

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:	
<input type="checkbox"/>	Preliminary Proxy Statement
<input type="checkbox"/>	Confidential, for Use of the Commission Only (as permitted by Rule 14a-6(e)(2))
<input checked="" type="checkbox"/>	Definitive Proxy Statement
<input type="checkbox"/>	Definitive Additional Materials
<input type="checkbox"/>	Soliciting Material under §240.14a-12



VERTEX PHARMACEUTICALS INCORPORATED

(Name of Registrant as Specified In Its Charter)
(Name of Person(s) Filing Proxy Statement, if other than the Registrant)

Payment of Filing Fee (Check all boxes that apply):	
<input checked="" type="checkbox"/>	No fee required
<input type="checkbox"/>	Fee paid previously with preliminary materials
<input type="checkbox"/>	Fee computed on table in exhibit required by Item 25(b) per Exchange Act Rules 14a-6(i)(1) and 0-11



2022 PROXY STATEMENT
VERTEX PHARMACEUTICALS INCORPORATED

Notice of Annual Meeting of Shareholders to be held on May 18, 2022



Dear Shareholders:

2021 was an important year for Vertex, and one that has positioned us well for the future as we continue discovering, developing, and commercializing transformative medicines for people with serious diseases. Our unique and differentiated corporate strategy, which is driven by a focus on serial innovation, is delivering both exceptional financial performance and unprecedented clinical results across multiple programs. The disciplined execution of our strategy has enabled us to meaningfully expand our leadership position in cystic fibrosis (CF), where we have already discovered, developed, and commercialized four transformative medicines, and to simultaneously expand and accelerate our clinical-stage pipeline in multiple additional disease areas and therapeutic modalities. During the last year, we significantly increased our annual product revenues by 22% to \$7.57 billion and delivered industry-leading operating margins while continuing to invest the majority of our operating expenses in research and development. Our investment in innovation allowed us to progress our pipeline with new proof-of-concept results obtained in type 1 diabetes and APOL1-mediated kidney disease, and to progress our mid- to late-stage clinical development programs in sickle cell disease, beta thalassemia, and pain.

In CF, we are treating more patients than ever before, and we have solidified our long-term leadership position in three important ways. First, with more than 20 new reimbursement agreements secured in 2021 and the launch of TRIKAFTA for children with CF 6 to 11 years of age in the United States, thousands of new patients have initiated treatment with TRIKAFTA, or KAFTRIO as it is known in Europe. Second, we have continued to accumulate unparalleled long-term and real-world data about our medicines showing a breadth of clinical benefits that go beyond what we have demonstrated in our Phase 3 studies. Third, we have made important progress advancing once-a-day, next-generation CFTR modulators, now in Phase 3 development, that have the potential for improved efficacy and enhanced economics, and made a significant breakthrough in our mRNA approach for the remaining people with CF who cannot benefit from our small molecule medicines. Based on these results, we are confident that we will reach our goal of bringing transformative therapies to all people with this devastating disease.

Beyond CF, we have a broad and deep pipeline that is both advancing and delivering important clinical results. In 2021, we made significant advances in key pipeline programs, laying the groundwork for multiple important clinical milestones in 2022. In sickle cell disease and beta thalassemia, we completed enrollment for the pivotal studies for CTX001, a one-time gene-editing therapy that is our most advanced program outside of CF and has the potential to be a functional cure for people living with these diseases. In type 1 diabetes, we announced the first clinical data for VX-880, our stem cell-derived fully differentiated pancreatic islet cell therapy, which, while still early, are unprecedented and bring great hope that we will be able to deliver a functional cure to people suffering from this disease. In APOL1-mediated focal segmental glomerulosclerosis, we established clinical proof-of-concept with unprecedented results for VX-147, our small molecule targeting APOL1-mediated kidney disease, and announced plans to move into pivotal development. We also initiated and have now completed and announced positive data for two Phase 2 proof-of-concept studies for VX-548, our small molecule NaV1.8 inhibitor for the treatment of acute pain. 2021 also saw significant progress in our research pipeline for diseases including Duchenne muscular dystrophy, myotonic dystrophy type 1 and alpha-1 antitrypsin deficiency. The speed at which our clinical programs are progressing is a direct result of our differentiated research and development strategy, in which we target causal human biology, focusing on validated targets and on diseases with biomarkers that translate from bench to bedside. With six programs in mid- to late-stage development, we are positioned for multiple milestones and significant value creation in 2022 and beyond.

In addition to advancing our approved and pipeline medicines, we remained committed to supporting our communities and our workforce. In 2021, Vertex and the Vertex Foundation increased support to organizations focused on STEAM education, social innovation, and healthy families – and also continued with targeted efforts in response to COVID-19 and equity, diversity, and social justice. We increased support for our employees, offering a variety of new benefits and growth opportunities designed to enhance their well-being and development now and into the future. We are proud of our committed and talented team and are focused on ensuring that Vertex remains a great place to work for all.

Building on a successful 2021, we have the people, the programs, and the financial strength to successfully execute on our strategy: bringing our CF medicines to more people, advancing our broad and deep pipeline of first-in-class or best-in-class medicines for multiple serious diseases, growing both revenues and profits, and investing in internal and external innovation. In our roles as Executive Chairman and Chief Executive Officer, we are committed to the successful execution of our strategy of serial innovation that has been the foundation of Vertex's successes, and we are confident that this strategy will continue to drive exceptional results for patients and the medical community as well as for our shareholders.

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 18, 2022

9:30 a.m. (Eastern Time)

<https://meetnow.global/MYNFZZ5>

Dear Shareholders:

You are invited to attend the Vertex Pharmaceuticals Incorporated 2022 Annual Meeting of Shareholders. At the annual meeting, shareholders will vote:

- to elect the 11 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 2023 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 2022;
- to approve our 2021 named executive officer compensation in an advisory vote; and
- to approve an amendment and restatement of our 2013 Stock and Option Plan to increase the number of shares authorized for issuance under this plan by 13.5 million shares.

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, 2021 ("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 CONTINUED CONCERNS RELATED TO THE 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 [HTTPS://MEETNOW.GLOBAL/MYNFZZ5](https://meetnow.global/MYNFZZ5). THERE IS NO PHYSICAL LOCATION FOR THE ANNUAL MEETING THIS YEAR.

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 5:00 p.m. (Eastern Time) on May 13, 2022. 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 18, 2022.

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:

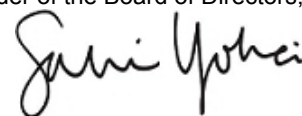
Only Vertex shareholders of record at the close of business on March 24, 2022 are entitled to receive notice of, and vote at, the annual meeting, and, subject to applicable law, any adjournment or postponement thereof.

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 7, 2022

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, 2021 are first being made available to holders of record of our common stock on or about April 7, 2022. 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 2021, we continued to execute on our strategy of investing in scientific innovation to create transformative medicines for people with serious diseases. In so doing, we grew our cystic fibrosis (“CF”) business, advanced our pipeline of potential treatments for patients in multiple new disease areas, and further strengthened our financial position.

In CF, our fourth approved medicine, TRIKAFTA, or KAFTRIO as it is known in Europe, has the potential to treat approximately 90% of people with CF. In 2021, we continued to make progress bringing TRIKAFTA/KAFTRIO to many more eligible patients both within and outside of the U.S. Beyond CF, we are advancing programs in several serious diseases: sickle cell disease and beta thalassemia, APOL1-mediated kidney disease, type 1 diabetes, pain, alpha-1 antitrypsin deficiency, Duchenne muscular dystrophy, and myotonic dystrophy type 1.

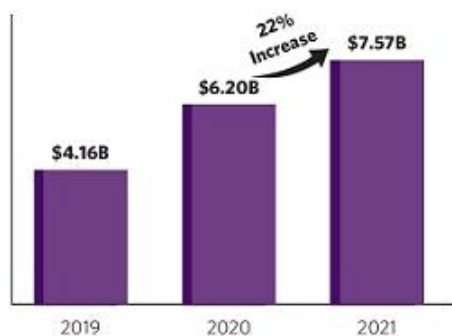
Our outstanding performance in 2021 resulted in net product revenues of \$7.57 billion and strong operating margins. As a result, we are well-positioned to continue creating long-term value for both our patients and our shareholders with a portfolio of approved high value medicines for CF, a broad and deep pipeline beyond CF, therapeutic modalities that span small molecules to genetic and cell therapies, and a strong financial profile.

Financial Performance

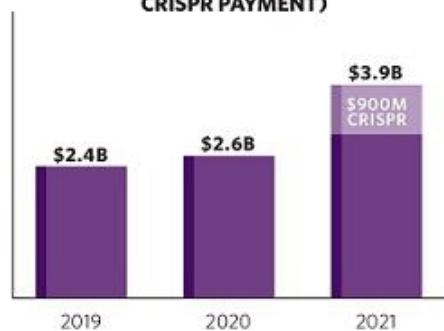
Our CF medicines, TRIKAFTA/KAFTRIO, SYMDEKO/SYMKEVI, ORKAMBI, and KALYDECO, are transforming the lives of eligible patients around the globe and continue to drive our financial performance.

- Our CF net product revenues increased to \$7.57 billion in 2021, up 22% or approximately \$1.4 billion, from our 2020 net product revenues.
- Our total R&D and SG&A expenses increased to \$3.9 billion compared to \$2.6 billion in 2020 primarily due to a \$900 million upfront payment we made to CRISPR in connection with an amendment to our CTX001 collaboration in 2021, and incremental investments to support the advancement and expansion of our pipeline and to support the launches of our medicines globally.

INCREASING CF NET PRODUCT REVENUES



TOTAL R&D AND SG&A EXPENSES (INCLUDING 2021 \$900 MILLION CRISPR PAYMENT)

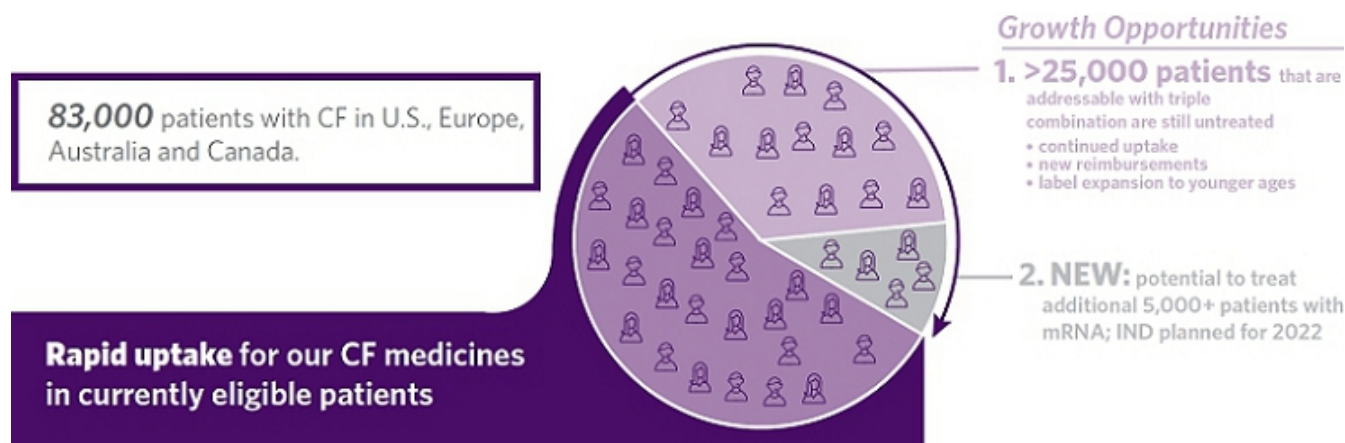


Marketed Products

Our deliberate strategy of continuous serial innovation has significantly solidified our leadership position in CF and moved us ever 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.

