revoke a proxy and/or change their vote prior to the completion of voting at the annual meeting by: signing another proxy card with a later date and delivering it to our Secretary, Michael J. LaCascia, 50 Northern

Avenue, Boston, Massachusetts 02210, before the annual meeting; or

voting at the annual meeting, if you are a shareholder of record or hold your shares in street name and have obtained a legal proxy from your bank or broker.

WHAT IF I DO NOT SPECIFY A CHOICE FOR A MATTER WHEN RETURNING A PROXY?

Shareholders should specify their choice for each matter following the directions described on their proxy card. If no specific instructions are given, proxies that are signed and returned will be voted:

FOR the election of all director nominees;

FOR approval of the amendment to our Restated Articles of Organization;

FOR approval of the amendment and restatement of our 2013 Stock and Option Plan;

FOR ratification of the appointment of Ernst & Young LLP as our independent registered public accounting firm for the year ended December 31, 2015;

FOR our executive compensation program;

AGAINST the shareholder proposal regarding a proxy access by-law; and

AGAINST the shareholder proposal requesting a report on specialty drug prices.

ARE MY SHARES VOTED IF I DO NOT PROVIDE A PROXY?

If you are a shareholder of record and do not provide a proxy, you must attend the annual meeting in order to vote. If you hold shares through an account with a bank or broker, your shares may be voted by the bank or broker if you do not provide voting instructions. Banks and brokers have the authority under applicable rules to vote shares on routine matters for which their customers do not provide voting instructions. The ratification of Ernst & Young LLP as our independent registered public accounting firm is considered a routine matter. Each of the other proposals, including the

election of directors, the approval of the amendment to our Restated Articles of Organization, the approval of the amendment and restatement of our 2013 Stock and Option Plan, the advisory vote with respect to our executive compensation program and the two shareholder proposals are not considered routine, and banks and brokers cannot vote shares without instruction on those matters. Shares that banks and brokers are not authorized to vote on those matters are counted as "broker non-votes" and other than with respect to the approval of the amendment to our Restated Articles of Organization, will have no effect on the results of those votes. Broker non-votes will have the same effect on the result of the proposal to amend our Restated Articles of Organization as votes against the proposal.

WHAT VOTE IS REQUIRED TO APPROVE EACH PROPOSAL AND HOW ARE VOTES COUNTED?

Item 1: Election of Directors

The nominees for director in an uncontested election who receive a majority of the votes from shareholders present in person or represented by proxy at the annual meeting (more votes cast "FOR" such director than "WITHHELD" from such director) will be elected. Abstentions are not counted for purposes of electing directors. You may vote either FOR or WITHHOLD your vote from any one or more of the nominees.

Item 2: Approval of the Amendment to our Restated Articles of Organization

To be approved, this proposal must receive an affirmative vote from shareholders present in person or represented by proxy at the annual meeting representing a majority of our outstanding shares of common stock as of the record date. Abstentions and broker non-votes will have the same effect on the result of this vote as votes against the proposal.

Item 3: Approval of the Amendment and Restatement of our 2013 Stock and Option Plan

To be approved, this proposal must receive an affirmative vote from shareholders present in person or represented by proxy at the annual meeting representing a majority of the votes cast on the proposal. Abstentions will have no effect on the results of this vote.

Item 4: Ratification of the Appointment of Independent Registered Public Accounting Firm

To be approved, this proposal must receive an affirmative vote from shareholders present in person or represented by proxy at the annual meeting representing a majority of the votes cast on the proposal. Abstentions will have no effect on the results of this vote.

FREQUENTLY ASKED QUESTIONS REGARDING THE ANNUAL MEETING (continued)

Item 5: Advisory Vote to Approve Named Executive Officer Compensation

To be approved, this proposal must receive an affirmative vote from shareholders present in person or represented by proxy at the annual meeting representing a majority of the votes cast on the proposal. Abstentions will have no effect on the results of this vote.

Item 6: Shareholder Proposal Regarding a Proxy Access By-law

To be approved, this proposal must receive an affirmative vote from shareholders present in person or represented by proxy at the annual meeting representing a majority of the votes cast on the proposal. Abstentions will have no effect on the results of this vote.

