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

☑ Filed by the Registrant ☐ Filed by a Party other than the Registrant

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

VERTEX
THE SCIENCE of POSSIBILITY

VERTEX PHARMACEUTICALS INCORPORATED

(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:


VERTEX
THE SCIENCE of POSSIBILITY
2021 PROXY STATEMENT
VERTEX PHARMACEUTICALS INCORPORATED
Notice of Annual Meeting of Shareholders
to be held on May 19, 2021

Dear Shareholders:

2020 was an important year for Vertex, and we are better positioned today than ever before to continue discovering and developing medicines for serious diseases. Led by TRIKAFTA, we are treating more patients than ever with a Vertex CFTR modulator. As a result, in 2020, we delivered extraordinary commercial results - $6.2 billion in net product revenues, representing an increase of approximately 50% as compared to 2019 net product revenues; we advanced our pipeline meaningfully with proof-of-concept results obtained in both transfusion-dependent beta thalassemia and sickle cell disease and first-in-class or best-in-class programs in the clinic across multiple disease areas; and we significantly strengthened our financial position. Notably, we achieved these results despite the challenges brought on by the COVID-19 pandemic, which disrupted governments, businesses and people around the world.

Since 2012, we have executed on our corporate strategy of investing in scientific innovation to create transformative medicines for people with serious diseases in specialty markets, a strategy we believe both maximizes benefits for patients and generates significant long-term value for shareholders. The disciplined execution of our strategy has enabled Vertex to serially innovate to discover, develop and commercialize four transformative medicines for people with cystic fibrosis (CF) around the world and advance our growing pipeline of small molecule, cell and genetic therapies sourced from internal and external innovation.

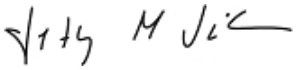
The latest of our approved CF medicines, TRIKAFTA, or KAFTRIO, as it is known in Europe, has the potential to treat up to 90% of people with CF. In 2020, we made significant progress in bringing TRIKAFTA to nearly all eligible people in the U.S. in its first full year of approval. Outside of the U.S., we successfully launched KAFTRIO after receiving early approval in the E.U. and securing reimbursement in numerous countries. Over the next three to five years in CF, we have line of sight to continued, significant revenue growth as we secure new regulatory approvals and reimbursement agreements in additional geographies and work to expand the TRIKAFTA / KAFTRIO label for younger patients. We are also focused on developing once-a-day next-generation corrector therapies with improved efficacy, as well as genetic therapies for the remaining 10% of people with CF who may not be helped by our current CF medicines. We remain committed to bringing transformative therapies to all people with this devastating disease.

Beyond CF, our unique and differentiated research and development strategy has delivered a broad and deep pipeline. In 2020, we continued to meaningfully advance multiple compounds and are currently in clinical development with programs across six diseases outside of CF: alpha-1 antitrypsin deficiency, APOL1-mediated focal segmental glomerulosclerosis, pain, beta thalassemia, sickle cell disease, and type 1 diabetes. We established proof-of-concept for CTX001, the investigational CRISPR/Cas9-based gene-editing therapy we are developing with our partner CRISPR Therapeutics, for the treatment of transfusion-dependent beta thalassemia, the most severe form of beta thalassemia, and sickle cell disease. The results to date have shown that CTX001 has the potential to be a one-time functional cure for people living with these diseases. We advanced our Phase 2 proof-of-concept clinical trial evaluating VX-864 for the treatment of people with alpha-1 antitrypsin deficiency who have two copies of the Z mutation, we initiated a Phase 2 proof-of-concept clinical trial of VX-147 in people with APOL1-mediated focal segmental glomerulosclerosis, and we continued to progress a portfolio of NaV1.8 inhibitors for the treatment of pain into pre-clinical and early clinical development. In early 2021, we initiated the Phase 1/2 clinical trial for VX-880, our first cell therapy for type 1 diabetes, a particularly significant achievement, as it is Vertex's first cell-based therapy to enter clinical development, as well as the only fully differentiated pancreatic islet cell program in clinical development.

COVID-19 continues to be disruptive for individuals, families, industries and economies across the globe. Despite this, Vertex remains well-positioned to fulfill its mission of providing transformative medicines to people with serious diseases. We also remain committed to supporting our patient and local communities, with direct donations from the Vertex Foundation to support STEAM education, targeted efforts in response to the spread of COVID-19, and contributions in support of social justice and healthy families, as part of our long-standing commitment to inclusion, diversity, and equity.

As we look towards the future, we look forward to bringing our CF medicines to more people, advancing our broad and deep pipeline of first-in-class or best-in-class assets in multiple serious diseases, growing both revenues and profits, and utilizing our financial strength to continue to invest in internal and external innovation. In our roles as Executive Chairman and CEO, we are committed to the continued execution of our strategy of serial innovation that has been the foundation of Vertex's successes over the last decade and that will be critical to our long-term success.

Sincerely,



Jeffrey M. Leiden, M.D., Ph.D.
Executive Chairman

Reshma Kewalramani, M.D.
Chief Executive Officer and President

Notice of Annual Meeting of Shareholders

Wednesday, May 19, 2021

9:30 a.m. (Eastern Time)

www.meetingcenter.io/237308243

Dear Shareholders:

You are invited to attend the Vertex Pharmaceuticals Incorporated 2021 Annual Meeting of Shareholders. At the annual meeting, shareholders will vote:

- to elect the ten director nominees that are set forth in the attached proxy statement to our board of directors to serve for a one-year term until the 2022 annual meeting of shareholders and until his or her successor has been duly elected and qualified;
- to ratify the selection of Ernst & Young LLP as our independent registered public accounting firm for 2021;
- to approve our 2020 named executive officer 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

PROXY MATERIALS:

We are using the “Notice and Access” method of providing proxy materials to you via the Internet. We are mailing to you a Notice of Internet Availability of Proxy Materials instead of paper copies of this notice, our proxy statement and our Annual Report on Form 10-K for the year ended December 31, 2020 (“Annual Report”). Notice and Access provides a convenient way for you to access our proxy materials. The Notice of Internet Availability of Proxy Materials includes instructions on how to access this notice, our proxy statement and our Annual Report and how to vote your shares. The Notice of Internet Availability of Proxy Materials also contains instructions on how to receive a paper copy of the proxy materials and our Annual Report, if you prefer.

MEETING ACCESS:

IN LIGHT OF THE PUBLIC HEALTH AND TRAVEL SAFETY CONCERNS RELATED TO THE ONGOING SPREAD OF THE GLOBAL COVID-19 PANDEMIC, VERTEX WILL HOLD A VIRTUAL ANNUAL MEETING. THE VIRTUAL ANNUAL MEETING WILL FACILITATE SHAREHOLDER ATTENDANCE AND PARTICIPATION BY ENABLING SHAREHOLDERS TO PARTICIPATE FROM ANY LOCATION AND AT NO COST. YOU WILL BE ABLE TO PARTICIPATE IN THE MEETING ONLINE, VOTE YOUR SHARES ELECTRONICALLY AND SUBMIT YOUR QUESTIONS DURING THE MEETING BY VISITING WWW.MEETINGCENTER.IO/237308243.

Shareholders will need their unique control number, which appears on the Notice of Internet Availability of Proxy Materials or proxy card (printed in the shaded bar), or within the body of the email sending the proxy statement. If you hold shares beneficially through a bank, broker or other nominee (that is, in “street name”), you must register in advance to gain access to the virtual meeting and to vote shares during the meeting. To register, you will need to obtain a legal proxy from your bank, broker or other nominee. Once you have received

a legal proxy from them, you must submit a copy of this legal proxy, along with your name and email address to Computershare at legalproxy@computershare.com. Alternatively, you may mail your legal proxy to the following address: Computershare, Vertex Pharmaceuticals Incorporated Legal Proxy, P.O. Box 43001, Providence, RI 02940-3001. Requests for registration must be labeled as “Legal Proxy” and received no later than 5 p.m. Eastern Time on May 14, 2021. You will receive an email from Computershare confirming your registration and providing your control number. You will need your control number to access the virtual annual meeting, submit your questions and vote your shares electronically. The annual meeting will begin promptly at 9:30 a.m., Eastern Time, on May 19, 2021. The password for the meeting is **VRTX2021.**

We will make a list of our shareholders of record available electronically during the annual meeting. A shareholder wishing access to the list during the annual meeting should contact our corporate secretary in advance of the meeting.

RECORD DATE:

Only Vertex shareholders of record at the close of business on March 25, 2021 are entitled to receive notice of, and vote at, the annual meeting, and, subject to applicable law, any adjournment or postponement thereof.

VOTING:

Your vote matters. *Whether or not you plan to attend the annual meeting, we urge you to vote as promptly as possible by Internet, telephone or signing, dating and returning a printed proxy card. If you attend the annual meeting, you may vote your shares during the annual meeting even if you previously voted your proxy. Please vote as soon as possible to ensure that your shares will be represented and counted at the annual meeting.*

April 8, 2021

By Order of the Board of Directors,

Sabrina Yohai
Corporate Secretary

IMPORTANT NOTICE REGARDING INTERNET AVAILABILITY OF PROXY MATERIALS. This notice, our proxy statement and our Annual Report on Form 10-K for the year ended December 31, 2020 are first being made available to holders of record of our common stock on or about April 8, 2021. These materials 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

In 2020, we continued to execute on our decade-long strategy of investing in scientific innovation to create transformative medicines for people with serious diseases. We were disciplined in continuing to implement our unique research and development approach by focusing on validated targets that play a causal role in the human biology of a disease, creating biological assays and identifying clinical biomarkers that we believe will be predictive of clinical responses, and advancing multiple compounds into clinical trials. This approach has yielded a broad and deep pipeline and increases the speed and likelihood of successfully bringing medicines to patients.

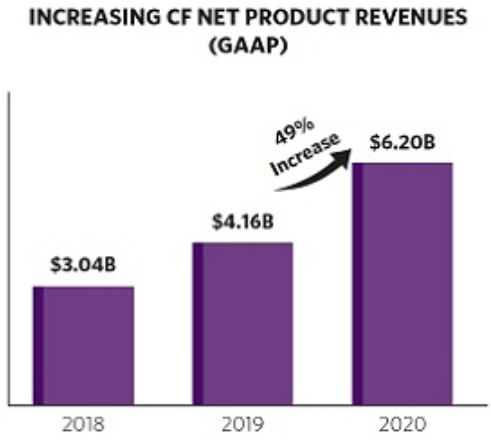
In cystic fibrosis ("CF"), our fourth approved medicine, TRIKAFTA, or KAFTRIO, as it is known in Europe, has the potential to treat up to 90% of people with CF. In 2020, we made significant progress bringing TRIKAFTA to nearly all eligible patients in the U.S. Outside of the U.S., we received early approval for KAFTRIO in the E.U. and secured reimbursement in numerous countries. As a result of these successful activities and launches in Europe, thousands of eligible patients, including those in Germany, England, and Ireland, gained access to KAFTRIO by year end. Beyond CF, we are advancing clinical programs in six serious diseases: alpha-1 antitrypsin ("AAT") deficiency, APOL1-mediated focal segmental glomerulosclerosis ("FSGS"), pain, sickle cell disease ("SCD"), beta thalassemia and type 1 diabetes ("T1D"). In 2020, we and our collaborator, CRISPR Therapeutics AG ("CRISPR"), established proof-of-concept in transfusion-dependent beta thalassemia ("TDT"), the most severe form of beta thalassemia, and SCD, and announced positive interim data from 10 people treated with CTX001. To date, more than 20 people have been dosed with CTX001. In January 2021, the FDA cleared our Investigational New Drug Application ("IND") for VX-880, our program involving transplantation of fully differentiated islet cells alone, for people with T1D. We have recently initiated a Phase 1/2 clinical trial to evaluate VX-880 in people who have T1D with impaired hypoglycemic awareness and severe hypoglycemia.

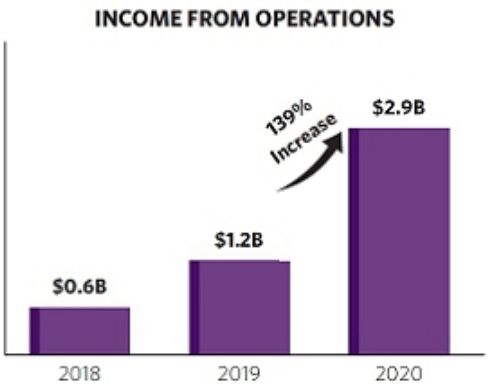
Our outstanding performance in 2020 resulted in net product revenues of $6.2 billion and expansion of our operating margins and operating income. As we enter 2021, we are positioned to continue creating long-term value for both our patients and our shareholders with a portfolio of approved medicines for CF, a broad and deep pipeline beyond CF, therapeutic modalities that span small molecules to genetic and cell therapies, and a strong financial profile. Our strategy of serial innovation continues to play out as planned and positions us for significant growth into the future.

Financial Performance

Our CF medicines, TRIKAFTA/KAFTRIO, SYMDEKO/SYMKEVI, ORKAMBI and KALYDECO, are transforming the lives of eligible patients around the globe and, as we increase the number of patients eligible for our medicines, driving our financial performance.

- Our CF net product revenues increased to $6.2 billion in 2020, up 49% from our 2019 GAAP net product revenues and up 55% from our 2019 non-GAAP net product revenues (*See Appendix A for a reconciliation of GAAP net product revenues to non-GAAP net product revenues*).
- Our net income increased to $2.7 billion in 2020, driven by our increased net product revenues.
- We increased income from operations by approximately $1.7 billion, or 139%, in 2020 compared to 2019.
- Our total cash, cash equivalents and marketable securities increased by approximately $2.9 billion to approximately $6.7 billion.

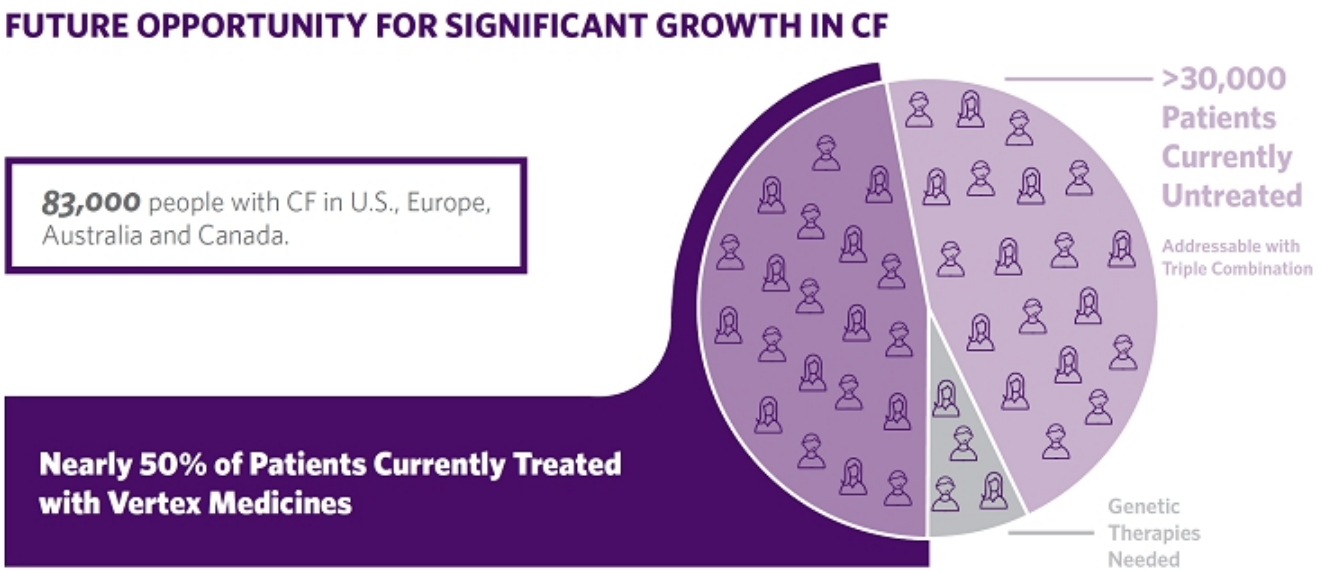




Cystic Fibrosis

Advances in our pipeline and disciplined execution of our strategy have moved us closer to our goal of delivering highly effective treatments to all patients with CF. In January 2012, KALYDECO was first approved to treat approximately 1,000 patients with the *G551D* mutation in the U.S. Since then, we have focused on expanding the number of patients eligible for our medicines and seeking improved treatment options for all patients with CF. Collectively, our four medicines are approved to treat the majority of the approximately 83,000 people with CF in North America, Europe and Australia. In 2020, we made significant progress bringing TRIKAFTA to nearly all eligible patients in the U.S. Outside of the U.S., we received early approval for KAFTRIO in the E.U., and secured reimbursement in numerous countries. As a result of these successful activities and launches in Europe, thousands of eligible patients, including those in Germany, England and Ireland, gained access to KAFTRIO by year end.

Currently, approximately half of the people with CF in North America, Europe and Australia are being treated with our medicines. We believe that more than 30,000 additional patients in these geographies could benefit from Vertex medicines. The majority of these patients are 12 years of age and older, who we expect will be treated through the continued uptake and reimbursement of KAFTRIO in Europe and other countries, and through approvals in additional countries. The remaining patients are in lower age groups or have other mutations, which we expect will be addressed through label expansions. We also are pursuing once-a-day next-generation small molecule therapies with increased efficacy for currently treated patients with the goal of achieving carrier levels of cystic fibrosis transmembrane conductance regulator ("CFTR") activity for the 90% of people with CF who respond to CFTR modulators, as well as genetic therapies for the remaining 10% of people with CF who may not be helped by CFTR modulators in support of our goal of bringing transformative therapies to all people with CF.



Since the beginning of 2020, we have made important progress in expanding the number of people who are eligible for our CFTR modulators, including:

- We obtained early approval from the European Commission for KAFTRIO for treatment of people with CF 12 years of age and older who have one *F508del* mutation and one minimal function mutation, or two *F508del* mutations.
- The FDA expanded the eligibility for TRIKAFTA to include people with CF 12 years of age and older with certain rare mutations that are responsive to TRIKAFTA.
- The FDA approved KALYDECO for treatment of infants with CF four months of age and older who have at least one mutation in their CFTR gene that is responsive to KALYDECO.
- The European Commission approved KALYDECO for treatment of infants with CF four months of age and older who have the *R117H* mutation or certain gating mutations.
- The FDA approved SYMDEKO and the European Commission approved SYMKEVI for treatment of people with CF 6 years of age and older with certain mutations.
- In January 2021, the FDA accepted and granted Priority Review to our supplemental New Drug Application ("sNDA") for TRIKAFTA for treatment of children 6 to 11 years of age with at least one *F508del* mutation or with certain mutations that are responsive to TRIKAFTA.

Research and Development

We invest in research and development in order to discover and develop transformative medicines for people with serious diseases with a focus on specialty markets. Our strategy is to combine transformative advances in the understanding of human disease and the science of therapeutics in order to discover and develop new medicines. Our approach to drug discovery has been validated through our success in moving multiple novel small molecule drug candidates into clinical trials and obtaining marketing approvals for five transformative medicines in the past decade.

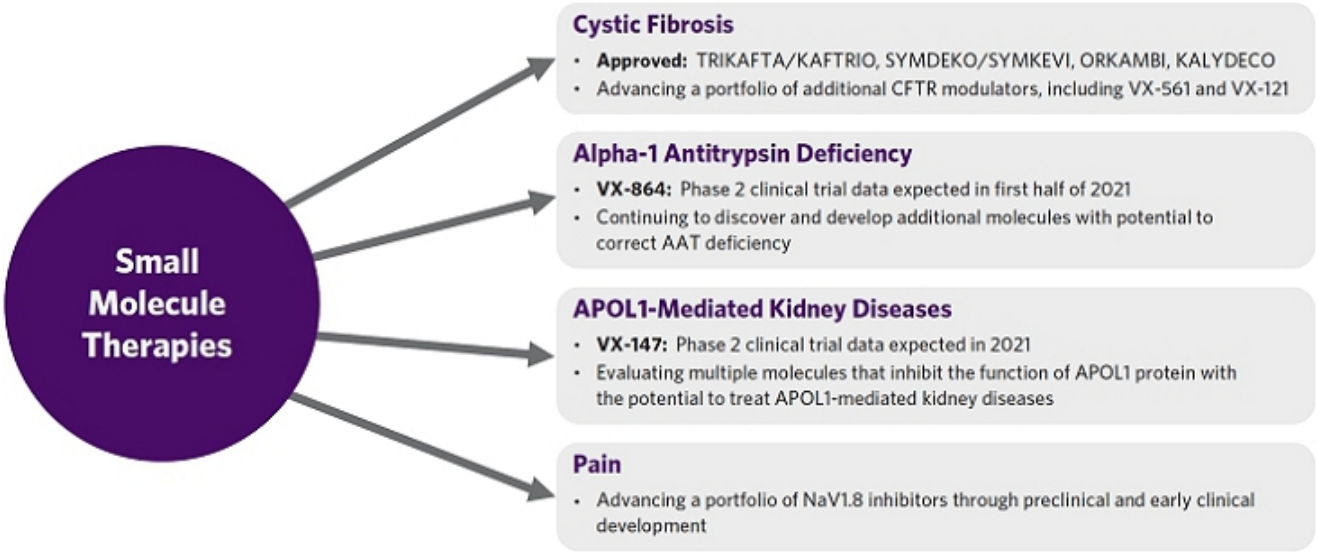
We continue to research and develop small molecule drug candidates for the treatment of serious diseases, including CF, AAT deficiency, APOL1-mediated kidney diseases, and pain. Our research and development approach includes advancing multiple small molecules into clinical trials, pursuing multiple modalities and evaluating clinical and non-clinical data to inform drug discovery and development, with the goal of bringing best-in-class therapies to patients. We are also focused on developing cell and genetic therapies for various diseases in our pipeline, including SCD, beta thalassemia, T1D, Duchenne muscular dystrophy ("DMD"), myotonic dystrophy type 1 ("DM1") and CF. Over the last several years, we have expanded our capabilities to include additional innovative therapeutic approaches for cell and genetic therapies, which have the potential to treat, and in some cases, cure diseases by addressing the underlying cause of the disease.

In 2020, we had novel medicines in clinical trials in six diseases - CF, AAT deficiency, APOL1-mediated FSGS, pain, SCD and beta thalassemia. In 2021, we were cleared to begin our clinical program involving transplantation of fully differentiated islet cells alone in people with T1D, our seventh disease area in clinical development and our first cell-based therapy. We have recently initiated a Phase 1/2 clinical trial to evaluate VX-880 in people who have T1D with impaired hypoglycemic awareness and severe hypoglycemia.

Small Molecule Programs

Since the beginning of 2020, we have advanced several promising small molecule programs:

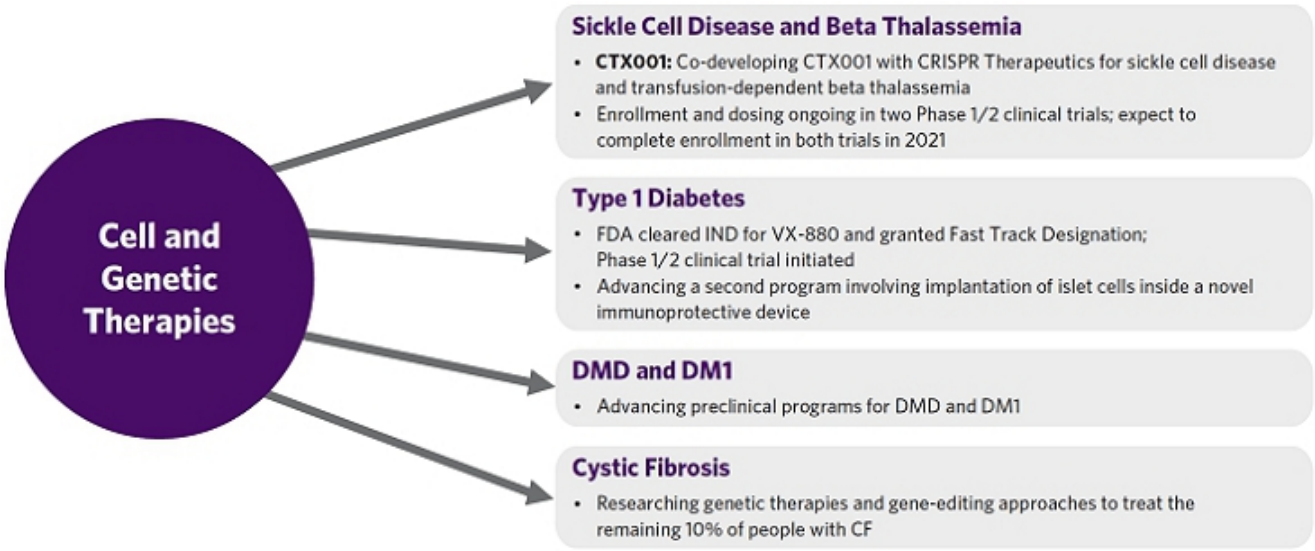
- *AAT Deficiency:* We are focused on identifying and developing multiple drug candidates with the potential to increase the levels of functional AAT in the blood to address the lung and liver manifestations of AAT deficiency. In 2020, we progressed a Phase 2 proof-of-concept clinical trial for VX-864, an investigational small molecule corrector for the treatment of AAT deficiency.
- *APOL1-mediated Kidney Diseases:* We are evaluating inhibitors of APOL1 function to reduce levels of protein in the urine, or proteinuria, in people with serious kidney diseases, including APOL1-mediated FSGS. In 2020, we initiated a Phase 2 proof-of-concept clinical trial designed to evaluate the reduction in proteinuria in people with APOL1-mediated FSGS after treatment with VX-147.
- *Pain:* We progressed a portfolio of NaV1.8 inhibitors for the treatment of acute pain and chronic neuropathic pain into pre-clinical and early clinical development.
- *Cystic Fibrosis:* We continued to identify and develop additional CFTR modulators, including once-a-day next-generation small molecule therapies, with the goal of achieving carrier levels of CFTR activity for the 90% of people with CF who respond to CFTR modulators.



Cell and Genetic Therapies

Since the beginning of 2020, we have made important progress in the advancement of our pipeline of potentially transformative cell and genetic therapies.

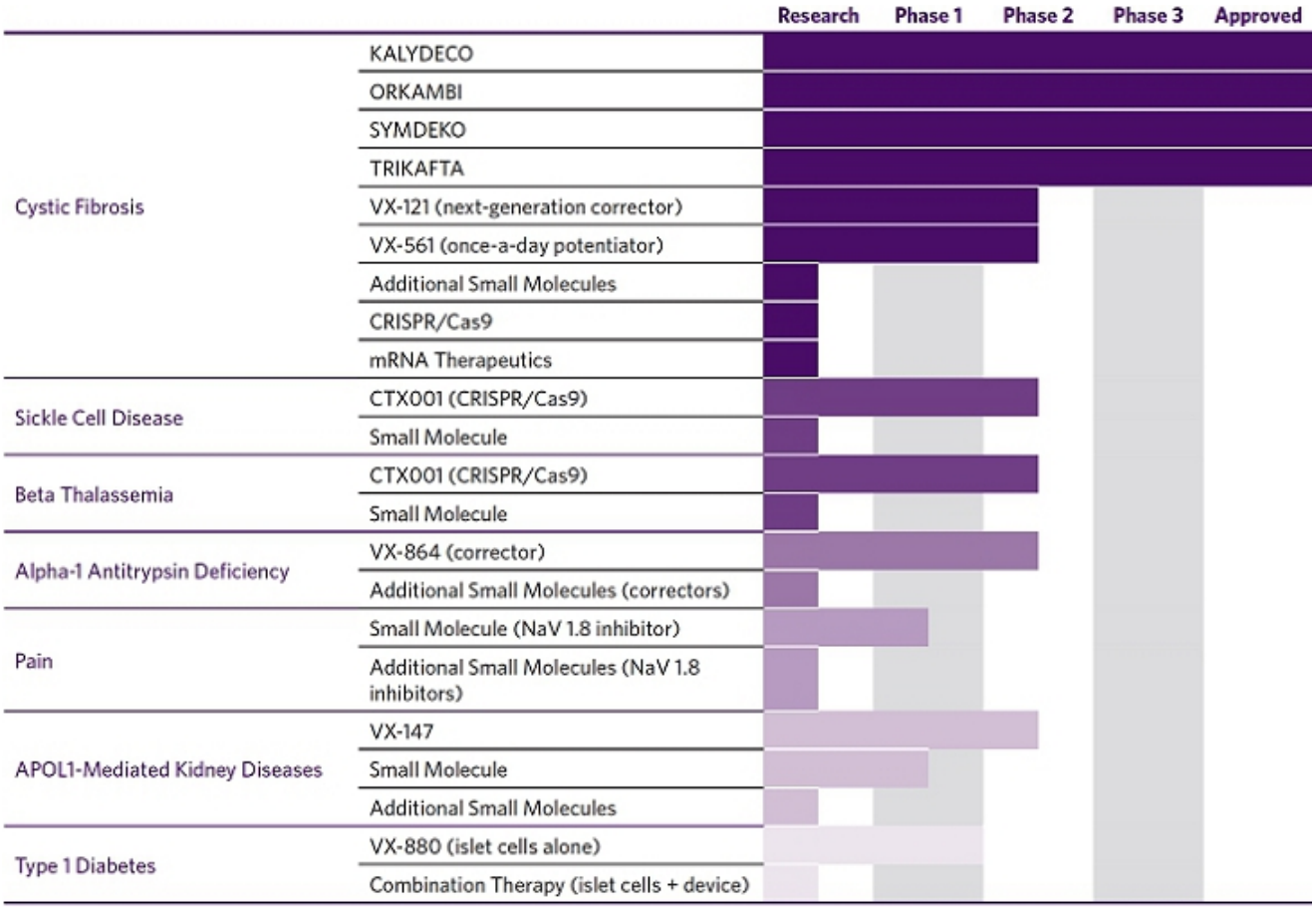
- *Sickle Cell Disease and Beta Thalassemia:* We are co-developing CTX001, an investigational CRISPR/Cas9-based gene-editing therapy for SCD and TDT with CRISPR. Enrollment and dosing are ongoing in two Phase 1/2 clinical trials to evaluate CTX001 as a potential one-time curative therapy for people with severe SCD and TDT. In summer of 2020, we established proof-of-concept in TDT. In December 2020, we established proof-of-concept in SCD and we announced positive interim data from 10 people treated with CTX001. As of December, all seven people with TDT were transfusion independent at last follow-up and all three people with SCD were free of vaso-occlusive crises from CTX001 infusion through the last follow-up. To date, more than 20 people have been dosed with CTX001. We expect to complete enrollment in both clinical trials in 2021.
- *Type 1 Diabetes:* We are pursuing two programs for the transplant of functional islets into patients: transplantation of islet cells alone, using immunosuppression to protect the implanted cells, and implantation of the islet cells inside an immunoprotective device. In early 2021, the FDA cleared our IND for VX-880, our program involving transplantation of fully differentiated islet cells alone for people with T1D, and we recently initiated a Phase 1/2 clinical trial to evaluate VX-880 in people who have T1D with impaired hypoglycemic awareness and severe hypoglycemia.
- *DMD and DM1:* We continue to focus on gene-editing therapies aimed at treating the underlying cause of DMD by restoring expression of near-full length dystrophin protein, and, in DM1, by addressing the repeat expansion that causes the disease.
- *Cystic Fibrosis:* We continue to research genetic therapies, such as messenger ribonucleic acid, or mRNA, and gene-editing approaches, to treat the remaining 10% of people who do not make CFTR protein and, are not eligible for CFTR modulators.
- *External Innovation:* We continue to collaborate with biopharmaceutical and technology companies and other organizations to advance research in our areas of therapeutic interest. This includes accessing tools and technologies to execute on our strategy to deliver transformational therapies for serious diseases, such as novel proteins to advance the development of gene-editing therapies, new capsid technologies to deliver gene therapies, and innovative platforms to discover small molecules that modulate RNA splicing.