Today, our four approved medicines are being used to treat the majority of the approximately 83,000 people with CF in North America, Europe, and Australia. However, we believe that there are more than 25,000 untreated patients in these geographies who could still benefit from our medicines. Over the next several years, we plan to reach these patients through continued uptake of our medicines, expansion of our TRIKAFTA/KAFTRIO label to lower age groups, and additional approvals and reimbursement agreements. In support of our goal of bringing transformative therapies to all people with CF, we also are pursuing genetic therapies for the remaining people with CF who may not be helped by our current CF medicines. During the last year, we have significantly advanced our pre-clinical messenger ribonucleic acid (“mRNA”) program for these patients and expect to enter the clinic with this new therapy in 2022.

CONTINUED GROWTH AHEAD IN CF



Since the beginning of 2021, notable progress that has resulted from our efforts includes:

- The U.S. Food and Drug Administration (“FDA”) approved the use of TRIKAFTA for children with CF 6 through 11 years of age who have at least one F508del mutation or at least one other mutation that is responsive to TRIKAFTA.
- Health Canada granted marketing authorization for TRIKAFTA for people with CF 12 years of age and older who have at least one F508del mutation. Our application for approval of TRIKAFTA for children with CF 6 through 11 years of age has been accepted for priority review by Health Canada.
- In January 2022, the European Commission and the Medicines and Healthcare products Regulatory Agency granted marketing authorization for KAFTRIO for the treatment of children with CF 6 through 11 years of age who have at least one F508del mutation in the CFTR gene.
- More than 20 countries outside the U.S. have now approved and reimbursed or made accessible TRIKAFTA/KAFTRIO.

Research and Development

We invest in research and development to discover and develop transformative medicines for people with serious diseases with a focus on specialty markets. Our research and development strategy is to combine transformative advances in the understanding of human disease and the science of therapeutics to discover and develop new medicines. This approach has yielded a broad and deep pipeline and increases the speed and likelihood of successfully bringing medicines to patients. Our differentiated approach to drug discovery has been validated by 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.

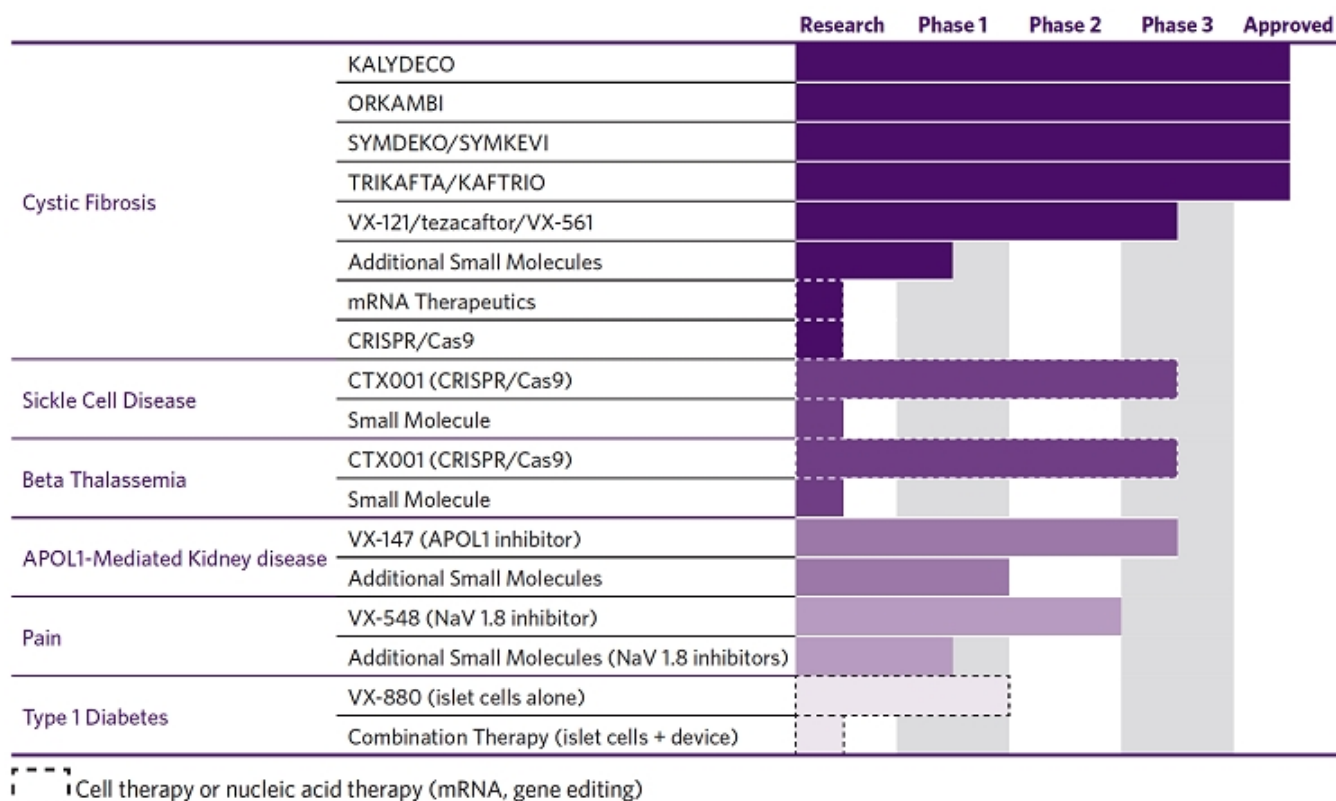
We continue to research and develop small molecule product candidates for the treatment of serious diseases, including CF, APOL1-mediated kidney disease (“AMKD”), pain, alpha-1 antitrypsin (“AAT”) deficiency, and myotonic dystrophy type 1 (“DM1”). Our research and development approach includes advancing multiple candidates 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. In 2022, we expect to have several small molecule programs in pivotal development (AMKD, CF, pain). In addition to expanding our small molecule programs during the last seven years, we also have assembled an industry-leading portfolio of programs in cell and gene therapies. In collaboration with our partner, CRISPR Therapeutics AG (“CRISPR”), we have developed the first human gene editing approach for two serious genetic diseases, sickle cell disease (“SCD”) and beta thalassemia. Based on our acquisition of Semma Therapeutics, we have recently reported unprecedented clinical data for the first stem cell-derived therapy for type 1 diabetes (“T1D”). We also continue to advance our late-stage pre-clinical gene editing program for Duchenne muscular dystrophy (“DMD”).

We are advancing programs across multiple disease areas and modalities, including:

- **Cystic Fibrosis.** We are evaluating in Phase 3 clinical trials a new, once-daily investigational triple combination of VX-121/tezacaftor/VX-561 (deutivacaftor). We also are researching mRNA therapies as well as gene-editing approaches to treat the remaining people with CF who are not expected to benefit from our small molecule medicines. We expect to submit an IND for our CF mRNA program in 2022.
- **Sickle Cell Disease and Beta Thalassemia.** We are evaluating in Phase 3 clinical trials CTX001, an investigational CRISPR/Cas9-based gene-editing therapy for severe sickle cell disease and transfusion-dependent beta thalassemia (“TDT”) with CRISPR. Enrollment is complete, and we anticipate regulatory submissions for CTX001 in late 2022.
- **APOL1-Mediated Kidney Disease.** Based on positive Phase 2 data for VX-147, our small molecule for the treatment of APOL1-mediated focal segmental glomerulosclerosis (“FSGS”), we advanced VX-147 into pivotal development in a broader population of people with AMKD in the first quarter of 2022.
- **Type 1 Diabetes.** We are evaluating VX-880, a stem-cell derived therapy involving the transplantation of fully differentiated pancreatic islet cells, for the treatment of T1D in a Phase 1/2 clinical trial, and announced positive Day 150 data for the first T1D patient in this clinical trial. Our trials in the U.S. and Canada are ongoing, and we continue to dose patients. We also are pursuing additional programs in T1D, in which the implanted islet cells are encapsulated in an immunoprotective device or modified to produce hypoimmune cells. We are conducting IND-enabling studies for the cells and device program and expect to submit an IND for this program in 2022.
- **Pain.** We recently announced positive Phase 2 data for VX-548, a Nav 1.8 inhibitor, for the non-opioid treatment of acute pain. We expect to advance VX-548 into pivotal development in the second half of 2022.
- **Alpha-1 Antitrypsin Deficiency.** We obtained proof-of-mechanism for VX-864 in a Phase 2 study of protein folding correction of the Z-AAT protein. We plan to advance into the clinic one or more novel small molecule correctors intended to address the lung and liver manifestations of AAT deficiency in 2022.
- **Duchenne muscular dystrophy and myotonic dystrophy type 1.** We are focused on advancing gene-editing therapies aimed at treating the underlying cause of DMD and DM1. We are also exploring potential small molecule approaches to address the underlying causal biology for DM1.
- In addition to the programs listed above, we have a number of early-stage research programs aimed at other targets that represent the causal human biology of serious diseases.

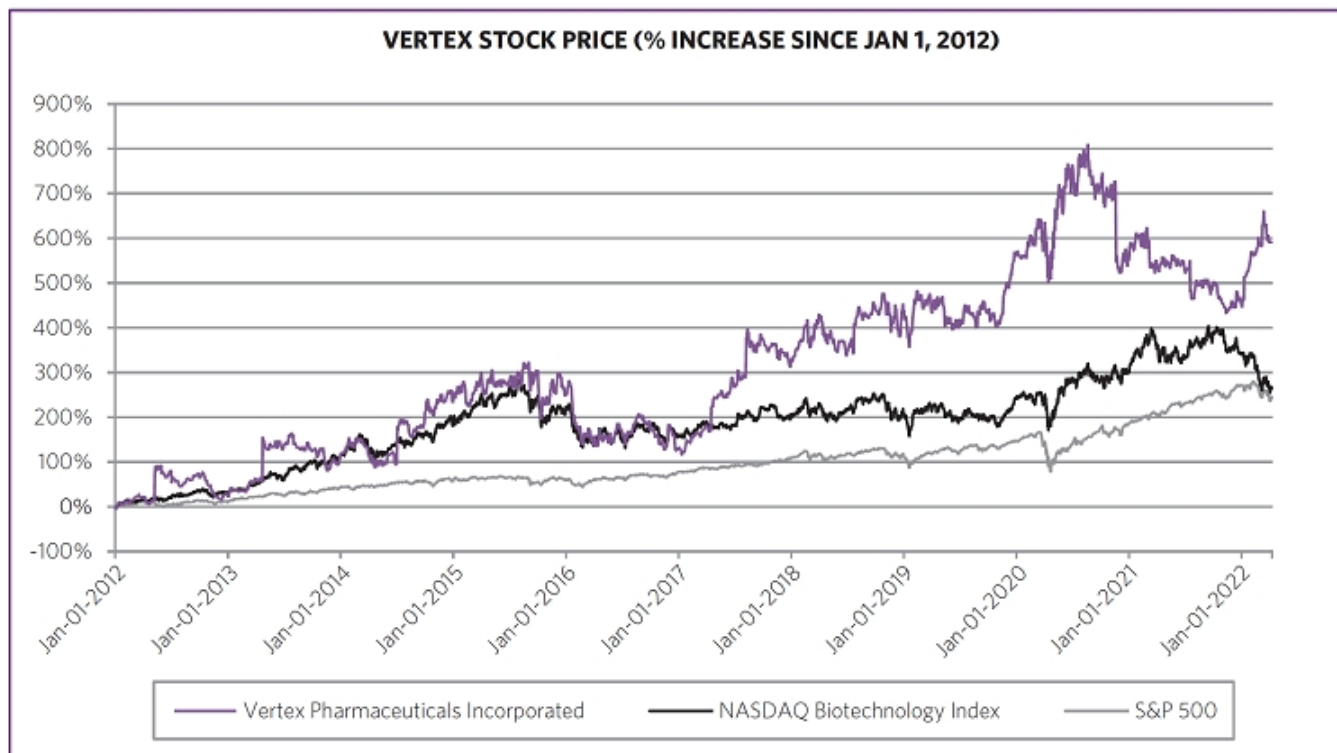
We will continue investing in our research and development programs and fostering scientific innovation by identifying additional product candidates through our internal research efforts and investing in business development transactions to access emerging technologies, products and product candidates.