Item 7: Shareholder Proposal Requesting a Report on Specialty Drug Prices

To be approved, this proposal must receive an affirmative vote from shareholders present in person or represented by proxy at the annual meeting representing a majority of the votes cast on the proposal. Abstentions will have no effect on the results of this vote.

WHERE CAN I FIND MORE INFORMATION ABOUT MY VOTING RIGHTS AS A SHAREHOLDER? The SEC has an informational website that provides shareholders with general information about how to cast their vote and why voting should be an important consideration for shareholders. You may access that website at

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sec.gov/spotlight/proxymatters.shtml.

ITEM 1 - ELECTION OF DIRECTORS

Our board of directors has nominated Jeffrey M. Leiden and Bruce I. Sachs for re-election and Sangeeta N. Bhatia for election at our 2015 annual meeting of shareholders to hold office until our 2018 annual meeting of shareholders. Our board of directors is our company's ultimate decision-making body, except with respect to those matters reserved to the shareholders. Our board selects our senior management team, who in turn are responsible for the day-to-day operations of our company. Our board acts as an advisor and counselor to senior management and oversees its performance.

Our board consists of directors divided into three classes, with each class holding office for a three-year term. Jeffrey M. Leiden and Bruce I. Sachs, current Class II Directors, and Sangeeta N. Bhatia, who would join our board as a Class II Director upon election by our shareholders, have been nominated by our board for election at the 2015 annual meeting of shareholders for three-year terms that will expire at the 2018 annual meeting of shareholders. Each of the nominees has agreed to be named in this proxy statement and to serve if elected. We believe that all of the nominees will be able and willing to serve if elected. However, if any nominee should become unable for any reason or unwilling to serve, proxies may be voted for another person nominated as a substitute by our board, or our board may reduce the number of directors.

BOARD STRUCTURE AND COMPOSITION

The corporate governance and nominating committee of our board of directors is responsible for recommending the composition and structure of our board and for developing criteria for board membership. This committee regularly reviews director competencies, qualities and experiences, with the goal of ensuring that our board is comprised of an effective team of directors who function collegially and who are able to apply their experience toward meaningful contributions to general corporate strategy and oversight of corporate performance, risk management, organizational development and succession planning.

Our by-laws provide that the size of our board may range between three and eleven members. We currently have nine members on our board. We have nominated Sangeeta N. Bhatia, who was recommended by our corporate governance and nominating committee, for election at the 2015 annual meeting of shareholders to fill the vacant tenth seat on our board. Our corporate governance and nominating committee may seek one additional director candidate who meets the criteria below in order to complement the qualifications and experience of our existing board members. Our corporate governance and nominating committee may engage a search firm to recommend candidates who satisfy the criteria.

Director Criteria, Qualifications and Experience; Diversity. The corporate governance and nominating committee seeks to recommend for nomination directors of stature who have a substantive knowledge of our business and industry or who can bring to the board specific and valuable strategic or management capabilities acquired in other industries. The committee expects each of our directors to have proven leadership, sound judgment, integrity and a commitment to the success of our company. We also seek personal qualities that foster a respectful environment in which our directors listen to one another and are engaged and constructive. These goals for our board composition presuppose a diverse range of viewpoints, experiences and specific expertise. The corporate governance and nominating committee considers a nominee's personal characteristics and business experience relative to those of our existing board members, including the type of prior management experience, levels of expertise relevant to our business and its growth stage, prior board service, reputation in the business community, personal characteristics such as gender and race and other factors that the committee believes to be important. At this time, our commitment to racial and gender diversity is demonstrated by the make-up of our board, which includes three members or nominees who are women and one member who is African-American.

The key experience, qualifications, attributes and skills brought by our directors to our board that are important to our business include:

Corporate leadership experience. We believe that directors who have held significant corporate leadership positions over extended periods of time provide our company with special insights. These people generally have a practical understanding of organizational processes and strategy that is valuable during periods of organizational change and growth.