SEVEN DISEASE AREAS ACTIVE IN CLINICAL DEVELOPMENT

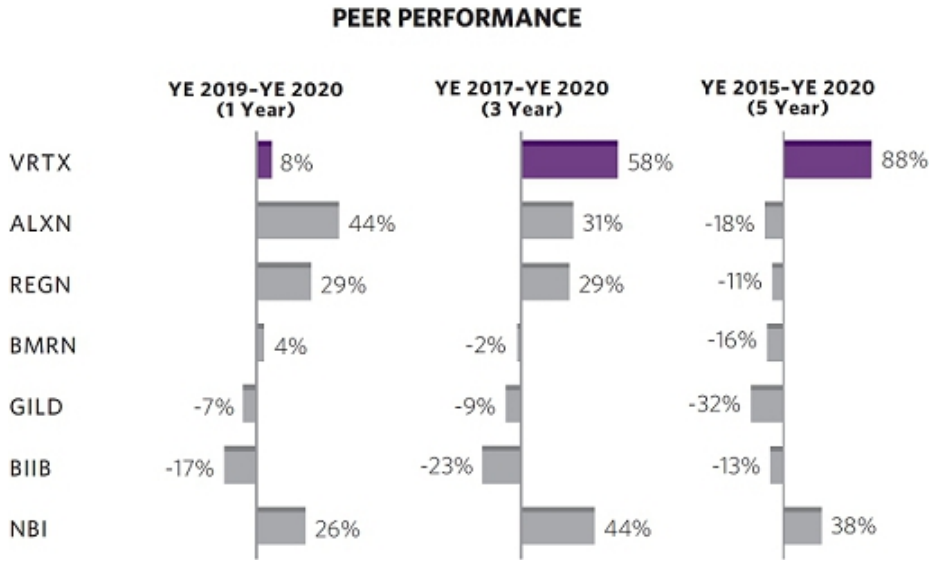
Portfolio Approach with Lead Molecules and Rapidly Avancing Follow-On Programs

The following chart represents our pipeline by disease and by stage, reflecting our programs that have lead assets already in the clinic.



Increased Shareholder Value

Driven by our business performance, our stock price increased by 8% from $218.95 per share at the end of 2019 to $236.34 per share at the end of 2020. Although we were pleased with our performance in 2020, biotechnology companies are best measured over the long term and in comparison to their peers, as opposed to in one-year increments and in isolation. The following chart shows our total shareholder return during the 1-year, 3-year and 5-year periods ending December 31, 2020 compared to the Nasdaq Biotechnology Index ("NBI") and the following members of our peer group: Alexion, Regeneron, BioMarin, Gilead and Biogen. These peers are the companies we consider most similar to our Company based on their business models (see pages 51 and 52).



Corporate Responsibility

Vertex has grown into a leading global biotechnology company that serially innovates to bring transformative medicines to people with serious diseases. As we have grown, we have maintained and expanded upon our commitment to corporate responsibility, including through a ten-year $500 million corporate giving commitment previously announced by the company. Our progress and efforts have been recognized, with Vertex named to the Points of Light Civic 50, *Investor Business Daily's* list of Best Environmental, Social and Governance Companies and the *Boston Business Journal's* Most Charitable Companies in Massachusetts top 20 ranking.

Community	In 2020, Vertex and its employees supported more than 1,600 nonprofit organizations in 14 countries through Vertex Volunteers and the Vertex Foundation's Matching Gift Program. The Vertex Foundation, a nonprofit 501(c)(3) organization, seeks to improve the lives of people with serious diseases and contribute to the communities where Vertex is located through education, innovation, and health. In 2020, the Vertex Foundation made $17.4 million in grants to nonprofit organizations, including $5 million for global COVID-19 response efforts and $4 million to support racial and social justice initiatives and organizations in the U.S. As part of its focus on racial and social justice, the Vertex Foundation committed $1.5 million to support the new Boston University Center for Antiracist Research. The Vertex Foundation Matching Gift Program saw more than $3.3 million donated by employees and the Vertex Foundation. The Vertex Foundation also continued to make grants in support of its focus areas (STEAM education, social innovation and healthy families) and to support projects and organizations with a strong commitment to inclusion, diversity and equity.
Workplace	Our commitment to diversity and inclusion on our board and in our workforce is long-standing and deeply ingrained in our culture. Four of our ten directors, including our CEO, are women, and four of our ten directors are from diverse racial and ethnic groups. As of December 31, 2020, women represent 53% of our global workforce and 38% of our leadership (VP and above). In the U.S., approximately 34% of our workforce and 44% of new hires are from diverse racial and ethnic groups. We have been recognized for our inclusion efforts, receiving a perfect score of 100 on the Human Rights Campaign's Corporate Equality Index and being listed on the Forbes 2020 Best Employers for Diversity List.
Environment	We are committed to limiting our environmental impacts and to operating our business in a sustainable manner. In 2020, we sourced 100% renewable energy for our International Headquarters in London, joining our Oxford, UK facility, which has done so since 2018, and began the installation of a solar array panel at our San Diego research facility, which is expected to provide approximately 20% of the building's energy. We continue to make progress towards our global goal of reducing our absolute greenhouse gas emissions by 20% by 2023 over a 2018 baseline.

Director Nominees

The following table provides summary information regarding our ten director nominees. For detailed information about each nominee's background and areas of expertise, please see "*Proposal No. 1: Election of Directors*."

Name, Occupation or Experience	Age	Director Since	Independent	Committees			
				AC	MDCC	CGNC	S&T
Jeffrey Leiden Executive Chairman, Vertex Former CEO and President, Vertex	65	2009	No				
Reshma Kewalramani CEO and President, Vertex	48	2020	No				
Sangeeta Bhatia John J. and Dorothy Wilson Professor of Health Sciences & Technology/Electrical Engineering & Computer Science, MIT	52	2015	Yes			✔	C
Lloyd Carney CEO, Carney Global Ventures	59	2019	Yes	✔			
Alan Garber Provost, Harvard University	65	2017	Yes	✔			✔
Terrence Kearney Former Chief Operating Officer, Hospira	66	2011	Yes	C	✔		
Yuchun Lee CEO, Allego Executive Chairman, Clarabridge	55	2012	Yes	✔	✔		
Margaret McGlynn Former President, Vaccines and Infectious Diseases, Merck & Co. Former President, Hospital and Specialty Products, Merck & Co.	61	2011	Yes			C	✔
Diana McKenzie Former Chief Information Officer, Workday Former Chief Information Officer, Amgen	56	2020	Yes			✔	
Bruce Sachs General Partner, Charles River Ventures	61	1998	Yes		C	✔	

CEO Succession

In 2020, we successfully executed a leadership succession plan with the transition of Dr. Reshma Kewalramani to the role of Chief Executive Officer and our former Chief Executive Officer, Dr. Jeffrey Leiden, to the role of Executive Chairman. This transition was the culmination of a deliberate and comprehensive multi-year planning process led by our independent directors. In his role as Executive Chairman, Dr. Leiden continues to focus on strategy and business development, our cell and genetic therapy programs, and government and community affairs activities, along with serving as the Chairman of our Board. Bruce Sachs continues in his role as Lead Independent Director. The Board believes this structure will help ensure continuity of strong and effective leadership.

2020 Compensation Decisions and Pay-for Performance

In 2020, our executive compensation program received substantial support, approved by approximately 95% of the votes cast at the annual meeting of shareholders. We believe this support is consistent with our shareholders' understanding of our business model and the long-term value we are creating. In 2020, our board of directors and management development and compensation committee ("MDCC"), reviewed our compensation programs and made the following key decisions:

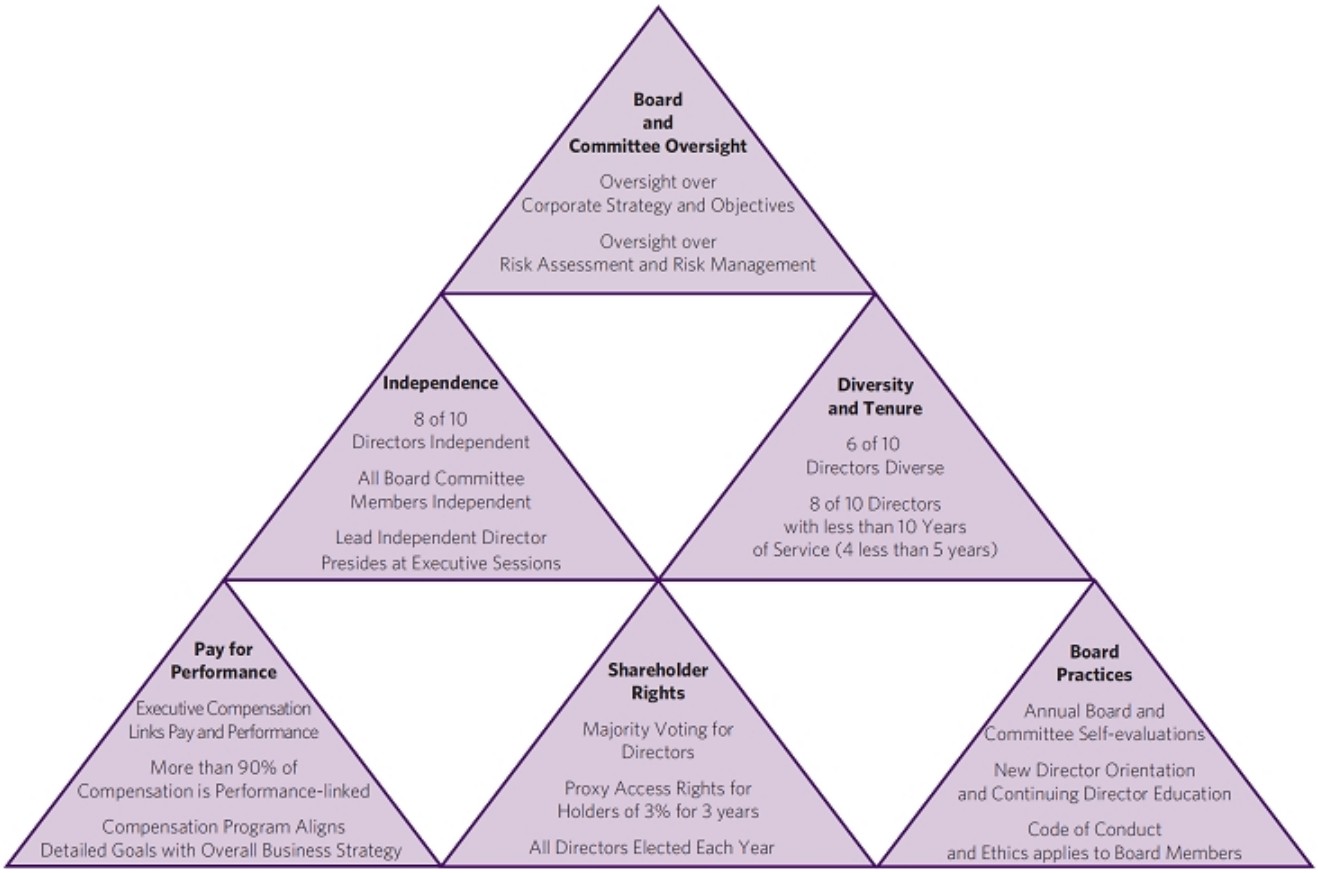
- Dr. Reshma Kewalramani, our CEO and President, maintained a base salary of $1.15 million, a target cash bonus of 120% of base salary and a target equity level of $11.0 million.
- Pursuant to his employment agreement, Dr. Jeffrey Leiden maintained a base salary of $1.0 million and a target cash bonus of 100% of base salary for his first year as Executive Chairman. Dr. Leiden will not receive a base salary or cash bonus for the remainder of his three-year term in this position. Dr. Leiden additionally received equity grants of $9.0 million for his first year as Executive Chairman pursuant to the terms of his employment agreement and will receive additional equity awards with declining values for his second and third years in this role.
- For each of our other named executive officers ("NEOs"), we maintained base salary, a target cash bonus of 70% of base salary and a target equity level of $4.0 million based on a comparative analysis with companies in our peer group.
- The company's outstanding performance in 2020 resulted in a leading rating (138 out of a potential 150) for 2020 and annual cash bonuses near the high end of the range for 2020, commensurate with the performance described above.
- We maintained the mix of equity granted under our compensation program with 50% consisting of performance stock units that vest upon achievement of rigorous performance goals and 50% consisting of time-vesting restricted stock units that reward stock price appreciation and serve as a long-term retention tool.

Shareholder Engagement

We believe that a robust shareholder outreach program is an important component of maintaining our strong corporate governance practices. We strive for a collaborative approach with investors to solicit and understand a variety of perspectives. During 2020, we solicited feedback from institutional investors representing approximately 60% of our outstanding shares. In our discussions with investors, we seek their input on a variety of corporate governance and sustainability topics and other issues that may impact our business or reputation.

Corporate Governance

We are committed to maintaining strong corporate governance practices that promote the long-term interests of our shareholders and strengthen board and management accountability.



Voting Roadmap

Item 1: Election of Each of the Director Nominees for One Year Term Expiring in 2022	FOR all Nominees
Item 2: Ratify Selection of Independent Auditor for 2021	FOR
Item 3: Approve, on an Advisory Basis, Our Named Executive Officer Compensation	FOR
Item 4: Shareholder Proposal Regarding a Report on Our Lobbying Activities	AGAINST
Item 5: Shareholder Proposal Regarding a Report on Our Political Spending	AGAINST

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PROXY STATEMENT

This proxy statement is being made available to shareholders of Vertex Pharmaceuticals Incorporated in connection with the solicitation by our board of directors of proxies to be voted at our 2021 annual meeting of shareholders and at any postponement or adjournment thereof. The annual meeting will be held on Wednesday, May 19, 2021, at 9:30 a.m., Eastern Time, as a virtual meeting conducted exclusively via live webcast at www.meetingcenter.io/237308243. See “Frequently Asked Questions Regarding the Annual Meeting - How May I Attend the Annual Meeting?” below for information regarding attending the virtual annual meeting.

PROPOSAL NO. 1: ELECTION OF DIRECTORS

Our board of directors currently consists of ten directors, including eight independent directors, our Executive Chairman, and our Chief Executive Officer. The board of directors has nominated all ten directors - Sangeeta Bhatia, Lloyd Carney, Alan Garber, Terrence Kearney, Reshma Kewalramani, Yuchun Lee, Jeffrey Leiden, Margaret McGlynn, Diana McKenzie, and Bruce Sachs - for election at our 2021 annual meeting of shareholders to hold office until our 2022 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 or unwilling to serve for any reason, proxies may be voted for another person nominated as a substitute by our board or our board may reduce the number of directors.

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, which in turn is 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.

Board Structure and Composition

The corporate governance and nominating committee ("CGNC") of our board of directors is responsible for the composition and structure of our board, including identifying, developing, and recommending qualified candidates for board membership. The CGNC regularly reviews director competencies, qualities, skills and experiences with the goal of ensuring that our board is comprised of directors who function collegially and effectively 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 ten members on our board and expect to have ten members of our board following the 2021 annual meeting of shareholders. Our CGNC may seek additional director candidates in the future who meet the criteria below in order to complement the qualifications and experience of our existing board members. Our CGNC may engage a search firm to recommend candidates who satisfy the above criteria.

Director Criteria, Qualifications and Experience; Diversity

The CGNC seeks to recommend for nomination experienced directors who have 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, the highest ethics and integrity and a commitment to the success of our company. It also seeks personal qualities that foster a respectful environment in which our directors listen to one another and hold engaged and constructive discussions. These goals for our board composition presuppose a diverse range of viewpoints, experiences and specific expertise. The CGNC 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, 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. When considering whether or not to re-nominate a director for board service, the CGNC also considers whether the director has served as a member of our board for more than 20 years and whether the director is over 72 years of age.

Our commitment to diversity and inclusion is demonstrated by the composition of our board, which currently includes four women and four members of diverse racial and ethnic minority groups.

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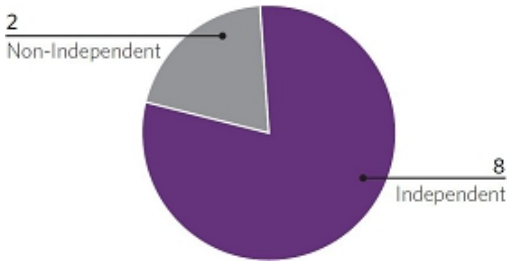
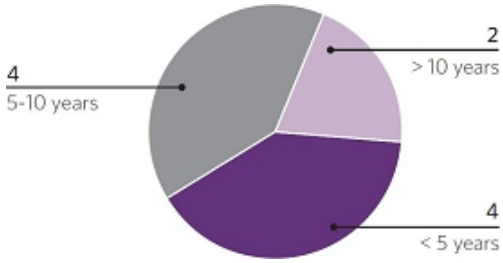
The follow table and charts provide information regarding our director nominees:

	Bhatia	Carney	Garber	Kearney	Kewalramani	Lee	Leiden	McGlynn	McKenzie	Sachs
Leadership Experience. We believe that directors who have held significant leadership positions over extended periods of time provide our company with special insights.	✔	✔	✔	✔	✔	✔	✔	✔	✔	✔
Industry Knowledge. We seek directors with substantive knowledge of the healthcare and biotechnology industries to successfully advise and oversee the strategic development and direction of our company.	✔		✔	✔	✔		✔	✔	✔	
Financial Expertise. We believe that an understanding of finance is important for members of our board, and our budgeting processes and financial and strategic transactions require our directors to be financially knowledgeable.		✔	✔	✔	✔	✔	✔	✔	✔	✔
International Perspective. We have significant operations outside the United States and value directors with experience in the operation of complex multinational organizations.		✔	✔	✔	✔	✔	✔	✔	✔	✔
Public Policy and Regulation. We operate in a highly-regulated industry and seek directors who have experience in public policy and the regulation of medicines.			✔		✔		✔	✔		
Academic Experience or Technological Background. As a biotechnology company that seeks to develop transformative medicines for patients with serious diseases, we look for directors with backgrounds in academia, 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.	✔	✔	✔	✔	✔	✔	✔	✔	✔	✔
Independence	Y	Y	Y	Y	N	Y	N	Y	Y	Y
Age	52	59	65	66	48	55	65	61	56	61
Tenure on Board	5	2	3	9	1	8	11	9	1	22
Gender	F	M	M	M	F	M	M	F	F	M
Ethnic or Racial Diversity	✔	✔			✔	✔				

DIRECTOR INDEPENDENCE

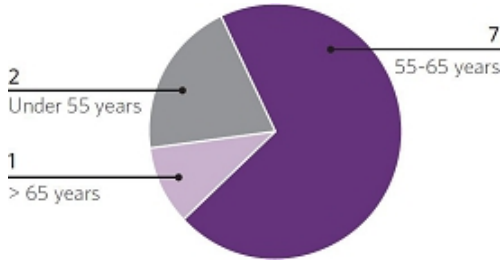


DIRECTOR TENURE



OVERALL BOARD DIVERSITY

DIRECTOR AGE



Shareholder-Recommended Director Candidates

The CGNC 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 2022 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 2022 Annual Meeting and Nominations for Director* on page 80 of this proxy statement.

Our by-laws provide for proxy access, a process that allows qualifying shareholders to nominate a director candidate for consideration at an annual meeting of shareholders and have such candidate be included in our proxy materials for the applicable shareholder meeting. The key elements of our proxy access by-law are as follows:

Provision	Requirement
Ownership Threshold and Holding Period	Available to shareholders owning 3% or more of our shares continuously for at least 3 years.
Number of Board Seats	Total number of proxy access nominees is capped at 20% of the existing board seats (or the closest whole number below 20%), with a minimum of two.
Aggregation Limits	20-shareholder limit on the number of shareholders who can aggregate their shares to satisfy the 3% ownership requirement.
Proxy Fights	Proxy access nominees will not be included in the proxy materials if we receive notice that a shareholder intends to nominate a candidate who is not to be included in our proxy materials.
Future Ineligibility	Proxy access nominees who fail to receive at least 10% of the votes cast “for” such nominee may not be re-nominated as a proxy access nominee for the next two annual meetings.

The above table is only a summary of our proxy access by-law and is qualified in its entirety by our by-laws. A shareholder who wishes to nominate a proxy access nominee to be considered for election as a director at the 2022 annual meeting of shareholders must follow the procedures set forth in our by-laws as well as those described in *Other Information—Shareholder Proposals for the 2022 Annual Meeting and Nominations for Director* on page 80 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, director nominees in an uncontested election who receive more votes cast “for” such director nominee than “against” 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 “against” 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 CGNC 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 CGNC’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 CGNC or board considerations, recommendations or actions with respect to the tendered resignation.

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Director Nominees

Sangeeta Bhatia

Age: 52
Director Since: 2015

Committee Assignments:
- Chair - Science and Technology Committee
- Member - Corporate Governance and Nominating Committee

Dr. Bhatia is a professor at the Massachusetts Institute of Technology, or MIT, where she currently serves as the John J. and Dorothy Wilson Professor of Health Sciences & Technology/Electrical Engineering & Computer Science. In 2020, Dr. Bhatia co-founded Satellite Bio, a private company focused on developing satellite organs as living therapeutic solutions. In 2018, Dr. Bhatia co-founded Glympse Bio, a private company focused on developing in vivo sensing technology dedicated to disease monitoring, while on sabbatical from MIT. Prior to joining MIT in 2005, 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 a Sc.B. in biomedical engineering from Brown University, an S.M. and Ph.D. in Mechanical Engineering from MIT 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 provides valuable insights to our board of directors, including with respect to our key research and development initiatives.

Lloyd Carney

Age: 59
Director Since: 2019

Committee Assignments:
- Member - Audit and Finance Committee

Mr. Carney has been the Chief Executive Officer of Carney Global Ventures, LLC, an early round investor, since March 2007. He has been the Chief Acquisition Officer of Carney Technology Acquisition Corp. II, a special purpose acquisition corporation, since October 2020. Mr. Carney was the Chief Executive Officer of ChaSerg Technology Acquisition Corp., a technology acquisition company, from September 2018 until March 2020. He was the Chief Executive Officer of Brocade Communications Systems Inc., or Brocade, a global supplier of networking hardware and software, from January 2013 until November 2017, when it was acquired by Broadcom. Prior to Brocade, Mr. Carney served as Chief Executive Officer of Xsigo Systems, a cloud-based infrastructure solutions provider, until its acquisition by Oracle in 2012. He has also served as the Chief Executive Officer and Chairman of Micromuse Inc., a software solutions provider for business and service assurance, until its acquisition by IBM. Earlier in his career he had held senior leadership roles at Juniper Networks, Inc., Nortel Networks Inc., and Bay Networks, Inc. Mr. Carney serves as a member on the Board of Directors of Visa Inc., Nuance Communications, Inc. and Grid Dynamics Holdings, Inc. He holds a Bachelor of Science degree in Electrical Engineering Technology from Wentworth Institute of Technology, a Master of Science degree in Applied Business Management from Lesley College, and an Honorary Doctorate degree in Engineering from Wentworth Institute of Technology.

Skills and Qualifications: Mr. Carney brings strong business judgment, honed through his time as a senior executive and board member of multiple global technology companies, to our board of directors. Mr. Carney has extensive corporate leadership experience, including service as the CEO of several technology companies, as well as financial expertise.

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Alan Garber

Age: 65
Director Since: 2017

Committee Assignments:
- Member - Science and Technology Committee
- Member - Audit and Finance Committee

Dr. Garber is Provost of Harvard University and the Mallinckrodt Professor of Health Care Policy at Harvard Medical School, a Professor of Economics in the Faculty of Arts and Sciences, Professor of Public Policy in the Harvard Kennedy School of Government, and Professor in the Department of Health Policy and Management in the Harvard T.H. Chan School of Public Health. From 1998 until he joined Harvard in 2011, he was the Henry J. Kaiser Jr. Professor, a Professor of Medicine, and a Professor (by courtesy) of Economics, Health Research and Policy, and of Economics in the Graduate School of Business at Stanford University. Dr. Garber is a member of the National Academy of Medicine, the American Society of Clinical Investigation, the Association of American Physicians, and the American Academy for Arts and Sciences. He is a Fellow of the American Association for the Advancement of Science, the American College of Physicians, and the Royal College of Physicians. Dr. Garber is also a Research Associate with the National Bureau of Economic Research and served as founding Director of its Health Care Program for nineteen years. He also has served as a member of the National Advisory Council on Aging at the National Institutes of Health, as a member of the Board of Health Advisers of the Congressional Budget Office and as Chair of the Medicare Evidence Development and Coverage Advisory Committee at the Centers for Medicare and Medicaid Services. Dr. Garber has been a member of the Board of Directors of Exelixis, Inc., a biopharmaceutical company, since 2005. Dr. Garber holds an A.B. summa cum laude, an A.M. and a Ph.D., all in Economics, from Harvard University, and an M.D. with research honors from Stanford University.

Skills and Qualifications: Dr. Garber brings extensive leadership experience and knowledge regarding science, medicine and the healthcare industry and in particular healthcare economics to our board of directors. The insights he has developed as an expert in health care policy and as an advisor to government agencies provides our board important perspectives on the issues facing our company.

Terrence Kearney

Age: 66
Director Since: 2011

Committee Assignments:
- Chair - Audit and Finance Committee
- 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 has served as a member of the Board of Directors at Acceleron Pharma Inc., a biopharmaceutical company, since July 2014. He served as a member of the Board of Directors of Innoviva (formerly known as Theravance, Inc.), a royalty management company, from October 2014 through April 2016, and as member of the Board of Directors of AveXis, Inc., a gene therapy company, from January 2016 until its acquisition in May 2018. Mr. Kearney has been a member of the Board of Directors of Levo Therapeutics, Inc., a biotechnology company focused on developing treatments for Prader-Willi Syndrome, since 2018. 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" with particular experience in matters faced by the audit committee of a company with pharmaceutical product revenues and related expenses.

Reshma Kewalramani

Age: 48
Director Since: 2020

Position:
- Chief Executive Officer and President

Dr. Kewalramani has been our Chief Executive Officer and President since April 2020 and a member of our board since February 2020. Dr. Kewalramani was our Executive Vice President and Chief Medical Officer from April 2018 through March 2020. She was our Senior Vice President, Late Development from February 2017 until April 2018. From August 2004 to January 2017, she served in roles of increasing responsibility at Amgen Inc., most recently as Vice President, Global Clinical Development, Nephrology & Metabolic Therapeutic Area and as Vice President, U.S. Medical Organization. From 2014 through 2019, Dr. Kewalramani was the industry representative to the FDA's Endocrine and Metabolic Drug Advisory Committee. She completed her internship and residency in Internal Medicine at the Massachusetts General Hospital and her fellowship in Nephrology at the Massachusetts General Hospital and Brigham and Women's Hospital combined program. Dr. Kewalramani holds a B.A. from Boston University and an M.D. from Boston University School of Medicine. Dr. Kewalramani also completed the General Management Program at Harvard Business School and is an alumnus of the school.

Skills and Qualifications: Dr. Kewalramani has extensive industry knowledge and leadership experience garnered through her scientific and medical expertise, as well as her role as a global senior leader across multiple disease areas and all stages of drug development. She provides our board of directors with in-depth knowledge of our company gained during her various senior management roles within Vertex and through the day-to-day leadership of our executives.

Yuchun Lee

Age: 55
Director Since: 2012

Committee Assignments:
- Member - Audit and Finance Committee
- Member - Management Development and Compensation Committee

Mr. Lee has served as the Chief Executive Officer of Allego, a technology company focused on modern sales learning and enablement, since 2013 and has been Executive Chairman of Clarabridge, Inc. since 2013. Mr. Lee also serves as an Executive in Residence of General Catalyst Partners, a venture capital firm, a position he has held since 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 and customer engagement and business and financial experience 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 an important perspective on the issues facing the company.

Jeffrey Leiden

Age: 65
Director Since: 2009

Position:
- Executive Chairman

Dr. Leiden became our Executive Chairman in April 2020. He was our Chief Executive Officer and President from 2012 through March 2020. He has been a member of our Board of Directors since July 2009, 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 serves as a director of Massachusetts Mutual Life Insurance Company, an insurance company, and serves as the Chairman of Revolution Healthcare Acquisition Corp., a special purpose acquisition corporation. 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 a director of Quest Diagnostics, a medical diagnostics company, from December 2014 to May 2019. 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 a senior executive in the biotech and pharmaceutical industries 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. As our former CEO and as a former senior executive at Abbott Laboratories he brings a global perspective to our business and public policy issues facing our company. He also provides our board of directors with in-depth knowledge of our company and guidance with respect to our corporate strategy.

Margaret McGlynn

Age: 61
Director Since: 2011

Committee Assignments:
- Chair - Corporate Governance and Nominating Committee
- Member - Science and Technology Committee

Ms. McGlynn retired from Merck & Co. in 2009, where she served as President, Vaccines and Infectious Diseases and as President, Hospital and Specialty Products. During her 26-year career at Merck, she also held various leadership roles in the U.S. and globally in marketing, sales, managed care and business development. Following her retirement, Ms. McGlynn 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, from 2011 until 2015. Ms. McGlynn served as a member of the Board of Directors for Air Products and Chemicals, Inc., a company specializing in gases and chemicals for industrial uses, from 2005 to November 2020. Ms. McGlynn currently serves as a member of the Board of Directors of Amicus Therapeutics, Inc., a biopharmaceutical company, and Novavax, Inc., a vaccine development 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 and an Honorary Doctorate from the State University of New York at Buffalo.

Skills and Qualifications: Ms. McGlynn's 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 boards of Amicus Therapeutics and Novavax, 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 and commercialization of products across several therapeutic areas, and in her board roles and advocacy in rare diseases, provides her with a valuable understanding of the scientific, public policy, regulatory and marketplace issues we face in the drug development and commercialization process.

Diana McKenzie

Age: 56
Director Since: 2020

Committee Assignments:
- Member - Corporate Governance and Nominating Committee

Ms. McKenzie was the Chief Information Officer of Workday, Inc., a cloud-based financial and human capital management software company, from February 2016 until April 2019. From 2004 through February 2016, she held roles of increasing responsibility at Amgen Inc., a biotechnology company, most recently serving as Senior Vice President and Chief Information Officer. Ms. McKenzie served for 17 years at Eli Lilly and Company, a pharmaceutical company, in various leadership roles, focused on drug development, reducing time to market and improving technology and security standards. She currently serves as a member on the Board of Directors of MetLife, Inc., Change Healthcare, Inc., and Paradox AI, and as a Special Advisor to Brighton Park Capital. Ms. McKenzie holds a Bachelor of Science degree in Computer Information Systems from Purdue University and completed the Information Technology Management Program at University of California, Los Angeles and the CERT Certification for Cybersecurity Oversight from Carnegie Mellon's Software Engineering Institute.

Skills and Qualifications: Ms. McKenzie has corporate leadership experience and industry knowledge that make her a valuable contributor to our board of directors. Her service as an executive and innovator in the biotechnology and technology industries and as a member of the board of directors of public companies involved in healthcare issues provide her with multiple perspectives on our industry. Ms. McKenzie is well-positioned to provide valuable guidance and support to our management and our board of directors.

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Bruce Sachs

Age: 61
Director Since: 1998
Lead Independent Director

Committee Assignments:
- Chair - Management Development and Compensation Committee
- Member - Corporate Governance and Nominating 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 of 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, honed through his experience developing business strategy as a senior executive and in venture capital, to our board of directors. Mr. Sachs has a deep understanding of our business and the global business environment along with expertise in the technology that supports our infrastructure and operations. In addition, Mr. Sachs has extensive business leadership experience, including service as a CEO at a technology company, as well as financial expertise.

Board Recommendation

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

Our board of directors unanimously recommends that you vote **FOR** each of the nominees.

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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, Executive Chairman and Lead Independent Director

Our board of directors has determined that eight of our ten directors qualify as "independent" under the definition of that term adopted by The Nasdaq Stock Market LLC, or Nasdaq. Our independent directors are Dr. Bhatia, Mr. Carney, Dr. Garber, Mr. Kearney, Mr. Lee, Ms. McGlynn, Ms. McKenzie, and Mr. Sachs.

Our independent directors meet in executive session without management at each regularly scheduled board meeting. Each of the board committees is composed of independent directors.

Dr. Leiden, our executive chairman and former chief executive officer and president, and Dr. Kewalramani, our current chief executive officer and president, are not considered "independent" directors.