The following chart represents our pipeline programs by disease area, stage of development, and modality, for programs that have lead assets in the clinic.

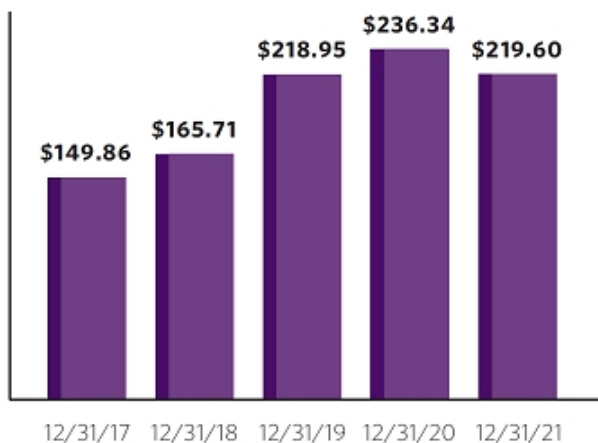


Increasing Shareholder Value

We believe that execution of our differentiated serial innovation strategy will continue to create shareholder value over the long term. The biotechnology sector is subject to short-term volatility and many biotechnology companies, including Vertex, experienced stock price fluctuations in 2021. Notwithstanding these short-term fluctuations, our executive team has outperformed on our CF business and successfully executed on our focused strategy, creating significant shareholder returns over the last several years. The following charts show our total shareholder return relative to the Nasdaq Biotechnology Index (“NBI”) and S&P 500 indices since the beginning of 2012, when KALYDECO was first approved, as well as our stock price performance over multiple periods.



STOCK PRICE



Corporate Responsibility

Vertex is a leading global biotechnology company that serially innovates to bring transformative medicines to people with serious diseases. Over the past several years, 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 broadly, with Vertex named to the Points of Light Civic 50, JUST Capital's list of the top 100 Companies Supporting Healthy Families and Communities, and the Boston Business Journal's Most Charitable Companies in Massachusetts top 10 ranking.



Community

In 2021, we supported nearly 2,000 nonprofit organizations in 29 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 2021, the Vertex Foundation awarded more than \$9 million to support STEAM education, social innovation, and healthy families with a focus on projects and organizations demonstrating a strong commitment to inclusion, diversity, and equity. The Vertex Foundation Matching Gift Program saw nearly \$3.9 million in donations by employees and the Vertex Foundation, driven in part by two special match campaigns: an annual campaign in June focused on racial and social justice, COVID-19 relief, and patient support, and a second, offered for Giving Tuesday in November.



Workplace

Our commitment to inclusion, diversity, and equity on our board and in our workforce is long-standing and deeply ingrained in our culture. Four of our eleven director nominees, including our chief executive officer ("CEO"), are women, and five of our eleven director nominees are from ethnic and racial minorities. As of December 31, 2021, women represented 54% of our global workforce and 41% of our global leadership (VP and above). In the U.S., employees from ethnic and racial minorities represented approximately 36% of our workforce and 43% of new hires. We are pleased to have been awarded a score of 100 on the Human Rights Campaign's 2021 Corporate Equality Index and to have been recognized by numerous workplace lists, including Seramount's (previously Working Mother) 100 Best Companies & 100 Best Companies for Dads.



Environment

We are committed to limiting our environmental impacts and to operating our business in a sustainable manner and continue to make progress towards our global goal of a 20% reduction in our absolute greenhouse gas emissions by the end of 2023 over a 2018 baseline. In 2021, we sourced 100% renewable energy for our International Headquarters in London and our Oxford, UK facility, and completed installation of a solar panel array at our San Diego research site. We completed construction on the Jeffrey Leiden Center for Cell and Genetic Therapies in Boston, Massachusetts, which incorporates sustainability into all aspects of its construction and design. We continue to take steps to minimize waste across all of our sites through employee engagement initiatives, vendor takeback programs, and improved product distribution processes.

Director Nominees

The following table provides summary information regarding our eleven 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	66	2009	No				
Reshma Kewalramani CEO and President, Vertex	49	2020	No				
Sangeeta Bhatia John J. and Dorothy Wilson Professor of Health Sciences & Technology/Electrical Engineering & Computer Science, MIT	53	2015	Yes			✓	Ⓞ
Lloyd Carney Founder and Chief Acquisition Officer, Carney Technology Acquisition Corp. II	60	2019	Yes	✓	✓		
Alan Garber Provost, Harvard University	66	2017	Yes	✓			✓
Terrence Kearney Former Chief Operating Officer, Hospira	67	2011	Yes	Ⓞ	✓		
Yuchun Lee CEO, Allego	56	2012	Yes	✓	✓		
Margaret McGlynn Former President, Vaccines and Infectious Diseases, Merck & Co. Former President, Hospital and Specialty Products, Merck & Co.	62	2011	Yes			Ⓞ	✓
Diana McKenzie Former Chief Information Officer, Workday Former Chief Information Officer, Amgen	57	2020	Yes			✓	
Bruce Sachs General Partner, Charles River Ventures	62	1998	Yes		Ⓞ	✓	
Suketu "Suky" Upadhyay Executive Vice President and Chief Financial Officer, Zimmer Biomet	53	Nominee	Yes				

2021 Compensation Decisions and Pay-for Performance

In 2021, our executive compensation program received substantial support, approved by approximately 91% of the votes cast at the annual meeting. We believe this support is consistent with our shareholders' understanding of our business model and the long-term value we are creating. Since the beginning of 2021, our board of directors and management development and compensation committee ("MDCC") reviewed our compensation programs and made the following key decisions:

- We increased the base salary and target equity level for Dr. Reshma Kewalramani, our CEO and President, based on a comparative analysis of companies in our peer group. Dr. Kewalramani's target cash bonus as a percentage of base salary was unchanged for 2021.
- We increased compensation for select named executive officers ("NEOs") based on a comparative analysis of companies in our peer group, including Mr. Arbuckle in connection with his promotion to Chief Operating Officer, and Mr. Wagner, our Chief Financial Officer.
- We extended Dr. Leiden's employment agreement by one year, until 2024. Under his amended employment agreement, Dr. Leiden will not receive any cash compensation for his role as Executive Chairman other than an annual cash payment intended to facilitate participation in the company's benefit plans, and he will continue to receive equity awards for his third and fourth years of service.
- The company's outstanding performance in 2021 resulted in the board determining that the company had achieved a leading rating (138 out of a potential 150) for 2021, with the payment of annual cash bonuses near the high end of the range for 2021, commensurate with the performance described above.
- We maintained the mix of equity granted to our NEOs 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.

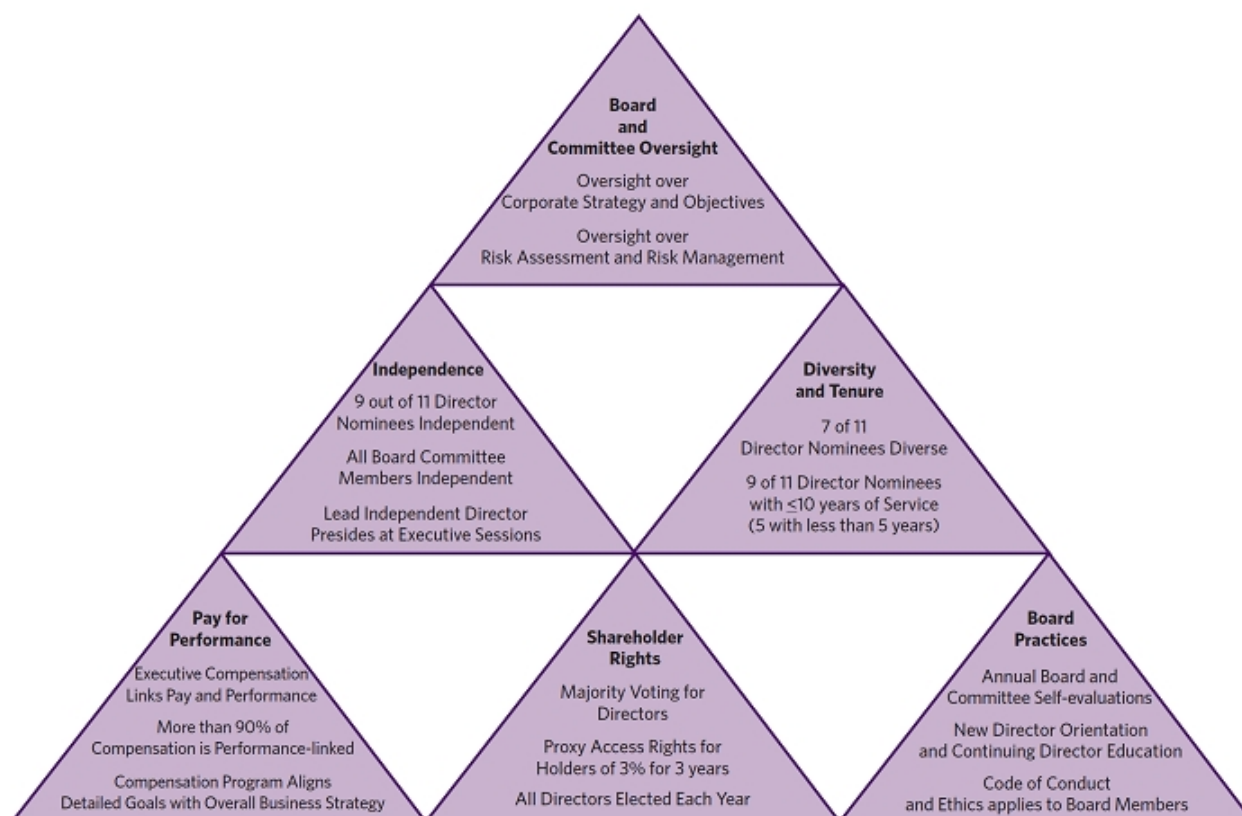
Shareholder Engagement

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 shareholders to solicit and understand a variety of perspectives and interests, and our practice has been to engage with our top shareholders regularly over the course of the year.

During 2021, we solicited feedback regarding our corporate governance practices from our top 40 shareholders representing approximately 60% of our outstanding shares. Our integrated outreach team included leaders from our Investor Relations, Human Resources, Corporate Responsibility, and Legal teams, and we discussed numerous topics of shareholder interest, including our business strategy, research and development, diversity initiatives and metrics, employee engagement and development, political and lobbying disclosures, executive compensation, sustainability and climate change matters, and COVID-related impacts to our employees, patients, and our business.

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 2023

FOR

all Nominees

Item 2:

Ratify Selection of Independent Auditor for 2022

FOR

Item 3:

Approve, on an Advisory Basis, Our Named Executive Officer Compensation

FOR

Item 4:

Approve the Amendment and Restatement of 2013 Stock and Option Plan

FOR

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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 2022 annual meeting of shareholders and at any postponement or adjournment thereof. The annual meeting will be held on Wednesday, May 18, 2022, at 9:30 a.m., Eastern Time, as a virtual meeting conducted exclusively via live webcast at <https://meetnow.global/MYNFZZ5>. 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 CEO. The board of directors has nominated all current directors - Sangeeta Bhatia, Lloyd Carney, Alan Garber, Terrence Kearney, Reshma Kewalramani, Yuchun Lee, Jeffrey Leiden, Margaret McGlynn, Diana McKenzie, and Bruce Sachs - as well as Suketu "Suky" Upadhyay - for election at our 2022 annual meeting of shareholders to hold office until our 2023 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 consists 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 eleven members of our board following the 2022 annual meeting of shareholders. Our CGNC may seek additional director candidates in the future who meet the criteria below to complement the qualifications and experience of our existing board members. Our CGNC may engage a search firm to recommend candidates who satisfy the such criteria.