Industry knowledge. We seek directors with substantive knowledge of the biotechnology, pharmaceutical or related industries. We believe that having a substantial portion of our board of directors comprised of individuals with

ITEM 1 - ELECTION OF DIRECTORS (continued)

experience as executives or directors in these industries provides our board with the background necessary to counsel our management regarding the issues facing our company.

Financial expertise. We believe that an understanding of finance is important for our board of directors, and our budgeting processes and financial and strategic transactions require our directors to be financially knowledgeable. In addition, we seek to have a number of directors qualified to serve on our audit and finance committee and at least one director with in-depth knowledge of financial statements and financial reporting processes sufficient to qualify as an audit committee financial expert under applicable regulatory standards.

Scientific experience. As a biopharmaceutical company that seeks to develop transformative medicines for patients with serious diseases, we look for directors with backgrounds in science and technology and in particular the research and development of pharmaceutical products.

Commitment to company values and goals. We seek directors who are committed to our company and its values and goals and who value the contributions that can be provided by individuals who believe in our company and its prospects for success.

SHAREHOLDER-RECOMMENDED DIRECTOR CANDIDATES

The corporate governance and nominating committee will consider director candidates recommended by shareholders using the same criteria for director selection described above under Director Criteria, Qualifications and Experience; Diversity. Shareholders recommending candidates for consideration should submit any pertinent information regarding the candidate, including biographical information and a statement by the proposed candidate that he or she is willing to serve if nominated and elected, by mail to our corporate secretary at our offices at 50 Northern Avenue, Boston, Massachusetts 02210. If a shareholder wishes to nominate a candidate to be considered for election as a director at the 2016 annual meeting of shareholders using the procedures set forth in our by-laws, the shareholder must follow the procedures described in Other Information—Shareholder Proposals for the 2016 Annual Meeting and Nominations for Director on page 85 of this proxy statement.

MAJORITY VOTE STANDARD

Our by-laws provide for a majority vote standard for uncontested elections of our directors. Under our by-laws, as amended, director nominees in an uncontested election who receive more votes cast "for" such director nominee than "withheld" from such director nominee are elected. Our board's policy is that any nominee for director in an uncontested election who receives a greater number of votes "withheld" than votes "for" the nominee's election shall promptly tender his or her resignation to the chair of our board following certification of the shareholder vote. Our corporate governance and nominating committee will promptly consider the tendered resignation. Based on all factors it deems in its discretion to be relevant, the committee will recommend that our board either accept or reject the resignation and may recommend that the board adopt measures designed to address any issues perceived to underlie the election results. Our board will then act on the corporate governance and nominating committee's recommendation. We will promptly disclose our board's decision, including, if applicable, the reasons for rejecting the tendered resignation. Any director whose resignation is being considered under this policy will not participate in the corporate governance and nominating committee or board considerations, recommendations or actions with respect to the tendered resignation. OUR BOARD OF DIRECTORS RECOMMENDS THAT SHAREHOLDERS VOTE FOR EACH OF THE NOMINEES.

ITEM 1 - DIRECTOR NOMINEES

In each of the director nominee and continuing director biographies that follow, we highlight the specific experience, qualifications, attributes and skills that led the board of directors to conclude that the director nominee or continuing director should serve on our board at this time.

DIRECTOR NOMINEES

CLASS II DIRECTORS—PRESENT TERMS EXPIRING IN 2015 AND PROPOSED TERMS TO EXPIRE IN 2018 Jeffrey M. Leiden, M.D., Ph.D. Chairman, Chief Executive Officer and President