Our board believes that strong, independent board leadership is a critical aspect of effective corporate governance. Our corporate governance principles require that if the chair is not an independent director, the independent directors shall elect one or more lead independent director(s). Since December 2011, Mr. Sachs has served as a lead independent director. We believe this structure provides our board independent leadership, while providing the benefit of having our former chief executive officer chair regular board meetings and our current chief executive officer participate in regular board meetings as a director. Combined with the lead independent director and experienced and independent committee members, our board structure provides strong independent oversight of management.

Our lead independent director's responsibilities include:

- calling and leading regular and special meetings of the independent directors;
- serving as a liaison between our management and 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, each of which has a written charter, to assist in discharging its duties: the audit and finance committee ("audit committee"), the CGNC, the MDCC, and the science and technology committee ("S&T committee"). Each member of the audit committee, CGNC, MDCC and S&T committee is an independent director as that term is defined by the applicable SEC and Nasdaq rules. The primary responsibilities of each of the committees are set forth below, and the committee memberships are provided in the table appearing on page 27 of this proxy statement.

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

Risk Management

Our board of directors and its committees oversee risk and risk management for the company and regularly receive updates from management regarding our most significant strategic, compliance and operational risks. This includes presentations throughout the year, as well as an annual review of our key risks as identified by our Enterprise Risk Management ("ERM") Program. As part of our ERM Program, we obtain input from our senior leaders and relevant subject-matter experts to identify our key enterprise risks based on likelihood of occurrence and potential impact to the business, as well as root causes of those risks. The ERM Program also assigns risk owners who are responsible for implementing controls and mitigations to reduce the likelihood or impact of each risk. The identified risks and related controls and mitigations are actively monitored and regularly reviewed with senior management. We face considerable risks related to the commercialization of our approved products, including regulatory risks 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 additionally face risks related to our research programs, clinical development programs and business development activities, including considerable risks that our programs will not ultimately result in a commercially successful pharmaceutical product.

For certain specific risk types, our board has delegated oversight responsibility to board committees as follows:

- Our audit committee oversees our policies and programs related to our financial and accounting systems, accounting policies and investment strategies, internal audit function and cybersecurity. The audit 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, and management development and selection processes.
- Our CGNC oversees risks related to the company's governance structure.
- Our S&T committee oversees risks related to our research and development investments.
- Our MDCC and CGNC work together to oversee succession planning, including planning related to our CEO transition in 2020.

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. We routinely review our Code of Conduct and make updates as necessary. 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 principal executive, financial or accounting officers or controller or persons performing similar functions 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.

Board Attendance, Committee Meetings and Committee Membership

During 2020, our board of directors met eight times. Each of our directors attended at least 75% of the total meetings of the board and the board committees on which he or she served that were held during the time he or she was a director in 2020. Dr. Kewalramani joined our board in February 2020 and Ms. McKenzie joined our board in June 2020.

The following table sets information regarding the current membership of our board of directors.

Director[1]	Independence	Board	Audit Committee	CGNC	MDCC	S&T Committee	2020 Attendance at Meetings[2]
Sangeeta N. Bhatia	✔					C	100%
Lloyd Carney	✔						95%
Alan Garber	✔						100%
Terrence C. Kearney	✔		C				100%
Reshma Kewalramani							100%
Yuchun Lee	✔						100%
Jeffrey M. Leiden		C					100%
Margaret G. McGlynn	✔			C			94%
Diana McKenzie	✔						100%
Bruce I. Sachs	✔	★			C		100%
2020 Meetings		8	11	5	6	5	

= Member

C = Chair

★ = Lead Independent Director

(1) All directors attended our 2020 annual shareholders meeting.

(2) Includes meetings of the board of directors and meetings of each committee of the board while the director served on such committee.

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Audit and Finance Committee

The primary purposes of the audit committee are to:

- appoint, oversee and replace, if necessary, our independent registered public accounting firm;
- assist our board's oversight of our accounting and financial reporting processes, including financial controls, and audits of our financial statements;
- review and make recommendations to our board concerning our financial structure and financing strategy;
- oversee our policies and programs and address risks related to our programs our financial and accounting systems, accounting policies and investment strategies, internal audit function and cybersecurity;
- address risks arising from related party transactions;
- oversee our internal audit function; and
- assist our board's oversight of our Code of Conduct.

Our independent registered public accounting firm reports directly to, and is held accountable by, our audit committee in connection with the audit of our annual financial statements and related services.

Mr. Kearney, the chair of our audit committee, is our "audit committee financial expert" as that term is defined in applicable rules and regulations of the SEC, and is independent according to the applicable listing standards of Nasdaq. In addition, other members of the audit committee are qualified to serve as an audit committee financial expert under the SEC rules and regulations. The report of the audit committee appears on page 36 of this proxy statement.

Our audit committee reviews and, if appropriate, recommends for approval or ratification by our board, all transactions with related persons that are required to be disclosed by us pursuant to Item 404(a) of Regulation S-K promulgated by the SEC, except for transactions, if any, related to the employment of executive officers, which would be recommended for approval by the MDCC. Our policies and procedures with respect to transactions with related persons are governed by our written Related Party Transaction Policy. Pursuant to this policy, related party transactions include transactions, arrangements or relationships in which our company is a participant, the amount involved exceeds $120,000, and one of our executive officers, directors, director nominees or 5% shareholders or their immediate family members, whom we refer to as related persons, has a direct or indirect material interest, except where disclosure of such transaction would not be required pursuant to Item 404(a) of Regulation S-K. As appropriate for the circumstances, our audit committee reviews and considers the related person's interest in the related party transaction and such other factors as it deems appropriate. In 2020, we had no transactions considered to be a related party transaction pursuant to Item 404(a) of Regulation S-K.

Corporate Governance and Nominating Committee

The primary purposes of the CGNC are to:

- assist our board of directors in developing and implementing our corporate governance principles;
- recommend the size and composition of our board and its committees;
- develop and recommend to our board an annual self-evaluation process to assess the effectiveness of our board and its committees, and oversees this process;
- oversee risks related to the company's governance structure;
- review and make recommendations with respect to our committee charters;
- identify and recommend to our board qualified individuals for board membership; and
- assist the board in external recruiting and evaluating potential candidates for the CEO position.

Management Development and Compensation Committee

The primary purposes of the MDCC are to:

- oversee and make recommendations to the board regarding compensation and development of our executives;
- recommend to the board (i) ratings for the company performance against company goals for the prior year and (ii) goals and weighting of goals for the next year;
- assist the board in evaluating potential internal candidates for the CEO position and executive succession plans;
- oversee risks associated with our compensation policies, management resources and structure, and management development and selection processes;

- oversee and make recommendations to the board regarding the compensation of our non-employee directors; and
- review and approve our benefit and equity plans.

The MDCC has the authority to delegate any of its responsibilities to individual members to the extent deemed appropriate by the MDCC in its sole discretion, but subject always to the general oversight of the board.

See *Compensation Discussion and Analysis—Detailed Discussion* below for a discussion of the MDCC's role in overseeing executive compensation.

The report of the MDCC appears on page 65 of this proxy statement.

Science and Technology Committee

Our S&T committee discharges our board of directors' responsibilities relating to the oversight of our investment in pharmaceutical research and development. In furtherance of that oversight function, the S&T committee:

- reviews and assesses our current and planned research and development programs and technology initiatives from a scientific perspective;
- oversees risks related to our research and development investments;
- assesses the capabilities of our key scientific personnel and the depth and breadth of our scientific resources; and
- provides strategic advice to our board regarding emerging science and technology issues and trends.

Compensation Committee Interlocks and Insider Participation

Messrs. Kearney, Lee, Sachs and William Young, a former member of our board of directors, served on the MDCC during 2020. Each member of the MDCC was an independent director while serving on the MDCC. None of the members of the MDCC has been an officer or employee of the Company. None of the members of our MDCC had a relationship with the Company or any of its subsidiaries during 2020 that would be required to be disclosed pursuant to Item 404(a) of Regulation S-K. During 2020, none of our executive officers served as a member of the board of directors or compensation committee of another company that has one or more executive officers serving as a member of our board or MDCC.

Public Policy and Engagement

Vertex recognizes the importance of public policy in supporting our mission of creating transformative medicines for people with serious diseases. We engage with various policymakers and trade and industry groups to help promote an environment in which we can continue to innovate and develop transformative medicines for the benefit of patients with serious diseases.

Our board has oversight over our public policy activities, including political contributions and lobbying, and reviews our public policy and lobbying priorities at least annually. Our Head of U.S. Public Affairs is responsible for approving all corporate political contributions and ensuring that they align with our mission and business priorities.

We meet all federal, state and local laws and reporting requirements governing corporate political contributions. We file quarterly reports listing the issues for which we conduct federal lobbying activities in compliance with the Honest Leadership and Open Government Act of 2007. These reports are available to the public at the U.S. Senate Office of Public Records website and U.S. House of Representatives Office of the Clerk website. Our website includes links to federal and state websites where we file lobbying reports, as well as a list of contributions made to support state and local candidates and political organizations.

We are a member of select industry and trade groups that are generally aligned with our business objectives and political contribution philosophy. These organizations represent the biotechnology industry and/or businesses more broadly in engaging with policy makers on issues that affect our industry. The industry and trade organizations to which Vertex paid more than $25,000 in dues have been disclosed on our website. Our governmental affairs executives regularly evaluate our participation in these organizations to ensure that they continue to be aligned with our contribution criteria and principles. We do not direct, nor do we have discretion over, how our membership dues are used and do not always agree with positions taken by these organizations and/or their members.

We recognize that increasingly, investors are asking public companies to provide additional visibility regarding their political engagement and contributions and to provide information about accountability and oversight. We have made available on our website our political engagement principles, which provide transparency on our approach to political contributions, including lobbying activities. We have shared this with shareholders, engaged in productive dialogues on this topic and have committed to updating this information annually.

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DIRECTOR COMPENSATION

Non-Employee Director Compensation Program

We have designed and implemented our compensation program for our non-employee directors to attract, motivate and retain individuals who are committed to our values and goals and who have the expertise and experience that we need to achieve those goals.

The compensation program for our non-employee directors is:

Compensation Elements		
Cash		
Annual Cash Retainer		$ 100,000
Annual Committee Chair Retainer	Audit and Finance Committee	$ 30,000
	Management Development and Compensation Committee	$ 25,000
	Corporate Governance and Nominating Committee	$ 20,000
	Science and Technology Committee	$ 20,000
Committee Membership Retainer		
	Audit and Finance Committee	$ 15,000
	Management Development and Compensation Committee	$ 12,500
	Corporate Governance and Nominating Committee	$ 10,000
	Science and Technology Committee	$ 10,000
Annual Lead Independent Director Retainer		$ 40,000
Equity		
Initial Equity Grant	A $400,000 value-based award in restricted stock units vesting after 12 months	
Annual Equity Retainer	On May 1 of each year, a $400,000 value-based award, which the directors can elect to receive in the form of: • options that are fully-vested upon grant; • restricted stock units that vests on the first anniversary of the date of grant; or • a 50/50 mix of options and restricted stock units	

Each of our non-employee directors is eligible to defer 50% or 100% of the cash and restricted stock portion of his or her compensation set forth above and elect to receive deferred stock units that are paid out in common stock upon the earliest to occur of (i) termination of the non-employee director's service on our board of directors, (ii) a change of control and (iii) the non-employee directors disability or death.

Our non-employee directors also are reimbursed for their business-related expenses incurred in connection with attendance at board and committee meetings and related activities. Our two employee directors, Dr. Leiden and Dr. Kewalramani, do not receive separate compensation for service in such capacity.

We annually review the compensation program for our non-employee directors. We did not make any material changes to the compensation program for our non-employee directors in 2020.

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2020 Summary Compensation

Director	Fees Earned or Paid in Cash	Stock Awards[1]	Option Awards[1]	All Other Compensation[4]	Total
Sangeeta N. Bhatia	$130,000	$ 400,205	$ —	$ —	$ 530,205
Lloyd Carney	$115,000	$ 400,205	$ —	$ 25,000	$ 540,205
Alan Garber	$125,000	$ 200,103	$ 200,074	$ —	$ 525,177
Terrence C. Kearney	$142,500	$ —	$ 400,060	$ —	$ 542,560
Yuchun Lee	$127,500	$ —	$ 400,060	$ 9,750	$ 537,310
Margaret G. McGlynn	$125,797	$ 200,103	$ 200,074	$ 25,000	$ 550,974
Diana McKenzie[2]	$ 60,057	$ 400,265	$ —	$ 14,500	$ 474,822
Bruce I. Sachs[3]	$179,204	$ —	$ 400,060	$ —	$ 579,264
William Young	$ 52,163	$ —	$ 400,060	$ —	$ 452,223

(1) The amounts set forth under the captions “Stock Awards” and “Option Awards” in the table above represent the grant-date fair value for financial statement reporting purposes of the equity awards granted during 2020. Our methodology, including underlying estimates and assumptions, for calculating these values is set forth in Note N to our consolidated financial statements included in our 2020 Annual Report on Form 10-K, filed with the SEC on February 11, 2021.

(2) Ms. McKenzie joined our board on June 3, 2020 and elected to defer her quarterly cash retainers, which were paid in deferred stock units, on each of the quarterly payment dates occurring on the 15th of the month following the quarter end in an amount equal to the dollar value of the cash amount that would have been paid on such date divided by the fair market value of a share of common stock on each such date. The per share fair market values of our common stock on each of those dates was $292.77, $222.81 and $225.99.

(3) Mr. Sachs elected to defer his quarterly cash retainers, which were paid in deferred stock units, on each of the quarterly payment dates occurring on the 15th of the month following the quarter end in an amount equal to the dollar value of the cash amount that would have been paid on such date divided by the fair market value of a share of common stock on each such date. The per share fair market values of our common stock on each of those dates was $258.56, $292.77, $222.81 and $225.99.

(4) Mr. Carney, Mr. Lee, Ms. McGlynn and Ms. McKenzie participated in the Vertex Foundation Matching Gift Program.

2020 Equity Grants

Grant	Date	Shares	Exercise Price	Grant-Date Fair Value
Annual Non-Employee Director - 100% Option Grants	June 1, 2020	4,527	$ 286.27	$ 400,060
Annual Non-Employee Director - 50% Option Grants	June 1, 2020	2,264	$ 286.27	$ 200,074
Annual Non-Employee Director - 100% Restricted Stock Unit Grants	June 1, 2020	1,398	N/A	$ 400,205
Annual Non-Employee Director - 50% Restricted Stock Unit Grants	June 1, 2020	699	N/A	$ 200,103
Initial Restricted Stock Unit Grant to Diana McKenzie	June 3, 2020	1,435	N/A	$ 400,265

Outstanding Equity

As of December 31, 2020, our non-employee directors had outstanding restricted stock units, deferred stock units and stock options to purchase our common stock as follows:

Director	Outstanding Restricted Stock Units	Outstanding Deferred Stock Units	Exercisable Options	Total Outstanding Options
Sangeeta N. Bhatia	1,398	—	3,845	3,845
Lloyd Carney	1,398	—	—	—
Alan Garber	1,249	—	13,478	14,143
Terrence C. Kearney	—	—	33,051	33,051
Yuchun Lee	—	1,801	86,783	86,783
Margaret G. McGlynn	699	3,989	44,520	44,520
Diana McKenzie	1,435	138	—	—
Bruce I. Sachs	—	12,629	71,783	71,783

Non-Employee Director Stock Ownership Guidelines

We have stock ownership guidelines for our non-employee directors pursuant to which our non-employee directors should, within five years of becoming subject to the guidelines, hold shares of (a) our common stock, (b) unvested restricted stock units, and/or (c) deferred stock units, having a value of at least five times the annual cash retainer. As of March 31, 2021, each of our non-employee directors was in compliance with our stock ownership guidelines, and each of our non-employee directors, except for Ms. McKenzie, satisfied the individual holding requirements. Ms. McKenzie joined our board of directors in June 2020 and has five years to satisfy the individual holding requirements.

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CORPORATE RESPONSIBILITY

Vertex has grown into a leading global biotechnology company that repeatedly innovates to bring transformative medicines to people with serious diseases. As we have grown, we have maintained and expanded on our commitment to corporate responsibility, including through a ten-year $500 million corporate giving commitment previously announced by the company. Our progress and efforts have been recognized, with Vertex named to the Points of Light Civic 50, *Investor Business Daily's* list of Best Environmental, Social and Governance Companies and the *Boston Business Journal's* Most Charitable Companies in Massachusetts top 20 ranking.

Community

At Vertex, volunteering and giving is in our DNA. In 2020, Vertex and its employees supported more than 1,600 nonprofit organizations in 14 countries through Vertex Volunteers and the Vertex Foundation Matching Gift Program.

The Vertex Foundation, a nonprofit 501(c)(3) organization, seeks to improve the lives of people with serious diseases and contribute to the communities where Vertex is located through education, innovation and health. In 2020, the Vertex Foundation made $17.4 million in grants to nonprofit organizations, including $5 million for global COVID-19 response efforts and $4 million to support racial and social justice initiatives and organizations in the U.S. As part of its focus on racial and social justice, the Vertex Foundation committed $1.5 million to support the new Boston University Center for Antiracist Research. The Vertex Foundation Matching Gift Program saw more than $3.3 million donated by employees and the Vertex Foundation, and also offered employees two special matching campaigns, resulting in nearly $900,000 in donations to select organizations responding to the COVID-19 pandemic and supporting racial and social justice in our communities. The Vertex Foundation also continued to make grants in support of its focus areas (STEAM education, social innovation and healthy families) and support projects and organizations with a strong commitment to inclusion, diversity, and equity.

Throughout the year, we encourage our employees to participate in community service activities through the Vertex Volunteers program, including activities such as pro bono service conducted by members of our legal and compliance group and our annual global Day of Service. Last year, 36% of Vertex employees in 14 countries collectively volunteered more than 3,200 hours in their local communities, primarily through virtual and remote opportunities.

Our corporate giving extends and expands our long-term commitment to patients with serious diseases and our communities, including a focus on STEAM education. In 2020, we transitioned our in-person Learning Labs programming in San Diego and Boston to a virtual environment that engaged more than 1,200 students and 40 high school interns. In 2020, we provided 87 scholarships to people with CF and their family members who are pursuing two-year, four-year or graduate degrees. Vertex is also committed to supporting programs and initiatives in the countries in which we operate to educate healthcare professionals, strengthen CF research and development, raise disease awareness and provide support to nonprofit organizations.

Workplace

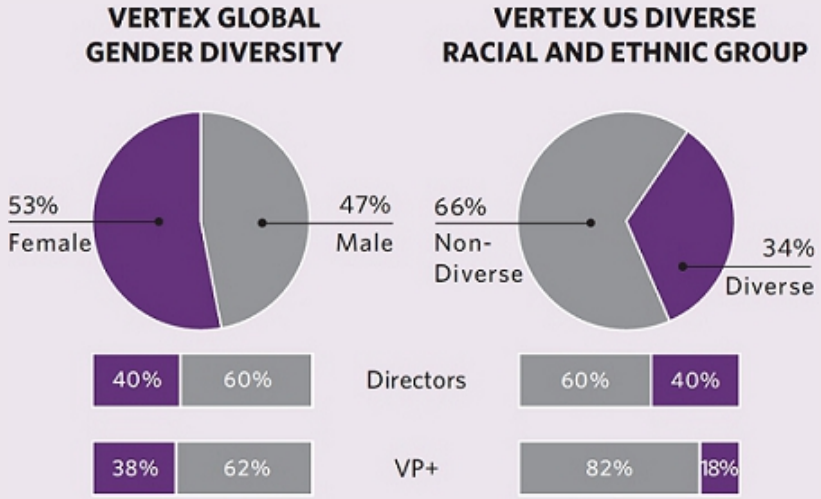
We are committed to building an outstanding, committed and passionate team at Vertex. We believe that we can do our best work for patients when we foster a culture and environment where all points of view are respected and heard. At Vertex, we view diversity as a catalyst for innovation, and as a key driver in making better decisions and achieving the best outcomes.

We are pleased to have been awarded:

- a perfect score of 100 on the Human Rights Campaign's Corporate Equality Index (CEI);
- recognition in the list of Best Places to Work for LGBTQ Equality; and
- a listing on Forbes 2020 Best Employers for Diversity List.

Six of our ten directors are women and/or from diverse racial and ethnic groups. This includes four female directors.

On a global basis, as of December 31, 2020, our employee population is 53% women and 47% men. In the U.S., approximately 34% of our workforce and 44% of new hires are from diverse racial and ethnic groups. As of December 31, 2020, 38% of our global leadership (VP and above) were women and 18% of U.S. leadership were from diverse racial and ethnic groups.



Environment

We are committed to limiting our environmental impacts and to operating our business in a sustainable manner. We make strong local efforts to reduce our impact on the environment. In 2020, we sourced 100% renewable energy for our International Headquarters in London, joining our Oxford, UK facility, which has done so since 2018. We began the installation of a solar panel array at our San Diego research facility that is expected to provide approximately 20% of the building's energy. In 2020, the use of reusable, thermal boxes for patient deliveries allowed us to avoid the use of 20,000 single use boxes, or the equivalent of 78,000 kgs of waste not generated. In addition, our facilities in Boston and in San Diego are LEED Gold certified and our office in London achieved a BREEAM rating of excellent.

In 2020, we received a score of B on the CDP Climate Change survey by demonstrating management and coordinated action on climate issues. We also conducted a climate risk assessment that will be used to inform a global mitigation and resiliency plan in 2021. And finally, we continue to make progress towards our global goal of reducing our absolute greenhouse gas emissions 20% by the end of 2023 over a 2018 baseline.

PROPOSAL NO. 2: RATIFICATION OF THE APPOINTMENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

Engagement of Ernst & Young LLP

Our audit and finance committee is responsible for the appointment, compensation and oversight of our independent registered public accounting firm. Ernst & Young LLP has been our independent registered public accounting firm since 2005, and we believe that the selection of Ernst & Young LLP as our independent registered accounting firm for the year ending December 31, 2021 is in the best interest of our company and our shareholders.

In determining whether to reappoint our independent registered public accounting firm, our audit and finance committee undertakes an annual formal evaluation of the independent registered public accounting firm, during which it considers the quality of its discussions with, and the performance of, the lead audit partner, the audit team assigned to our account, the potential impact of changing our independent registered public accounting firm, the overall strength and reputation of the firm and issues pertaining to auditor independence, including fees that our independent registered public accounting firm receives for non-audit services. In accordance with applicable requirements, we are required to change our lead audit partner every five years.

Representatives of Ernst & Young LLP are expected to attend the annual meeting, will have the opportunity to make a statement if they desire to do so and will be available to respond to appropriate questions from shareholders.

Effect of Vote

Although we are not required to have shareholders ratify the selection of Ernst & Young LLP, our board is submitting this proposal to our shareholders for ratification as a matter of good corporate practice. If our shareholders do not ratify the selection, our audit and finance committee will reconsider the selection of Ernst & Young LLP for the ensuing year, but may determine that continued retention of Ernst & Young LLP is in our company's and our shareholders' best interests. Even if the appointment is ratified, the audit and finance committee, in its discretion, may direct the appointment of a different independent registered public accounting firm at any time during the year if it determines that such a change would be in our company's and our shareholders' best interests.

Independent Registered Public Accounting Firm Fees

The audit and finance committee works with our management in order to negotiate appropriate fees with Ernst & Young LLP and is ultimately responsible for approving those fees. The following is a summary and description of fees for services provided by Ernst & Young LLP in 2020 and 2019.

Service	2020	2019
Audit fees	$ 3,594,000	$ 3,891,000
Audit-related fees	—	—
Tax fees	4,212,000	3,194,000
All other fees	8,000	10,000
TOTAL	**$ 7,814,000**	**$ 7,095,000**

"Audit fees" represented the aggregate fees for professional services rendered for the audit of our annual consolidated financial statements, and our internal controls over financial reporting, for the reviews of the consolidated financial statements included in our Form 10-Q filings, for statutory audits of our international operations and providing consents with respect to registration statements.

"Audit-related fees" refer to fees for accounting consultations.

"Tax fees" consisted of fees related to tax compliance, worldwide tax planning and tax advice. The tax fees for 2020 and 2019 consisted of:

- tax compliance and preparation fees, including the preparation of original and amended tax returns and refund claims, and tax payment planning of $1,660,000 and $1,720,000, respectively; and
- tax advice and planning fees of $2,552,000 and $1,474,000, respectively.

"All other fees" consisted of licensing fees paid to Ernst & Young LLP for access to its proprietary accounting research database.

Audit and Finance Committee Pre-Approval Policies and Procedures

Our audit and finance committee has established a policy to pre-approve all audit and permissible non-audit services provided by our independent registered public accounting firm. Prior to the engagement of the firm for each year's audit, management submits to our audit and finance committee for approval a description of services expected to be rendered during that year for each of the following four categories of services and a budget for those services in the aggregate.

- **Audit fees** include fees for audit work performed in the preparation of financial statements, as well as work that generally only our independent registered public accounting firm can reasonably be expected to provide, including comfort letters, statutory audits, consents and attestation services.
- **Audit-related fees** relate to services for assurance and related services that traditionally are performed by the independent registered public accounting firm, including due diligence related to mergers and acquisitions, employee benefit plan audits, special procedures required to meet certain regulatory requirements and consultation regarding financial accounting and/or reporting standards.
- **Tax fees** include fees for all services performed by the independent registered public accounting firm's tax personnel except those services specifically related to the audit of our financial statements, and include fees in the areas of tax compliance, tax planning and tax advice.
- **All other fees** are those associated with services not captured in the three preceding categories.

Prior to the engagement of our independent registered public accounting firm, our audit and finance committee pre-approves these services by category of service. The fees are budgeted and our audit and finance committee requires the independent registered public accounting firm and management to report actual fees versus the budget periodically throughout the year by category of service. During the year, circumstances may arise when it may become necessary to engage the independent registered public accounting firm for additional services not contemplated in the original pre-approval. In those instances, our audit and finance committee requires that we obtain its specific pre-approval for these services.

The audit and finance committee may delegate pre-approval authority to one or more of its members. The member to whom such authority is delegated must report any pre-approval decisions to our audit and finance committee at its next scheduled meeting.

All of the services set forth above in the categories "audit-related fees," "tax fees" and "all other fees" were pre-approved and none were approved by our audit and finance committee pursuant to Rule 2-01(c)(7)(i)(C) of Regulation S-X, which relates to the approval of a *de minimis* amount of non-audit services after the fact but before completion of the audit.

The affirmative vote of a majority of the shares represented and entitled to vote on this matter is required for the approval of this proposal.

Our board of directors unanimously recommends that you vote **FOR** ratification of the appointment of Ernst & Young LLP as our independent registered public accounting firm for the year ending December 31, 2021.

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AUDIT AND FINANCE COMMITTEE REPORT

The Audit and Finance Committee of the Board of Directors (the "Audit Committee") oversees the Company's accounting, auditing and financial reporting process, financial risk assessment and management process and for monitoring compliance with certain regulatory and compliance matters, on behalf of the Board of Directors. Management of the Company is responsible for preparing the financial statements, for establishing and maintaining adequate internal financial and disclosure controls, and for the public reporting process. Ernst & Young LLP ("Ernst & Young"), the Company's independent registered public accounting firm, is responsible for expressing an opinion on the conformity of the Company's audited financial statements with generally accepted accounting principles and on the Company's internal control over financial reporting.

The Audit Committee reviewed and discussed the Company's audited financial statements for the year ended December 31, 2020 with Ernst & Young and the Company's management and Ernst & Young's audit of the Company's internal control over financial reporting. In addition, the Audit Committee has discussed with Ernst & Young the matters that are required to be discussed by the applicable requirements of the Public Company Accounting Oversight Board (the "PCAOB") and the SEC. These communications and discussions are intended to assist the Audit Committee in overseeing the financial reporting and disclosure process.

The Audit Committee also has received from Ernst & Young the written disclosures and the letter concerning independence as required by the applicable requirements of the PCAOB regarding Ernst & Young's communications with the Audit Committee regarding independence, and has discussed with Ernst & Young the firm's independence. The Audit Committee has also concluded that Ernst & Young's provision of audit and non-audit services to the Company is compatible with Ernst & Young's independence from the Audit Committee and the Company's management.

Based on the review and discussions noted above, the Audit Committee recommended to the Company's Board of Directors that the audited financial statements for the year ended December 31, 2020 be included in the Company's Annual Report on Form 10-K for filing with the SEC. This report is provided by the following independent directors, who comprise the Audit Committee:

Terrence C. Kearney (*Chair*)
Lloyd Carney
Alan Garber
Yuchun Lee

PROPOSAL NO. 3: ADVISORY VOTE TO APPROVE NAMED EXECUTIVE OFFICER COMPENSATION

Our compensation program is designed to attract, retain and motivate talented and experienced individuals across all areas of our business and to align the interests of our executive officers with the interests of our shareholders as we seek to create value through the discovery, development and commercialization of transformative medicines.

In 2020, our annual advisory vote on executive compensation received support from approximately 95% of the votes cast at the annual meeting of shareholders. We believe this support is consistent with our shareholders' understanding of our business model and the long-term value we are creating. We plan to continue a high level of shareholder engagement regarding executive compensation.

Our focus is and continues to be maintaining the strong link between our compensation programs and our ability to continue to develop transformative medicines while delivering sustained company performance, with approximately 90% of our named executive officer ("NEO") compensation linked to performance. Our board and MDCC routinely review our compensation programs and made the following key decisions with respect to 2020 compensation:

- Pursuant to her employment agreement, Dr. Reshma Kewalramani, our CEO and President, maintained a base salary of $1.15 million, a target cash bonus of 120% of base salary and a target equity level of $11.0 million.
- Pursuant to his employment agreement, Dr. Jeffrey Leiden maintained a base salary of $1.0 million and a target cash bonus of 100% of base salary for his first year as Executive Chairman. Dr. Leiden will not receive a base salary or cash bonus for the remaining two years of his term in this position. Dr. Leiden additionally received equity grants of $9.0 million for his first year as Executive Chairman pursuant to the terms of his employment agreement. Dr. Leiden's second year as Executive Chairman commenced on April 1, 2021.
- For each of our other NEOs, we maintained base salary, a target cash bonus of 70% of base salary and a target equity level of $4.0 million based on a comparative analysis with companies in our peer group.
- The company's outstanding performance in 2020 resulted in a leading rating (138 out of a potential 150) for 2020 and annual cash bonuses near the high end of the range for 2020, commensurate with the performance described above.
- We maintained the mix of equity granted under our compensation program with 50% consisting of performance stock units that vest solely upon achievement of rigorous performance goals and 50% consisting of time-vesting restricted stock units that reward stock price appreciation but also serve as a long-term retention tool.

Our executive compensation program, including our performance and the compensation of our NEOs, is discussed in greater detail in the *Compensation Discussion and Analysis* section beginning on page 42 of this proxy statement.

As required by Section 14A of the Exchange Act, our board of directors is asking that shareholders cast a non-binding, advisory vote FOR the following resolution:

> *RESOLVED, that the compensation of our named executive officers, as disclosed pursuant to the rules of the Securities and Exchange Commission, including the Compensation Discussion and Analysis, the Compensation and Equity Tables and the related narrative executive compensation disclosures contained in this proxy statement, is hereby APPROVED.*

The vote on this resolution is advisory and not binding on the board. However, our MDCC and board intend to consider carefully the outcome of the shareholder vote when considering future executive compensation program matters. We will hold an annual advisory, non-binding vote of our shareholders on the compensation of our NEOs. The next shareholder vote on the frequency of such advisory vote is expected to be held at the 2023 annual meeting of shareholders.

Our board of directors unanimously recommends that you vote **FOR** the approval of the resolution set forth above.

PROPOSAL NO. 4: SHAREHOLDER PROPOSAL REGARDING REPORT ON OUR LOBBYING ACTIVITIES

We expect the following shareholder proposal will be presented for consideration at the 2021 annual meeting of shareholders. Our board of directors unanimously recommends a vote AGAINST this shareholder proposal for the reasons set forth following the proposal.

THE SHAREHOLDER PROPOSAL

Friends Fiduciary Corporation, 1700 Market Street, Suite 1535, Philadelphia, Pennsylvania 19103, an owner of at least $2,000 worth of shares of our common stock as of December 28, 2020, has given notice that it intends to present for action at our 2020 annual meeting of shareholders the following resolution:

WHEREAS, we believe in full disclosure of our company's direct and indirect lobbying activities and expenditures to assess whether Vertex's lobbying is consistent with its expressed goals and in shareholder interests.