Director Criteria, Qualifications and Experience; Diversity

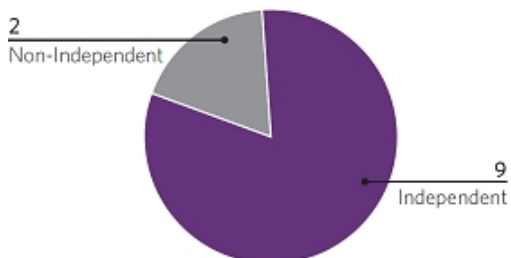
The CGNC seeks to recommend for nomination experienced directors who have substantive knowledge of our business and industry or who can bring to the board specific and valuable strategic or management capabilities acquired in other industries. The committee expects each of our directors to have proven 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. Suky Upadhyay was selected and recommended as a nominee for our board of directors by the CGNC based on the criteria outlined above.

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

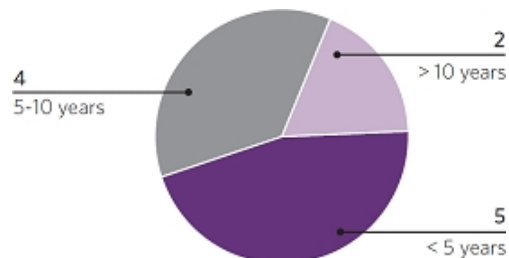
The follow table and charts provide information regarding our director nominees:

	Bhatia	Carney	Garber	Kearney	Kewalramani	Lee	Leiden	McGlynn	McKenzie	Sachs	Upadhyay
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	Y
Age	53	60	66	67	49	56	66	62	57	62	53
Tenure on Board	6	3	4	10	2	9	12	10	2	23	0
Gender	F	M	M	M	F	M	M	F	F	M	M
Ethnic or Racial Minority	✓	✓			✓	✓					✓

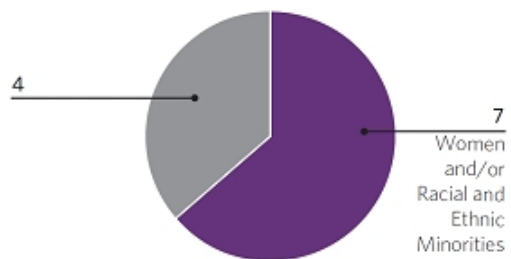
NOMINEE INDEPENDENCE



NOMINEE TENURE



NOMINEE DIVERSITY



NOMINEE AGE



Board Diversity Matrix

The table below provides certain self-identified characteristics of our current directors, in accordance with Nasdaq Rule 5605(f).

Board Diversity Matrix as of April 7, 2022

Total Number of Directors	10			
	Female	Male	Non-Binary	Did Not Disclose Gender
Part I: Gender Identity				
Directors	4	6	0	0
Part II: Demographic Background				
African American or Black	0	1	0	0
Alaskan Native or Native American	0	0	0	0
Asian	2	1	0	0
Hispanic or Latinx	0	0	0	0
Native Hawaiian or Pacific Islander	0	0	0	0
White	2	4	0	0
Two or More Races or Ethnicities	0	0	0	0
LGBTQ			0	
Did Not Disclose Demographic Background			0	

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 2023 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 and Nominations for Director for the 2023 Annual Meeting* on page 81 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:

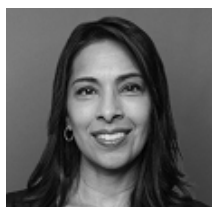
Provision	Requirement
Ownership Threshold and Holding Period	Available to shareholders owning 3% or more of our shares continuously for at least 3 years.
Number of Board Seats	Total number of proxy access nominees is capped at 20% of the existing board seats (or the closest whole number below 20%), with 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 2023 annual meeting of shareholders must follow the procedures set forth in our by-laws as well as those described in *Other Information—Shareholder Proposals and Nominations for Director for the 2023 Annual Meeting* on page 81 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. The CGNC will promptly consider the tendered resignation. Based on all factors it deems in its discretion to be relevant, the CGNC 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.

Director Nominees



Sangeeta Bhatia

Age: 53

Director Since: 2015

Board Committees:

- Chair – Science and Technology Committee
- Member – Corporate Governance and Nominating Committee

Experience:

- Professor at the Massachusetts Institute of Technology, or MIT; John J. and Dorothy Wilson Professor of Health Sciences & Technology/Electrical Engineering & Computer Science, since 2005
- Co-founder of Satellite Bio, a private company focused on developing satellite organs as living therapeutic solutions, since 2020
- Co-founder of Glympse Bio, a private company focused on developing in vivo sensing technology dedicated to disease monitoring, since 2018
- Professor of bioengineering and medicine at the University of California at San Diego, from 1998 through 2005
- 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
- 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

Key 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.

Other Public Company

Boards:

- None

**Lloyd Carney****Age:** 60**Director Since:** 2019**Board Committees:**

- Member – Audit and Finance Committee
- Member – Management Development and Compensation Committee

Experience:

- Chief Acquisition Officer of Carney Technology Acquisition Corp. II, a special purpose acquisition corporation, since October 2020
- Chief Executive Officer of ChaSerg Technology Acquisition Corp., a technology acquisition company, from September 2018 until March 2020
- Chief Executive Officer of Brocade Communications Systems Inc., a global supplier of networking hardware and software, from January 2013 until it was acquired by Broadcom in November 2017
- Chief Executive Officer of Xsigo Systems, a cloud-based infrastructure solutions provider, until it was acquired by Oracle in 2012
- Chief Executive Officer and Chairman of Micromuse Inc., a software solutions provider for business and service assurance, until it was acquired by IBM
- Previously held senior leadership roles at Juniper Networks, Inc., Nortel Networks Inc., and Bay Networks, Inc.
- Member of the Board of Directors of Nuance Communications Inc., a publicly traded AI-enabled communication company, until it was acquired by Microsoft Corp in March 2022
- 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

Key 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 chief executive officer of several technology companies, as well as financial expertise.

Other Public Company Boards:

- Visa Inc.
- Grid Dynamics Holdings Inc.

**Alan Garber****Age:** 66**Director Since:** 2017**Board Committees:**

- Member – Audit and Finance Committee
- Member – Science and Technology Committee

Experience:

- 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, since 2011
- 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, from 1998 until 2011
- 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
- Fellow of the American Association for the Advancement of Science, the American College of Physicians, and the Royal College of Physicians
- Former Research Associate with the National Bureau of Economic Research and served for nineteen years as founding Director of its Health Care Program
- Previously 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
- 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

Key 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.

Other Public Company Boards:

- Exelixis, Inc.

**Terrence Kearney****Age:** 67**Director Since:** 2011**Board Committees:**

- Chair – Audit and Finance Committee
- Member – Management Development and Compensation Committee

Experience:

- Chief Operating Officer of Hospira, Inc., a specialty pharmaceutical and medication delivery company, from April 2006 until January 2011
- Senior Vice President, Finance, and Chief Financial Officer of Hospira from April 2004 to April 2006; Acting Chief Financial Officer through August 2006
- Vice President and Treasurer of Abbott Laboratories, from 2001 to April 2004
- Divisional Vice President and Controller for Abbott's International Division, from 1996 until 2001
- Member of the Board of Directors of Levo Therapeutics, Inc., a biotechnology company focused on developing treatments for Prader-Willi Syndrome, since 2018
- Member of the Board of Directors of Acceleron Pharma Inc., a publicly traded biopharmaceutical company, until it was acquired by Merck in 2021; Innoviva (formerly known as Theravance, Inc.), a publicly traded royalty management company, from October 2014 through April 2016; and AveXis, Inc., a publicly traded gene therapy company, from January 2016 until it was acquired by Novartis in May 2018
- Holds a B.S. in biology from the University of Illinois and an M.B.A. from the University of Denver

Key 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. Mr. Kearney 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:** 49**Director Since:** 2020**Position:**

- Chief Executive Officer and President

Experience:

- Chief Executive Officer and President of Vertex Pharmaceuticals Incorporated since April 2020
- Executive Vice President and Chief Medical Officer of Vertex from April 2018 through March 2020
- Senior Vice President, Late Development of Vertex from February 2017 until April 2018
- Served in roles of increasing responsibility at Amgen Inc. from August 2004 to January 2017, most recently as Vice President, Global Clinical Development, Nephrology & Metabolic Therapeutic Area and as Vice President, U.S. Medical Organization
- Industry representative to the FDA's Endocrine and Metabolic Drug Advisory Committee from 2014 through 2019
- Holds a B.A. from Boston University and an M.D. from Boston University School of Medicine; Dr. Kewalramani 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 also completed the General Management Program at Harvard Business School and is an alumna of the school

Key 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 as CEO.

- Other Public Company Boards:**
- Ginkgo Bioworks Holdings, Inc.

**Yuchun Lee****Age:** 56**Director Since:** 2012**Board Committees:**

- Member – Audit and Finance Committee
- Member – Management Development and Compensation Committee

Experience:

- Chief Executive Officer of Allego, a technology company focused on modern sales learning and enablement, since 2013
- Executive Chairman of DSP Concepts, an Audio of Things (AoT) platform company, since 2022
- Executive in Residence of General Catalyst Partners, a venture capital firm, since 2013
- Executive Chairman of Clarabridge, Inc. until it was acquired by Qualtrics in 2021
- Vice President of IBM's Enterprise Marketing Management Group from November 2010 through January 2013
- Co-founder of Unica Corporation, a provider of software and services used to automate marketing processes, in 1992, and served as Unica's President and/or Chief Executive Officer from 1992 through November 2010, until it was acquired by IBM
- Senior consultant at Digital Equipment Corporation, a supplier of general computing technology and consulting services, from 1989 to 1992
- 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

Key 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.

Other Public Company Boards:

- None

**Jeffrey Leiden****Age:** 66**Director Since:** 2009**Position:**

- Executive Chairman

Experience:

- Chief Executive Officer and President of Vertex Pharmaceuticals Incorporated from 2012 through March 2020
- Chairman of Board of Directors of Vertex since May 2012; previously served as lead independent director from October 2010 through December 2011
- Managing Director at Clarus Ventures, a life sciences venture capital firm, from 2006 through January 2012
- 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
- Held several academic appointments from 1987 to 2000, 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
- Elected member of both the American Academy of Arts and Sciences and the Institute of Medicine of the National Academy of Sciences
- Member of the Board of Directors of Massachusetts Mutual Life Insurance Company, an insurance company
- Member of the Board of Directors of Quest Diagnostics Incorporated, a publicly traded medical diagnostics company, from December 2014 to May 2019; member of the Board of Directors and non-executive Vice Chairman of Shire plc, a specialty biopharmaceutical company, from 2006 to January 2012
- Dr. Leiden received his M.D., Ph.D. and B.A. degrees from the University of Chicago

Key Skills and Qualifications:

Dr. Leiden possesses strong leadership qualities, demonstrated through his service as a senior executive in the biotechnology 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.

Other Public Company Boards:

- Revolution Healthcare Acquisition Corp.

**Margaret McGlynn****Age:** 62**Director Since:** 2011**Board Committees:**

- Chair – Corporate Governance and Nominating Committee
- Member – Science and Technology Committee

Experience:

- Retired from Merck & Co. in 2009, where she served as President, Vaccines and Infectious Diseases and as President, Hospital and Specialty Products
- Held various leadership roles in the U.S. and globally in marketing, sales, managed care, and business development during her 26-year career at Merck
- 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
- Member of the National Industrial Advisory Committee at the University at Buffalo School of Pharmacy and Pharmaceutical Sciences
- Member of the Board of Directors of Air Products and Chemicals, Inc., a publicly traded company specializing in gases and chemicals for industrial uses, from 2005 to November 2020
- Holds a B.S. in Pharmacy, an M.B.A. in Marketing, and an Honorary Doctorate from the State University of New York at Buffalo

Key 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, Inc. and Novavax, Inc., and previously on 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:** 57**Director Since:** 2020**Board Committees:**

- Member – Corporate Governance and Nominating Committee

Experience:

- Chief Information Officer of Workday, Inc., a cloud-based financial and human capital management software company, from February 2016 until April 2019
- Held roles of increasing responsibility at Amgen Inc., a biotechnology company, from 2004 through February 2016, most recently serving as Senior Vice President and Chief Information Officer
- Held various leadership roles at Eli Lilly and Company, a pharmaceutical company, for 17 years, focused on drug development, reducing time to market and improving technology and security standards
- Member of the Board of Directors of Paradox AI; member of the Board of Directors of GenapSys Inc.; Special Advisor to Brighton Park Capital
- 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

Key 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 provides valuable guidance and support to our management and our board of directors.