Age: 59

Director Since: 2009

Dr. Leiden has held the positions of Chief Executive Officer and President since February 2012 after joining us as CEO Designee in December 2011. He has been the Chairman of our Board of Directors since May 2012, and served as our lead independent director from October 2010 through December 2011. Dr. Leiden was a Managing Director at Clarus Ventures, a life sciences venture capital firm, from 2006 through January 2012. Dr. Leiden was President and Chief Operating Officer of Abbott Laboratories, Pharmaceuticals Products Group, and a member of the Board of Directors of Abbott Laboratories from 2001 to 2006. From 1987 to 2000, Dr. Leiden held several academic appointments, including the Rawson Professor of Medicine and Pathology and Chief of Cardiology and Director of the Cardiovascular Research Institute at the University of Chicago, the Elkan R. Blout Professor of Biological Sciences at the Harvard School of Public Health, and Professor of Medicine at Harvard Medical School. He is an elected member of both the American Academy of Arts and Sciences, and the Institute of Medicine of the National Academy of Sciences. Dr. Leiden is a senior advisor to Clarus Ventures. Dr. Leiden has served as a director of Quest Diagnostics Inc., a medical diagnostics company, since December 2014. Dr. Leiden was a director and the non-executive Vice Chairman of the board of Shire plc, a specialty biopharmaceutical company, from 2006 to January 2012, and was also a member of the Board of Directors of Millennium Pharmaceuticals, Inc. from October 2007 until it was acquired in June 2008. Dr. Leiden received his M.D., Ph.D. and B.A. degrees from the University of Chicago. Skills and Qualifications: Dr. Leiden possesses strong leadership qualities, demonstrated through his service as an executive in the pharmaceutical industry and as a life sciences venture capitalist, and has extensive knowledge of the science underlying drug discovery and development through his experiences as a distinguished physician, scientist and teacher. He also provides our board of directors with in-depth knowledge of our company through the day-to-day leadership of our executives.

Bruce I. Sachs Co-lead Independent Director

Age: 55 Chair – Management Development and Compensation Committee

Director Since: 1998 Member – Audit and Finance Committee

Mr. Sachs is a General Partner at Charles River Ventures, a venture capital firm he joined in 1999. From 1998 to 1999, he served as Executive Vice President and General Manager of Ascend Communications, Inc. From 1997 until 1998, Mr. Sachs served as President and Chief Executive Officer of Stratus Computer, Inc. From 1995 to 1997, he served as Executive Vice President and General Manager of the Internet Telecom Business Group at Bay Networks, Inc. From 1993 to 1995, he served as President and Chief Executive Officer at Xylogics, Inc. Mr. Sachs holds a B.S.E.E. in electrical engineering from Bucknell University, an M.E.E. in electrical engineering from Cornell University, and an M.B.A. from Northeastern University.

Skills and Qualifications: Mr. Sachs brings strong business judgment and financial analytical skills, honed through his experience developing business strategy at a senior management level and his success in building companies and in venture capital, to our board of directors. In addition, Mr. Sachs has extensive business leadership experience, including service as a CEO at a technology company, as well as financial expertise.

ITEM 1 - DIRECTOR NOMINEES (continued)

DIRECTOR NOMINEE—PROPOSED TERM TO EXPIRE IN 2018

Sangeeta N. Bhatia, M.D., Ph.D.

Age: 46

Dr. Bhatia has been a professor at the Massachusetts Institute of Technology since 2005, where she currently serves as the John J. and Dorothy Wilson Professor of Health Sciences & Technology/Electrical Engineering & Computer Science. Prior to joining the Massachusetts Institute of Technology, Dr. Bhatia was a professor of bioengineering and medicine at the University of California at San Diego from 1998 through 2005. Dr. Bhatia also is an investigator for the Howard Hughes Medical Institute, a member of the Department of Medicine at Brigham and Women's Hospital, a member of the Broad Institute and a member of the Koch Institute for Integrative Cancer Research. Dr. Bhatia holds an Sc.B. in biomedical engineering from Brown University, an S.M. and Ph.D. in Mechanical Engineering from the Massachusetts Institute of Technology and an M.D. from Harvard Medical School.

Skills and Qualifications: Dr. Bhatia is a leading academic scientist and medical researcher. Her extensive experience in the field of biomedical engineering and in-depth understanding on the use of advanced technologies in medical research will provide valuable insights to our board, including with respect to our key research and development initiatives.

ITEM 1 - CONTINUING DIRECTORS

CONTINUING DIRECTORS

CLASS III DIRECTORS—TERMS EXPIRING IN 2016

Joshua Boger, Ph.D.