RESOLVED, the shareholders of Vertex Pharmaceuticals Incorporated ("Vertex") request the preparation of a report, updated annually, disclosing:

1. Company policy and procedures governing lobbying, both direct and indirect, and grassroots lobbying communications.
2. Payments by Vertex used for (a) direct or indirect lobbying or (b) grassroots lobbying communications, in each case including the amount of the payment and the recipient.
3. Vertex's membership in and payments to any tax-exempt organization that writes and endorses model legislation.
4. Description of the decision-making process and oversight by management and the Board for making payments described in section 2 and 3 above.

For purposes of this proposal, a "grassroots lobbying communication" is a communication directed to the general public that (a) refers to specific legislation or regulation, (b) reflects a view on the legislation or regulation and (c) encourages the recipient of the communication to take action with respect to the legislation or regulation. "Indirect lobbying" is lobbying engaged in by a trade association or other organization of which Vertex is a member.

Both "direct and indirect lobbying" and "grassroots lobbying communications" include efforts at the local, state and federal levels.

The report shall be presented to the Audit Committee or other relevant oversight committees and posted on Vertex's website.

SUPPORTING STATEMENT

As shareholders, we encourage transparency in Vertex's use of funds to lobby, both directly and indirectly. While we commend Vertex on its recently published lobbying policy, disclosure gaps remain. Vertex discloses trade associations receiving more than $25,000 and the amounts used to lobby, including the Biotechnology Innovation Organization (BIO), but its disclosure covers only dues, not other payments, which can be significant. Additionally, this disclosure does not include 501(c)(4) social welfare organizations, such as the Alliance for Patient Access (AfPA). Vertex's undisclosed membership in AfPA poses reputational risks on drug pricing and opioids. The AfPA has been described as a non-profit pharmaceutical industry front group ("Non-Profit Alliance for Patient Access Uses Journalists and Politicians to Push Big Pharma's Agenda," *Health News Review*, October 2, 2017) and has attracted negative scrutiny for its role in passing legislation that weakened the Drug Enforcement Administration's ability to stop suspicious drug shipments by drug distributors, thereby exacerbating the opioid crisis ("Opioid Lobbyist Left a Digital Footprint on a Campaign by Patient Advocates," *The Intercept*, October 22, 2017").

We are concerned Vertex's payments to third party groups may be used for undisclosed grassroots lobbying. For example, BIO funds the Alliance to Protect Medical Innovation, described as a front group formed in response to the campaign by Patients for Affordable Drugs ("Anonymous 'Ghost Ship' is Among Groups Flooding Drug Pricing Debate," *The Washington Post*, January 22, 2019). Grassroots lobbying does not get reported at the federal level under the Lobbying Disclosure Act, and disclosure is uneven or absent in states.

Transparent reporting would reveal whether company assets are being used for objectives contrary to Vertex's long-term interests. We are concerned that Vertex's lack of indirect lobbying disclosures, and any potential negative publicity for opposing drug price initiatives, may present reputational risks for Vertex.

YOUR COMPANY'S RESPONSE

Our board of directors recommends a vote AGAINST this shareholder proposal.

Vertex recognizes the importance of public policy in supporting our mission of creating transformative medicines for people with serious diseases. We engage with various policymakers and trade and industry groups to help promote an environment in which we can continue to innovate and develop transformative medicines for the benefit of patients with serious diseases.

In 2020, we published our political engagement principles on our website (https://www.vrtx.com/sites/default/files/Political_ Engagement_Principles.pdf). In our principles, we outline the majority of the information requested by this shareholder proposal, including Vertex's approach to political contributions and lobbying, details of our political contributions (including links to our federal and state lobbying reports), Vertex's membership in - and payments to -trade and industry groups to which we contribute $25,000 per year (including amounts that are attributable to lobbying), and board and management oversight over our political contributions and lobbying activities. We do not engage in grassroots lobbying communications.

Our political engagement principles are aligned with similar peer company disclosures. We have shared them with shareholders, engaged in productive dialogues on this topic and have committed to updating this information annually.

In light of the above, our board believes that the proposal's additional detailed reporting obligation would be duplicative of existing disclosures and would impose an unnecessary administrative burden and expense on the company when sufficient meaningful disclosure already exists.

The affirmative vote by the holders of a majority of the votes cast in person or by proxy on this matter is required for the approval of this proposal.

For all of the above reasons, our board of directors unanimously recommends that you vote **AGAINST** this shareholder proposal.

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PROPOSAL NO. 5: SHAREHOLDER PROPOSAL REGARDING REPORT ON OUR POLITICAL SPENDING

We expect the following shareholder proposal will be presented for consideration at the 2021 annual meeting of shareholders. Our board of directors unanimously recommends a vote AGAINST this shareholder proposal for the reasons set forth following the proposal.

THE SHAREHOLDER PROPOSAL

Newground Social Investment, 111 Queen Anne N, #500, Seattle, Washington 98109, representing its client, Seattle Mennonite Church, 3120 NE 125 Street, Seattle, Washington 98125, which is an owner of at least $2,000 worth of shares of our common stock as of December 28, 2020, has given notice that it intends to present for action at our 2021 annual meeting of shareholders the following resolution:

RESOLVED: The shareholders of Vertex Pharmaceuticals Inc. ("Vertex" or "Company") hereby request the Company to prepare and semiannually update a report, which shall be presented to the pertinent board of directors committee and posted on the Company's website, that discloses the Company's:

a. Policies and procedures for making electoral contributions and expenditures (direct and indirect) with corporate funds, including the board's role (if any) in that process; and

b. Monetary and non-monetary contributions or expenditures that could not be deducted as an "ordinary and necessary" business expense under section 162(e)(1)(B) of the Internal Revenue Code, including (but not limited to) contributions or expenditures on behalf of candidates, parties, and committees and entities organized and operating under section 501(c)(4) of the Internal Revenue Code, as well as the portion of any dues or payments made to any tax-exempt organization (such as a trade association) used for an expenditure or contribution that, if made directly by the Company, would not be deductible under section 162(e)(1)(B) of the Internal Revenue Code.

The report shall be made available within 12 months of the annual meeting and identify all recipients and the amount paid to each recipient from Company funds. This proposal does not encompass lobbying spending.

SUPPORTING STATEMENT

As long-term Vertex shareholders, we support transparency and accountability in corporate electoral spending. Disclosure is in the best interest of both the Company and its shareholders.

The Supreme Court recognized this in its 2010 Citizens United decision, which said: "[D]isclosure permits citizens and shareholders to react to the speech of corporate entities in a proper way. This transparency enables the electorate to make informed decisions and give proper weight to different speakers and messages."

Public records show Vertex has contributed more than $3.3 million in corporate funds since the 2010 election cycle.

Vertex discloses a policy on corporate political spending and its direct contributions to candidates, parties, committees, and 527 groups; however, this is only a small part of the overall picture because Vertex does not disclose its:

1. Direct independent expenditures;
2. Payments to trade associations that that can be used for election-related purposes (amounts nondeductible under section 162(e)(1)(B));
3. Payments to any other tax-exempt organizations – such as 501(c)(4)s – that can be used for election-related purposes; and,
4. Payments to influence the outcome of ballot measures.

Information on indirect electoral spending through trade associations and 501(c)(4) groups cannot be obtained by shareholders without Company disclosure. This proposal seeks disclose of all of Vertex's electoral spending – both direct and indirect.

This would bring Vertex in line with a growing number of leading peer companies, including: **Alexion Pharmaceuticals Inc., Biogen Inc., and Gilead Sciences Inc.,** each of whom present this information on their websites.

Vertex shareholders and the Board need comprehensive disclosure to be able to fully evaluate the use of corporate assets in elections.

THEREFORE: We urge your support FOR this critical governance reform.

YOUR COMPANY'S RESPONSE

Our board of directors recommends a vote AGAINST this shareholder proposal.

Vertex recognizes the importance of public policy in supporting our mission of creating transformative medicines for people with serious diseases. We engage with various policymakers and trade and industry groups to help promote an environment in which we can continue to innovate and develop transformative medicines for the benefit of patients with serious diseases.

In 2020, we published our political engagement principles on our website (https://www.vrtx.com/sites/default/files/Political_ Engagement_Principles.pdf). In our principles, we outline the majority of the information requested by this shareholder proposal, including Vertex's approach to political contributions, details of our political contributions, Vertex's membership in - and payments to - trade and industry groups to which we contribute $25,000 per year (including amounts that are non-deductible under 162(e)(1)(B) of the Internal Revenue Code, as reported to us by these organizations), and board and management oversight over our political contributions and related activities. We do not make payments to influence the outcome of ballot measures, nor do we make direct independent expenditures.

Our political engagement principles are aligned with similar peer company disclosures. We have shared them with shareholders, engaged in productive dialogues on this topic and have committed to updating this information annually.

In light of the above, our board believes that the proposal's additional detailed reporting obligation would be duplicative of existing disclosures and would impose an unnecessary administrative burden and expense on the company when sufficient meaningful disclosure already exists.

The affirmative vote by the holders of a majority of the votes cast in person or by proxy on this matter is required for the approval of this proposal.

For all of the above reasons our board of directors unanimously recommends that you vote **AGAINST** this shareholder proposal.

COMPENSATION DISCUSSION AND ANALYSIS

Letter from Management Development and Compensation Committee to Our Shareholders

Dear Fellow Shareholders,

The Management Development and Compensation Committee's stewardship of Vertex's compensation programs is guided by Vertex's mission of developing transformative medicines for people with serious diseases and by so doing, creating value for our shareholders. Toward that end, we have designed the company's compensation programs to closely align management's incentives with Vertex's strategic long- and short-term goals and with the interests of Vertex's shareholders. We believe that this alignment has contributed to Vertex's remarkable accomplishments over the last decade as it has significantly increased the number of patients benefiting from Vertex medicines each year, established a strong financial position with significant growth in revenues, operating margins and cash flows, and accelerated the advancement of its pipeline of small molecule drug candidates and cutting edge cell and genetic therapies, all in accordance with its core strategy of investing in scientific innovation to create transformative medicines for people with serious diseases. These accomplishments have been recognized by the company's shareholders and have been reflected in the increasing value that the company's shareholders have attributed to the company. Vertex's market capitalization has increased from approximately $7 billion in early 2012 to more than $61 billion at the end of 2020.

We take seriously our role in the governance of compensation programs and the importance of attracting and retaining critical executive talent. The success of the company and the execution of Vertex's business strategy over the last several years has depended upon the stability and operational excellence of our senior executive team. In 2020, we successfully executed a leadership succession plan with the transition of Dr. Reshma Kewalramani to the role of Chief Executive Officer and Dr. Jeffrey Leiden, our former Chief Executive Officer, to the role of Executive Chairman.

Despite the global COVID-19 pandemic, 2020 was an important year for Vertex and the company continued to execute successfully on its business strategy. By the end of 2020, the vast majority of eligible people in the U.S. were taking TRIKAFTA. Vertex also obtained approval of TRIKAFTA for people with CF 12 years of age and older in the U.S. with certain rare mutations and submitted an sNDA for TRIKAFTA for people with CF 6-11 years of age, which will further expand the number of patients treated in the U.S. In addition, the company obtained early approval for KAFTRIO in the E.U., secured reimbursement in multiple countries, and successfully executed product launches in Europe. Vertex also obtained several label expansions for our medicines, including for TRIKAFTA in the U.S. and SYMKEVI in the E.U. The research and development team significantly expanded the Vertex pipeline, establishing proof-of-concept in two disease areas, advancing several clinical programs, spanning multiple modalities, including our first cell-based therapy in T1D that entered clinical development in 2021, and continuing to make strategic investments in external innovation. The company additionally delivered outstanding financial performance in 2020 achieving CF net product revenues of $6.2 billion, a 49% increase compared to 2019. This revenue growth drove significant growth in earnings and cash flow, and the company finished the year in a strong financial position with $6.7 billion in cash, cash equivalents and marketable securities. Finally, the team strengthened its organizational capabilities, recruiting and onboarding top-tier talent across the organization, including filling all identified critical hires with superior and diverse talent.

The company's success in 2020 reflects both the company's strong performance in 2020 and the consistent differentiated corporate strategy that Vertex's senior management team has championed since 2012. Consistent with these outstanding results, for 2020 our executives received above-target cash bonuses and payouts on performance stock unit awards based both on one-year business and financial goals and three-year research and development goals. We believe these outcomes are aligned with our commitment to directly linking pay to performance. Looking ahead, we will continue to focus on the strong link between Vertex's compensation programs and execution of its corporate strategy. Central to executing our corporate strategy is the ability to attract and retain an outstanding and fully aligned executive team while also establishing an executive compensation approach with a strong performance orientation and focus on creating long-term shareholder value.

Sincerely,

Bruce I. Sachs *(Chair)*
Terrence C. Kearney
Yuchun Lee

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Overview

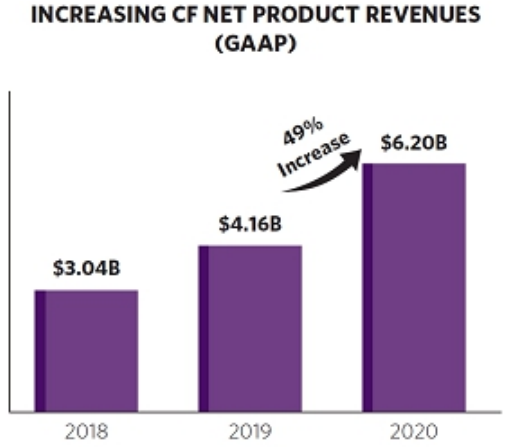
This section discusses the principles underlying our policies and decisions with respect to the compensation of our NEOs and all material factors we believe are relevant to an analysis of these policies and decisions. Our NEOs for 2020 are listed below. Michael Parini, our former Executive Vice President, Chief Administrative, Legal and Business Development Officer, voluntarily left the company effective March 1, 2021.

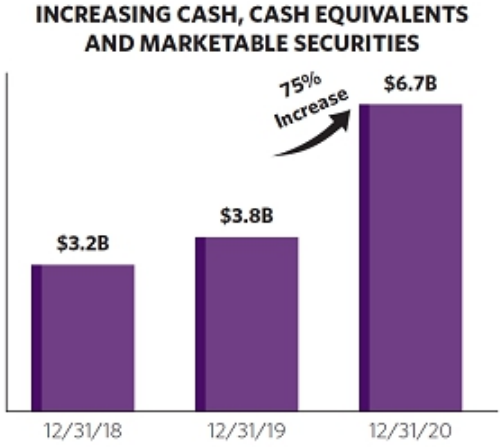
Name	Position
Reshma Kewalramani	Chief Executive Officer and President (Executive Vice President, Chief Medical Officer until March 31, 2020)
Jeffrey M. Leiden	Executive Chairman (Chief Executive Officer, President and Chairman until March 31, 2020)
Charles F. Wagner, Jr.	Executive Vice President, Chief Financial Officer
Stuart A. Arbuckle	Executive Vice President, Chief Commercial and Operations Officer
David Altshuler	Executive Vice President, Global Research and Chief Scientific Officer
Michael Parini	Executive Vice President, Chief Administrative, Legal and Business Development Officer (through March 1, 2021)

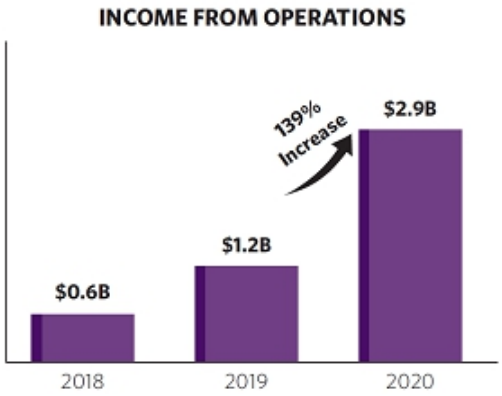
Financial Performance

Our CF medicines, TRIKAFTA/KAFTRIO, SYMDEKO/SYMKEVI, ORKAMBI and KALYDECO, are transforming the lives of eligible patients around the globe and, as we increase the number of patients eligible for our medicines, driving our financial performance.

- Our CF net product revenues increased to $6.2 billion in 2020, up 49% from our 2019 GAAP net product revenues and up 55% from our 2019 non-GAAP net product revenues (*See Appendix A for a reconciliation of GAAP net product revenues to non-GAAP net product revenues*).
- Our net income increased to $2.7 billion in 2020, driven by our increased net product revenues.
- We increased income from operations by approximately $1.7 billion, or 139%, in 2020 compared to 2019.
- Our total cash, cash equivalents and marketable securities increased by approximately $2.9 billion to approximately $6.7 billion.



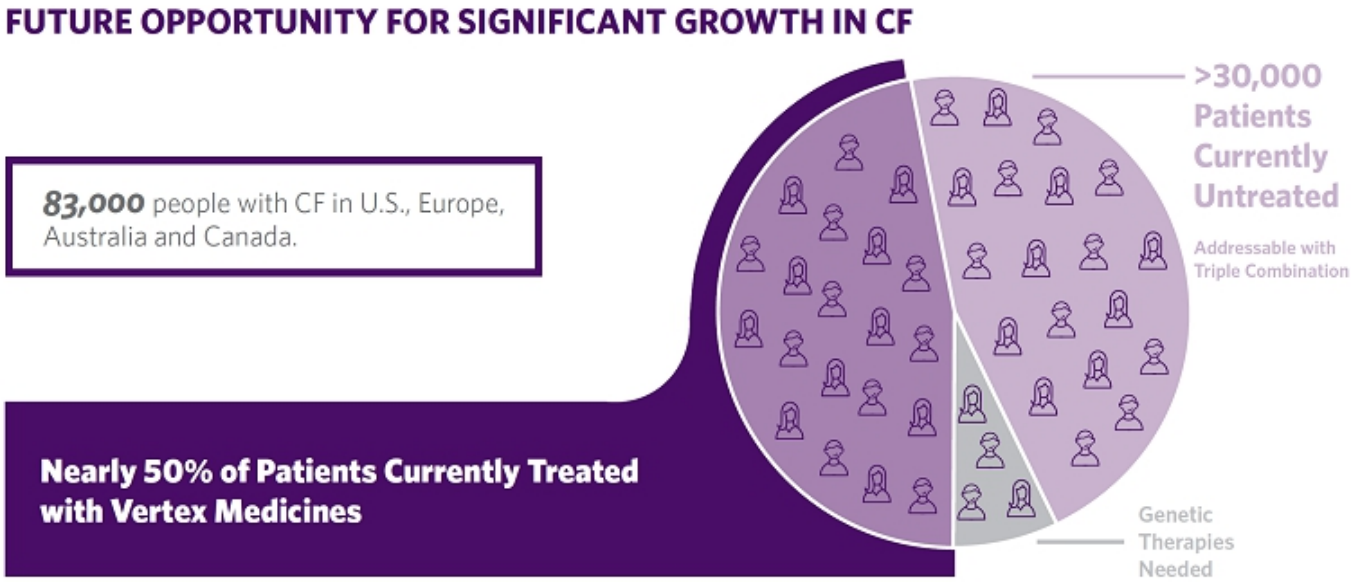




Cystic Fibrosis

Advances in our pipeline and disciplined execution of our strategy have moved us closer to our goal of delivering highly effective treatments to all patients with CF. In January 2012, KALYDECO was first approved to treat approximately 1,000 patients with the *G551D* mutation in the U.S. Since then, we have focused on expanding the number of patients eligible for our medicines and seeking improved treatment options for all patients with CF. Collectively, our four medicines are approved to treat the majority of the approximately 83,000 people with CF in North America, Europe and Australia. In 2020, we made significant progress bringing TRIKAFTA to nearly all eligible patients in the U.S. Outside of the U.S., we received early approval for KAFTRIO in the E.U., and secured reimbursement in numerous countries. As a result of these successful activities and launches in Europe, thousands of eligible patients, including those in Germany, England and Ireland, gained access to KAFTRIO by year end.

Currently, approximately half of the people with CF in North America, Europe and Australia are being treated with our medicines. We believe that more than 30,000 additional patients in these geographies could benefit from Vertex medicines. The majority of these patients are 12 years of age and older, who we expect will be treated through the continued uptake and reimbursement of KAFTRIO in Europe and other countries, and through approvals in additional countries. The remaining patients are in lower age groups or have other mutations, which we expect will be addressed through label expansions. We also are pursuing once-a-day next-generation small molecule therapies with increased efficacy for currently treated patients with the goal of achieving carrier levels of CFTR for the 90% of people with CF who respond to CFTR modulators, as well as genetic therapies for the remaining 10% of people with CF who may not be helped by CFTR modulators in support of our goal of bringing transformative therapies to all people with CF.



Since the beginning of 2020, we have made important progress in expanding the number of people who are eligible for our CFTR modulators, including:

- We obtained early approval from the European Commission for KAFTRIO for treatment of people with CF 12 years of age and older who have one *F508del* mutation and one minimal function mutation, or two *F508del* mutations.
- The FDA expanded the eligibility for TRIKAFTA to include people with CF 12 years of age and older with certain rare mutations that are responsive to TRIKAFTA.
- The FDA approved KALYDECO for treatment of infants with CF four months of age and older who have at least one mutation in their CFTR gene that is responsive to KALYDECO.
- The European Commission approved KALYDECO for treatment of infants with CF four months of age and older who have the *R117H* mutation or certain gating mutations.
- The FDA approved SYMDEKO and the European Commission approved SYMKEVI for treatment of people with CF 6 years of age and older with certain mutations.
- In January 2021, the FDA accepted and granted Priority Review to our sNDA for TRIKAFTA for treatment of children 6 to 11 years of age with at least one *F508del* mutation or with certain mutations that are responsive to TRIKAFTA.

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Research and Development

We invest in research and development in order to discover and develop transformative medicines for people with serious diseases with a focus on specialty markets. Our strategy is to combine transformative advances in the understanding of human disease and the science of therapeutics in order to discover and develop new medicines. Our approach to drug discovery has been validated through our success in moving multiple novel small molecule drug candidates into clinical trials and obtaining marketing approvals for five transformative medicines in the past decade.

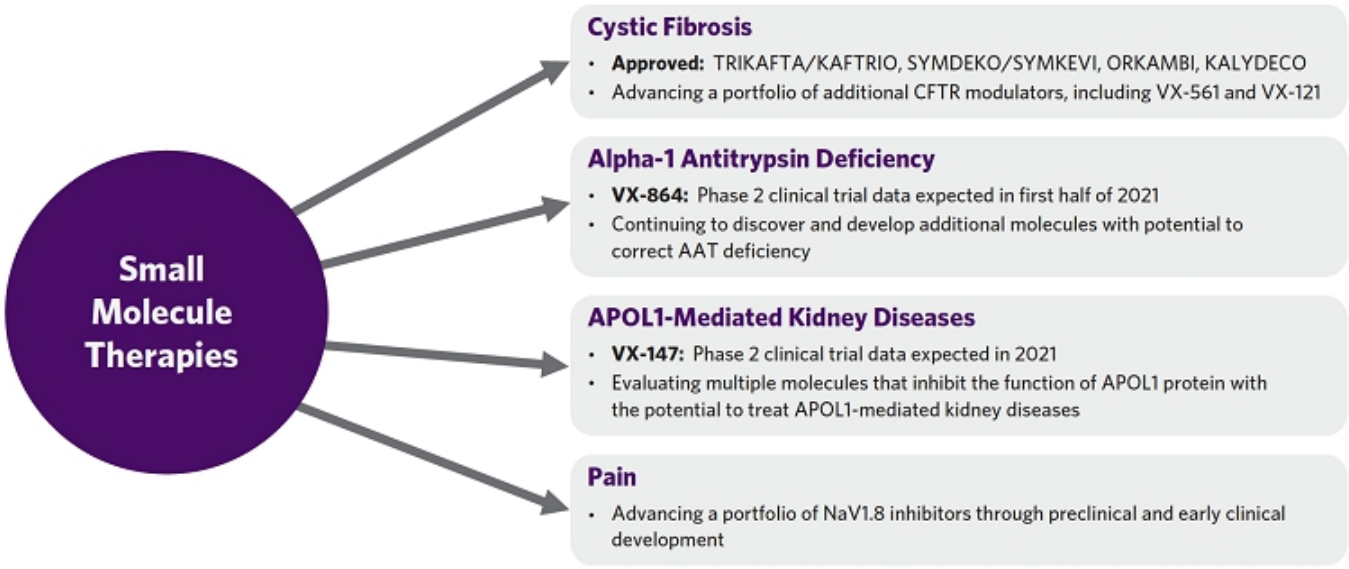
We continue to research and develop small molecule drug candidates for the treatment of serious diseases, including CF, AAT deficiency, APOL1-mediated kidney diseases, and pain. Our research and development approach includes advancing multiple small molecules into clinical trials, pursuing multiple modalities and evaluating clinical and non-clinical data to inform drug discovery and development, with the goal of bringing best-in-class therapies to patients. We are also focused on developing cell and genetic therapies for various diseases in our pipeline, including SCD, beta thalassemia, T1D, DMD, DM1 and CF. Over the last several years, we have expanded our capabilities to include additional innovative therapeutic approaches for cell and genetic therapies, which have the potential to treat, and in some cases, cure diseases by addressing the underlying cause of the disease.

In 2020, we had novel medicines in clinical trials in six diseases - CF, AAT deficiency, APOL1-mediated FSGS, pain, SCD and beta thalassemia. In 2021, we were cleared to begin our clinical program involving transplantation of fully differentiated islet cells alone in people with T1D, our seventh disease area in clinical development and our first cell-based therapy. We have recently initiated a Phase 1/2 clinical trial to evaluate VX-880 in people who have T1D with impaired hypoglycemic awareness and severe hypoglycemia.

Small Molecule Programs

Since the beginning of 2020, we advanced several promising small molecule programs:

- *AAT Deficiency:* We are focused on identifying and developing multiple drug candidates with the potential to increase the levels of functional AAT in the blood to address the lung and liver manifestations of AAT deficiency. In 2020, we progressed a Phase 2 proof-of-concept clinical trial for VX-864, an investigational small molecule corrector for the treatment of AAT deficiency.
- *APOL1-mediated Kidney Diseases:* We are evaluating inhibitors of APOL1 function to reduce levels of proteinuria in people with serious kidney diseases, including APOL1-mediated FSGS. In 2020, we initiated a Phase 2 proof-of-concept clinical trial designed to evaluate the reduction in proteinuria in people with APOL1-mediated FSGS after treatment with VX-147.
- *Pain:* We progressed a portfolio of NaV1.8 inhibitors for the treatment of acute pain and chronic neuropathic pain into pre-clinical and early clinical development.
- *Cystic Fibrosis:* We continued to identify and develop additional CFTR modulators, including once-a-day next-generation small molecule therapies, with the goal of achieving carrier levels of CFTR activity for the 90% of people with CF who respond to CFTR modulators.



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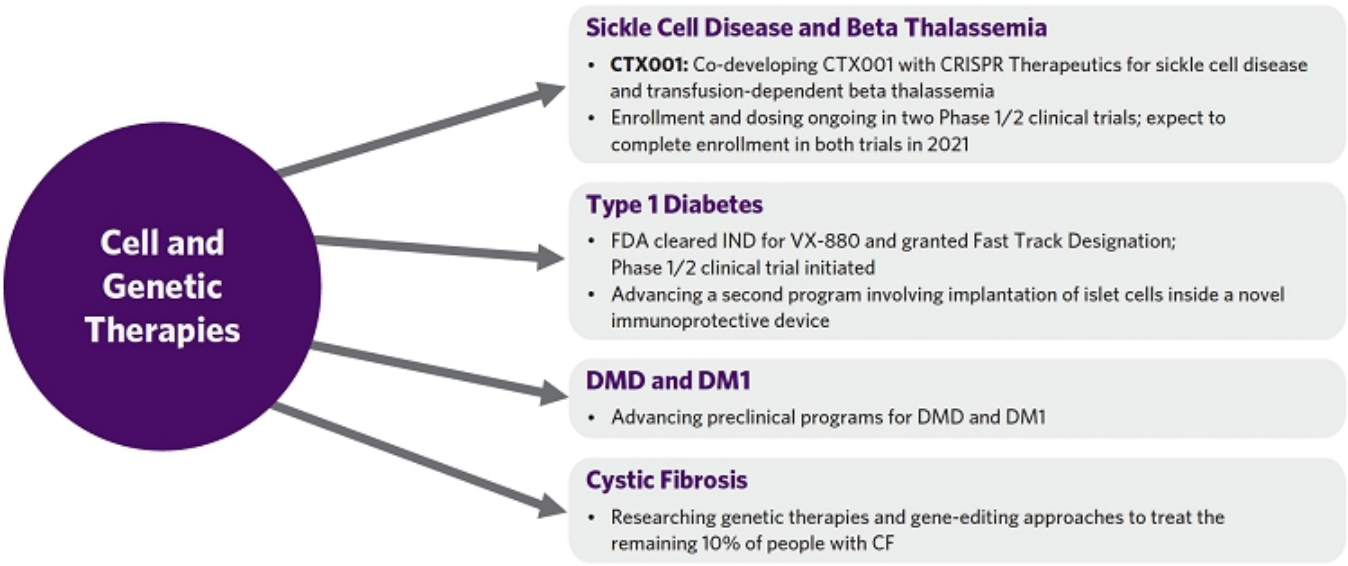
Cell and Genetic Therapies

Since the beginning of 2020, we have made important progress in the advancement of our pipeline of potentially transformative cell and genetic therapies.

- *Sickle Cell Disease and Beta Thalassemia:* We are co-developing CTX001, an investigational CRISPR/Cas9-based gene-editing therapy for SCD and TDT, the most severe form of beta thalassemia, with CRISPR. Enrollment and dosing are ongoing in two Phase 1/2 clinical trials to evaluate CTX001 as a potential one-time curative therapy for people with severe SCD and TDT. In summer of 2020, we established proof-of-concept in TDT. In December 2020, we established proof-of-concept in SCD and we announced positive interim data from 10 people treated with CTX001. As of December, all seven people with TDT were transfusion independent at last follow-up and all three people with SCD were free of vaso-occlusive crises from CTX001 infusion through the last follow-up. To date, more than 20 people have been dosed with CTX001. We expect to complete enrollment in both clinical trials in 2021.
- *Type 1 Diabetes:* We are pursuing two programs for the transplant of functional islets into patients: transplantation of islet cells alone, using immunosuppression to protect the implanted cells, and implantation of the islet cells inside an immunoprotective device. In early 2021, the FDA cleared our IND for VX-880, our program involving transplantation of fully differentiated islet cells alone for people with T1D, and we recently initiated a Phase 1/2 clinical trial to evaluate VX-880 in people who have T1D with impaired hypoglycemic awareness and severe hypoglycemia.
- *DMD and DM1:* We continue to focus on gene-editing therapies aimed at treating the underlying cause of DMD by restoring expression of near-full length dystrophin protein, and, in DM1, by addressing the repeat expansion that causes the disease.
- *Cystic Fibrosis:* We continue to research genetic therapies, such as mRNA and gene-editing approaches, to treat the remaining 10% of people who do not make CFTR protein and, are not eligible for CFTR modulators.
- *External Innovation:* We continue to collaborate with biopharmaceutical and technology companies and other organizations to advance research in our areas of therapeutic interest. This includes accessing tools and technologies to execute on our strategy to deliver transformational therapies for serious diseases, such as novel proteins to advance the development of gene-editing therapies, new capsid technologies to deliver gene therapies, and innovative platforms to discover small molecules that modulate RNA splicing.