Other Public Company Boards:

- MetLife Inc.
- Change Healthcare, Inc.

**Bruce Sachs****Age:** 62**Director Since:** 1998**Board Committees:**

- Chair – Management Development and Compensation Committee
- Member – Corporate Governance and Nominating Committee

Experience:

- General Partner at Charles River Ventures, a venture capital firm, since 1999
- Executive Vice President and General Manager of Ascend Communications, Inc. from 1998 to 1999
- President and Chief Executive Officer of Stratus Computer, Inc. from 1997 to 1998
- Executive Vice President and General Manager of the Internet Telecom Business Group at Bay Networks, Inc. from 1995 to 1997
- President and Chief Executive Officer of Xylogics, Inc. from 1993 to 1995
- 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

Key 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 technology company CEO, as well as financial expertise.

Other Public Company Boards:

- None

**Suketu "Suky" Upadhyay****Age:** 53**Director Nominee****Experience:**

- Executive Vice President and Chief Financial Officer of Zimmer Biomet, a leading global innovator and manufacturer of orthopedic solutions, since July 2019
- Senior Vice President, Global Financial Operations at Bristol-Myers Squibb from November 2016 to June 2019
- Executive Vice President and Chief Financial Officer of Endo International from September 2013 to November 2016
- Previously served as interim Chief Financial Officer and Senior Vice President of Finance, Corporate Controller and Principal Accounting Officer of Becton Dickinson and Senior Vice President of Global Financial Planning and Analysis and Vice President and Chief Financial Officer of Becton Dickinson's international business
- Previously held a number of global finance and strategy roles across AstraZeneca and Johnson & Johnson, including Research and Development, Supply Chain, Commercial Operations and Business Development
- Spent the early part of his career in public accounting with KPMG, earning his CPA designation and his CMA designation (each designation currently inactive)
- Holds a Bachelor of Science in Finance from Albright College and an MBA from The Fuqua School of Business at Duke University

Key Skills and Qualifications:

Mr. Upadhyay has extensive experience in the health care industry in financial roles covering all major areas of a fully integrated life sciences business. His service as an executive in the pharmaceutical and health care industries provide him with multiple perspectives on our industry. We believe this knowledge and expertise will make him a valuable contributor to our board of directors and management.

Other Public Company Boards:

- None

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.

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 (“Nasdaq”). Our independent directors are Dr. Bhatia, Mr. Carney, Dr. Garber, Mr. Kearney, Mr. Lee, Ms. McGlynn, Ms. McKenzie, and Mr. Sachs. Mr. Upadhyay, if elected, also will qualify as “independent.”

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.

Since 2020, Dr. Leiden has served as our Executive Chairman. In this role, 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. Dr. Leiden and Dr. Kewalramani 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 CEO chair regular board meetings and our current CEO 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 28 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 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, business development activities, and operations, 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, if any.
- 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 and CEO succession planning.
- Our S&T committee oversees risks related to our research and development investments.

Code of Conduct

We have adopted a Code of Conduct that applies to all of our directors and employees, including our CEO 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 2021, our board of directors met nine times. Each of our incumbent 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 2021.

The following table sets information regarding the current membership of our board of directors. Mr. Upadhyay has been nominated for our board of directors and is therefore not included in the table below.

Director ⁽¹⁾	Independence	Board	Audit Committee	CGNC	MDCC	S&T Committee	2021 Attendance at Meetings ⁽²⁾
Sangeeta N. Bhatia	✓	●	●	●	●	●	100%
Lloyd Carney	✓	●	●		●		100%
Alan Garber	✓	●	●			●	100%
Terrence C. Kearney	✓	●	●		●		100%
Reshma Kewalramani		●					100%
Yuchun Lee	✓	●	●		●		100%
Jeffrey M. Leiden		●					100%
Margaret G. McGlynn	✓	●		●		●	100%
Diana McKenzie	✓	●		●			100%
Bruce I. Sachs	✓	★		●	●		100%
2021 Meetings		9	9	5	6	5	

- = Member
- = Chair
- ★ = Lead Independent Director

(1) All directors attended our 2021 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.

Audit and Finance Committee

The primary purposes of the audit committee are to:

- assist our board's oversight of our accounting and financial reporting processes, including financial controls and audits of our financial statements;
- appoint, oversee, and replace, if necessary, our independent registered public accounting firm engaged for the purpose of preparing or issuing an audit report or performing other audit, review, or attestation services;
- review and discuss our annual audit, quarterly reviews and related disclosures, and oversee our internal audit function;
- review and make recommendations to our board concerning our financial structure, financial strategy, and risks;
- 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 person transactions; and
- assist our board's oversight of our Code of Conduct, related policies and procedures, and ongoing compliance matters as needed.

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 37 of this proxy statement.

Our audit committee reviews and approves 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 2021, 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, composition, and leadership structure of our board and its committees;
- identify and recommend to our board qualified individuals for board membership, accounting for the appropriate balance of knowledge, experience, skills, expertise, tenure, and diversity;
- oversee the CEO succession planning process and assist the board in recruiting and evaluating potential candidates;
- develop and recommend to our board an annual self-evaluation process to assess the effectiveness of our board and its committees, and coordinate this process;
- oversee risks related to the company's governance structure; and
- review and make recommendations with respect to our committee charters.

Management Development and Compensation Committee

The primary purposes of the MDCC are to:

- assess the overall compensation programs of the company and adopt a written statement of compensation philosophy and objectives;
- 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;
- 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.

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

The report of the MDCC appears on page 67 of this proxy statement.

Science and Technology Committee

Our S&T committee assists our board of directors in its 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 depth and breadth of our scientific personnel and resources; and
- provides strategic advice to our board regarding emerging science and technology issues and trends.

Each board committee has the authority to delegate any of its responsibilities to one or more subcommittees comprised of at least one member of the committee to the extent deemed appropriate but subject always to the general oversight of the board.

Compensation Committee Interlocks and Insider Participation

Messrs. Carney, Kearney, Lee, and Sachs served on the MDCC during 2021. 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 2021 that would be required to be disclosed pursuant to Item 404(a) of Regulation S-K. During 2021, 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 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 do not make independent political expenditures or make payments to influence ballot measures.

At times, we may contribute to certain 501(c)(4) organizations that engage in lobbying or political activity. We will disclose such organizations annually on our website, and, to the extent available to us, the portion of those payments used for activities that are not deductible under Chapter 162(e) of the Internal Revenue Code. We do not contribute funds intended for elections to 501(c)(4) organizations.

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.

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 highly experienced individuals who have strong industry knowledge, 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	\$ 25,000
	Science and Technology Committee	\$ 25,000
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:	
	<ul style="list-style-type: none"> ■ options that are fully-vested upon grant; 	
	<ul style="list-style-type: none"> ■ restricted stock units that vests on the first anniversary of the date of grant; or 	
	<ul style="list-style-type: none"> ■ 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 director's 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 compensation for their service as directors.

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 2019 or 2020. In 2021, based on a comparative analysis of companies in our peer group, we increased the annual committee chair retainer for the CGNC and the S&T committees from \$20,000 to \$25,000.

2021 Summary Compensation

Director	Fees Earned or Paid in Cash	Stock Awards ⁽¹⁾	Option Awards ⁽¹⁾	All Other Compensation ⁽³⁾	Total
Sangeeta N. Bhatia	\$130,000	\$ 400,082	\$ —	\$ —	\$ 530,082
Lloyd Carney	\$118,125	\$ 400,082	\$ —	\$ 25,000	\$ 543,207
Alan Garber	\$125,000	\$ —	\$ 400,058	\$ —	\$ 525,058
Terrence C. Kearney	\$142,500	\$ —	\$ 400,058	\$ —	\$ 542,558
Yuchun Lee	\$127,500	\$ —	\$ 400,058	\$ 7,000	\$ 534,558
Margaret G. McGlynn	\$130,000	\$ 200,041	\$ 200,062	\$ 25,000	\$ 555,103
Diana McKenzie ⁽²⁾	\$110,000	\$ 400,082	\$ —	\$ 24,000	\$ 534,082
Bruce I. Sachs ⁽²⁾	\$175,000	\$ —	\$ 400,058	\$ 10,000	\$ 585,058

(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 2021. 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 2021 Annual Report on Form 10-K, filed with the SEC on February 9, 2022.

(2) Ms. McKenzie and Mr. Sachs elected to defer their 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 \$220.17, \$198.00, \$182.07 and \$230.58.

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

2021 Equity Grants

Grant	Date	Shares	Exercise Price	Grant-Date Fair Value
Annual Non-Employee Director - 100% Option Grants	May 1, 2021	6,067	\$ 217.20	\$ 400,058
Annual Non-Employee Director - 50% Option Grants	May 1, 2021	3,034	\$ 217.20	\$ 200,062
Annual Non-Employee Director - 100% Restricted Stock Unit Grants	May 1, 2021	1,842	—	\$ 400,082
Annual Non-Employee Director - 50% Restricted Stock Unit Grants	May 1, 2021	921	—	\$ 200,041

Outstanding Equity

As of December 31, 2021, 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	1,842	—	3,845	3,845
Lloyd Carney	1,842	—	—	—
Alan Garber	—	—	20,210	20,210
Terrence C. Kearney	—	—	39,118	39,118
Yuchun Lee	—	1,801	92,850	92,850
Margaret G. McGlynn	921	4,688	47,554	47,554
Diana McKenzie	1,842	674	—	—
Bruce I. Sachs	—	13,483	77,850	77,850

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, 2022, each of our non-employee directors was in compliance with our stock ownership guidelines, and each of our non-employee directors satisfied the individual holding requirements.

CORPORATE RESPONSIBILITY



Community

Vertex is a leading global biotechnology company that serially innovates to bring transformative medicines to people with serious diseases. Over the past several years, 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, JUST Capital's list of the top 100 Companies Supporting Healthy Families and Communities, and the *Boston Business Journal's* Most Charitable Companies in Massachusetts top 10 ranking.

At Vertex, volunteering and giving back are core to our culture. In 2021, we supported nearly 2,000 nonprofit organizations in 29 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 2021, the Vertex Foundation awarded more than \$9 million to support STEAM education, social innovation, and healthy families with a focus on projects and organizations demonstrating a strong commitment to inclusion, diversity, and equity. The Vertex Foundation Matching Gift Program saw nearly \$3.9 million in employee donations, driven in part by two special match campaigns: an annual campaign in June focused on racial and social justice, COVID-19 relief, and patient support, and a second, offered for Giving Tuesday in November.

Throughout the year, we encourage our employees to participate in community service through our 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, 40% of Vertex employees collectively volunteered 5,000+ hours in their local communities through these programs.