Age: 64

Chair – Science and Technology Committee

Director Since: 1989

Dr. Boger is the founder of Vertex. He was our Chief Executive Officer from 1992 through May 2009. He was our Chairman of our board of directors from 1997 until May 2006 and our President from our inception until December 2000, and from 2005 through February 2009. He was our Chief Scientific Officer from 1989 until May 1992. Prior to founding Vertex in 1989, Dr. Boger held the position of Senior Director of Basic Chemistry at Merck Sharp & Dohme Research Laboratories in Rahway, New Jersey, where he headed both the Department of Medicinal Chemistry of Immunology & Inflammation and the Department of Biophysical Chemistry. Dr. Boger holds a B.A. in chemistry and philosophy from Wesleyan University and M.S. and Ph.D. degrees in chemistry from Harvard University. Skills and Qualifications: Dr. Boger's qualifications for our board of directors include his extensive industry knowledge and leadership experience. Dr. Boger brings an in-depth knowledge of issues facing our company and our industry as a result of his experience founding and leading Vertex and his distinguished career as a scientist. Terrence C. Kearney

Age: 60 Chair – Audit and Finance Committee

Director Since: 2011 Member – Management Development and Compensation

Committee

Mr. Kearney served as the Chief Operating Officer of Hospira, Inc., a specialty pharmaceutical and medication delivery company, from April 2006 to January 2011. From April 2004 to April 2006, he served as Hospira's Senior Vice President, Finance, and Chief Financial Officer, and he served as Acting Chief Financial Officer through August 2006. Mr. Kearney served as Vice President and Treasurer of Abbott Laboratories from 2001 to April 2004. From 1996 to 2001, Mr. Kearney was Divisional Vice President and Controller for Abbott's International Division. Mr. Kearney serves as a member of the Board of Directors at Acceleron Pharma Inc., a biopharmaceutical company, and Theravance, Inc., a royalty management company. He received his B.S. in biology from the University of Illinois and his M.B.A. from the University of Denver.

Skills and Qualifications: Mr. Kearney's corporate leadership experience, industry knowledge and financial expertise make him a valuable contributor to our board of directors. He has a practical perspective on the management of global pharmaceutical operations, including commercial, manufacturing and research and development activities, and financial management strategies. He is an "audit committee financial expert" as defined in SEC regulations, with particular experience in matters faced by the audit committee of a company with pharmaceutical product revenues and related expenses.

ITEM 1 - CONTINUING DIRECTORS (continued)

Yuchun Lee

Age: 49 Member – Audit and Finance Committee Director Since: 2012 Member – Science and Technology Committee

Mr. Lee has served as an Executive in Residence (XIR) and Partner of General Catalyst Partners, a venture capital firm, since April of 2013. Mr. Lee was the Vice President of IBM's Enterprise Marketing Management Group from November 2010 through January 2013. Mr. Lee co-founded Unica Corporation, a provider of software and services used to automate marketing processes, in 1992, and was Unica's President and/or Chief Executive Officer from 1992 through November 2010, when Unica was acquired by IBM. From 1989 to 1992, Mr. Lee was a senior consultant at Digital Equipment Corporation, a supplier of general computing technology and consulting services. Mr. Lee holds a B.S. and an M.S. in electrical engineering and computer science from the Massachusetts Institute of Technology and an M.B.A. from Babson College.

Skills and Qualifications: Mr. Lee's expertise in marketing processes, customer engagement and business and financial expertise make him a valuable contributor to our board of directors. Mr. Lee is an innovator who founded and managed the growth of a successful technology company and gained further leadership experience while serving as an executive at IBM. Mr. Lee's experiences outside of the biopharmaceutical sector provide the board with a fresh perspective on the issues facing the company.