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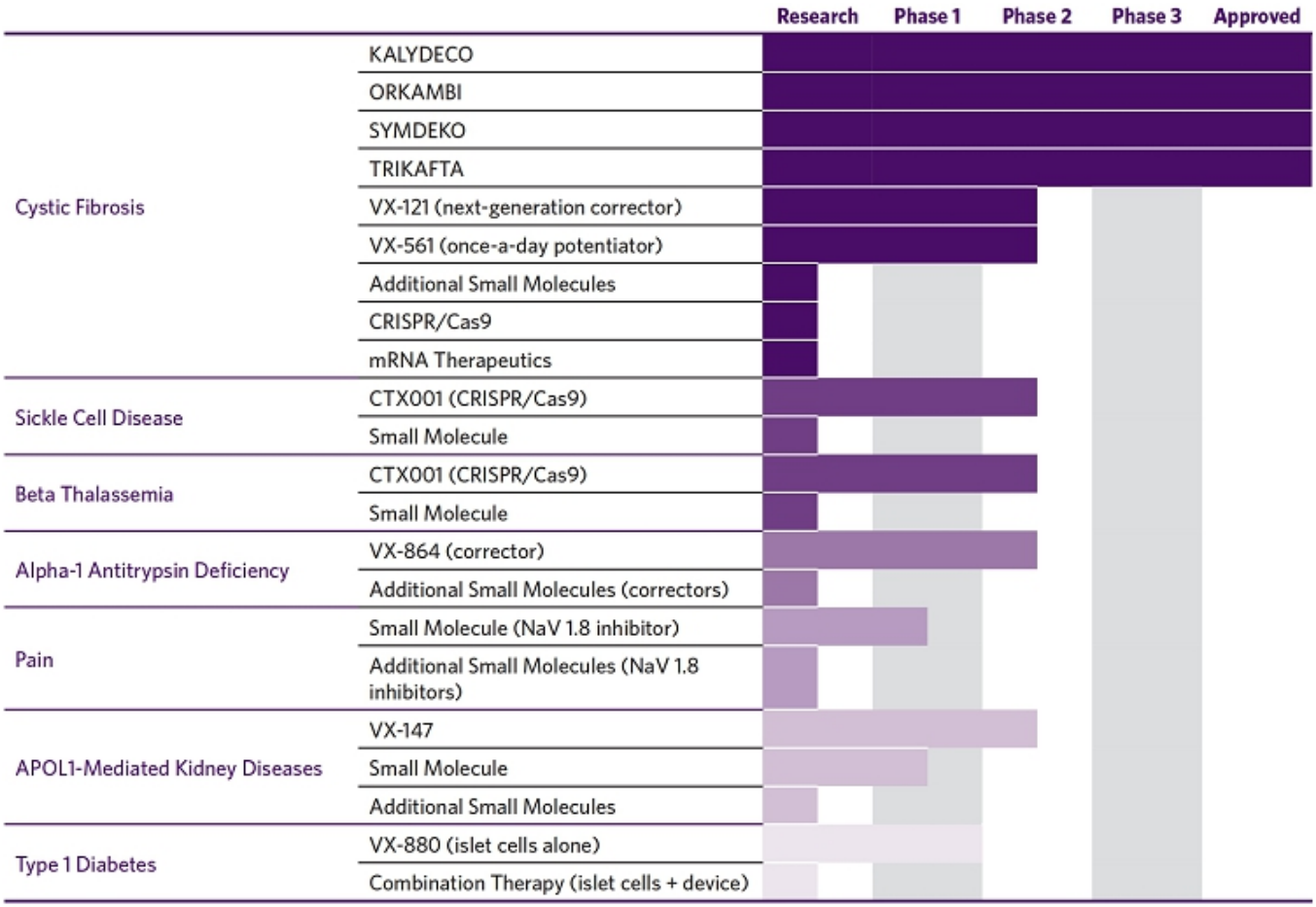
SEVEN DISEASE AREAS ACTIVE IN CLINICAL DEVELOPMENT

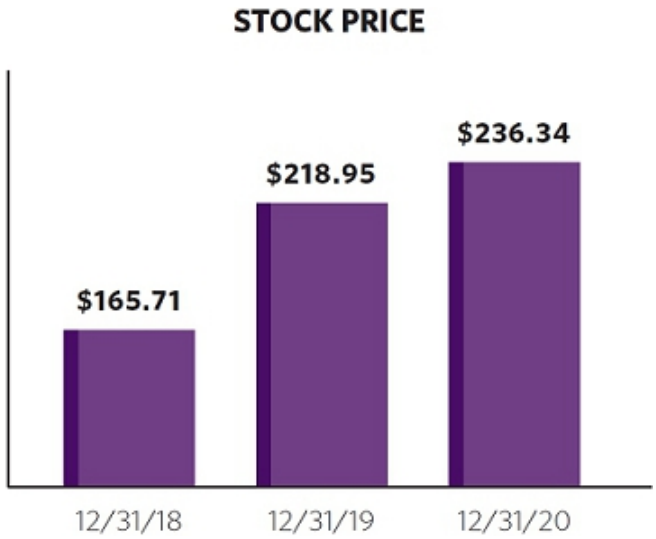
Portfolio Approach with Lead Molecules and Rapidly Avancing Follow-On Programs

The following chart represents our pipeline by disease and by stage, reflecting our programs that have lead assets already in the clinic.



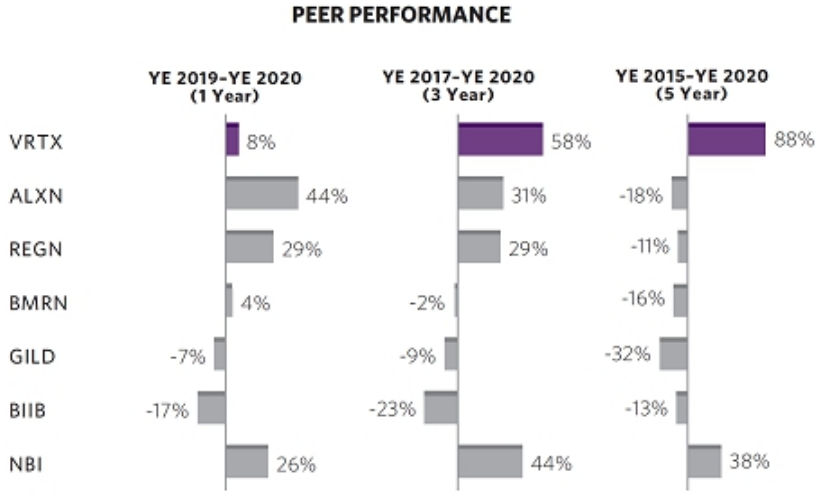
Increased Shareholder Value

Driven by our business performance, our stock price increased by 8% from $218.95 per share at the end of 2019 to $236.34 per share at the end of 2020.

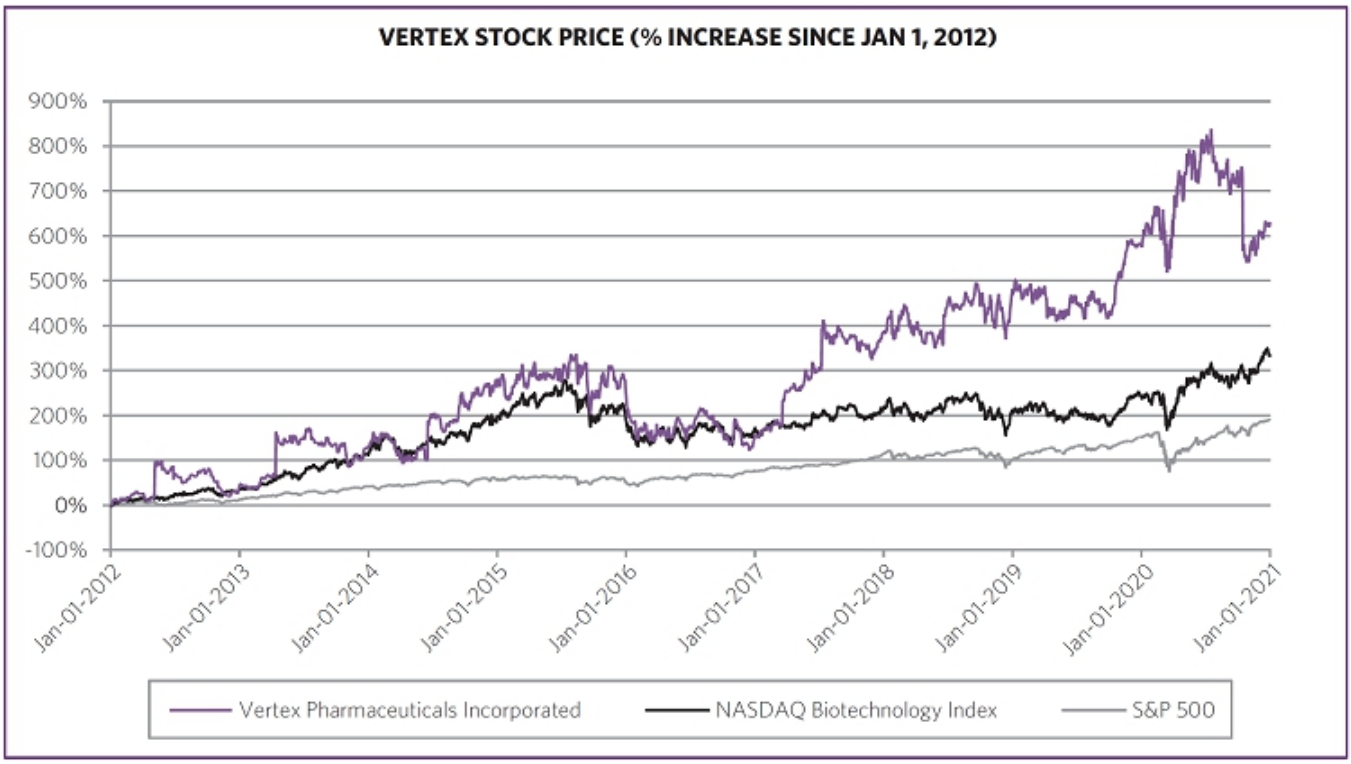


Although we were pleased with our performance in 2020, biotechnology companies are best measured over the long term and in comparison to their peers, as opposed to in one-year increments and in isolation. The following chart shows our total shareholder return during the 1-year, 3-year

and 5-year periods ending December 31, 2020 compared to the NBI and the following members of our peer group: Alexion, Regeneron, BioMarin, Gilead and Biogen. These peers are the companies we consider most similar to our company based on their business models (see pages 51 and 52). Based on this comparison, our performance exceeded our peers, including the NBI, on both of the three- and five-year performance periods.



The following chart further shows our total shareholder return relative to the NBI and S&P 500 indices since the beginning of 2012, when KALYDECO was first approved, through December 31, 2020.



CEO Succession

In 2020, we successfully executed a leadership succession plan with the transition of Dr. Reshma Kewalramani to the role of Chief Executive Officer and our former Chief Executive Officer, Dr. Jeffrey Leiden, to the role of Executive Chairman. This transition was the culmination of a deliberate and comprehensive multi-year planning process led by our independent directors. In his role as Executive Chairman, Dr. Leiden continues to focus on strategy and business development, our cell and genetic therapy programs, and government and community affairs activities, along with serving as the Chairman of our Board. Bruce Sachs continues in his role as Lead Independent Director. The Board believes this structure will help ensure continuity of strong and effective leadership.

2020 Compensation Decisions and Pay-for Performance

In 2020, our executive compensation program received substantial support, approved by approximately 95% of the votes cast at the annual meeting of shareholders. We believe this support is consistent with our long-term shareholders' understanding of our business model and the long-term value we are creating. Our executive compensation program is intended to align executive compensation with the company's long-term performance and to provide the compensation and incentives required to attract, motivate and retain our high-caliber executives who are crucial to Vertex's long-term success. **Our compensation program is highly performance-based, with approximately 90% of our NEO compensation tied to performance**.

Retention of our talented executives is critical, as their outstanding performance over the last nine years has led to the company's advancement and the creation of significant shareholder value.

In 2020, our board of directors and MDCC reviewed our compensation programs and made the following key decisions:

- **Program Design:** We maintained our compensation program design that directly ties pay with performance and has contributed to our short-and long-term successes.
- **Base Salary:** Dr. Reshma Kewalramani's employment agreement, which was negotiated in 2019, provides for a base salary of $1.15 million for her role as CEO. Dr. Jeffrey Leiden's employment agreement provides for a base salary of $1.0 million for his first year in the role of Executive Chairman. We maintained the base salaries of our other NEOs.
- **Annual Cash Bonus:** We maintained Dr. Kewalramani's target bonus of 120% of base salary. Dr. Leiden's employment agreement provides for a target bonus of 100% of base salary for 2020. We maintained a target cash bonus of 70% of base salary for our other NEOs. The company's outstanding performance in 2020, as described above, resulted in a leading rating (a company rating of 138 out of a potential 150) for 2020 and annual cash bonuses near the high end of the range for 2020, commensurate with this performance.
- **Long-Term Equity Program:**
  - For 2020, Dr. Kewalramani, our CEO, maintained a target equity level of $11.0 million. Dr. Leiden received equity grants of $9.0 million for his first year as Executive Chairman pursuant to the terms of his employment agreement. We maintained the target equity grants for our other NEOs at $4.0 million based on a comparative analysis with companies in our peer group.
  - We maintained our mix of equity granted under our compensation program with 50% consisting of performance stock units that vest solely upon achievement of rigorous performance goals and 50% consisting of time-vesting restricted stock units that reward stock price appreciation but also serve as a retention tool. The number of restricted stock units awarded may be adjusted to reflect an executive officer's individual performance for the relevant performance period, and are, thus, considered to be performance-based awards.
  - In early 2020, the MDCC established financial and non-financial metrics for the PSUs, with payouts earned based on achievement of these metrics. Fifty percent of the PSUs were tied to CF net product revenues in 2020, while the remaining fifty percent are tied to specific clinical and research milestones over a three-year period.

Shareholder Engagement

We believe that a robust shareholder outreach program is an important component of maintaining our strong corporate governance practices. We strive for a collaborative approach with investors to solicit and understand a variety of perspectives. During 2020, we solicited feedback from institutional investors representing approximately 60% of our outstanding shares. In our discussions with investors, we seek their input on a variety of corporate governance and sustainability topics and other issues that may impact our business or reputation.

Compensation Governance Practices

We continue to implement and maintain leading practices in our compensation program, shareholder outreach and related areas.

What We Do	What We Don't Do
Caps on awards	No excessive executive perquisites
Multiple performance factors	No supplemental pension benefits for executives
Range of awards; not all or nothing	No single-trigger vesting in connection with a change-in-control for equity awards
Compensation recoupment (clawback) policy	No hedging or pledging or speculative transactions in our securities by directors and executive officers
Balance of short- and long-term incentives (through annual cash bonuses and equity awards)	No re-pricing of equity awards without shareholder approval
Executive and Non-Employee Director Stock Ownership Guidelines	No payment of dividends on unvested performance shares or units
Independent compensation consultant	No 280G gross-ups
Robust shareholder outreach	

Detailed Discussion and Analysis

Compensation Philosophy

Our MDCC regularly reviews the elements of the individual compensation packages for our chief executive officer and executive officers to achieve the following primary objectives:

- attract, retain and motivate talented, experienced and high-performing individuals across all areas of our business;
- align the interests of our executive officers with the interests of our shareholders as we seek to create value through the discovery, development and commercialization of transformative medicines; and
- ensure that the vast majority of compensation is tied to performance.

Our executive officers have had long and varied careers and possess diverse backgrounds and skills that make them extremely valuable members of our executive team and to our company as a whole. The stability and commitment of this team have been instrumental in building Vertex into the company it is today, with a leadership position in the treatment of CF, a pipeline of small molecule and cell and genetic therapies that has advanced significantly over the last several years, increasing revenues and a strong financial profile. All of these factors position Vertex to achieve its strategic objectives in future years.

Our MDCC and our board of directors seek to connect the achievement of our strategic objectives with our compensation program in a number of ways, including through detailed and measurable company goals that underlie our annual cash bonuses and the performance goals that are included in our equity awards. Our company goals involve a mix of goals relating to revenues from our current products, achievement of research and development objectives, our organizational capabilities and our financial strength. These objectives are selected specifically because they are considered by our board to be measurable milestones that our company must achieve if it is to maintain its significant revenue growth and superior profitability. Our MDCC and board expects to continue to seek to balance the use of financial metrics and research and development goals in order to motivate our executive team to achieve financial objectives, while providing appropriate incentives for our management to continue to make investments in our business for the long term.

In determining compensation, we consider compensation paid by similar companies as reference points, but do not strictly benchmark or target compensation at any particular level. Our MDCC retains flexibility to structure compensation based on good governance practices, our objectives of building our company and creating value for our shareholders.

Compensation Decision-Making Process

Role of MDCC and Chief Executive Officer in Setting Executive Compensation

The MDCC has responsibility for overseeing the design, development and implementation of the compensation program for our chief executive officer and other executive officers. The MDCC evaluates the performance of our chief executive officer and other executive officers. Our chief executive officer and our human resources group assist the MDCC in evaluating the performance of our other executive officers, including the NEOs other than the chief executive officer. Our chief executive officer does not make any recommendations to the MDCC regarding CEO compensation and does not participate in the portions of MDCC meetings or meetings of the board of directors when CEO compensation is discussed and determined. Similarly, our Executive Chairman does not make any recommendations to the MDCC regarding his compensation and does not participate in portions of MDCC meetings or meetings of the board of directors when Executive Chairman compensation is discussed and determined.

The members of the MDCC, each of whom is an independent director, make a recommendation regarding CEO compensation to the independent directors of the board, who together make final compensation decisions for the chief executive officer and other executive officers based on these assessments.

Role of Compensation Consultant

The MDCC (i) is directly responsible for the appointment and oversight of its compensation consultants, (ii) has the authority to determine the fees that we pay for services provided by such compensation consultants and (iii) prior to engaging any compensation consultant, considers applicable factors potentially affecting the independence of the compensation consultant, including the factors set forth in Nasdaq Marketplace Rule 5605(d)(3).

Annually, the MDCC engages a compensation consultant to conduct an analysis of all elements of our executive officer compensation compared to similar elements paid to similarly situated executives at companies in our peer group and to provide a written report and presentation of findings at the meeting of the MDCC that occurs in the summer each year. The compensation consultant also provides guidance on other matters that may arise from time to time and participates in regular discussions with the MDCC Chair, as requested. In 2020, the MDCC selected Pearl Meyer as its compensation consultant. Pearl Meyer is compensated for advice provided at the direction of the MDCC.

The MDCC considered the following information provided to it by Pearl Meyer:

- Pearl Meyer’s policies and procedures designed to prevent conflicts of interest;
- that fees paid by us to Pearl Meyer represent less than 1% of Pearl Meyer’s total annual revenues;

- the absence of business and personal relationships between the compensation consultant and the MDCC or any of our executive officers; and
- that Pearl Meyer's partners, consultants and employees who provide services to the MDCC, and their immediate family members, do not own shares of our common stock.

Based on these, and other factors considered by the MDCC, the MDCC determined that Pearl Meyer's work did not raise a conflict of interest.

Use of Peer Group Companies

In order to make judgments about elements of executive compensation on a competitive basis, the MDCC and our board of directors considers information about the compensation practices of a representative group of companies with whom we compete for executive talent, ("Peer Group"). We conduct a detailed analysis to select companies for this Peer Group on the basis of similarity and complexity of business model. Selecting a peer group for our company is difficult because of the limited number of companies that are similar in terms of complexity, including breadth of pipeline, variety of innovative therapies and level of revenues. As a result, we use a mix of quantitative and qualitative factors in order to establish our peers, including the following:

Factor Considered	What We Look For
Similar industry	Biotechnology or pharmaceutical industry
Importance of medicines to patients and society	Transformative medicines for serious diseases; therapeutics for unmet needs
Recognized focus on innovation	Breakthrough Therapy designations, priority review and/or other markers indicating unmet need
Global operations	Significant operations outside the U.S.
Commercial operations	Marketing and selling approved medicines
Significant R&D investment	Greater than $1B or 25% of revenue
Number of employees	Greater than 750 employees
Market capitalization and significance to broader economy	Market cap at least ¼ our size and/or inclusion on S&P 500 or NASDAQ 100
Labor market competitor	Companies we compete with for executive talent
Companies that use Vertex as a peer	Inclusion of Vertex in proxy reported peer group

Although we consider revenue as a factor, we do not emphasize it, as we do not believe it is an adequate reflection of whether companies have a similar business model or complexity particularly at our stage of maturity. A company with similar revenues may not have global or commercial operations like we have, or it may focus on generic medicines rather than innovative therapies; either of these factors would result in a different business model that required a relatively smaller investment in research and development. Moreover, companies with similar revenues may not focus on innovative therapies such as those designated as Breakthrough Therapies by the FDA, a designation which can expedite the development and review of medicines that are intended to treat serious conditions where preliminary clinical evidence indicates that the medicine may demonstrate substantial improvement over available therapy. As a result, we believe the factors listed above provide a better way to assess similarity versus a reliance on the combination of revenue and industry. We also note that it is unlikely for companies to align on all the factors listed above, so we look for companies meeting a majority of the criteria although we place greater weight on companies focused on innovation and importance of medicines to patients and society as we believe these are the key drivers of our business model. On a regular basis, we review and revise the list of companies with the goal of maintaining a group of comparators comprised of at least twelve companies.

As a result of this analysis, and on the basis of the criteria listed above, the MDCC selected the following comparator companies for 2020. In 2020, due to the acquisitions of Celgene Corporation and Shire plc, we added Eli Lilly and Company and SeaGen Inc. (formerly known as Seattle Genetics, Inc.) to our Peer Group. In 2021, we expect to make further changes due to the pending acquisition of Alexion Pharmaceuticals, Inc.

2020 Peer Companies		
Abbvie Inc.	BioMarin Pharmaceutical Inc.	Jazz Pharmaceuticals plc
Alexion Pharmaceuticals, Inc.	Eli Lilly and Company	Regeneron Pharmaceuticals, Inc.
Alkermes plc	Gilead Sciences, Inc.	SeaGen Inc. (formerly known as Seattle Genetics, Inc.)
Amgen Inc.	Incyte Corporation	United Therapeutics Corporation
Biogen Inc.		

We believe, based on our discussions with major shareholders, that the Peer Group identified by the MDCC is consistent with our shareholders' views of our relevant peers in the biotechnology industry. In addition, the Peer Group companies have many of the business model characteristics that we seek in comparator companies as set forth in the following table.

Company Information		R&D Expense[1]		Operational Focus		Innovative and Importance of Medicines				Market Position	
Company	Industry	$ (millions)	% of Revenue	Global	Commercial	Orphan/ Unmet Clinical Need	Breakthrough Therapy Designations[2]	Innovative Approved Drugs in Last 9 Years[3]	Uses Vertex as Peer	Nasdaq 100	S&P 500
AbbVie	Biotech	$ 7,755	17%	✔	✔	✔	7	7			✔
Alexion	Biotech	$ 1,003	17%	✔	✔	✔	2	3	✔	✔	✔
Alkermes	Biotech	$ 395	38%	✔	✔	✔	—	2			
Amgen	Biotech	$ 4,207	17%	✔	✔	✔	1	7		✔	✔
Biogen	Biotech	$ 4,066	30%	✔	✔	✔	—	5	✔	✔	✔
BioMarin	Biotech	$ 628	34%	✔	✔	✔	1	3	✔		
Eli Lilly	Pharma	$ 6,746	27%	✔	✔	✔	3	9			✔
Gilead	Biotech	$ 10,895	44%	✔	✔	✔	4	8		✔	✔
Incyte	Biotech	$ 2,224	83%	✔	✔	✔	1	3	✔	✔	✔
Jazz	Pharma	$ 846	36%	✔	✔	✔	—	3	✔		
Regeneron	Biotech	$ 2,735	33%	✔	✔	✔	5	6	✔	✔	✔
SeaGen	Biotech	$ 827	38%	✔	✔	✔	4	2	✔	✔	
United Therapeutics	Biotech	$ 358	24%	✔	✔	✔	—	3	✔		
Vertex	Biotech	$ 1,830	29%	✔	✔	✔	8	5		✔	✔

(1) R&D Expense (including certain expenses related to intangible assets) and R&D Expense as a % of Revenue reflect the trailing data for the most recent four quarters as of December 31, 2020 per the S&P Capital IQ database.

(2) Per the Center for Drug Evaluation and Research (CDER) Breakthrough Therapy Approvals report, which lists approvals for breakthrough therapy designated drugs.

(3) Innovative drugs in the last eight years include: VIEKIRA PAK, IMBRUVICA, VENCLEXTA, ORILISSA, MAVYRET, RINVOQ and SKYRIZI (Abbvie), STRENSIQ, ULTOMIRIS and KANUMA (Alexion), ARISTADA and VUMERITY (Alkermes), AIMOVIG, BLINCYTO, XGEVA, PROLIA, KYPROLIS, PARSABIV, and EVENITY (Amgen), TECFIDERA, ALPROLIX, SPINRAZA, ELOCTATE and VUMERITY (Biogen), BRINEURA, PALYNZIQ and VIMIZIM (BioMarin), CYRAMZA, EMGALITY, JARDIANCE, OLUMIANT, PORTRAZZA, RETEVMO, REYVOW, TALTZ and VERZENIO (Eli Lilly), YESCARTA, SOVALDI, HARVONI, VEMLIDY, CAYSTON, ZYDELIG, BIKTARVY and VEKLURY (Gilead), JAKAFI, OLUMIANT and PEMAZYRE (Incyte), VYXEOS, DEFITELIO and ZEPZELCA (Jazz), DUPIXENT, LIBTAYO, PRALUENT, EYLEA, ZALTRAP and INMAZEB (Regeneron), PADCEV and TUKYSA (Seagen) and REMODULIN, ORENITRAM and UNITUXIN (United Therapeutics).

We do not strictly benchmark to a particular level of compensation relative to compensation levels at the Peer Group companies, but rather make a judgment about where each executive should fall in comparison with executives with similar responsibilities at the Peer Group companies. We believe this should mitigate concerns regarding our Peer Group including companies that have significantly higher revenues than our current revenues. The MDCC looks at Peer Group information to confirm that our compensation levels are competitive with those of the Peer Group companies and consistent with our compensation philosophy. In addition, the MDCC reviews broader industry specific executive compensation surveys published by Radford, Mercer SIRS and Willis Towers Watson, but does not make any material compensation decisions based on any particular company participants in such surveys.

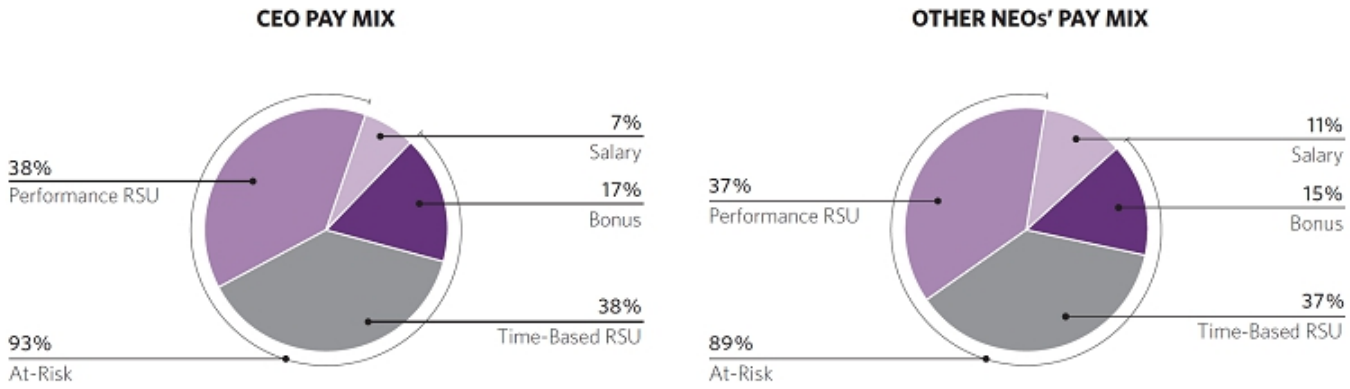
Elements of Annual Compensation

Our practice is to target total direct compensation including base salary, annual cash incentives targets and long-term incentive targets at market competitive levels depending upon the NEO's responsibilities, expertise and experience. At superior levels of performance, we aim for the design of our executive compensation program to result in actual total direct compensation at or above the seventy-fifth percentile of peer executives. Each year we review the balance of elements of our executive compensation program to ensure that they are appropriately designed in light of our goals to align the program with our shareholders' interests, the competitive environment and our business strategy.

Our executive compensation program uses a mix of long-term equity compensation awards to incent and reward those individuals who make the greatest contribution to our company performance over time. For the NEOs, this means compensation is primarily in the form of equity and directly tied to changes in shareholder value over time. For our 2020 equity grants, we maintained our mix of equity, which emphasizes performance restricted stock units and time-based restricted stock units.

Compensation Program

As shown in the following charts, our compensation program places an emphasis on performance-linked compensation, with approximately 90% of our NEO compensation tied to performance, or "at-risk" if performance is not achieved.



The charts above generally represent the values in the Summary Compensation Table for our NEOs using the target value for PSU grants instead of the fair value of these PSU grants. The CEO Pay Mix chart reflects the first equity grant Dr. Kewalramani received in February 2021 as CEO to provide a more accurate representation of our CEO compensation. These charts exclude the compensation of our Executive Chairman.

Performance-Linked Value-Based Program

We have a performance-linked program that is consistent with programs implemented by our peers and allows us to attract, retain and motivate talented and experienced individuals across all areas of our business. We focus on performance-linked elements as follows:

Compensation Element	Performance Link
Annual Cash Bonus	Annual bonus dependent on company performance factors and individual performance
Equity Awards	Grant date value of equity awards based on individual performance Value of shares granted based on target set by MDCC and Board, adjusted for individual performance ranging from 0% for below target individual performance, 100% at target performance, and up to 150% for above target individual performance
Performance Stock Unit Awards	• 50% of PSUs with range of shares issued **0% to 200%** of target based on one year financial metric (vesting in installments over a three-year period) • 50% of PSUs with range of shares issued **0% to 200%** of target based on three-year non-financial metrics (cliff-vesting after three years)
Time-Based Restricted Stock Units	• Value of awards increases or decreases based on increases or decreases in stock price

More specifically:

- **Performance Stock Units.** Our CEO and executive vice presidents ("EVPs") receive 50% of their annual target equity compensation in the form of PSUs. The PSUs vest, if at all, based half on financial goals (to date, CF net product revenue goals over a one-year period) and half on non-financial goals (to date, multiple clinical milestones over a three-year period). The financial PSUs vest over a three-year period and the non-financial PSUs cliff vest after three years. The potential shares earned pursuant to the performance stock unit awards range from 0% to 200% of the target shares with the number of shares actually issued based on financial and non-financial measures. The MDCC selected revenue and clinical development milestones because the MDCC determined that these milestones are important measurable metrics, the achievement of which would indicate successful execution toward our long-term strategic objectives and should build considerable shareholder value.
- **Time-based Restricted Stock Units.** Our CEO and EVPs receive 50% of their annual target equity compensation in the form of time-based restricted stock units which vest over a three-year period. With 50% of the annual long-term incentive award at risk pending successful execution of our strategic objectives, we believe that it is important to have a portion of the long-term equity annual award focused on retaining our key executive talent. As a result, we believe time-based restricted stock units encourage retention and focus on long-term value creation thereby aligning with the interests of our shareholders. In addition, we consider our time-vesting restricted stock unit awards to be performance based awards because the target number of restricted stock units awarded may be adjusted based on the corresponding executive's individual performance for the relevant performance period.

Maintenance of Broad-Based Equity Program While Reducing Dilution

Since our inception, we have compensated all eligible employees using a mix of cash and equity. The broad-based nature of our equity compensation program is an important element of our overall employee compensation program and reflects our philosophy that it is important for all of our employees to approach their jobs with a long-term commitment and perspective. Over the last several years, we have modified our equity

compensation programs. These modifications are consistent with modifications other biotechnology companies have made as they matured from development-stage companies to commercial-stage companies with a strong financial profile. As a result of these changes, we granted, on an absolute basis, equity awards representing 76% fewer shares of common stock in 2020 as compared to 2012 and reduced our "gross burn rate" from 3.6% in 2012 to 0.7% in 2020. These reductions were achieved while we significantly increased our headcount during this period.

Name	2012	2013	2014	2015	2016	2017	2018	2019	2020	% Change 2012 to 2020
	(in thousands, except percentages)									
Total Shares Granted Subject to Equity Awards	7,525	6,276	5,629	5,035	4,887	4,470	4,391	3,687	1,814	(76)%
Gross Burn Rate[1]	3.6%	2.8%	2.4%	2.1%	2.0%	1.8%	1.7%	1.4%	0.7%	
Awards Canceled, Forfeited or Expired	1,644	2,622	1,628	1,573	928	1,107	826	886	432	
Net Dilution	5,881	3,654	4,001	3,462	3,959	3,363	3,565	2,801	1,382	(77)%
Net Burn Rate	2.8%	1.6%	1.7%	1.4%	1.6%	1.4%	1.4%	1.1%	0.5%	

(1) "Burn rate" is defined as the number of equity awards granted in a specific year divided by the basic weighted average number of shares outstanding during that year.