Our corporate giving extends and expands on our long-term commitment to patients with serious diseases and our communities, with an on-going focus on STEAM education. In 2021, we continued to offer virtual opportunities for local students and teachers through our Learning Labs in Boston, San Diego, and Oxford, UK and expanded our paid high school internship programs. The Vertex Foundation provided 88 scholarships to people with CF and their family members who are pursuing two-year, four-year, or graduate degrees. Vertex also is 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

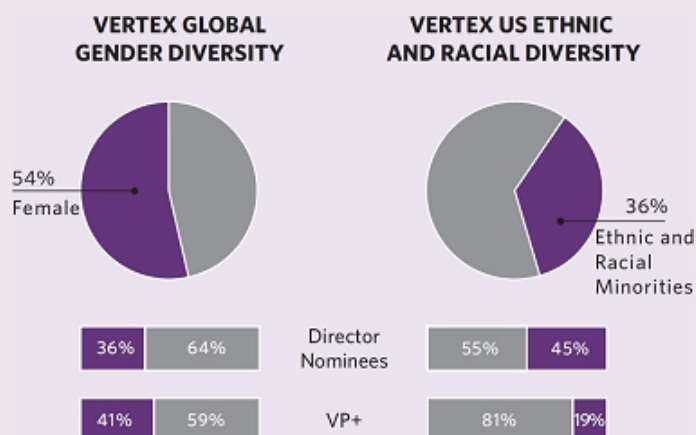
We are committed to building an outstanding, dedicated, and passionate team at Vertex. We believe that we can do our best work for patients when we foster a culture and environment where all points of view are respected and heard. At Vertex, we view diversity as a catalyst for innovation, and as a key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

We are pleased to have been awarded:

- a score of 100 on the Human Rights Campaign's 2021 Corporate Equality Index; and
- listings on Seramount's (previously Working Mother) 100 Best Companies & 100 Best Companies for Dads, Boston Globe's Top Places to Work, Science Magazine's Top Employers, and San Diego Business Journal's Best Places to Work.

Seven of our eleven director nominees are women and/or ethnic and racial minorities.

As of December 31, 2021, women represented 54% of our global workforce and men represented 46% of our global workforce. In the U.S., approximately 36% of our workforce and 43% of new hires are ethnic and racial minorities. As of December 31, 2021, 41% of our global leadership (VP and above) were women and 19% of U.S. leadership are ethnic and racial minorities.



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 2021, we sourced 100% renewable energy for our International Headquarters in London and our Oxford, UK facility, and we completed installation of a solar panel array at our San Diego research site. We completed construction on the Jeffrey Leiden Center for Cell and Genetic Therapies in Boston, Massachusetts, which incorporates sustainability into all aspects of its construction and design. We continue to take steps to minimize waste across all of our sites through employee engagement initiatives, vendor takeback programs and improved product distribution processes.

In 2022, we received a score of B, which is above the global average, on the CDP Climate Change survey by demonstrating management and coordinated action on climate issues. 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, 2022 is in the best interest of our company and our shareholders.

In determining whether to reappoint our independent registered public accounting firm, our audit 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 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 2021 and 2020.

Service	2021	2020
Audit fees	\$ 3,989,000	\$ 3,594,000
Audit-related fees	—	—
Tax fees	4,650,000	4,212,000
All other fees	6,000	8,000
TOTAL	\$ 8,645,000	\$ 7,814,000

“**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 2021 and 2020 consisted of:

- tax compliance and preparation fees, including the preparation of original and amended tax returns and refund claims, and tax payment planning of \$1,990,000 and \$1,660,000, respectively; and
- tax advice and planning fees of \$2,660,000 and \$2,552,000, 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 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, 2022.

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, 2021 with Ernst & Young and the company’s management, as well as 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, 2021 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 2021, our annual advisory vote on executive compensation received support from approximately 91% 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 our executive compensation program.

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 more than 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 2021 compensation:

- We increased the base salary and target equity level for Dr. Reshma Kewalramani, our CEO and President, based on a comparative analysis of companies in our peer group. Dr. Kewalramani's target cash bonus as a percentage of base salary was unchanged for 2021.
- Based on a comparative analysis of companies in our peer group, we increased compensation for Mr. Arbuckle in connection with his promotion to Chief Operating Officer, and for Mr. Wagner, our Chief Financial Officer.
- We extended Dr. Leiden's employment agreement by one year, until 2024. Under his amended employment agreement, Dr. Leiden will not receive any cash compensation for his Executive Chairman role other than an annual cash payment intended to facilitate participation in the company's benefit plans. Dr. Leiden will continue to receive equity awards for his third and fourth years in his Executive Chairman role.
- The company's outstanding performance in 2021 resulted in the board determining that the company had achieved a leading rating (138 out of a potential 150) for 2021, with the payment of annual cash bonuses near the high end of the range for 2021, commensurate with the performance described herein.
- 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 45 of this proxy statement.

As required by Section 14(a) 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: APPROVAL OF AMENDMENT AND RESTATEMENT OF 2013 STOCK AND OPTION PLAN

Our broad-based equity compensation program is essential to attract, retain and motivate people with the necessary talent and experience and to provide additional incentive to achieve our short- and long-term business objectives. Accordingly, we are requesting that our shareholders approve an amendment and restatement of our 2013 Stock and Option Plan (the “2013 Plan”), to increase the number of shares available for issuance under the 2013 Plan by 13.5 million shares.

On April 1, 2022, our board of directors amended and restated our 2013 Plan, subject to shareholder approval, to increase the number of shares of common stock authorized for issuance under the 2013 Plan by 13.5 million shares.

The 2013 Plan utilizes “fungible” shares, with stock options counting as one share against the total authorized shares and full value awards, such as restricted stock or restricted stock units, counting as 1.66 shares against the total authorized shares. We adopted this fungible share plan to provide flexibility in the types of awards we grant under our equity compensation program, while appropriately accounting for the difference between stock options and full value awards. Over the last several years, we have implemented changes in our equity compensation program for our employees, executives and our board that have significantly reduced dilution from our employee equity awards while maintaining a broad-based equity program. We believe that our equity compensation program has been fundamental to our success over the last several years and that the amendment and restatement of the 2013 Plan, which authorizes the issuance of additional shares, is necessary to support our equity compensation program going forward.

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 34% fewer shares of common stock in 2021 as compared to 2018 and reduced our “gross burn rate” from 1.7% in 2018 to 1.1% in 2021.

	2018	2019	2020	2021	% Change 2018 to 2021
	(in thousands, except percentages and employee numbers)				
Total Shares Granted Subject to Equity Awards	4,391	3,687	1,814	2,908	(34)%
Gross Burn Rate ⁽¹⁾	1.7%	1.4%	0.7%	1.1%	
Awards Canceled, Forfeited or Expired	826	886	432	646	
Net Dilution	3,565	2,801	1,382	2,262	(37)%
Net Burn Rate	1.4%	1.1%	0.5%	0.9%	
Average Employees During Fiscal Year ⁽²⁾	2,398	2,668	3,113	3,655	

(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.

(2) Average number of employees as of January 1st and December 31st.

Key Provisions of the 2013 Plan

The 2013 Plan includes a number of provisions designed to serve shareholders’ interests and facilitate effective corporate governance, including the following:

- **Fungible Shares:** Options granted at fair market value on the grant date (which is defined under the 2013 Plan as the average of the highest and lowest quoted selling prices on such date), and any other awards that we may in the future grant at a purchase price of 100% of the fair market value of a share of our common stock on the date of grant such as stock appreciation rights, count against the number of shares authorized under our 2013 Plan at a rate of one share for each share granted. Any restricted stock units, restricted stock or other “full value” awards granted under the 2013 Plan count against the number of shares authorized for issuance under our 2013 Plan at a rate of 1.66 shares for each share granted.

- **No Stock Option Re-pricing/Exchange:** Except in connection with specific corporate transactions (including stock dividends, stock splits, consolidations, mergers, recapitalizations and reorganizations), the 2013 Plan does not permit (i) the amendment of stock options or stock appreciation rights granted under the 2013 Plan to provide an exercise price that is lower than the then-current exercise price per share of such outstanding option or stock appreciation right, (ii) the cancellation of any outstanding option or stock appreciation right (whether or not granted under the 2013 Plan) and the grant in substitution thereof of any award under the 2013 Plan covering the same or a different number of shares of common stock and having an exercise price per share lower than the then-current exercise price per share of the cancelled option or stock appreciation right or (iii) the cancellation in exchange for a cash payment of any outstanding option or stock appreciation right with an exercise price per share above the then-current fair market value of our common stock without shareholder approval.
- **No Discounted Stock Options or SARs:** Stock options and stock appreciation rights cannot be granted with an exercise price less than the fair market value on the date of grant.
- **No “Evergreen” Provision:** The 2013 Plan does not contain an “evergreen” or similar provision. The 2013 Plan fixes the number of shares available for future grants and does not provide for any increase based on increases in the number of outstanding shares of common stock.
- **No Reload Rights:** Stock options granted under the 2013 Plan do not contain provisions entitling participants to automatic grants of additional stock options in connection with the exercise of the original option.
- **Limitation on Re-use of Shares:** Shares that are delivered to, or withheld by, the company under an award may not be reissued under the 2013 Plan. Shares may be delivered or withheld in connection with the exercise of stock options or the payment of required withholding taxes.
- **Limitations on Dividend Payments:** No dividends or dividend equivalents will be paid with respect to shares subject to stock options or stock appreciation rights unless and until such awards have vested and been exercised in accordance with their terms. Any dividends or dividend equivalents paid with respect to shares underlying stock rights other than stock options or stock appreciation rights will be subject to the same vesting terms otherwise applicable to the award.

Existing Plans

As of February 28, 2022, options to purchase (i) an aggregate of 3,165,632 shares having a weighted-average exercise price of \$147.70 per share and a weighted-average term before expiration of 5.58 years were outstanding under the 2013 Plan, and (ii) an aggregate of 252,327 shares having a weighted-average exercise price of \$74.66 per share and a weighted-average term before expiration of 1.69 years were outstanding under our Amended and Restated 2006 Stock and Option Plan (the “2006 Plan”). Also, as of February 28, 2022, there were outstanding an aggregate of 4,348,128 unvested shares of restricted stock units granted under the 2013 Plan and no unvested shares of restricted stock and restricted stock units granted under the 2006 Plan. As of this same date, there were outstanding purchase rights with respect to approximately 90,000 shares under our Employee Stock Purchase Plan (based on the closing price per share on February 28, 2022) and 1,777,228 shares remaining available for future issuance under this plan.

Submission of 2013 Plan

We are submitting an amendment and restatement of our 2013 Plan to our shareholders as required under applicable rules of Nasdaq and to ensure favorable federal income tax treatment under Section 422 of the Code, for any grants of incentive stock options that we may make under our 2013 Plan.

Summary of the Amended and Restated 2013 Stock and Option Plan

A summary of the principal features of our 2013 Plan is set forth below. A copy of our 2013 Plan, as amended and restated and in the form that would become effective upon shareholder approval of this proposal, is attached to this proxy statement as Appendix A.

Administration and Eligibility for Participation

The 2013 Plan is administered by our board of directors or any committee to which it delegates all or a part of its administrative responsibilities under the 2013 Plan. The term “administrator” as used in this summary refers to our board or any committee thereof that has been delegated the responsibility for administering the 2013 Plan. Subject to the provisions of the 2013 Plan, the administrator determines the persons to whom awards under the 2013 Plan will be granted, the number of shares to be covered by each award, the exercise price per share and the manner of exercise, the terms and conditions upon which awards are granted, whether to accelerate the vesting or extend the date of exercise of any installment of any award and how to interpret the provisions of the 2013 Plan. Awards may be granted under the 2013 Plan to our employees, including officers and directors who are employees, and to our consultants, advisors and non-employee directors. As of February 28, 2022, we and our subsidiaries had approximately 4,000 employees and 8 non-employee directors eligible to participate in the 2013 Plan. The number of consultants and advisors eligible for awards under the 2013 Plan varies from time to time and, as of February 28, 2022, approximately 50 consultants and advisors would be eligible to participate in the 2013 Plan. No participant may be granted awards in any calendar year for more than 1,000,000 shares, subject to adjustment for stock splits and similar recapitalizations.

Description of Awards

The 2013 Plan provides for the award of stock options, stock grants, and other stock-based awards. Any restricted stock grants, restricted stock units or other “full value” awards granted under the 2013 Plan will count against the number of shares authorized for issuance under the 2013 Plan at a rate of 1.66 shares for each share granted. Shares of common stock reserved for such awards granted under the 2013 Plan that lapse or are canceled or forfeited are added back to the share reserve at a rate of 1.66 shares for each share that lapses or is canceled or forfeited. Shares of common stock issued pursuant to restricted stock agreements and restricted stock unit awards may be purchased by employees for nominal value. If we were to permit shares of common stock to be delivered to us to pay the exercise price of a stock option or to be withheld to fund the payment of taxes, those shares would not be added back to the share reserve available for future awards. No option or stock appreciation right may be granted with a term exceeding ten years from the date of grant.