Elaine S. Ullian Co-lead Independent Director

Age: 67 Chair – Corporate Governance and Nominating Committee

Member – Management Development and Compensation Director Since: 1997

Committee

Ms. Ullian served as President and Chief Executive Officer of Boston Medical Center, a private, not-for-profit, 626-bed, academic medical center with a community-based focus, from 1996 through January 2010. From 1994 to 1996, she served as President and Chief Executive Officer of Boston University Medical Center Hospital. From 1987 to 1994, Ms. Ullian served as President and Chief Executive Officer of Faulkner Hospital. She also serves as a director of Thermo Fisher Scientific Inc. and Hologic, Inc. Ms. Ullian holds a B.A. in political science from Tufts University and an M.P.H. from the University of Michigan.

Skills and Qualifications: Ms. Ullian brings significant leadership experience acquired as the CEO of large health care providers to our board of directors. The knowledge she obtained serving as an executive, together with her extensive experience serving on the boards of directors of multiple public companies in the healthcare field, provide her with the expertise required to serve as one of our co-lead independent directors and as the chair of our corporate governance and nominating committee. She also provides the board with the perspective of providers, payors and patients, for whom our products are intended.

ITEM 1 - CONTINUING DIRECTORS (continued)

CLASS I DIRECTORS—TERMS EXPIRING IN 2017

Margaret G. McGlynn

Age: 55 Member – Science and Technology Committee

Director Since: 2011

Ms. McGlynn has served as the President and Chief Executive Officer of the International AIDS Vaccine Initiative, a global not-for-profit organization whose mission is to ensure the development of safe, effective and accessible HIV vaccines for use throughout the world, since July 2011. Ms. McGlynn served as President, Vaccines and Infectious Diseases of Merck & Co., Inc. from 2005 until 2009. Ms. McGlynn joined Merck in 1983 and served in a variety of marketing, sales and managed care roles. Ms. McGlynn serves as a member of the Board of Directors for Air Products and Chemicals, Inc., a company specializing in gases and chemicals for industrial uses, and Amicus Therapeutics, Inc., a biopharmaceutical company. She is also a member of the National Industrial Advisory Committee at the University at Buffalo School of Pharmacy and Pharmaceutical Sciences. Ms. McGlynn holds a B.S. in Pharmacy and an M.B.A. in Marketing from the State University of New York at Buffalo.

Skills and Qualifications: Ms. McGlynn's corporate leadership experience and industry knowledge make her a valuable contributor to our board of directors. Her service as an executive at Merck and her service on the board of Amicus Therapeutics and the board and audit committee of Air Products and Chemicals, Inc. give her a practical understanding of organizational practices valuable to a company at our stage of growth. Her experience in the development of treatments for infectious diseases provides her with a valuable understanding of the scientific issues we face in the drug development process.

Wayne J. Riley, M.D.

Age: 55 Member – Corporate Governance and Nominating Committee Director Since: 2010 Member – Science and Technology Committee

Dr. Riley is Clinical Professor of Medicine, Vanderbilt University School of Medicine and Adjunct Professor of Healthcare Management, Owen Graduate School of Management at Vanderbilt University. From January 2007 until July 2013, Dr. Riley was President and Chief Executive Officer of Meharry Medical College. At Meharry he held the rank of tenured Professor of Internal Medicine and was a Senior Health Policy Associate at the Robert Wood Johnson Center for Health Policy at Meharry. From May 2004 to December 2006, Dr. Riley served as a corporate officer and member of the executive management team as Vice President and Vice Dean for Health Affairs and Governmental Relations and Associate Professor of Medicine at Baylor College of Medicine, and Assistant Chief of Medicine at Ben Taub General Hospital. Dr. Riley is a member of the Board of Directors of HCA Holdings, Inc., the parent company of Hospital Corporation of America, a leading operator of hospitals and health facilities, where he serves on the Audit & Compliance Committee and the Nominating and Corporate Governance Committee and is the Chair of the Patient Safety and Quality Committee. Dr. Riley formerly served as a Director of Pinnacle Financial Partners and of the Nashville Branch Board of the Federal Reserve Bank of Atlanta. He is a member of the Institute of Medicine of the National Academy of Sciences, Dr. Riley earned a B.A. from Yale University, an M.P.H. in health systems management from Tulane University School of Public Health & Tropical Medicine, an M.D. from the Morehouse School of Medicine and an M.B.A. from Rice University's Jones Graduate School of Management. Skills and Qualifications: Dr. Riley is a valuable contributor to our board of directors due to the corporate leadership skills he has acquired through his experience as the President and CEO of Meharry Medical College and executive positions at Baylor College of Medicine and Ben Taub General Hospital. As a physician, executive, clinician educator, and public health and health policy expert, he brings a unique perspective on the scientific and medical issues we face in pharmaceutical development and commercialization.