Base Salary

The MDCC recommends base salaries for our executive officers based on multiple factors, including a competitive market analysis on a position-by-position basis. Annually, the MDCC reviews tables showing a comparison of each executive's prior year base salary and cash bonus opportunity, measured at the target level, to salaries and cash bonuses reported for executives with similar responsibilities at comparable companies. We do not strictly benchmark to a particular level of compensation relative to compensation levels at the Peer Group companies. Instead, our judgment about where each executive should fall in comparison with executives with similar responsibilities at the Peer Group companies takes into account the executive's general level of experience and capability, the significance of his or her job responsibilities to the achievement of our business strategy and company goals, and general performance over time, including demonstration of corporate values. On the basis of that information, including compensation at Peer Group companies, and taking into consideration the executive's base salary for the previous year, the MDCC recommends an appropriate salary for each executive officer, subject to final approval by our independent directors. Our current base salaries reflect each individual executive's past and expected future contributions, performance, experience, specific responsibilities relative to peer benchmarks and competitive positioning within the range around the median base salaries for peer counterparts in our Peer Group.

Dr. Kewalramani's base salary for 2020, as our CEO and President, was set at $1.15 million based on multiple factors, including her prior experience, her performance as our Executive Vice President and Chief Medical Officer and a competitive market analysis.

Pursuant to his employment agreement, Dr. Leiden's base salary for his first year as Executive Chairman was $1.0 million, and is reduced to zero for the second and third years of his term as Executive Chairman. Dr. Leiden's second year as Executive Chairman commenced on April 1, 2021.

In 2020, we maintained the base salary of $700,000 for Mr. Wagner, $725,000 for Dr. Altshuler, and $800,000 for each of Mr. Arbuckle and Mr. Parini.

Name	Base Salary
Reshma Kewalramani	$ 1,150,000
Jeffrey M. Leiden	$ 1,000,000
Charles F. Wagner, Jr.	$ 700,000
David Altshuler	$ 725,000
Stuart A. Arbuckle	$ 800,000
Michael Parini	$ 800,000

Company and Individual Ratings

The amounts for two of the principal elements of our executive compensation program - annual cash bonus and annual equity awards - are determined on the basis of annual company and individual performance ratings.

Overview of Company Performance Rating & Achievement in 2020

At the beginning of each year, our board of directors, in consultation with our CEO, establishes company-wide goals for that year. While our performance against these goals is the most important factor considered by our board in assessing our corporate performance, our board considers additional accomplishments and shortcomings and may increase or decrease the performance scores (although the company score may not exceed 150). The MDCC and our board of directors discuss and analyze the company's performance, including specific performance factors and accomplishment of company goals, and ultimately approve the company's annual performance rating.

For 2020, the board set company goals and assigned relative weights that reflected our operational, strategic and financial objectives for the year and the importance of these goals in achieving long-term growth and increasing profitability. Our revenue goals for marketed and approval stage products were designed to incentivize increasing access to our medicines through approvals of new transformative medicines, label-expansions for our existing medicines and obtaining government reimbursement in ex-U.S. markets and were not set, achieved through or dependent upon, price increases for our medicines. Our pipeline goals and our budgets were established with the expectation that we would reinvest in research and development and external innovation with the goal of developing additional transformative medicines.

Our 2020 weighted goals and the year-end score achieved by the company and assigned by the board are set forth in the following table:

Goal(s)	Maximum Score	Actual 2020 Performance Score
Marketed and Approval-Stage Products	**55**	**55**
• Achieve CF net product revenue goals through compliant marketing practices, including U.S. and ex-U.S. revenue goals • Successful U.S. launch of TRIKAFTA and strong start to E.U. launch of KAFTRIO		
Pipeline Growth	**60**	**43**
• Achieve proof-of-concept for two non-CF programs • Submit sNDA for triple combination in people with CF 6-11 years of age • Obtain approval in E.U. for KAFTRIO for people with CF 12 years and older • Obtain approval in E.U. for SYMKEVI for people with CF 6-11 years of age • Advance multiple non-CF development programs, including VX-880 • Advance multiple research programs, including CF and non-CF programs		
Organizational Development and Capability	**15**	**15**
• Fill critical positions with superior and diverse talent to support business growth • Improve infrastructure to support expanding business • Continue to ensure a strong compliance mindset and enterprise-wide risk management program		
Financial Strength	**20**	**20**
• Manage operating expenses and achieve financial targets		
Additional Accomplishments and Shortcomings, Net (see page 56 of this proxy statement)		**5**
TOTAL	**150**	**138**

Our 2020 company performance score was 138 out of a potential of 150. We did not change or adjust our goals in light of the COVID-19 pandemic. Our 2021 company performance will be evaluated against the broad categories set forth above, but with slightly different weighting with respect to Marketed and Approval-Stage Products (55 points), Pipeline Growth (65 points), Organizational Development and Capability (13 points) and Financial Strength (17 points).

Detailed Discussion of Company Performance Rating Factors and Achievements

Goals - Marketed and Approval-Stage Products

In 2020, CF net product revenues increased to $6.20 billion, up 49% as compared to 2019.

- Our CF net product revenues exceeded the mid-point of our initial CF net product revenues guidance by approximately $1.0 billion ($6.20 billion actual as compared to the mid-point of our initial guidance of $5.2 billion) as a result of the successful launch of TRIKAFTA and early approval of KAFTRIO in the E.U in the third quarter of 2020.

For marketed and approval-stage products goals, our board assigned the company a score of 55 out of 55, due to our exceeding our goals with respect to total CF net product revenues and the successful conclusion of reimbursement negotiations for our medicines in ex-U.S. markets.

Goals - Pipeline Growth (Late and Early-Stage)

Since the beginning of 2020, we made significant progress advancing our CF medicines, including providing improved treatment for people who are already eligible for one of our medicines.

- We obtained approval for KAFTRIO in the E.U. for people with CF 12 years of age and older.
- We expanded the eligibility of TRIKAFTA in the U.S. to include people with CF 12 years of age and older with certain rare mutations.
- We obtained approval for SYMKEVI in the E.U. for children 6-11 years of age.
- We obtained approval for KALYDECO in the E.U. for children with CF 6 months to 18 years of age with *R117H* mutation in the CFTR gene.
- We completed Phase 3 clinical trials evaluating our triple combination in children 6-11 years of age who have two *F508del* mutations or one *F508del* mutation and one minimal function mutation.

- We expanded eligibility in the U.S. for SYMDEKO to include people with CF 6 years of age and older, and KALYDECO to include infants 4 months of age and older, respectively.
- We expanded the eligibility in the E.U. for KALYDECO to include infants with CF four months of age and older and SYMKEVI in combination with KALYDECO to include children with CF 6 years of age and older.
- In January 2021, the FDA accepted and granted priority review of our sNDA for TRIKAFTA for the treatment of children with CF 6 to 11 years of age.

We also made significant progress advancing a broad pipeline of potentially transformative small molecule, cell and genetic therapies aimed at treating serious diseases. Since the beginning of 2020, we have made important progress in activities supporting these efforts.

- We progressed our Phase 2 clinical trial of VX-864, a small molecule drug candidate that we are evaluating as a potential treatment for AAT deficiency. We expect data from this trial in the first half of 2021.
- We initiated and progressed our Phase 2 clinical trial of VX-147, a small molecule drug candidate that we are evaluating as potential treatment for APOL1-mediated FSGS. We expect to see data from this trial in 2021.
- We achieved proof-of-concept for ex-vivo gene editing program with CTX001 in TDT and SCD.
- We obtained Priority Medicines Designation granted by the European Medicines Agency to CTX001 for the treatment of SCD.
- We filed an IND for VX-880, a cell-based therapy program as potential treatments for T1D. In March 2021, we initiated a Phase 1/2 clinical trial to evaluate VX-880 in people who have T1D with impaired hypoglycemic awareness and severe hypoglycemia.

Partially offsetting these achievements, were challenges advancing select molecules into the clinic due to the COVID-19 pandemic and delivering proof-of-concept for VX-814, the development of which was discontinued during Phase 2.

> ***On the basis of the accomplishments in advancing our research and development programs and, in particular the early approval of KAFTRIO, the achievement of proof-of-concept in TDT and SCD, and the advancement of multiple small molecule drug candidates and our cell and genetic therapies, and also taking into account shortcomings including the discontinuance of VX-814 for the treatment of AAT deficiency as well as delays in advancing select molecules due to COVID-19, our board assigned the company a score of 43 out of 60 for our pipeline growth goal.***

Goals - Organizational Development and Capability

Talent and expertise

We strengthened our organizational capabilities by attracting, developing and retaining the key talent necessary to operate our business, including filling 15 of 15 critical hires with superior and diverse talent.

Systems and Infrastructure

We continued improvement of infrastructure to support an increasingly complex organization, including enhancing policies, software platforms and business processes, while also adapting to the challenges of the COVID-19 pandemic.

Ethics and Compliance

We continued to promote effective governance, communication and training to support our company-wide compliance and risk management programs.

> ***To reflect the improvements to our organizational structure, processes and systems achieved in 2020, our board assigned the company a score of 15 out of 15 for our organizational development and capability goals.***

Goals - Financial Strength

We exceeded all of our financial goals in 2020. We increased our net product revenues to $6.20 billion, a 49% increase from 2019 and managed our operating expenses resulting in a GAAP operating margin of 46% and a non-GAAP operating margin of 56% (*see Appendix A for a reconciliation of non-GAAP figures*). As a result, we ended 2020 with cash, cash equivalents and marketable securities of approximately $6.7 billion, an increase of approximately $2.9 billion from 2019.

> ***As a result of our strong financial performance, including increasing revenues and managing operating expenses, our board assigned the company a score of 20 out of 20 for our financial strength goals.***

Additional Factors (accomplishments and/or shortcomings)

In connection with determining our 2020 company rating, our board of directors made positive and negative adjustments based on factors not anticipated when the company's original goals for 2020 were established. By design, the potential adjustment is capped at ±10% (or ±15 points) and used by the board to address and highlight important achievements and or shortcomings. The positive adjustments were primarily related to our success in significantly exceeding our forecasted net product revenue goal, obtaining multiple reimbursement agreements for KAFTRIO in important markets outside of the U.S., and successful leadership and management of our company by our executive team during the global

COVID-19 pandemic, including effectively establishing remote IT systems, hiring and onboarding talent virtually, and coordinating on-site issues. Overall, the board of directors increased our company rating by six points for positive additional accomplishments, which was offset by a one point downward adjustment related to a negative factor. As a result, our final company rating was increased by 5 points to a total of 138 points.

2020 Individual Performance Ratings - Overview

The MDCC evaluates executives' individual performance on a "results-based, values-tempered" basis, which takes into account not only "what" was accomplished, but "how" it was accomplished. The results-based component evaluates the executive officer's performance in his or her individual role and as a leader of our company in achieving our objectives. The possible individual results-based performance ratings are "not building," "building," "strong" or "leading." The values-tempered component of the individual evaluations builds upon our company core values: "uncompromising commitment to patients;" "innovation is our lifeblood;" "fearless pursuit of excellence" and "we wins" and are considered along with our leadership competencies which reflect our core values and leadership behaviors that we believe lead to successful execution of our strategy and continued emphasis on innovation and collaboration. We expect all employees to demonstrate our company core values and leadership behaviors in all aspects of job performance. We further expect that our executives will be stewards of our company culture, and the performance ratings assigned to them incorporate our board's assessment of the strength of their leadership with respect to, and demonstration of, values-based behavior. This evaluation results in ratings of "not demonstrating," "living the values" or "exemplary demonstration." The possible individual performance ratings under this program are as set forth in the following table:

		RESULTS EVALUATION			
		RESULTS - Not Building	RESULTS - Building	RESULTS - Strong	RESULTS - Leading
Values Evaluation	Exemplary Demonstration	Not Possible	Strong	Leading	Leading Exemplary
	Living the Values	Not Building	Building	Strong	Leading
	Not Demonstrating	Not Building	Not Building	Building	Not Possible

The 2020 results-based rating recommendation for each NEO, other than our CEO and Executive Chairman, is the combined result of the MDCC members' own observations and a review of the executive's role in the accomplishment of the corporate goals and recommendations, the latter of which is provided to the MDCC by our chief executive officer and is made on the basis of her independent assessment of each executive officer's performance. The MDCC, Dr. Leiden and Dr. Kewalramani discussed each recommendation at length, on both an individual and comparative basis. Upon completion of these discussions, the MDCC finalized its recommendation for the results-based rating for each executive. The final recommendations took into account Dr. Kewalramani's and Dr. Leiden's recommendations, the opinions of MDCC members (based on the executive's contributions and the MDCC members' interactions with the executive), as well as other factors. The MDCC gave Dr. Kewalramani's recommendations greater weight when determining the behaviors-based rating than when determining the results-based rating, as the behaviors-based rating is pertinent to the executive's daily interactions in carrying out his or her duties. Furthermore, the MDCC believes that, in her role as CEO, Dr. Kewalramani had greater visibility than the MDCC members into the quality of these interactions. Taking into account all of the factors raised in the discussion and the assigned individual performance rating, the MDCC assigns an individual performance factor for each NEO within the ranges set forth above. While the individual ratings are not 100% objective, we view them as critical factors indicative of management success and crucial to achieving the more objective goals discussed above. The results-based and behaviors-based evaluations for our CEO and Executive Chairman are based on a similar assessment of individual performance by our MDCC and independent directors.

2020 Actual Individual Ratings for Named Executive Officers

Dr. Reshma Kewalramani	2020 Rating:		Leading
Chief Executive Officer and President	2020 Salary:	$	1,150,000
(EVP and CMO through March 31, 2020)	2020 Bonus:	$	2,723,292
	LTI Equity Grants (Feb 2021):	$	12,485,000

On the basis of the MDCC's recommendation, our independent directors rated Dr. Kewalramani's overall performance for 2020 as "leading", with an individual performance factor of 143%. The performance rating for Dr. Kewalramani combined a "strong" results-based rating with an "exemplary demonstration" behaviors-based rating. Dr. Kewalramani's rating derived from her leadership of our executive team in 2020, including:

- Leadership in executing our corporate strategy to develop transformative medicines for serious diseases and achieving our business goals
- The substantial over-achievement of our financial goals including significantly increasing CF net product revenues, strengthening our balance sheet, expanding our operating margins, and increasing operating income
- The advancement of our CF programs, including the early approval of KAFTRIO outside of the U.S. and progress with respect to the CF pipeline
- Leadership in the advancement of our non-CF clinical development pipeline, including advancing the development of VX-864 and VX-147, and significant and rapid progress in the CTX001 and T1D clinical programs
- Exhibiting outstanding leadership qualities and advancing Vertex's values, including exemplary management and coordination throughout the COVID-19 pandemic

Dr. Jeffrey Leiden	2020 Rating:		Leading
Executive Chairman	2020 Salary:	$	1,000,000
(CEO and President through March 31, 2020)	2020 Bonus:	$	1,973,400
	Equity Grants (Feb 2021):	$	9,000,000

On the basis of the MDCC's recommendation, our independent directors rated Dr. Leiden's overall performance for 2020 as "leading," with an individual performance factor of 143%. The performance rating for Dr. Leiden combined a "strong" results-based rating with an "exemplary demonstration" behaviors-based rating. The rating derived principally from his leadership as Executive Chairman of our Board and his focus on our strategy and business development, our cell and genetic therapy efforts, and government and community affairs activities, which included:

- Exhibiting outstanding personal and leadership qualities and embodying Vertex's core values in enabling the successful stewardship of our company over the last year
- Collaborating with Dr. Kewalramani, the other members of our executive team, and the board to ensure a successful CEO transition
- Meaningfully advancing business development transactions that helped progress our pipeline and research programs, including collaborations with Affinia Therapeutics, Skyhawk Therapeutics and Moderna
- Leading the establishment and growth of the Vertex cell and genetic therapies organization
- Coordinating, as the chair of our board, clear, open and constructive communication between our board and management regarding key business and strategic issues

Charles F. Wagner, Jr.	2020 Rating:		Leading
EVP, Chief Financial Officer	2020 Salary:	$	700,000
	2020 Bonus:	$	946,680
	LTI Equity Grants (Feb 2021):	$	5,000,000

The MDCC recommended and the board adopted an overall rating of "leading" for Mr. Wagner based on a results-based rating of "leading" and a behaviors-based rating of "living the values" with an individual performance factor of 140%. Mr. Wagner's rating derived from his leadership of the finance, accounting, investor relations and operations organizations, including the following:

- Overseeing an outstanding financial year for Vertex, including managing operating expenses in accordance with our budget and guidance and successfully managing our capital allocation
- Successfully completing the integration of our two significant acquisitions, Exonics and Semma
- Successfully progressing construction of the Vertex Cell and Genetic Therapies buildings and facilitating the purchase of the continuous manufacturing facility
- Recruiting and developing multiple new senior members of the finance organization
- Exhibiting outstanding leadership qualities throughout the COVID-19 pandemic, including as an executive leader of the COVID Management Team

Dr. David M. Altshuler	2020 Rating:		Leading
EVP, Global Research and Chief Scientific Officer	2020 Salary:	$	725,000
	2020 Bonus:	$	1,015,508
	LTI Equity Grants (Feb 2021):	$	5,000,000

The MDCC recommended and the board adopted an overall rating of “leading” for Mr. Altshuler based on a results-based rating of “strong” and a behaviors-based rating of “exemplary demonstration” with an individual performance factor of 145%. Mr. Altshuler’s rating derived principally from his leadership of the research organization with respect to the following:

- The excellent performance of our internal research organization in advancing multiple programs toward the clinic
- Advancing collaborations with CRISPR, Moderna, and Affinia Therapeutics to progress our pipeline and research programs
- Significantly expanding the company’s expertise in various therapeutic modalities through internal research, recruiting and collaborations
- Collaborating with senior management to evolve Vertex’s cell and genetic therapy programs, including important progress in our beta thalassemia, sickle cell, and T1D programs
- Meeting or exceeding corporate goals related to pipeline diversification, including adding to our targeted disease areas
- Exhibiting outstanding leadership qualities throughout the COVID-19 pandemic, including as an executive leader of the COVID Management Team

Stuart A. Arbuckle	2020 Rating:		Leading Exemplary
EVP, Chief Commercial and Operations Officer	2020 Salary:	$	800,000
	2020 Bonus:	$	1,159,200
	LTI Equity Grants (Feb 2021):	$	6,000,000

The MDCC recommended and the board adopted an overall rating of “leading exemplary” for Mr. Arbuckle based on a results-based rating of “leading” and a behaviors-based rating of “exemplary demonstration” with an individual performance factor of 150%. Mr. Arbuckle’s rating derived from his leadership of the commercial organization, including the following:

- Delivering CF net product revenues of $6.2 billion in 2020, up 49% compared to 2019 and exceeding our initial revenue forecast by more than $1.0 billion
- Overseeing the continued U.S. launch of TRIKAFTA for patients 12 years of age with the vast majority of eligible patients on TRIKAFTA by year end
- Successfully leading the launch of KAFTRIO in the E.U. after receiving early approval for the medicine
- Obtaining reimbursement for KAFTRIO in several critical ex-U.S. markets, including the U.K.
- Enhancing the Company’s manufacturing capabilities, including for cell and genetic therapy, by recruiting an outstanding new leader of our manufacturing organization, focused internal organization and advancements in external partnerships

Michael Parini	2020 Rating:		Leading
EVP, Chief Administrative,	2020 Salary:	$	800,000
Legal and Business Development Officer	2020 Bonus:	$	1,081,920
	LTI Equity Grants (Feb 2021):	$	5,000,000

The MDCC recommended and the board adopted an overall rating of “leading” for Mr. Parini based on a results-based rating of “strong” and a behaviors-based rating of “exemplary demonstration” with an individual performance factor of 140%. Mr. Parini’s rating derived principally from his leadership of the legal, compliance, human resources, corporate communications, global information technology, and business development groups with respect to the following:

- Continuing to enhance the legal and compliance groups to meet the Company’s evolving legal and compliance needs
- Developing and implementing a new global information services (“GIS”) strategy and operating model and recruiting a new leader of our GIS organization
- Successfully executing collaborations with Affinia Therapeutics, Skyhawk Therapeutics and Moderna to advance our work in genetic therapies
- Spearheading our recruiting efforts, which resulted in over 600 hires, including all critical hires, with the majority of new employees hired and onboarded virtually in light of the pandemic
- Exhibiting outstanding leadership qualities throughout the COVID-19 pandemic, including as an executive leader of the COVID Management Team

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Annual Cash Bonus

The cash bonus for each NEO (referred to in the *Summary Compensation Table* on page 66 of this proxy statement as "Non-Equity Incentive Plan Compensation") is calculated by multiplying the NEO's target bonus by both the company performance factor and the individual performance factor, in accordance with the following formula in 2020:

Target Cash Bonus				Performance Factors				Cash Bonus
Base Salary	×	Individual Incentive Target (expressed as a percentage of base salary)	×	Company Performance Factor (expressed as a percentage of the target bonus)	×	Individual Performance Factor (expressed as a percentage of the target bonus)	=	Annual Cash Bonus Award
		70%-120% based on role		0%-150%		0-150%		

The individual incentive targets were established, and are reviewed annually, by the MDCC based on available data about Peer Group company compensation. Dr. Kewalramani's individual incentive target was 120% for 2020. Dr. Leiden's individual incentive target was 100% for 2020, and he will not be eligible for a cash bonus for 2021 or 2022 performance. The individual incentive target for each of our other NEOs remained at 70% during 2020. The resulting target annual bonuses of our executives approximate the median target annual bonuses for comparable executives at peer companies.

Company performance factors are determined annually and range from 0% to 150%. The possible individual ratings and corresponding individual performance factor ranges for our executive officers in 2020 are set forth in the table below:

Individual Rating	Individual Performance Factor
Not Building	0%
Building	50%-80%
Strong	80%-120%
Leading	120%-150%
Leading/Exemplary	140%-150%

On the basis of the factors described above, our independent directors approved, upon the MDCC's recommendation, individual performance factors and annual bonus awards for each of the NEOs, on account of 2020 performance, as set forth in the table below.

Name	2020 Base Salary		Individual Incentive Target		2020 Target Bonus		Company Performance Factor		Individual Performance Factor		2020 Performance Cash Bonus
Reshma Kewalramani	$ 1,150,000	x	120%	=	$ 1,380,000	x	138%	x	143%	=	$ 2,723,292
Jeffrey M. Leiden	$ 1,000,000	x	100%	=	$ 1,000,000	x	138%	x	143%	=	$ 1,973,400
Charles F. Wagner, Jr.	$ 700,000	x	70%	=	$ 490,000	x	138%	x	140%	=	$ 946,680
David Altshuler	$ 725,000	x	70%	=	$ 507,500	x	138%	x	145%	=	$ 1,015,508
Stuart A. Arbuckle	$ 800,000	x	70%	=	$ 560,000	x	138%	x	150%	=	$ 1,159,200
Michael Parini	$ 800,000	x	70%	=	$ 560,000	x	138%	x	140%	=	$ 1,081,920

Annual Equity Awards

Value-Based Guidelines for Annual NEO Equity Grants

Under our program, our CEO and EVPs were eligible for awards with the following target values based on 2020 performance:

	Not Building	Building	Strong	Leading	Leading Exemplary
CEO	$ —	$ 5,500,000	$ 11,000,000	$ 12,485,000	$ 13,970,000
EVP	$ —	$ 2,000,000	$ 4,000,000	$ 5,000,000	$ 6,000,000

The MDCC set a target equity value for Dr. Kewalramani, our CEO, of $11.0 million, and maintained the target equity value of $4.0 million for our EVPs. The number of shares subject to the time-vested restricted stock units and performance stock units is based on the fair value of our common stock on the date of grant. Dr. Leiden received equity grants of $9.0 million in the first quarter of 2021 pursuant to the terms of his employment agreement and will receive equity grants of $8.5 million in the first quarter of 2022 and $6.5 million in the first quarter of 2023 for his role as Executive Chairman.

February 2021 Grants Based on 2020 Performance

In February 2021, our independent directors approved, upon the MDCC's recommendation, individual performance factors and equity awards for 2020 performance for each of the NEOs set forth in the table below. Dr. Leiden's equity awards were determined by his employment agreement as described above.

Name	Individual Performance Rating	Performance-Based RSU (50%)	Time-based RSU (50%)	Total Equity Value
Reshma Kewalramani	Leading	$ 6,242,500	$ 6,242,500	$ 12,485,000
Charles F. Wagner, Jr.	Leading	$ 2,500,000	$ 2,500,000	$ 5,000,000
David Altshuler	Leading	$ 2,500,000	$ 2,500,000	$ 5,000,000
Stuart A. Arbuckle	Leading Exemplary	$ 3,000,000	$ 3,000,000	$ 6,000,000
Michael Parini	Leading	$ 2,500,000	$ 2,500,000	$ 5,000,000

Performance Units Results Table

We annually grant one-year financial-based performance restricted stock unit awards and three-year non-financial based performance restricted stock unit awards. We believe the combination of the one-year financial and three-year non-financial PSUs provides an appropriate balance of near- and long-term incentives for our management team. Our near-term objective of growing our CF business through increasing the number of patients eligible and able to receive our medicines complements our long-term strategic objectives, which require the reinvestment of revenues into research and development in order to develop additional transformative medicines for serious diseases.

The final performance multipliers for our 2020 financial-based performance restricted stock unit awards were determined by the MDCC and applied to the target units granted to determine the actual units earned and eligible to vest with a payout of 200% in February 2021. The following chart shows the pre-established financial goals and the actual results for the financial-based performance restricted stock unit awards granted in 2020:

Award Year	Company Goal	Below Threshold 0% Payout	Threshold 50% Payout	Target 100% Payout	Max 200% Payout	Results CF Revenue	Results Payout
2020	2020 CF Net Product Revenues	<$5.045 billion	$ 5.045 billion	5.205 to $ $5.225 billion	$ 5.4 billion	$ 6.20 billion	200.0%

Consistent with our philosophy of aligning compensation with performance in 2020, a year in which we substantially exceeded our CF net product revenue expectations, the payout on our one-year financial PSU awards achieved the maximum level.

The performance goals for the 2018 non-financial based performance restricted stock unit awards were established in February 2018 and our performance against these goals was determined in the first quarter of 2021. There were three non-financial goals and achievement of one goal would have resulted in a 50% payout, achievement of two goals would have resulted in a 100% payout and achievement of three goals resulted in a payout of 200%.

2018	CF Portfolio Milestone - Approval of TRIKAFTA in the U.S.	Achieved
	Complete a clinical trial designed to establish proof-of-concept for a nucleic acid therapy	Achieved
	First subject is dosed in a pivotal clinical trial for a drug candidate that is not a CFTR modulator	Achieved

The performance multiples for the 2019, 2020 and 2021 non-financial based performance restricted stock unit awards will be determined in the first quarter of 2022, 2023 and 2024, respectively, based on performance over the relevant three-year performance period. The non-financial goals contained in our three-year performance restricted stock unit awards for 2019, 2020 and 2021 are not disclosed for competitive reasons and because the relevant performance periods are ongoing.

Other Compensation Arrangements

Benefits

Our executives are eligible to participate in all of our benefit plans and programs on the terms made generally available to our employees, including medical insurance, dental insurance, payment of life insurance premiums, disability coverage, equity programs, including a career employment/ retirement provision and participation in our employee stock purchase plan and eligibility for matching contributions, subject to an annual $25,000 limit, to qualified charitable organizations pursuant to the Vertex Foundation Matching Gift Program. We have a defined contribution—a 401(k)—plan, in which our NEOs are eligible to participate. We make matching contributions to the 401(k) plan. The formula for determining the amount of our matching contributions is the same for our NEOs as for our other employees (and are subject to the same statutory maximum), but the actual contributions made to the accounts of our NEOs generally are at the top end of the range, due to the executives' higher salaries and correspondingly higher cash contribution levels. Other than the retirement provision under our equity program available to all employees, we do not provide any retirement benefits to our executive officers.

Employment Agreements and Post-Termination Compensation and Benefits

The initial compensation terms for newly hired members of our executive team are the result of negotiations between us, in consultation with the MDCC and our board of directors, and the executive being hired. In general, each newly hired executive team member enters into an employment agreement and a change of control agreement and is granted a restricted stock unit award and/or a stock option award, and in some cases a cash sign-on bonus, reimbursement of moving expenses, and other benefits. We also enter into employment and change of control agreements with EVPs who are promoted to our executive team, on the basis of standard terms and conditions that have been recommended by our MDCC and approved by our board for such circumstances. We have entered into agreements providing for severance and change of control payments with each EVP on our executive team because we believe that they are a fair and effective way to allow our executives to maintain focus on our business in the face of market and other volatility in our industry.

In general, each employment arrangement provides for cash severance and continuation of certain employee benefits in the event that an executive's employment is terminated by us without cause or is terminated by the executive for good reason. We use a "double trigger" with respect to benefits that are to be provided in connection with a change of control. A change of control does not itself trigger benefits; rather, benefits are paid only if the employment of the executive is terminated by us other than for cause, death or disability, or by the executive for good reason, during a specified period before or after a change of control. We believe a "double trigger" benefit maximizes shareholder value because it prevents a windfall to executives in the event of a change of control in which the executive retains significant responsibility as defined in his or her individual agreement, while still providing our executives appropriate incentives to cooperate in negotiating any change of control that may put their jobs at risk.

We offer a company-wide program that provides for accelerated vesting of equity awards held by qualified retirement-eligible participants. Equity awards granted, including those granted to our NEOs, contain a retirement vesting provision, under which a "qualified" participant who retires under the terms of the provision will receive accelerated vesting of an additional number of shares underlying the award, equal to the sum of (x) 50% plus 10% for each year of service in excess of five full years of service multiplied by (y) the number of unvested shares subject to the award. A "qualified" participant is a participant who is at least age 55 and has completed at least five full years of service or whose age plus full years of service is 65 or greater and who, has completed a mandatory transitional period of employment with the company following notice of his or her planned termination of service.

In addition to the benefits that only accrue in connection with a change of control, our agreements with our executive officers provide benefits if we terminate their employment with us without cause or they terminate their employment with us for good reason, as such terms are defined in the applicable agreement with the executive officer. A further discussion of the terms and projected payments under each of our agreements with our NEOs is set forth below under the heading *Employment Contracts and Change of Control Arrangements*.

Tax Considerations

We would like our compensation program to be reasonably cost and tax effective. To the extent consistent with our other goals, we seek to preserve corporate tax deductions, while maintaining the flexibility to approve compensation arrangements that we believe are in the best interests of the company and our shareholders. Following the introduction of U.S. tax reform, the performance-based exceptions and $1 million salary threshold for covered executives under Section 162(m) have been repealed. We continue to grant performance-based compensation as important elements of our compensation program that align corporate shareholder and company interests, even though these awards may not result in full tax deductibility.

Compensation Practices

Equity Grant Practices

Our board of directors generally grants annual equity awards to NEOs at a board meeting scheduled in advance for early February. Scheduling decisions are made without regard to anticipated earnings or other major announcements by the company. For all value-based equity grants, we convert value to shares on the date of grant using the average of the high and low price for the common stock on the day the equity grant is awarded.

Newly hired employees, including executive officers, are sometimes granted restricted stock units effective on the first day of employment. The employees' start dates are scheduled without regard to anticipated earnings or other major announcements by the company.

Compensation Recoupment ("Clawback") Policy

We have adopted a recoupment or clawback policy providing that, if our board of directors determines that an executive officer engaged in fraud or intentional misconduct that resulted in an incorrect determination that an incentive compensation performance goal had been achieved, the board may take appropriate action to recover from such executive officer any compensation that resulted from such determination. The board may require repayment for any bonus, equity or incentive compensation awarded to an executive officer who engaged in the fraud or intentional misconduct to the extent it was based on such incorrect determination.