On March 24, 2022, the last reported sale price of our common stock on Nasdaq was \$251.70 per share.

Stock Options

Stock options provide award recipients with the right, subject to the terms and conditions that are specified in connection with the option grant, to purchase a specified number of shares of our common stock at a specified exercise price. Stock options granted under the 2013 Plan may be awarded as either non-qualified stock options or as incentive stock options within the meaning of Section 422 of the Code, referred to as ISOs, however only employees may receive ISOs. The maximum value of shares of common stock—determined at the time of grant—that may be subject to ISOs that become exercisable by an employee in any one year is limited to \$100,000. Since 2003, we have only granted non-qualified stock options under our equity plans.

Stock options granted under the 2013 Plan may not be granted with an exercise price that is less than the fair market value of our common stock on the date of grant, which is defined under the 2013 Plan as the average of the highest and lowest quoted selling prices on such date. ISOs may not be granted with an exercise price that is less than 110% of fair market value in the case of employees or officers holding 10% or more of our voting stock. ISOs granted to an employee or officer holding 10% or more of our voting stock must expire not more than five years from the date of grant.

Stock options granted under the 2013 Plan can only be exercised by the option holder and are not transferable except by the laws of descent and distribution or pursuant to domestic relations orders or as otherwise determined by the administrator, provided such transfer is not for value.

The 2013 Plan provides for stock option grants to non-employee directors under our director compensation program. In addition to any other stock rights as may be determined by our board of directors, each non-employee director serving in office is granted annually, pursuant to our equity plans, a fully vested non-qualified option to purchase a specified number of shares determined from time to time by our board.

The 2013 Plan permits the administrator to determine the manner of payment of the exercise price of options. Such methods include payment by cash or check, or, at the discretion of the administrator, by means of a broker assisted “cashless exercise,” delivery to us of shares of our common stock, any combination of such methods or any other lawful means approved by the administrator, other than delivery of a promissory note.

Stock Grants

A stock grant is an award of shares of common stock. Stock grants may be issued subject to restrictions on transfer and vesting requirements, as determined by the administrator. Vesting requirements may take the form of our lapsing right to repurchase the stock from the award recipient, based on either continued employment for specified time periods or on the attainment of specified business performance goals set by the administrator. Subject to the transfer restrictions and our repurchase rights, if any, the grantee will have all rights with respect to unvested shares of common stock issued under a stock grant as are possessed by our other shareholders, including all voting and dividend rights, provided that dividends, if any, with respect to unvested shares shall accrue and be payable only upon the vesting of such shares.

Stock-Based Awards

The 2013 Plan provides that the administrator may grant other stock-based awards, including restricted stock units, share grants based upon specified conditions, the grant of securities convertible into shares, or the grant of stock appreciation rights, or phantom stock awards, in each case upon terms and conditions established by the administrator.

Performance Awards

Under the 2013 Plan, we have the discretionary authority to structure one or more awards so that the shares of common stock subject to those particular awards will not vest unless certain pre-established objective performance goals are achieved. Each objective performance measure that is a financial measure may be determined pursuant to generally accepted accounting principles (GAAP) or on a non-GAAP basis.

Such objective performance measures may reflect absolute entity or business unit performance or a relative comparison to the performance of a peer group of entities, an index or indices or other external measure of the selected performance criteria, and may be absolute in their terms or measured against or in relationship to other companies comparably, similarly or otherwise situated. The objective performance measures and any targets with respect thereto need not be based on an increase, a positive or improved result or the avoidance of loss. Such performance measures: (1) may vary by participant and may be different for different awards and (2) may be particular to a participant or the department, branch, line of business, subsidiary or other unit in which the participant works and may cover such performance period as may be specified by us.

Adjustments in the Event of Stock Dividends, Stock Splits, Recapitalizations or Reorganizations

The number of shares subject to stock rights and other terms applicable to such rights will be equitably adjusted if we issue a stock dividend, or in the event of a stock split, recapitalization or reorganization. In addition, in the event of certain consolidations or acquisitions or a sale of substantially all of our assets, either (i) the administrator or the entity assuming our obligations under the 2013 Plan shall make appropriate provision for the continuation of all outstanding stock rights under the 2013 Plan or grant replacement stock rights on an equitable basis as determined by the administrator or the relevant entity, or (ii) if there is no assumption or replacement, the vesting of all outstanding and unvested stock rights under the 2013 Plan will be accelerated and such stock rights will become fully exercisable immediately prior to such consolidation, acquisition or sale.

Effective Date, Amendment and Expiration

The 2013 Plan became effective on May 8, 2013 and was previously amended and restated effective as of June 4, 2015, June 8, 2017, May 17, 2018, October 16, 2018 and June 5, 2019. The amendment and restatement of our 2013 Plan will be effective, subject to shareholder approval, on May 18, 2022. The 2013 Plan will terminate on April 12, 2027. Our board of directors may terminate or amend the 2013 Plan at any time, subject to shareholder approval under certain circumstances as provided in the 2013 Plan. No amendment or termination of the 2013 Plan will adversely and materially affect the rights provided in any award made under the 2013 Plan prior to the plan amendment or termination. Neither our board nor the administrator has the authority to reduce the exercise price of any stock option after the date of grant, except in the case of an equitable adjustment required under the 2013 Plan. No award may be made under the 2013 Plan after the plan expiration date. Awards made prior to expiration of the 2013 Plan may extend beyond the plan expiration date.

U.S. Federal Income Tax Consequences

The discussion of federal income tax consequences that follows is based on an analysis of the Code as currently in effect, existing law, judicial decisions and administrative regulations and rulings, all of which are subject to change, and is applicable to optionees who are U.S. taxpayers.

Non-Qualified Options

Options that are designated as non-qualified options are not intended to qualify for treatment under Section 422 of the Code. Options otherwise qualifying as ISOs, to the extent the aggregate fair market value of shares with respect to which such options are first exercisable by an individual in any calendar year exceeds \$100,000, also will be treated as options that are not ISOs.

A non-qualified option ordinarily will not result in income to the optionee or a deduction for us for tax purposes at the time of grant. Instead, the optionee will recognize compensation income at the time of exercise of a non-qualified option in an amount equal to the excess of the fair market value of the shares at the time of exercise over the option exercise price. Any compensation income may be subject to withholding taxes, and a deduction may then be allowable to us in an amount equal to the optionee's compensation income.

An optionee's initial basis in shares so acquired will be the amount paid on exercise of the non-qualified option plus the amount of any corresponding compensation income. Any gain or loss as a result of a subsequent disposition of the shares so acquired will be capital gain or loss.

Incentive Stock Options

ISOs are intended to qualify for treatment under Section 422 of the Code. An ISO does not result in taxable income to the optionee or a deduction for us at the time it is granted or exercised, provided that the optionee does not dispose of the shares acquired pursuant to the option either within two years after the date of grant of the option or within one year after the shares are issued, referred to as the ISO holding period. However, the difference between the fair market value of the shares on the date of exercise and the option exercise price will be an

item of tax preference that is included in alternative minimum taxable income. Upon disposition of the shares after the expiration of the ISO holding period, the optionee generally will recognize long-term capital gain or loss based on the difference between the disposition proceeds and the option exercise price paid for the shares. If the shares are disposed of prior to the expiration of the ISO holding period, the optionee generally will recognize taxable compensation, and we will have a corresponding deduction, in the year of the disposition, equal to the excess of the fair market value of the shares on the date of exercise of the option over the option exercise price. Any additional gain realized on the disposition normally will constitute capital gain. If the amount realized upon such a disqualifying disposition is less than fair market value of the shares on the date of exercise, the amount of compensation income will be limited to the excess of the amount realized over the optionee's adjusted basis in the shares.

Stock Grants

With respect to stock grants that result in the issuance of shares that are either not restricted as to transferability or not subject to a substantial risk of forfeiture, the grantee must generally recognize ordinary income equal to the fair market value of shares received. Thus, deferral of the time of issuance generally will result in the deferral of the time the grantee will be liable for income taxes with respect to such issuance. We generally will be entitled to a deduction in an amount equal to the ordinary income recognized by the grantee.

With respect to stock grants involving the issuance of shares that are restricted as to transferability and subject to a substantial risk of forfeiture, the grantee generally must recognize ordinary income equal to the fair market value of the shares received at the time the shares become transferable or are not subject to a substantial risk of forfeiture, whichever occurs earlier. A grantee may elect to be taxed at the time of receipt of shares rather than upon lapse of restrictions on transferability or substantial risk of forfeiture, but if the grantee subsequently forfeits such shares, the grantee would not be entitled to any tax deduction, including as a capital loss, for the value of the shares on which the grantee previously paid tax. The grantee must file any such election with the Internal Revenue Service within 30 days of the receipt of the shares. We generally will be entitled to a deduction in an amount equal to the ordinary income recognized by the grantee.

Our ability to deduct compensation is subject to limitations under the Code.

Plan Benefits

The granting of awards under the 2013 Plan is discretionary and we cannot now determine the number or type of awards to be granted in the future to any particular person or group. For further information on awards to non-employee directors, see the section "Non-Employee Director Compensation Program" beginning on page 31 of this proxy statement.

The following table sets forth the awards that were granted to our named executive officers, our executive officers as a group, our non-employee directors as a group, and our other employees (who are not executive officers) as a group under the 2013 Plan during the 2021 fiscal year.

Name and Position	Number of Stock Options	Number of Restricted Stock Units (excluding Performance-Based Restricted Stock Units)	Number of Performance-Based Restricted Stock Units (assuming target performance)
Named Executive Officers			
Dr. Reshma Kewalramani, Chief Executive Officer and President	—	29,031	29,032
Charles F. Wagner, Jr., EVP, Chief Financial Officer	—	11,627	11,628
Stuart A. Arbuckle, EVP, Chief Operating Officer	—	13,952	13,952
Dr. Jeffrey Leiden, Executive Chairman	—	20,928	20,928
Nia Tatsis, EVP, Chief Regulatory and Quality Officer	—	13,952	13,952
All executive officers as a group (10 persons)	—	139,632	148,458
All non-employee directors as a group (8 persons)	27,302	7,836	—
All other employees, as a group	—	1,779,674	572,840

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** the approval of an amendment and restatement of our 2013 stock and option plan to increase the number of shares authorized for issuance under this plan by 13.5 million shares.

Equity Compensation Plan Information

As of February 28, 2022, there were 6,810,418 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, 2022, under our equity plans:

- Stock options covering 3,417,959 shares of our common stock, with a weighted average exercise price of \$142.30 and a weighted average remaining term of 5.3 years, were outstanding; and
- Unvested restricted stock units covering 4,348,128 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, 2021. 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, 2021. Accordingly, the figures in the table below do not reflect the equity grants made to our employees under the 2013 Plan, since December 31, 2021.

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⁾	7,597,354 ⁽²⁾	\$ 141.76 ⁽³⁾	11,335,271 ⁽⁴⁾
Equity Compensation Plans Not Approved by Shareholders	—	—	—
TOTAL	7,597,354		11,335,271

(1) These plans consist of the 2013 Plan, the 2006 Plan and our Employee Stock Purchase Plan. No further shares of common stock will be issued or distributed under the 2006 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 shareholder approved plans, as of December 31, 2021, and includes 3,319,214 options granted under the 2013 Plan, 2,887,873 restricted stock units granted under the 2013 Plan, 1,077,830 performance stock units ("PSU") (assuming the maximum number of PSUs will be earned) granted under the 2013 Plan, 20,646 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 291,791 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 shareholder approved equity compensation plans and consists of 9,558,043 shares available for future issuance under the 2013 Plan and 1,777,228 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, 2022.

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, continued delivery of strong 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 approximately \$56 billion at the end of 2021.