ITEM 1 - CONTINUING DIRECTORS (continued)

William D. Young

Age: 70 Member – Management Development and Compensation Director Since: 2014 Committee

Mr. Young is a Venture Partner at Clarus Ventures, a life sciences venture capital firm, which he joined in 2010. Prior to Clarus Ventures, Mr. Young served from 1999 until June 2009 as the Chairman and Chief Executive Officer of Monogram Biosciences, Inc., a biotechnology company acquired by Laboratory Corporation of America in June 2009. From 1980 to 1999, Mr. Young was employed at Genentech, Inc. in positions of increasing responsibility, including as Chief Operating Officer from 1997 to 1999, where he was responsible for all product development, manufacturing and commercial functions. Prior to joining Genentech, Mr. Young was with Eli Lilly & Co. for 14 years. Mr. Young currently serves at the Chairman of the Board of Directors of NanoString Technologies, Inc., and as a member of the Boards of Directors of Theravance BioPharma Inc. and BioMarin Pharmaceutical Inc. Mr. Young retired from Biogen Idec's Board of Directors in June 2014 where he served as a director from 1997 through 2014 and as Biogen's Chairman of the Board from 2010 through 2014. Mr. Young holds a B.S. in Chemical Engineering from Purdue University, an M.B.A. from Indiana University and an Honorary Doctorate in Engineering from Purdue University. Mr. Young was elected to the National Academy of Engineering in 1993 for his contributions to biotechnology. Skills and Qualifications: Mr. Young is a valuable contributor to our board of directors due to the in-depth knowledge of the pharmaceuticals industry that he acquired through his extensive experience as both a CEO and board member at numerous pharmaceutical and biotechnology organizations and as a venture capitalist focused on the life sciences industry. Mr. Young's strong leadership qualities, global industry knowledge and financial expertise provide him with the background to work collaboratively with both management and fellow board members in order to address issues facing our company.

CORPORATE GOVERNANCE AND RISK MANAGEMENT

We are committed to good corporate governance and integrity in our business dealings. Our governance practices are documented in our Statement of Corporate Governance Principles, which addresses the role and composition of our board of directors and the functioning of the board and its committees. You can find our governance documents, including our Statement of Corporate Governance Principles, charters for each committee of the board and our Code of Conduct, on our website www.vrtx.com under "Investors—Corporate Governance—Governance Documents." INDEPENDENCE, CHAIR AND CO-LEAD INDEPENDENT DIRECTORS

Our board of directors has determined that eight of our nine directors qualify as "independent" under the definition of that term adopted by The Nasdaq Stock Market LLC, or Nasdaq. These directors are Dr. Boger, Mr. Kearney, Mr. Lee, Ms. McGlynn, Dr. Riley, Mr. Sachs, Ms. Ullian and Mr. Young. Our board also has determined that Dr. Bhatia will be an independent director if elected at the 2015 annual meeting of shareholders and that Dr. Altshuler was an independent director prior to his resignation from the board on December 9, 2014 in order to become our Executive Vice President, Global Research and Chief Scientific Officer. Our independent directors generally meet in executive session at each regularly scheduled board meeting.

Dr. Leiden, our president and chief executive officer, serves as the chairman of our board. Our employment agreement with Dr. Leiden provides that he will serve as the chairman of our board through December 31, 2017. In addition, we have two co-lead independent directors who are elected by the independent directors. Each of the board committees is chaired by one of our independent directors.