Stock Ownership Guidelines

We have stock ownership guidelines for our NEOs and guidelines for our non-employee directors, as discussed in *Non-Employee Director Stock Ownership Guidelines* on page 31 of this proxy statement. The guidelines for our NEOs are set forth in the following table:

Employee	Minimum Shareholding Requirement
Chief Executive Officer and Executive Chairman	6X base salary
Executive Vice Presidents	4X base salary

Individual holdings, and holdings of immediate family members, of (a) common stock, (b) unvested restricted stock units and (c) shares held through our 401(k) plan count toward meeting these guidelines. As of March 31, 2021, each of our NEOs satisfied the individual holding requirements.

Anti-Hedging and Pledging Policy

Our Insider Trading Policy prohibits all of our directors and employees, including our NEOs, from (i) short selling or hedging our securities, (ii) purchasing or selling derivative securities based on our securities and (iii) pledging our securities.

Risk Mitigation

Our MDCC reviews the risks and rewards associated with our compensation programs. The programs are designed with features that mitigate risk without diminishing the incentive nature of the compensation. We believe our compensation programs encourage and reward prudent business judgment and appropriate risk-taking over the short term and the long term. Our MDCC regularly evaluates the risks involved with our compensation programs and does not believe that any of our compensation programs create risks that are reasonably likely to have a material adverse effect on our company.

Risk Mitigation Factors

We believe that our annual cash bonus and long-term equity compensation programs, which account for most of our executive officers' compensation, contain appropriate risk mitigation factors, as summarized below:

What We Do	What We Don't Do
Caps on awards	No excessive executive perquisites
Multiple performance factors	No supplemental pension benefits for executives
Range of awards; not all or nothing	No single-trigger vesting in connection with a change-in-control for equity awards
Compensation recoupment (clawback) policy	No hedging or pledging or speculative transactions in our securities by directors and executive officers
Balance of short- and long-term incentives (through annual cash bonuses and equity awards)	No re-pricing of equity awards without shareholder approval
Executive and Non-Employee Director Stock Ownership Guidelines	No payment of dividends on unvested performance shares or units
Independent compensation consultant	No 280G gross-ups
Robust shareholder outreach	

Emphasis on Long-term Value Creation and Mitigation of Short-term Risk Taking

Our board believes that a key element of its risk oversight responsibilities is ensuring that our executive compensation program encourages implementation of our corporate strategy of investing in scientific innovation to create transformative medicines for people with serious disease and discourages decisions focused on creating short-term financial gains at the expense of long-term value creation. The board reviews our business performance, focusing on financial metrics and non-financial metrics, as well as other strategic factors including talent development and diversity to ensure our leaders are focusing on long-term growth in a manner aligned with our values.

Our MDCC reviews the performance of our executive officers using the above metrics. It also oversees the design of our executive compensation programs to ensure that our executive compensation program does not incentivize our executive officers, either individually or as a group, to make excessively risky business decisions that could maximize short-term results at the expense of long-term value. The independent directors who serve on the MDCC are informed of our most significant risks, including those associated with research and development of new medicines, competition and the pricing of our medicines. Our MDCC, in consultation with its independent compensation consultant, ensures that our executive compensation programs are aligned with our long-term strategy and do not incentivize overly risky behavior.

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MANAGEMENT DEVELOPMENT AND COMPENSATION COMMITTEE REPORT

The Management Development and Compensation Committee has reviewed the Compensation Discussion and Analysis and discussed that analysis with management. Based on its review and its discussions with management, the Management Development and Compensation Committee recommended to Vertex's Board of Directors that the Compensation Discussion and Analysis be included in Vertex's proxy statement for its 2021 annual meeting of shareholders and incorporated by reference into Vertex's Annual Report on Form 10-K for the year ended December 31, 2020. This report is provided by the following directors who comprise the Management Development and Compensation Committee:

Bruce I. Sachs (Chair)
Terrence C. Kearney
Yuchun Lee

COMPENSATION AND EQUITY TABLES

Summary Compensation Table

The following table provides summary information concerning compensation each of our NEOs for 2020, 2019 and 2018. On April 1, 2020, Dr. Reshma Kewalramani became our CEO and President and Dr. Jeffrey Leiden transitioned from the role of CEO and President to the role of Executive Chairman.

Name and Principal Position	Year	Salary	Bonus	Stock Awards[1]	Option Awards[1]	Non-Equity Incentive Plan Compensation	All Other Compensation	Total
Reshma Kewalramani CEO and President (EVP & Chief Medical Officer through March 31, 2020)	2020	$1,097,308	$ —	$ 5,250,411	$ —	$ 2,723,292	$ 40,348	$ 9,111,359
	2019	$ 702,308	$ —	$ 3,215,952	$1,575,011	$ 1,260,000	$ 63,665	$ 6,816,936
Jeffrey M. Leiden Executive Chairman (CEO and President through March 31, 2020)	2020	$1,121,539	$ —	$13,335,168	$ —	$ 1,973,400	$ 43,138	$16,473,245
	2019	$1,300,000	$ —	$ 9,334,681	$4,572,039	$ 3,510,000	$ 73,265	$18,789,985
	2018	$1,300,000	$ —	$ 9,800,288	$4,243,973	$ 3,440,151	$ 14,735	$18,799,147
Charles F. Wagner, Jr.[2] EVP & Chief Financial Officer	2020	$ 726,923	$ —	$ 4,375,585	$ —	$ 946,680	$ 41,202	$ 6,090,390
	2019	$ 492,692	$ 140,000	$ 1,225,383	$ 600,039	$ 992,250	$ 36,849	$ 3,487,213
David Altshuler EVP & Global Research and Chief Scientific Officer	2020	$ 752,885	$ —	$ 5,250,411	$ —	$ 1,015,508	$ 41,780	$ 7,060,584
Stuart A. Arbuckle EVP & Chief Commercial and Operations Officer	2020	$ 830,769	$ —	$ 5,250,411	$ —	$ 1,159,200	$ 42,598	$ 7,282,978
	2019	$ 770,962	$ —	$ 3,215,952	$1,575,011	$ 1,260,000	$ 37,608	$ 6,859,533
	2018	$ 721,923	$ —	$ 2,625,244	$1,136,785	$ 824,175	$ 38,965	$ 5,347,092
Michael J. Parini (EVP & Chief Administrative, Legal and Business Development Officer through March 1, 2021)	2020	$ 830,769	$ —	$ 4,375,585	$ —	$ 1,081,920	$ 67,404	$ 6,355,678
	2019	$ 785,481	$ —	$ 2,679,897	$1,312,509	$ 1,218,000	$ 43,610	$ 6,039,497
	2018	$ 746,923	$ —	$ 2,625,244	$1,136,785	$ 823,384	$ 29,000	$ 5,372,336

(1) Pursuant to applicable SEC rules, the grant-date fair values of the equity awards granted in February 2020 for 2019 performance are included in 2020 compensation. Equity awards granted in February 2021 to Dr. Kewalramani, Mr. Wagner, Dr. Altshuler, Mr. Arbuckle and Mr. Parini for 2020 performance and the equity awards granted to Dr. Leiden pursuant to his employment agreement are not reflected in the Summary Compensation Table above and the value of those awards for our 2021 NEOs will be reflected in the Summary Compensation Table for next year's proxy.

(2) Mr. Wagner joined Vertex as our EVP and Chief Financial Officer in April 2019.

Bonus

Pursuant to applicable SEC rules, the annual cash bonuses earned by our NEOs are set forth under the caption "Non-Equity Incentive Plan Compensation." Other bonuses, such as sign-on bonuses, are listed separately under the caption "Bonus."

Stock Awards and Options Awards

The amounts set forth under the captions "Stock Awards" and "Option Awards" in the table above represent the grant-date fair value of awards granted during the applicable fiscal year. Each year, the equity awards reflected in the Summary Compensation Table for a specific year reflect equity grants made early in that calendar year based on the executive's performance in the year prior to the year the equity grants are awarded. Because a majority of our executive's compensation is in the form of equity awards, the total compensation reflected in each executive's compensation for 2020 in the table above is significantly affected by his or her performance during 2019. Our methodology for determining the grant-date fair value, including underlying estimates and assumptions for calculating these values and specifically the estimates used to apply the Black-Scholes option pricing model, is set forth in Note N to our consolidated financial statements included in our 2020 Annual Report on Form 10-K filed with the SEC on February 11, 2021.

The “Stock Awards” for 2020 consist of performance stock unit (“PSU”) awards and time-vested restricted stock unit awards granted in February 2020. In 2020, the non-financial PSU awards had a grant-date fair value of 50% of the fair value of the target shares, in accordance with U.S. GAAP. If the grant-date fair value of the non-financial PSU awards had been 100% of the fair value of the target shares, it would increase the amounts set forth in the table above by $1.9 million for Dr. Leiden, $750,000 for each of Dr. Kewalramani, Dr. Altshuler and Mr. Arbuckle and $625,000 for Mr. Wagner and Mr. Parini. The “Stock Awards” for 2019 consist of PSU awards and time-vested restricted stock unit awards granted to Mr. Wagner as a sign-on award in April 2019 and to the other executive officers in February 2019. In 2019, the non-financial PSU awards had a grant-date fair value of 50% of the fair value of the target shares, in accordance with U.S. GAAP. If the grant-date fair value of the non-financial PSU awards had been 100% of the fair value of the target shares it would increase the amounts set forth in the table above by $1.3 million for Dr. Leiden, $459,000 for Dr. Kewalramani and Mr. Arbuckle, and $175,000 for Mr. Wagner. The “Stock Awards” for 2018 consist of PSU awards and time-vested restricted stock unit awards granted in February 2018.

Non-Equity Incentive Plan Compensation—Annual Cash Bonus

The amounts set forth under the caption “Non-Equity Incentive Plan Compensation” in the table above represent annual cash bonuses for 2020, 2019 and 2018 performance, each of which was paid in the first quarter of the subsequent year. The cash bonus awards to the NEOs for 2020 performance were determined as follows:

Name	Base Salary		Individual Incentive Target		2020 Target Bonus		Company Performance Factor		Individual Performance Factor		2020 Performance Cash Bonus
Reshma Kewalramani	$ 1,150,000	x	120%	=	$ 1,380,000	x	138%	x	143%	=	$ 2,723,292
Jeffrey M. Leiden	$ 1,000,000	x	100%	=	$ 1,000,000	x	138%	x	143%	=	$ 1,973,400
Charles F. Wagner, Jr.	$ 700,000	x	70%	=	$ 490,000	x	138%	x	140%	=	$ 946,680
David Altshuler	$ 725,000	x	70%	=	$ 507,500	x	138%	x	145%	=	$ 1,015,508
Stuart A. Arbuckle	$ 800,000	x	70%	=	$ 560,000	x	138%	x	150%	=	$ 1,159,200
Michael Parini	$ 800,000	x	70%	=	$ 560,000	x	138%	x	140%	=	$ 1,081,920

All Other Compensation

The amounts set forth under the caption “All Other Compensation” in the table for 2020 consist of:

Name	401(k) Match	Life Insurance Premiums	Matching Gift Program	Other	Total
Reshma Kewalramani	$ 12,825	$ 1,810	$ 23,750	$ 1,963(1)	$ 40,348
Jeffrey M. Leiden	$ 12,825	$ 1,622	$ 25,000	$ 3,691(1)	$ 43,138
Charles F. Wagner, Jr.	$ 12,825	$ 1,247	$ 25,000	$ 2,130(1)	$ 41,202
David Altshuler	$ 12,825	$ 1,278	$ 25,000	$ 2,677(1)	$ 41,780
Stuart A. Arbuckle	$ 12,825	$ 1,372	$ 25,000	$ 3,401(1)	$ 42,598
Michael Parini	$ 12,825	$ 1,372	$ 25,000	$ 28,207(2)	$ 67,404

(1) Tax reimbursements.

(2) Includes tax reimbursements and reimbursements for business-related commuting costs incurred under temporary procedures for executives during the COVID-19 pandemic.

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Grants of Plan-Based Awards During 2020

The following table provides information with respect to grants of awards to each of our NEOs during 2020. Pursuant to SEC rules, (i) the threshold, target and maximum amounts payable pursuant to our 2020 annual cash bonus program are set forth in columns under "Estimated Possible Payouts under Non-Equity Incentive Plan Awards," (ii) the threshold, target and maximum number of shares that could vest pursuant to PSUs granted in 2020 are set forth in columns under "Estimated Future Payouts under Equity Incentive Plan Awards," and (iii) the number of shares granted pursuant to other restricted stock unit awards in 2020 is set forth under "All Other Stock Awards: Number of Shares of Stock or Units."

			Estimated Possible Payouts Under Non-Equity Incentive Plan Awards			Estimated Future Payouts Under Equity Incentive Plan Awards (shares)			All Other Stock Awards: Number of Shares of Stock or Units (#)	Grant-Date Fair Value of Stock and Option Awards ($)
Name		Grant Date	Threshold ($)	Target ($)	Maximum ($)	Threshold (#)	Target (#)	Maximum (#)		
Reshma Kewalramani	(1)		$ 0	$ 1,380,000	$ 3,105,000					
	(2a)	2/5/2020				—	6,194	12,388		$ 1,500,187
	(2b)	2/5/2020				—	6,194	12,388		$ 750,093
	(3)	2/5/2020							12,387	$ 3,000,131
Jeffrey M. Leiden	(1)		$ 0	$ 1,000,000	$ 2,250,000					
	(2a)	2/5/2020				—	15,731	31,462		$ 3,810,048
	(2b)	2/5/2020				—	15,731	31,462		$ 1,905,024
	(3)	2/5/2020							31,462	$ 7,620,096
Charles F. Wagner, Jr.	(1)		$ 0	$ 490,000	$ 1,102,500					
	(2a)	2/5/2020				—	5,162	10,324		$ 1,250,236
	(2b)	2/5/2020				—	5,162	10,324		$ 625,118
	(3)	2/5/2020							10,323	$ 2,500,231
David Altshuler	(1)		$ 0	$ 507,500	$ 1,141,875					
	(2a)	2/5/2020				—	6,194	12,388		$ 1,500,187
	(2b)	2/5/2020				—	6,194	12,388		$ 750,093
	(3)	2/5/2020							12,387	$ 3,000,131
Stuart A. Arbuckle	(1)		$ 0	$ 560,000	$ 1,260,000					
	(2a)	2/5/2020				—	6,194	12,388		$ 1,500,187
	(2b)	2/5/2020				—	6,194	12,388		$ 750,093
	(3)	2/5/2020							12,387	$ 3,000,131
Michael Parini	(1)		$ 0	$ 560,000	$ 1,260,000					
	(2a)	2/5/2020				—	5,162	10,324		$ 1,250,236
	(2b)	2/5/2020				—	5,162	10,324		$ 625,118
	(3)	2/5/2020							10,323	$ 2,500,231

(1) Annual Cash Bonus. The amounts in the "Estimated Possible Payouts Under Non-Equity Incentive Plan Awards" column represent the minimum threshold, target and maximum amounts that our NEOs were eligible for pursuant to our 2020 annual cash bonus program. Actual amounts paid to each of the NEOs under this program for 2020 performance are set forth in the *Summary Compensation Table* above.

(2) PSU. The amounts in the "Estimated Future Payouts Under Equity Incentive Plan Awards" column represent the minimum threshold, target and maximum amounts that could vest pursuant to PSUs granted in 2020. Pursuant to U.S. GAAP, the grant date value of the financial PSU awards (2a) was based on 100% of the fair value of the target shares and the grant date value of the non-financial PSU awards (2b) was based on 50% of the fair value of the target shares in 2020. These awards vest if, and only if, performance objectives are achieved, as described in the footnotes to the table *Outstanding Equity Awards at Fiscal Year-End for 2020* below.

(3) Time-Based Restricted Stock Units. The amounts in the "All Other Stock Awards: Number of Shares of Stock or Units" column represent the number of time-based restricted stock units granted to the NEOs in 2020, which generally vest annually over three years.

Narrative Disclosure to Summary Compensation Table and Grants of Plan-Based Awards Table

Each NEO has entered into an employment agreement with the company, which provides the executives the right to participate in all of the company's compensation and benefits plans and equity programs, as described in *Compensation Discussion & Analysis*.

Option Exercises and Stock Vested for 2020

The following table sets forth the value realized by our NEOs from options to purchase common stock exercised by the NEOs during 2020 and shares of stock that vested during 2020. The value realized per share for options is based on the difference between the exercise price and the fair market value of the shares of common stock on the date the options were exercised. The value realized on vesting of stock awards is based on the fair market value of the shares of common stock on the vesting date.

	Option Awards		Stock Awards	
Name	Number of Shares Acquired on Exercise	Value Realized on Exercise	Number of Shares Acquired on Vesting	Value Realized on Vesting
Reshma Kewalramani	6,221	$ 506,927	8,659	$ 2,076,321
Jeffrey M. Leiden	265,603	$ 36,356,882	214,627	$ 51,066,007
Charles F. Wagner, Jr.	—	$ —	2,464	$ 604,924
David Altshuler	15,061	$ 2,026,446	41,408	$ 9,970,987
Stuart A. Arbuckle	18,634	$ 2,065,973	32,384	$ 7,794,783
Michael Parini	30,130	$ 3,770,483	44,858	$ 10,768,627

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Outstanding Equity Awards at Fiscal Year-End for 2020

The following table provides information with respect to outstanding equity awards held by each of our NEOs on December 31, 2020, based on the closing price of $236.34 per share of our common stock on December 31, 2020:

		Option Awards				Stock Awards			
Name		Number of Securities Underlying Unexercised Options Exercisable (shares)[1]	Number of Securities Underlying Unexercised Options Unexercisable (shares)[1]	Option Exercise Price (per share)	Option Expiration Date	Number of Shares or Units of Stock That Have Not Vested (shares)	Market Value of Shares or Units of Stock That Have Not Vested	Equity Incentive Plan Awards: Number of Unearned Shares, Units or Other Rights That Have Not Vested (shares)	Equity Incentive Plan Awards: Market or Payout Value of Unearned Shares, Units or Other Rights That Have Not Vested
Reshma Kewalramani	**Time-based RSU**								
						6,533[3]	$ 1,544,009		
						12,387[4]	$ 2,927,544		
	Performance-based RSU								
						1,172[5]	$ 276,990		
						6,534[6]	$ 1,544,246		
						1,758[7]	$ 415,486		
						6,194[8]	$ 1,463,890		
								4,900[9]	$ 1,158,066
								6,194[10]	$ 1,463,890
	Stock Options								
		510	2,548	$ 155.57	2/5/2028				
		1,564	14,078	$ 187.53	2/5/2029				
Jeffrey M. Leiden	**Performance-based RSU**								
						15,749[7]	$ 3,722,119		
						15,731[8]	$ 3,717,865		
								14,222[9]	$ 3,361,227
								15,731[10]	$ 3,717,865
	Stock Options								
		103,550	0	$ 86.52	2/2/2027				
		93,866	0	$ 91.05	2/1/2026				
Charles F. Wagner, Jr.	**Time-based RSU**								
						2,465[3]	$ 582,578		
						10,323[4]	$ 2,439,738		
	Performance-based RSU								
						2,466[6]	$ 582,814		
						5,162[8]	$ 1,219,987		
								1,849[9]	$ 436,993
								5,162[10]	$ 1,219,987
	Stock Options								
		3,574	5,958	$ 189.38	4/9/2029				
David Altshuler	**Time-based RSU**								
						2,813[2]	$ 664,824		
						5,444[3]	$ 1,286,635		
						12,387[4]	$ 2,927,544		
	Performance-based RSU								
						2,814[5]	$ 665,061		
						5,444[6]	$ 1,286,635		
						4,219[7]	$ 997,118		
						6,194[8]	$ 1,463,890		
								4,083[9]	$ 964,976
								6,194[10]	$ 1,463,890
	Stock Options								
		2,330	2,330	$ 86.52	2/2/2027				
		1,223	6,115	$ 155.57	2/5/2028				
		2,607	11,731	$ 187.53	2/5/2029				

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		Option Awards				Stock Awards			
Name		Number of Securities Underlying Unexercised Options Exercisable (shares)[1]	Number of Securities Underlying Unexercised Options Unexercisable (shares)[1]	Option Exercise Price (per share)	Option Expiration Date	Number of Shares or Units of Stock That Have Not Vested (shares)	Market Value of Shares or Units of Stock That Have Not Vested	Equity Incentive Plan Awards: Number of Unearned Shares, Units or Other Rights That Have Not Vested (shares)	Equity Incentive Plan Awards: Market or Payout Value of Unearned Shares, Units or Other Rights That Have Not Vested
Stuart A. Arbuckle	**Time-based RSU**								
						2,813[2]	$ 664,824		
						6,533[3]	$ 1,544,009		
						12,387[4]	$ 2,927,544		
	Performance-based RSU								
						2,814[5]	$ 665,061		
						6,534[6]	$ 1,544,246		
						4,219[7]	$ 997,118		
						6,194[8]	$ 1,463,890		
								4,900[9]	$ 1,158,066
								6,194[10]	$ 1,463,890
	Stock Options								
		0	1,554	$ 86.52	2/2/2027				
		2,446	6,115	$ 155.57	2/5/2028				
		3,128	14,078	$ 187.53	2/5/2029				
Michael Parini	**Time-based RSU**								
						2,813[2]	$ 664,824		
						5,444[3]	$ 1,286,635		
						10,323[4]	$ 2,439,738		
	Performance-based RSU								
						2,814[5]	$ 665,061		
						5,444[6]	$ 1,286,635		
						4,219[7]	$ 997,118		
						5,162[8]	$ 1,219,987		
								4,083[9]	$ 964,976
								5,162[10]	$ 1,219,987
	Stock Options								
		0	2,330	$ 86.52	2/2/2027				
		1,223	6,115	$ 155.57	2/5/2028				
		2,607	11,731	$ 187.53	2/5/2029				

(1) Unvested stock options vest in 16 quarterly installments during the first four years of their ten-year terms. The option expiration dates listed above reflect the final expiration date for each of the listed options. If the NEO's service with us is terminated, the options would expire, subject to certain exceptions, 90 days after the termination of service.

(2) These time-based restricted stock unit awards vest in three annual installments. The shares listed on the table above represent the third annual installment, which vested on February 17, 2021.

(3) These time-based restricted stock unit awards vest in three annual installments. The shares listed on the table above represent the second and third annual installments, which vested on February 24, 2021 and were scheduled to vest February 24, 2022, respectively.

(4) These time-based restricted stock unit awards vest in three annual installments. The shares listed on the table above represent the three annual installments, which vested on February 10, 2021, and were scheduled to vest in two remaining annual installments on February 10, 2022 and 2023.

(5) This performance stock unit award was based on the achievement of one-year financial performance metrics tied to our net product revenue for medicines for the treatment of CF during 2018. In February 2019, our MDCC certified as to the level of performance at 200% of the number of target shares with the earned shares vesting in annual installments on February 17, 2019, 2020 and 2021. The shares listed on the table above represent the final installment of earned shares, which vested on February 17, 2021.

(6) This performance stock unit award was based on the achievement of one-year financial performance metrics tied to our net product revenue for medicines for the treatment of CF during 2019, with vesting of the earned shares in three equal installments on each of February 24, 2020, 2021 and 2022. In February 2020, our MDCC certified as to the level of performance at 200% of the number of target shares. The shares listed on the table above represent the second and third installments of earned shares, which vested on February 24, 2021 and were scheduled to vest on February 24, 2022, respectively.

(7) This performance stock unit award is based on the achievement of three-year non-financial performance metrics. The awards provide for multiple clinical and research milestones, with a payout range of zero to 200%. In February 2021, our MDCC certified as to the level of performance at 200% of the number of target shares. The earned shares vested on February 17, 2021.

(8) This performance stock unit award was based on the achievement of one-year financial performance metrics tied to our net product revenue for medicines for the treatment of CF during 2020, with vesting of the earned shares generally occurring in three equal installments scheduled for each of February 10, 2021, 2022 and 2023. In February 2021, our MDCC certified as to the level of performance at 200% of the number of target shares.

(9) This performance stock unit award is based on the achievement of three-year non-financial performance metrics. The awards provide for multiple clinical and research milestones, with a payout range of zero to 200%. The specific clinical and research milestones are not disclosed for competitive reasons. Performance against these goals will be certified by our MDCC in early 2022.

(10) This performance stock unit award is based on the achievement of three-year non-financial performance metrics. The awards provide for multiple clinical and research milestones, with a payout range of zero to 200%. The specific clinical and research milestones are not disclosed for competitive reasons. Performance against these goals will be certified by our MDCC in early 2023.

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SUMMARY OF TERMINATION AND CHANGE OF CONTROL BENEFITS

The amounts shown in the following table are calculated based on the amounts that would have been payable by us had the listed current NEO experienced an employment termination on December 31, 2020.

	Voluntary Termination or Retirement/ Termination for Cause	Separate From a Change of Control, Involuntary Termination Other Than for Cause/ Termination by Executive for Good Reason	In Connection With a Change of Control, Involuntary Termination Other Than for Cause/ Termination by Executive for Good Reason	Disability	Death
Reshma Kewalramani					
Cash Severance Benefits	$ —	$ 6,440,000	$ 8,944,700	$ 1,380,000	$ 1,380,000
Continuation of Employee Benefits	—	44,230	44,230	—	—
Accelerated Vesting of Stock Options	—	469,965	892,949	892,949	892,949
Accelerated Vesting of Restricted Stock Units	—	3,700,415	10,794,121	10,794,121	10,794,121
TOTAL	**$ —**	**$10,654,610**	**$20,676,000**	**$ 13,067,070**	**$ 13,067,070**
Jeffrey M. Leiden					
Cash Severance Benefits	$ —	$25,250,000	$25,250,000	$ 10,250,000	$ 10,250,000
Continuation of Employee Benefits	—	29,725	29,725	—	—
Accelerated Vesting of Stock Options	—	—	—	—	—
Accelerated Vesting of Restricted Stock Units	—	—	—	—	—
TOTAL	**$ —**	**$25,279,725**	**$25,279,725**	**$ 10,250,000**	**$ 10,250,000**
Charles F. Wagner, Jr.					
Cash Severance Benefits	$ —	$ 1,190,000	$ 1,680,000	$ —	$ —
Continuation of Employee Benefits	—	26,667	26,667	—	—
Accelerated Vesting of Stock Options	—	—	279,788	279,788	279,788
Accelerated Vesting of Restricted Stock Units	—	—	6,482,097	6,482,097	6,482,097
TOTAL	**$ —**	**$ 1,216,667**	**$ 8,468,552**	**$ 6,761,885**	**$ 6,761,885**
David Altshuler					
Cash Severance Benefits	$ —	$ 1,232,500	$ 1,740,000	$ —	$ —
Continuation of Employee Benefits	—	29,487	29,487	—	—
Accelerated Vesting of Stock Options	—	—	1,415,579	1,066,499	1,415,579
Accelerated Vesting of Restricted Stock Units	—	—	11,720,573	11,720,573	11,720,573
TOTAL	**$ —**	**$ 1,261,987**	**$14,905,639**	**$ 12,787,072**	**$ 13,136,152**
Stuart A. Arbuckle					
Cash Severance Benefits	$ —	$ 1,360,000	$ 1,920,000	$ —	$ —
Continuation of Employee Benefits	—	29,487	29,487	—	—
Accelerated Vesting of Stock Options	—	—	1,413,876	1,181,056	1,413,876
Accelerated Vesting of Restricted Stock Units	—	—	12,428,648	12,428,648	12,428,648
TOTAL	**$ —**	**1,389,487**	**15,792,011**	**13,609,704**	**13,842,524**

The amounts in the table above do not include any life insurance payments or disability insurance payments that the executive or the executive's estate may receive under existing insurance policies. The assumptions underlying the calculations in the table include:

- The value of each share subject to an option to purchase common stock that would be accelerated or continue to vest in the circumstances described below under Employment Contracts and Change of Control Arrangements equals $236.34 per share (the closing price on the last trading day of 2020), minus the exercise price per share.
- The value of each share of restricted stock unit that would be accelerated or continue to vest, in each case in the circumstances described below, equals $236.34 per share (the closing price on the last trading day of 2020).
- Appropriate provision for the continuation of all then-outstanding options would be made in connection with a change of control.
- Our board of directors would elect not to pay a pro rata portion of an executive's target bonus for the year of termination in cases where the executive's employment is terminated voluntarily by the executive (for any reason, including retirement) or for cause, under our policy that cash bonuses are payable only to employees who are otherwise eligible and who remain employed by us on the date of bonus payment, typically in February of the next year.
- Our board of directors would have assigned the same 2020 individual and company performance ratings on December 31, 2020 as they assigned in the first quarter of 2021.
- Under his amended and restated employment agreement and equity agreements and consistent with a program applicable to all our employees, in March 2020, when he completed his service to us as Chief Executive Officer and President, Dr. Leiden received acceleration of his outstanding equity. PSUs granted to Dr. Leiden in his role as CEO vest following certification of the corresponding performance criteria.
- Mr. Parini voluntarily left the company effective March 1, 2021 and, as a result, was not entitled to any severance or termination payments.

The actual amounts that the current NEOs could receive in the future as a result of a termination of employment would likely differ materially from the amounts set forth above as a result of, among other things, changes in our stock price, changes in the officers' base salary, target bonus amounts and actual bonus amounts, and the vesting and grants of additional equity awards.

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EMPLOYMENT CONTRACTS AND CHANGE OF CONTROL ARRANGEMENTS

Executive Severance Arrangements

We have entered into agreements and maintain plans that require us to provide to our NEOs cash compensation, benefits and/or acceleration of the vesting of equity awards in the event of termination of employment or service as a director under specified circumstances. In addition to the agreements described below, outstanding options granted under our stock and option plans provide that, in the event of certain changes of control, either appropriate provision for the continuation of all then-outstanding options must be made, or the vesting of those options will be accelerated and they will become fully exercisable immediately prior to such change of control. As described below, the benefits that are to be provided in connection with a change of control are subject to a "double trigger." A change of control does not itself trigger benefits; rather, benefits are paid only if the employment of the executive is terminated by us other than for cause, death or disability or by the executive for good reason during a specified period before or after a change of control. The following descriptions are qualified in the entirety by the agreements with the NEOs, which have been filed with the SEC.

In addition to the benefits described below, under programs applicable to all employees, if a NEO dies while an employee, his or her estate and/ or beneficiaries would receive full acceleration of all outstanding equity awards, and if a NEO's employment is terminated due to disability, the executive officer would receive full acceleration of equity grants made since 2018. None of our current employment agreements provide for a so-called Section 4999 excise tax "gross-up," and we have a policy against providing so-called Section 4999 excise tax "gross-up" in the future.

Agreements with Reshma Kewalramani

Dr. Kewalramani's written employment agreement provides that she is entitled to receive compensation as determined by our board of directors and is eligible to receive the benefits generally made available to our executives. In addition, Dr. Kewalramani has agreed not to engage in specified competitive activities for 12 months after her employment with us terminates.

Under our arrangements with Dr. Kewalramani, if (i) Dr. Kewalramani's employment is terminated by us without cause or (ii) she terminates her employment for good reason, she would be entitled to receive, subject to limited exceptions:

Severance Payment:	A) 200% of the sum of her (i) base salary at the time of termination and (ii) target bonus for the year in which her employment is terminated B) Any annual bonus for the year prior to the year in which the termination occurs, if not yet paid C) A pro-rated bonus for the year in which the termination occurs based on her target bonus for the year in which the termination occurs
Equity:	Outstanding options and restricted stock units unvested on the termination date would receive partial vesting based on the portion of the award(s) that would have vested during the 12-month period following the termination date.
Employee Benefits:	Continuation of certain employee benefits for up to 18 months

If (i) Dr. Kewalramani's employment is terminated by us without cause or (ii) she terminates her employment for good reason, in each case, within 90 days prior to or 12 months after a change of control of the company, she would instead be entitled to receive:

Severance Payment:	A) 299% of the sum of her (i) base salary at the time of termination and (ii) target bonus for the year in which her employment is terminated B) A pro-rated bonus for the year in which the termination occurs C) All cash incentive awards earned by Dr. Kewalramani, if not yet paid
Equity:	Full vesting of all outstanding options and restricted stock unit awards (using target or earned shares, as applicable, for performance-based awards)
Employee Benefits:	Continuation of certain employee benefits for up to 18 months

Severance payments to Dr. Kewalramani in connection with a change of control may be reduced to increase their value to Dr. Kewalramani if such payments would be subject to an excise tax under Section 4999 of the Code.