Our board believes that strong, independent board leadership is a critical aspect of effective corporate governance, and our corporate governance principles require that if the chair is not an independent director, that the independent directors elect a lead independent director. Since December 2011, Mr. Sachs and Ms. Ullian have served as our co-lead independent directors. We believe this structure provides our board independent leadership, while providing the benefit of having our chief executive officer, the individual with primary responsibility for managing our day-to-day operations, chair regular board meetings as we discuss key business and strategic issues. Combined with the co-lead independent directors and experienced and independent committee chairs, this structure provides strong independent oversight of management.

Our co-lead independent directors' responsibilities include:

ealling and leading regular and special meetings of the independent directors;

serving as a liaison between our executive leaders and the independent directors;

reviewing the planned dates for regularly scheduled board meetings and the primary agenda items for each meeting; and

reviewing with the chair of each board committee agenda items that fall within the scope of the responsibilities of that committee.

BOARD COMMITTEES

Our board of directors has established various committees to assist in discharging its duties: the audit and finance committee, the corporate governance and nominating committee, the management development and compensation committee, or MDCC, and the science and technology committee. Each member of the audit and finance committee, corporate governance and nominating committee and MDCC is an independent director as that term is defined by the SEC and Nasdaq. The primary responsibilities of each of the committees are set forth below, and the committee memberships are provided in the table appearing on page 20 of this proxy statement.

Each of the committees has the authority, as its members deem appropriate, to engage legal counsel or other experts or consultants in order to assist the committee in carrying out its responsibilities.

CORPORATE GOVERNANCE AND RISK MANAGEMENT (continued)

RISK MANAGEMENT

Our board of directors discharges its overall responsibility to oversee risk management with a focus on our most significant risks. We face considerable risk related to the commercialization of our approved products, including regulatory risk with respect to our promotional activities and competition from approved drugs and investigational drug candidates that may have product profiles superior to our approved products. We continue to invest significant resources in research programs and clinical development programs as part of our strategy to develop transformative medicines for patients with serious diseases. With respect to each of our drug development and commercialization programs, we face considerable risk that the program will not ultimately result in a commercially successful pharmaceutical product. Our board and its committees monitor and manage the strategic, compliance and operational risks related to KALYDECO (ivacaftor), the potential commercialization of lumacaftor in combination with ivacaftor, if approved, and our research and development programs through regular board and committee discussions that include presentations to the board and its committees by our executive officers as well as during in-depth short- and long-term strategic reviews held at least annually.

For certain specific risk types, our board has delegated oversight responsibility to board committees as follows: Our audit and finance committee oversees our enterprise risk management programs and policies, including those related to our financial and accounting systems, accounting policies and investment strategies, intellectual property strategy, information technology systems and steps our management has taken to monitor, mitigate and report on those exposures. The audit and finance committee also is responsible for addressing risks arising from related party transactions.

Our MDCC oversees risks associated with our compensation policies, management resources and structure, succession planning, and management development and selection processes.

Our corporate governance and nominating committee oversees risks related to the company's governance structure. Our science and technology committee oversees risks related to our research and development investments. CODE OF CONDUCT

We have adopted a Code of Conduct that applies to all of our directors and employees, including our chief executive officer and chief financial and accounting officers. Our Code of Conduct is available on our website www.vrtx.com under "Investors—Corporate Governance—Governance Documents." Disclosure regarding any amendments to, or waivers from, provisions of the Code of Conduct that apply to our directors or principal executive, financial or accounting officers will be posted on our website or included in a Current Report on Form 8-K within four business days following the date of the amendment or waiver.

CORPORATE GOVERNANCE AND RISK MANAGEMENT (continued)

BOARD ATTENDANCE, COMMITTEE MEETINGS AND COMMITTEE MEMBERSHIP

		Aud	lit	Corporate	Management	Science	2014
Director (1) Independence Bo		d and		Governance and Development and and			Attendance at
		Fina	ınce	Nominating	Compensation	Technology	Meetings (2)
Joshua Boger	X					Chair	93%
Terrence C. Kearne	yX	Cha	ir				100%
Yuchun Lee	X						100%
Jeffrey M. Leiden	Cha	r					100%
Margaret G.	X						
McGlynn	Λ						