If Dr. Kewalramani's employment is terminated as a result of death or disability, for equity awards not covered by the company-wide equity program described above, she would be entitled to receive:

- a pro-rated bonus for the year of employment termination;
- vesting of any options then unvested at the time of termination.

Agreement with Jeffrey Leiden

Dr. Leiden's employment agreement has a three-year term that commenced on April 1, 2020 and provides for (i) a base salary and bonus in the first year, (ii) annual equity grants with declining values over the three-year term and (iii) eligibility to receive the other benefits generally made available to our executives. In addition, Dr. Leiden has agreed not to engage in specified competitive activities for 18 months after his employment with us terminates.

If (a) Dr. Leiden's employment is terminated by us without cause or (b) he terminates his employment for good reason, he would be entitled to receive, subject to limited exceptions: (i) any base salary or annual bonus amounts for the first year remaining unpaid, (ii) a cash payment equal to grant date value of any remaining annual equity awards he would have received following the termination date under his agreement and (iii) continuation of certain employee benefits for up to 18 months.

If Dr. Leiden's employment is terminated as a result of death or disability, he would be entitled to receive any base salary or annual bonus amounts for the first year remaining unpaid and a cash payment equal to the grant date value of the next annual equity award he would have received on the grant date immediately following the date of his termination.

Consistent with a program applicable to all our employees, in March 2020, when he completed his service to us as Chief Executive Officer and President, Dr. Leiden received acceleration of his outstanding equity and extension of the expiry of his outstanding options. PSUs granted to Dr. Leiden in his role as CEO vest following certification of the corresponding performance criteria.

Agreements with Dr. Altshuler, Mr. Arbuckle, Mr. Parini and Mr. Wagner

Employment Agreements

The terms and conditions of Dr. Altshuler's, Mr. Arbuckle's, Mr. Parini's and Mr. Wagner's employment are governed by written employment contracts that were entered into at the time the respective officers joined our company. Each of these officer's employment agreement provides that he is entitled to receive compensation as determined by our board of directors and is eligible to receive the benefits generally made available to our executives. In addition, each officer has agreed not to engage in specified competitive activities for a period of one year after the termination of his employment with us.

Under each employment agreement, (i) if the officer's employment is terminated without cause or (ii) the officer terminates his employment with us for good reason within 30 days of the event giving rise to his right to terminate for good reason, subject to notice and cure provisions, he would be entitled to receive:

Severance Payment:	The sum of his (i) base salary at the time of termination and (ii) target bonus for the year in which his employment is terminated
Employee Benefits:	Continuation of certain employee benefits for up to 12 months

Change of Control Agreements

We have a change of control agreement with each of Dr. Altshuler, Mr. Arbuckle, Mr. Parini and Mr. Wagner that were entered into at the time the respective officer joined our company. Under this agreement and the executive's equity agreements, if we terminate the employment of the officer without cause on a date within the 90 days prior to or the 12 months after a change of control or any of these individuals terminates his employment within 30 days of an event giving rise to a right to terminate for good reason, subject to notice and cure provisions, and the event occurs on a date within the 90 days prior to or the 12 months after a change of control, he would be entitled to receive:

Severance Payment:	A) The sum of his (i) base salary at the time of termination and (ii) target bonus for the year in which his employment is terminated B) A pro rata portion of his target bonus for the year in which the termination occurs
Equity	Full vesting of all outstanding options and restricted stock unit awards (using target or earned shares, as applicable, for performance-based awards)
Employee Benefits:	Continuation of certain employee benefits for up to 12 months

Severance payments to the officer in connection with a change of control may be reduced to increase their value to the applicable officer if such payments would be subject to an excise tax under Section 4999 of the Code.

PAY RATIO

CEO Pay Ratio

Under the Dodd-Frank Wall Street Reform and Consumer Protection Act, the SEC requires annual disclosure of the ratio of the annual total compensation of our CEO to that of our median employee. During 2020, we had two individuals serving (non-concurrently) as CEO. For purposes of providing the required pay ratio disclosure, we selected Dr. Kewalramani because she was serving as CEO as of October 1, 2020, the date when we selected our median employee.

We identify our median employee using target total annual compensation. Our measure of compensation for identifying the median employee was consistently applied to all employees (converting all non-USD currencies into USD based on 12-month foreign exchange rates for the 12-month period ending October 1, 2020) and includes:

- Base salary
- Target cash bonus
- Target long-term equity awards

Our methodology includes all 3,388 Company employees as of October 1, 2020, and includes employees in 21 countries. We identified a new median employee in 2020 because of a change in our compensation program in 2019.

After identifying the median employee, we calculated the median employee's annual total compensation using the same methodology used to calculate CEO's annual total compensation for the Summary Compensation Table. In 2020, the total annual compensation for our median employee, other than the CEO, equaled $215,509.

In 2020, Dr. Kewalramani's total annualized compensation as CEO equaled $9,164,051. The ratio of total annual compensation for Dr. Kewalramani to our median employee's total annual compensation was 43:1.

If we adjusted Dr. Kewalramani's base salary as if she had served as CEO for the full year and adjusted her long-term equity award to reflect an award as if she were CEO for the full year, Dr. Kewalramani's adjusted annual total compensation for 2020, with no additional changes to other amounts included in the Summary Compensation Table, would be $14,838,266. After giving effect to those adjustments, the ratio of total annual compensation for Dr. Kewalramani to that of our median employee would be 69:1.

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SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT

The following table sets forth information regarding beneficial ownership of our common stock as of March 25, 2021, by:

- each shareholder known by us to be the beneficial owner of more than 5% of our common stock on that date;
- each of our directors;
- each NEO; and
- all directors and executive officers as a group.

Name and Address	Shares Beneficially Owned[1]	Percentage of Total[2]
BlackRock, Inc.[3] 55 East 52nd Street New York, New York 10055	24,268,895	9.4%
The Vanguard Group[4] 100 Vanguard Blvd. Malvern, Pennsylvania 19355	20,433,050	7.9%
T. Rowe Price Associates, Inc.[5] 100 E. Pratt Street Baltimore, Maryland 21202	19,626,208	7.6%
FMR LLC[6] 245 Summer Street Boston, Massachusetts 02210	13,506,870	5.2%
Sangeeta N. Bhatia[7]	6,355	*
Lloyd Carney[7]	2,161	*
Alan Garber[7]	18,451	*
Terrence C. Kearney[7]	38,862	*
Reshma Kewalramani[7]	17,781	*
Yuchun Lee[7]	90,459	*
Jeffrey M. Leiden[7]	247,532	*
Margaret G. McGlynn[7]	49,386	*
Diana McKenzie[7]	467	*
Bruce I. Sachs[7]	110,816	*
David Altshuler[7]	13,542	*
Stuart A. Arbuckle[7]	15,387	*
Michael Parini[7]	6,356	*
Charles F. Wagner, Jr.[7]	12,132	*
All directors and executive officers as a group (20 persons)[7]	730,369	0.3%

* Less than 1%

(1) Beneficial ownership of shares for purposes of this proxy statement is determined in accordance with applicable SEC rules and includes shares of common stock as to which a person has or shares voting power and/or investment power, including dispositive power. The persons and entities named in the table have sole voting and investment power with respect to all shares shown as beneficially owned by them, except as noted below. Information with respect to persons other than directors and executive officers is based solely upon Schedules 13G and amendments thereto filed with the SEC in the first quarter of 2021.

(2) Percentage ownership is based on 258,821,254 shares of our common stock outstanding on March 25, 2021.

(3) Reflects the securities beneficially owned by clients of one or more investment advisers directly or indirectly owned by BlackRock, Inc. BlackRock, Inc. has sole voting power with respect to 21,772,420 shares and sole dispositive power with respect to 24,268,895 shares.

(4) Includes shares beneficially owned by Vanguard Asset Management Limited, Vanguard Fiduciary Trust Company, Vanguard Global Advisors, LLC, Vanguard Group (Ireland) Limited, Vanguard Investments Australia Ltd., Vanguard Investments Canada Inc., Vanguard Investments Hong Kong Limited and Vanguard Investments UK, Limited, each of which are wholly-owned subsidiaries of The Vanguard Group, Inc. The Vanguard Group, Inc. has sole voting power with respect to 0 shares, shared voting power with respect to 485,633 shares, sole dispositive power with respect to 19,237,602 shares, and shared dispositive power with respect to 1,195,448 shares.

(5) Reflects the securities beneficially owned by clients of one or more investment advisers directly or indirectly affiliated with T. Rowe Price Associates, Inc. T. Rowe Price Associates, Inc. has sole voting power with respect to 7,122,529 shares and sole dispositive power with respect to 19,626,208 shares.

(6) Reflects the securities beneficially owned, or that may be deemed to be beneficially owned, by FMR LLC, certain of its subsidiaries and affiliates, and other companies. FMR LLC has sole voting power with respect to 2,394,198 shares and sole dispositive power with respect to 13,506,870 shares.

(7) Includes shares that may be acquired upon the exercise of options exercisable within 60 days after March 25, 2021, unvested shares of restricted stock as of March 25, 2021, unvested restricted stock units vesting within 60 days of March 25, 2021 and deferred stock units as of March 25, 2021 issued pursuant to our Non-Employee Director Deferred Compensation Plan, as follows:

	Stock Options Exercisable Within 60 Days of March 25, 2021	Unvested Restricted Units Vesting Within 60 Days of March 25, 2021	Deferred Stock Units as of March 25, 2021
Sangeeta N. Bhatia	3,845	—	—
Lloyd Carney	—	—	—
Alan Garber	13,810	—	—
Terrence C. Kearney	33,051	—	—
Reshma Kewalramani	6,222	—	—
Yuchun Lee	86,783	—	1,801
Jeffrey M. Leiden	197,416	—	—
Margaret G. McGlynn	44,520	—	4,688
Diana McKenzie	—	—	260
Bruce I. Sachs	71,783	—	12,823
David Altshuler	13,542	—	—
Stuart A. Arbuckle	11,149	—	—
Michael Parini	6,356	—	—
Charles F. Wagner, Jr.	4,766	1,232	—
All directors and executive officers as a group (20 persons)	559,767	5,988	19,572

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EQUITY COMPENSATION PLAN INFORMATION

As of February 28, 2021, there were 10,640,130 shares remaining available for award under our 2013 Plan. Under our 2013 Plan, all awards may be granted as full value awards but count as 1.66 shares for each full value share awarded.

As of February 28, 2021, under our equity plans:

- Stock options covering 4,112,176 shares of our common stock, with a weighted average exercise price of $141.13 and a weighted average remaining term of 6.15 years, were outstanding; and
- Unvested restricted stock units covering 3,785,558 shares of our common stock were outstanding.

The following table provides aggregate information with respect to all of our equity compensation plans in effect as of December 31, 2020. We are required under applicable SEC rules to disclose in this table the number of shares remaining available for issuance under our equity plans as of December 31, 2020. Accordingly, the figures in the table below do not reflect the equity grants made to our employees under our 2013 Stock and Option Plan (the "2013 Plan"), since December 31, 2020.

Plan Category	Number of Securities to be Issued Upon Exercise of Outstanding Options, Restricted Stock Units and Rights	Weighted-Average Exercise Price of Outstanding Options and Rights	Number of Securities Remaining Available for Future Issuance Under Equity Compensation Plans (excluding securities reflected in first column)
Equity Compensation Plans Approved by Shareholders[1]	7,615,677[2]	$140.47[3]	15,381,642[4]
Equity Compensation Plans Not Approved by Shareholders	—	—	—
TOTAL	**7,615,677**		**15,381,642**

(1) These plans consist of our 2013 Plan, our 2006 Stock and Option Plan ("2006 Plan") and our Employee Stock Purchase Plan. No further shares of common stock will be issued or distributed under the 2006 Stock and Option Plan.

(2) Represents the number of underlying shares of common stock associated with outstanding options, restricted stock units, performance stock units, and deferred stock units granted under stockholder approved plans, as of December 31, 2020, and includes 3,854,523 options granted under the 2013 Plan, 2,702,040 restricted stock units granted under the 2013 Plan, 656,039 PSUs (assuming the maximum number of PSUs will be earned) granted under the 2013 Plan, 19,257 deferred stock units attributable to compensation deferred by non-employee directors participating in the Director Plan and distributable in the form of shares of common stock under the 2013 Plan (and which are treated as outstanding "stock rights" under the 2013 Plan), and 383,818 options granted under the 2006 Plan.

(3) Represents the weighted-average exercise price of options outstanding under the 2013 Plan and 2006 Plan. See note (2) above with respect to restricted stock units, PSUs and deferred stock units (credited under the Director Plan) outstanding under the 2013 Plan. The weighted-average exercise price does not take these awards into account.

(4) Represents the number of shares available for future issuance under stockholder approved equity compensation plans and is comprised of 13,385,321 shares available for future issuance under the 2013 Plan and 1,996,321 shares available for future issuance under the Employee Stock Purchase Plan, including shares to be purchased at the end of the current offering period ending May 15, 2021.

OTHER INFORMATION

Other Matters

The 2021 annual meeting of shareholders is called for the purposes set forth in the notice. Our board of directors does not know of any other matters to be considered by the shareholders at the 2021 annual meeting other than the matters described in this proxy statement. However, the enclosed proxy confers discretionary authority on the persons named in the proxy card with respect to matters that may properly come before the annual meeting and that are not known to our board at the date this proxy statement was printed. It is the intention of the persons named in the proxy card to vote in accordance with their best judgment on any such matter.

Shareholder Proposals for the 2022 Annual Meeting and Nominations for Director

In order to be considered for inclusion in the proxy statement for our 2022 annual meeting of shareholders, shareholder proposals must be received by us no later than December 9, 2021. If we do not receive notice of a matter to be considered for presentation at the 2022 annual meeting of shareholders by February 22, 2022, our proxy holders will have the right to exercise discretionary voting authority with respect to the proposal without including information regarding the proposal in our proxy materials. Proposals should be sent to the attention of our corporate secretary at our offices at 50 Northern Avenue, Boston, Massachusetts 02210.

If a shareholder wishes to nominate a candidate for election to our board of directors at the 2022 annual meeting of shareholders, but is not eligible or does not elect to have such candidate included in the proxy statement for our 2022 annual meeting of shareholders, such nomination may be submitted to our corporate secretary no later than February 18, 2022, and must include:

- the name and address of the shareholder who intends to make the nomination and of the person or persons to be nominated;
- a representation that the shareholder is a holder of record of our stock entitled to vote at such meeting and intends to appear in person or by proxy at the meeting to nominate the person or persons specified in the notice;
- a description of all arrangements or understandings between the shareholder and each nominee and any other person or persons (naming such person or persons) pursuant to which the nomination or nominations are to be made by the shareholder;
- the other information regarding each nominee proposed by the shareholder that would be required to be included in a proxy statement filed pursuant to the proxy rules of the SEC; and
- the consent of each nominee to serve on our board of directors if so elected.

If a shareholder wishes to nominate a candidate for election to our board at the 2022 annual meeting of shareholders, and is eligible and elects to have such candidate included in the proxy statement for our 2022 annual meeting of shareholders pursuant to our proxy access by-law, such nomination must be submitted to our corporate secretary no later than February 18, 2022 and must include, in addition to the information set forth above for other shareholder nominees, the information set forth in Section 8(e) of Article II of our by-laws.

Shareholder Communications to the Board

Generally, shareholders who have questions or concerns should contact our investor relations department at (617) 341-6100. However, any shareholder who wishes to address questions regarding our business directly with our board of directors, or any individual director(s), should direct his or her questions, in writing, in care of our corporate secretary, to our offices at 50 Northern Avenue, Boston, Massachusetts 02210. Under procedures approved by our board, including a majority of our independent directors, all substantive communications shall be reviewed by our corporate secretary and forwarded or reported to the chair of the CGNC, the independent directors and/or our full board, as deemed appropriate, with the exception of those communications relating to ordinary or routine business affairs, personal grievances or matters as to which we tend to receive repetitive or duplicative communications.

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Householding of Annual Meeting Materials

Some banks, brokers and other nominee record holders may be participating in the practice of “householding” proxy materials. This means that only one copy of our Notice of Internet Availability of Proxy Materials or proxy statement and annual report may have been sent to multiple shareholders in your household. We will promptly deliver a separate copy of these documents to you if you write or call our corporate secretary at the following address or phone number: 50 Northern Avenue, Boston, Massachusetts 02210, telephone (617) 341-6100. If you want to receive separate copies of the proxy materials in the future, or if you are receiving multiple copies and would like to receive only one copy for your household, you should contact your bank, broker, or other nominee record holder, or you may contact us at the above address and phone number.

Solicitation

We will bear the cost of soliciting proxies, including expenses in connection with preparing this proxy statement and hosting the virtual annual meeting. We have retained Morrow Sodali to assist in the solicitation of proxies at an estimated cost of approximately $20,000. Proxies also may be solicited by our directors and employees by mail, by telephone, in person or otherwise. Neither directors nor employees will receive additional compensation for solicitation efforts. In addition, we will request banks, brokers and other custodians, nominees and fiduciaries to forward proxy material to the beneficial owners of common stock and to obtain voting instructions from the beneficial owners. We will reimburse those firms for their reasonable expenses in forwarding proxy materials and obtaining voting instructions.

Forward-Looking Statements

This proxy statement contains forward-looking statements as defined in the Private Securities Litigation Reform Act of 1995, including, without limitation, statements regarding our medicines, statements with respect to potential regulatory approval of our drug candidates and expected clinical development plans and timing, as well as statements with respect to Vertex’s potential future financial performance and our beliefs regarding the number of people with CF and those potentially eligible for our medicines. While we believe the forward-looking statements contained in this proxy statement are accurate, these forward-looking statements represent our beliefs only as of the date of this proxy statement and there are a number of risks and uncertainties that could cause actual events or results to differ materially from those indicated by such forward-looking statements. Those risks and uncertainties include, among other things, that the company’s expectations regarding its future financial performance may be incorrect (including because one or more of the company’s assumptions underlying its expectations may not be realized), that COVID-19 may have different or more significant impacts on the company’s business or operations than the company currently expects, that data from preclinical testing or early clinical trials, especially if based on a limited number of patients, may not be indicative of final results, that regulatory authorities may not approve regulatory filings for our pipeline products on a timely basis, or at all, that data from the company’s developmental programs may not support registration or further development programs may not support registration or further development of its potential medicines in a timely manner, or at all, due to safety, efficacy or other reasons, and other risks listed under the heading “Risk Factors” in our Annual Report on Form 10-K for the fiscal year ended December 31, 2020 and available through the company’s website at www.vrtx.com. We disclaim any obligation to update the information contained in this proxy statement as new information becomes available.

Website references are provided throughout this document for convenience. The content on the referenced website does not constitute part of and is not incorporated by reference into this proxy statement.

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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 ratification of the appointment of Ernst & Young LLP as our independent registered public accounting firm;
- An advisory vote on our 2020 named executive officer compensation;
- A shareholder proposal regarding a report on our lobbying activities, if properly presented at the meeting; and
- A shareholder proposal regarding a report on our political spending, if properly presented at the meeting.

Management, members of our board and representatives of Ernst & Young LLP are expected to attend the annual meeting and be available to respond to appropriate 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. The board of directors has designated Jeffrey Leiden, Reshma Kewalramani, Joy Liu and Sabrina Yohai 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 rules of the SEC and other applicable laws require us to give you, as a shareholder, the information in this proxy statement and our Annual Report when we are soliciting your vote.

Why did I receive a “Notice of Internet Availability of Proxy Materials” but no proxy materials?

We are distributing our proxy materials to shareholders via the Internet under the “Notice and Access” approach permitted by rules of the SEC. This approach provides a timely and convenient method of accessing the materials and voting. On or about April 8, 2021, we will begin mailing a “Notice of Internet Availability of Proxy Materials” to shareholders. This notice includes instructions on how to access our notice of annual meeting of shareholders, this proxy statement and our Annual Report on Form 10-K for the year ended December 31, 2020 and how to vote your shares. The Notice of Internet Availability of Proxy Materials also contains instructions on how to receive a paper copy of the proxy materials and our Annual Report, if you prefer.

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 the Notice of Internet Availability of Proxy Materials was sent directly to you by Computershare.

Street Name Holders. If you hold your shares in an account at a bank, broker or other nominee, then you are the beneficial owner of shares held in “street name.” The Notice of Internet Availability of Proxy Materials was forwarded to you by your bank, broker or other nominee. As a beneficial owner, you have the right to direct your bank or broker how to vote the shares held in your account.

How May I Attend the Annual Meeting?

In light of the public health and travel safety concerns related to the ongoing COVID-19 pandemic, we will hold a virtual annual meeting this year. The virtual meeting will facilitate shareholder attendance and participation by enabling all shareholders to attend and participate in the annual meeting from any location and at no cost. Visit www.meetingcenter.io/237308243 to attend and submit questions during the meeting. The password for the meeting is **VRTX2021.**

To attend the virtual meeting, shareholders of record will not need to register in advance but will need the control number included on their Notice of Internet Availability of Proxy Materials or proxy card, or within the body of the email sending the proxy statement. Shareholders whose shares are held in street name may attend the annual meeting by registering and obtaining a control number in advance using the instructions below under the heading “How do I Register to Attend the Virtual Annual Meeting on the Internet.” The control number will be required to attend and participate in the virtual annual meeting, including voting your shares electronically and submitting questions. The meeting webcast will begin promptly at 9:30 a.m. (Eastern Time). We encourage you to access the meeting prior to the start time. You should allow for ample time for the check-in procedures.

If you would like to submit a question related to the business of the meeting, you may do so during the meeting by logging into the virtual annual meeting website and entering the control number included on your Notice of Internet Availability of Proxy Materials, proxy card, voting instruction form or electronic notification when prompted. We will respond to these questions during the meeting.

What if I have Trouble Accessing the Virtual Annual Meeting?

The virtual annual meeting platform is fully supported across MS Edge, Firefox, Chrome and Safari browsers and devices (desktops, laptops, tables and cell phones) running the most up-to-date version of applicable software and plugins. Please note that Internet Explorer is no longer supported by the platform. You should ensure that you have a strong WiFi connection wherever you intend to participate in the meeting. We encourage you to access the meeting prior to the start time. If you encounter any technical difficulties accessing the virtual annual meeting during the check-in or meeting time, a link on the meeting page will provide further assistance should you need it or you may call +1-888-724-2416 (U.S. toll-free) or +1-781-575-2748 (outside of the U.S.).

How do I Register to Attend the Virtual Annual Meeting on the Internet?

If you are a shareholder of record, you do not need to register in advance to attend the virtual annual meeting on the Internet. Please follow the instructions on the Notice of Internet Availability of Proxy Materials or the proxy card that you received.

If you hold your shares in street name, you must register and obtain a control number in advance to attend the virtual annual meeting on the Internet. To register to attend the virtual annual meeting you will need to obtain a legal proxy from your bank, broker or other nominee. Once you have received a legal proxy from them, you must send an email attaching an image of your legal proxy from your bank, broker or other nominee to legalproxy@computershare.com, along with your name and email address. Alternatively, you may mail your legal proxy to the following address: Computershare, Vertex Pharmaceuticals Incorporated Legal Proxy, P.O. Box 43001, Providence, RI 02940-3001. Requests for registration must be labeled as “Legal Proxy” and be received no later than 5:00 p.m., Eastern Time, on May 14, 2021. After Computershare receives your registration materials, you will receive an email from Computershare confirming your registration and providing your control number which will allow you to fully participate in the virtual annual meeting.

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. Shares present virtually during the annual meeting will be considered shares of common stock represented in person at the meeting. If you are a shareholder of record, your shares are counted as present if you properly vote by Internet, telephone, return a proxy card by mail or if you attend the annual meeting online. 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 or obtain a legal proxy to vote online at the annual meeting. 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.

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How Can I Vote My Shares?

If you are a shareholder of record, you may vote your shares by one of the following methods:

1. **Vote by Internet** by going to the web address www.envisionreports.com/VRTX before the annual meeting and following the instructions for Internet voting on the Notice of Internet Availability or proxy card. Have the Notice of Internet Availability of Proxy Materials, which contains your control number, available when voting by Internet.
2. **Vote by proxy card,** if you have received written proxy materials, by completing, signing, dating, and mailing your proxy card in the envelope provided. **If you vote by Internet, please do not mail your proxy card.**
3. **Vote by telephone** by following the instructions on the Notice of Internet Availability of Proxy Materials or proxy card.
4. **By attending the annual meeting online.** During the annual meeting, you may vote online by following the instructions at www.meetingcenter.io/237308243. Have the Notice of Internet Availability of Proxy Materials, which contains your control number, available when you access the virtual meeting webpage.

If you are a street name holder, your bank, broker or other nominee will provide you with a form seeking instruction on how your shares should be voted.

What is the Record Date and What Does it Mean?

The record date for the annual meeting is March 25, 2021 and was established by our board of directors. On the record date, there were 258,821,254 shares of our common stock outstanding, each of which is entitled to one vote on each matter properly brought before the annual meeting. 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
- 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:

- subsequently submitting a vote by Internet at www.envisionreports. com/VRTX or by telephone by following the directions on the Notice of Internet Availability of Proxy Materials, voting instruction form or your proxy card;
- signing another proxy card with a later date and delivering it to our corporate secretary at 50 Northern Avenue, Boston, Massachusetts 02210, before the annual meeting; or
- voting at the annual meeting online, 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 Notice of Internet Availability of Proxy Materials or proxy card. If no specific instructions are given, proxies that are signed and returned will be voted:

- FOR the election of each director nominee;
- FOR ratification of the appointment of Ernst & Young LLP as our independent registered public accounting firm for the year ending December 31, 2021;
- FOR our 2020 named executive officer compensation;
- AGAINST the shareholder proposal regarding a report on our lobbying activities; and
- AGAINST the shareholder proposal regarding a report on our political spending.

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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 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 will have no effect on the results of those votes.

What Vote is Required to Approve Each Proposal and How are Votes Counted?

Proposal No. 1: Election of Directors

To be elected, the number of votes cast “FOR” each director nominee must exceed the number of votes cast “AGAINST” that nominee. Abstentions will have no effect on the results of this vote. Our Corporate Governance Principles contain procedures to be followed in the event that one or more directors do not receive a majority of the votes cast “FOR” his or her election.

Proposal No. 2: 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 and broker non-votes will have no effect on the results of this vote.

Proposal No. 3: 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.

Proposal No. 4: Shareholder Proposal Regarding a Report on Our Lobbying Activities

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 and broker non-votes will have no effect on the results of this vote.

Proposal No. 5: Shareholder Proposal Regarding a Report on Our Political Spending

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 and broker non-votes 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 sec.gov/spotlight/proxymatters.shtml.

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APPENDIX A NON-GAAP FINANCIAL MEASURES

In this proxy statement, our financial results are provided in accordance with accounting principles generally accepted in the United States (GAAP). We also include non-GAAP net product revenue growth and operating margin. Our non-GAAP net product revenues for 2019 excluded an adjustment to GAAP net product revenues to reflect the conclusion of our early access program for ORKAMBI in France in 2019. Our non-GAAP operating income for 2020 excluded (i) stock-based compensation expense, (ii) an increase in the fair value of contingent consideration, (iii) revenues and expenses related to collaboration agreements and (iv) acquisition-related costs. Reconciliations of GAAP net product revenues to non-GAAP net product revenues and GAAP operating income to non-GAAP operating income are included below.

GAAP AND NON-GAAP NET PRODUCT REVENUES

	Twelve Months Ended December 31,		
	2020	2019	% Change
	(in thousands, except percentages)		
GAAP net product revenues	$ 6,202,783	$ 4,160,726	49%
ORKAMBI adjustment	—	(155,773)	
Non-GAAP net product revenues	$ 6,202,783	$ 4,004,953	55%

GAAP AND NON-GAAP OPERATING INCOME

	Twelve months ended December 31, 2020
	(in thousands, except percentages)
Net product revenues	$ 6,202,783
GAAP operating income	$ 2,856,290
Stock-based compensation expense	429,461
Increase in fair value of contingent consideration	13,100
Collaborative revenues and expenses	181,700
Acquisition-related costs	10,682
Non-GAAP operating income	$ 3,491,233
GAAP operating margin	46%
Non-GAAP operating margin	56%

These results should not be viewed as a substitute for our GAAP results and are provided as a complement to results provided in accordance with GAAP. Management believes non-GAAP net product revenues and non-GAAP operating margin help indicate underlying trends in our business, are important in comparing current results with prior period results and provide additional information regarding our financial position that management believes is helpful to an understanding of our ongoing business. Management also uses these non-GAAP financial measures to establish budgets and operational goals that are communicated internally and externally and to manage our business and to evaluate our performance.

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VOTE

Your vote matters – here's how to vote!

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

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

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

AT THE VIRTUAL MEETING
To access the virtual Annual Meeting, please visit www.meetingcenter.io/237308243
If prompted for a password, please enter VRTX2021

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

Annual Meeting Proxy Card

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

A **Proposals – The Board of Directors recommends a vote FOR each Director Nominee in proposal 1, FOR proposals 2 and 3, and AGAINST proposals 4 and 5.**

1. Election of Directors:

	For	Against	Abstain		For	Against	Abstain		For	Against	Abstain
01 - Sangeeta Bhatia	☐	☐	☐	02 - Lloyd Carney	☐	☐	☐	03 - Alan Garber	☐	☐	☐
04 - Terrence Kearney	☐	☐	☐	05 - Reshma Kewalramani	☐	☐	☐	06 - Yuchun Lee	☐	☐	☐
07 - Jeffrey Leiden	☐	☐	☐	08 - Margaret McGlynn	☐	☐	☐	09 - Diana McKenzie	☐	☐	☐
10 - Bruce Sachs	☐	☐	☐								

	For	Against	Abstain
2. Ratification of Ernst & Young LLP as independent Registered Public Accounting firm for the year ending December 31, 2021.	☐	☐	☐
3. Advisory vote to approve named executive officer compensation.	☐	☐	☐
4. Shareholder proposal, if properly presented at the meeting, regarding a report on lobbying activities.	☐	☐	☐
5. Shareholder proposal, if properly presented at the meeting, regarding a report on political spending.	☐	☐	☐

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

Please sign name exactly as name appears. When signing in a fiduciary capacity, please give full title. Co-fiduciaries and joint owners should each sign.

Date (mm/dd/yyyy) – Please print date below.	Signature 1 – Please keep signature within the box.	Signature 2 – Please keep signature within the box.
/ /		

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The 2021 Annual Meeting of Shareholders of Vertex Pharmaceuticals Incorporated
will be held on
May 19, 2021, at 9:30 a.m. Eastern Time
virtually via the internet at
www.meetingcenter.io/237308243.

To access the virtual meeting, you will need the 15-digit control number
that is printed in the shaded bar located on the reverse side of this form.

The password for this meeting is VRTX2021.

Important Notice Regarding the Availability of Proxy Materials for the Shareholder Meeting to be held on May 19, 2021:
The Notice of Annual Meeting of Shareholders, Proxy Statement and Annual Report are available at
http://www.envisionreports.com/vrtx

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

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VERTEX™

Proxy – Vertex Pharmaceuticals Incorporated

ANNUAL MEETING OF SHAREHOLDERS – May 19, 2021

THIS PROXY IS SOLICITED ON BEHALF OF THE BOARD OF DIRECTORS

The undersigned does hereby constitute and appoint Jeffrey Leiden, Reshma Kewalramani, Joy Liu, and Sabrina Yohai, and each of them, the attorney(s) and proxy of the undersigned, with full power of substitution, with all the powers that the undersigned would possess if personally present, to vote all stock of Vertex Pharmaceuticals Incorporated that the undersigned is entitled to vote at the Annual Meeting of Shareholders of Vertex Pharmaceuticals Incorporated to be held on Wednesday, May 19, 2021 at 9:30 A.M. Eastern Time, via live audio webcast available at www.meetingcenter.io/237308243 and at any postponement or adjournment thereof, and hereby acknowledges receipt of the proxy statement for such meeting and revokes all previous proxies.

This proxy, when properly executed, will be voted as directed. If no direction is made, this proxy will be voted FOR each of the nominees in proposal 1, FOR proposals 2 and 3, and AGAINST proposals 4 and 5 and, in the case of other matters that legally come before the meeting or any postponement or adjournment thereof, as said proxies may deem advisable.

Please vote, sign and date on the reverse side and return this proxy card promptly.

C Non-Voting Items

Change of Address – Please print new address below.

Comments – Please print your comments below.

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