We take seriously our role in the governance of compensation programs and the importance of attracting, recruiting, 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.

2021 was an important year for Vertex and the company continued to execute successfully on its business strategy. Vertex solidified its long-term leadership in CF in numerous ways and continued to treat more people with CF than ever before. Vertex obtained approval of TRIKAFTA for children with CF 6 to 11 years of age in the U.S. and entered into more than 20 new reimbursement agreements in 2021, securing access to our medicines for thousands of new patients. In early 2022, Vertex obtained approval of KAFTRIO for children with CF 6 to 11 years of age in Europe. Beyond CF, the research and development team advanced numerous programs, including completing enrollment for pivotal studies for CTX001, a one-time gene-editing therapy for patients with sickle cell disease and beta thalassemia; obtaining the first clinical data for VX-880, a fully differentiated pancreatic islet cell therapy; and establishing clinical proof-of-concept for VX-147, a small molecule targeting APOL1-mediated kidney disease. The team also initiated and has now completed and announced positive data for two Phase 2 proof-of-concept studies for VX-548, a small molecule NaV1.8 inhibitor for the treatment of acute pain. In addition, 2021 saw significant progress in our research pipeline for diseases, including DMD, DM1 and AAT deficiency. These advances position the company for multiple important milestones and significant value creation in 2022 and beyond.

The company delivered outstanding financial performance in 2021, achieving CF net product revenues of \$7.57 billion, a 22% increase compared to 2020. This revenue growth drove significant growth in earnings and cash flow, and the company finished the year in a strong financial position with \$7.5 billion in cash, cash equivalents, and marketable securities. The senior management team additionally strengthened its organizational capabilities, recruiting and onboarding top-tier talent across the organization, including filling critical hires with superior and diverse talent.

The company's successes in 2021 reflect both the company's strong performance in 2021 and the differentiated corporate strategy that its senior management team continues to champion. Consistent with these outstanding results, for 2021, 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)
Lloyd Carney
Terrence C. Kearney
Yuchun Lee

Overview

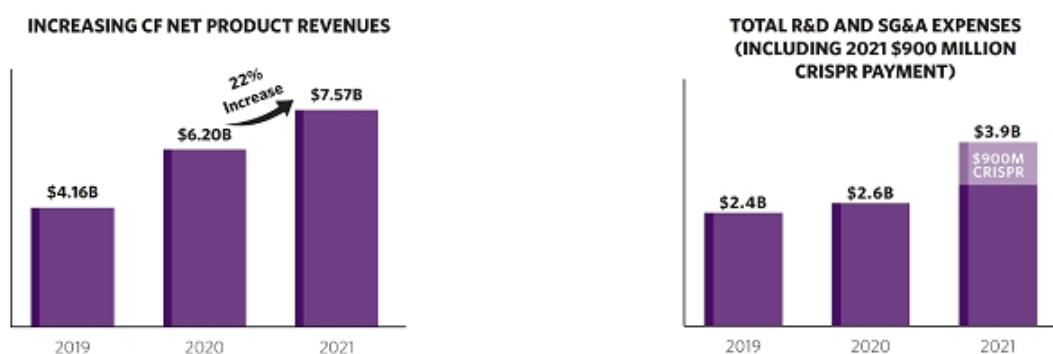
This section discusses the principles underlying our policies and decisions with respect to the compensation of our NEOs for 2021 and the factors we believe are relevant to an analysis of these policies and decisions. Our NEOs for 2021 are listed below.

Name	Position
Reshma Kewalramani	Chief Executive Officer and President
Charles F. Wagner, Jr.	Executive Vice President, Chief Financial Officer
Stuart A. Arbuckle	Executive Vice President, Chief Operating Officer
Jeffrey M. Leiden	Executive Chairman
Nia Tatsis	Executive Vice President, Chief Regulatory and Quality Officer

Financial Performance

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

- Our CF net product revenues increased to \$7.57 billion in 2021, up 22% or approximately \$1.4 billion, from our 2020 net product revenues.
- Our total R&D and SG&A expenses increased to \$3.9 billion compared to \$2.6 billion in 2020 primarily due to a \$900 million upfront payment we made to CRISPR in connection with an amendment to our CTX001 collaboration in 2021, and incremental investments to support the advancement and expansion of our pipeline and to support the launches of our medicines globally.

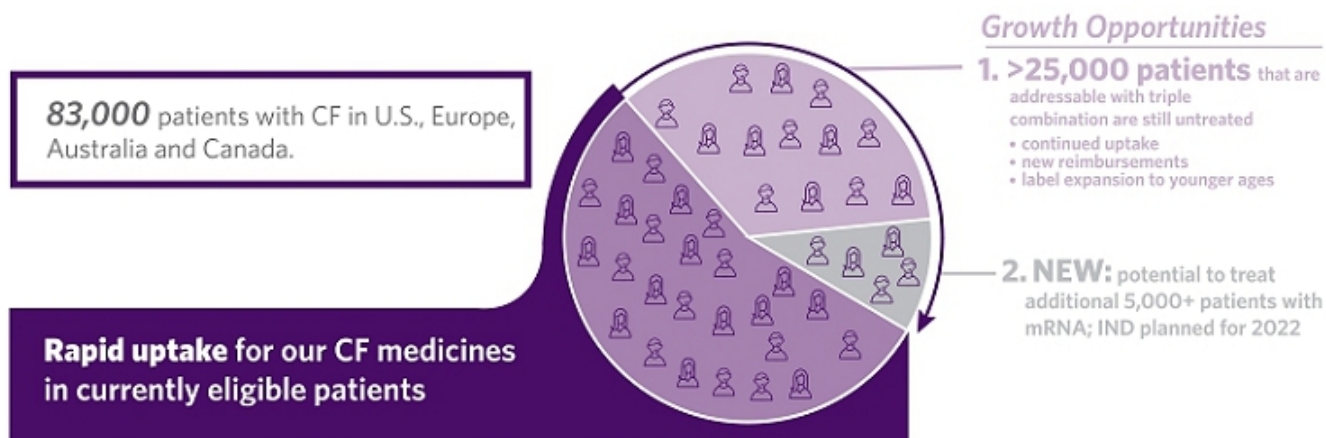


Marketed Products

Our deliberate strategy of continuous serial innovation has significantly solidified our leadership position in CF and moved us ever 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.

Today, our four approved medicines are being used to treat the majority of the approximately 83,000 people with CF in North America, Europe and Australia. However, we believe that there are more than 25,000 untreated patients in these geographies who could still benefit from our medicines. Over the next several years, we plan to reach these patients through continued uptake of our medicines, expansion of our TRIKAFTA/KAFTRIO label to lower age groups, and additional approvals and reimbursement agreements. In support of our goal of bringing transformative therapies to all people with CF, we also are pursuing genetic therapies for the remaining people with CF who may not be helped by our current CF medicines. During the last year, we have significantly advanced our pre-clinical mRNA program for these patients and expect to enter the clinic with this new therapy in 2022.

CONTINUED GROWTH AHEAD IN CF



Since the beginning of 2021, notable progress that has resulted from our efforts includes:

- The FDA approved the use of TRIKAFTA for children with CF 6 through 11 years of age who have at least one F508del mutation or at least one other mutation that is responsive to TRIKAFTA.
- Health Canada granted marketing authorization for TRIKAFTA for people with CF 12 years of age and older who have at least one F508del mutation. Our application for approval of TRIKAFTA for children with CF 6 through 11 years of age has been accepted for priority review by Health Canada.
- In January 2022, the European Commission and the Medicines and Healthcare products Regulatory Agency granted marketing authorization for KAFTRIO for the treatment of children with CF 6 through 11 years of age who have at least one F508del mutation in the CFTR gene.
- More than 20 countries outside the U.S. have now approved and reimbursed or made accessible TRIKAFTA/KAFTRIO.

Research and Development

We invest in research and development to discover and develop transformative medicines for people with serious diseases with a focus on specialty markets. Our research and development strategy is to combine transformative advances in the understanding of human disease and the science of therapeutics to discover and develop new medicines. This approach has yielded a broad and deep pipeline and increases the speed and likelihood of successfully bringing medicines to patients. Our differentiated approach to drug discovery has been validated by 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.

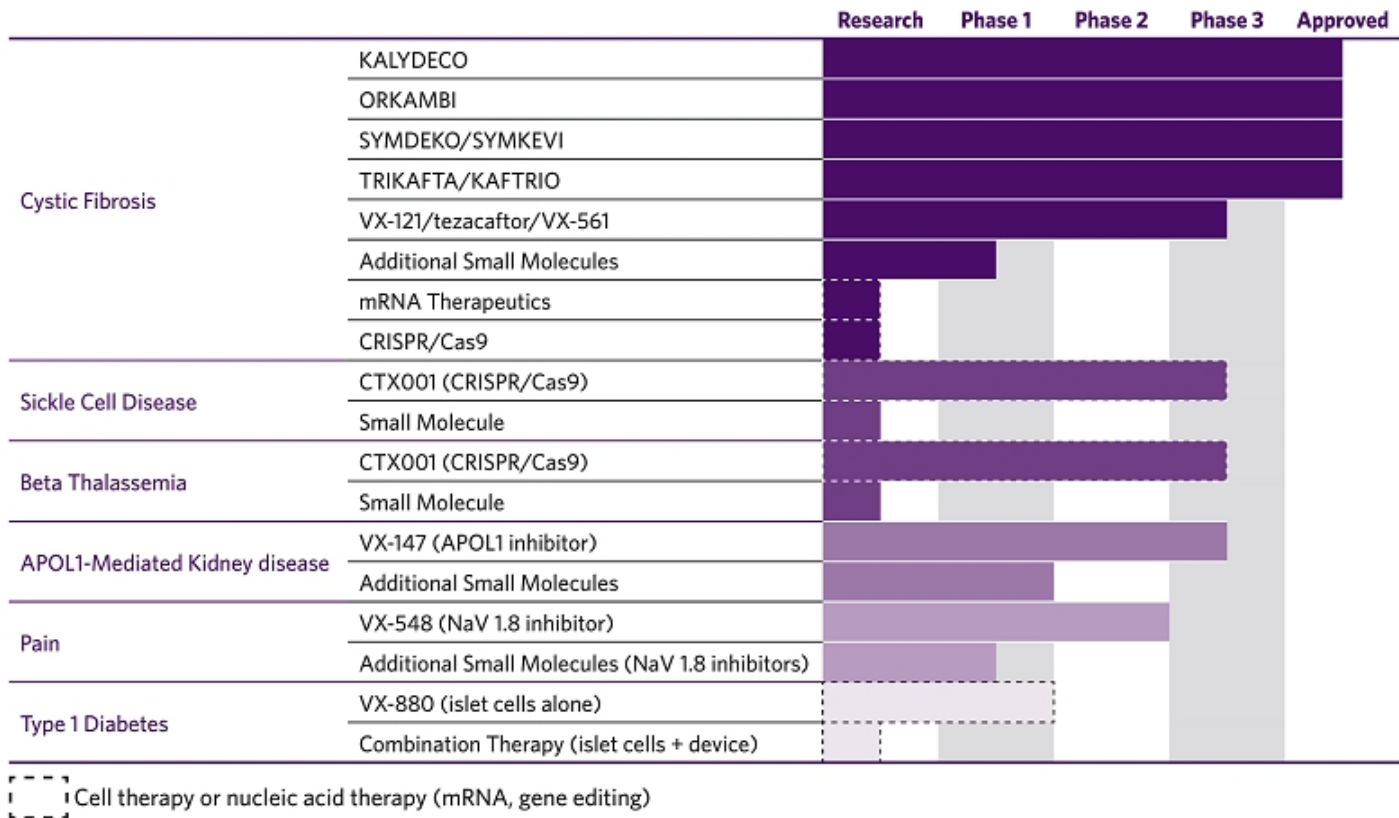
We continue to research and develop small molecule product candidates for the treatment of serious diseases, including CF, AMKD, pain, AAT deficiency, and DM1. Our research and development approach includes advancing multiple candidates into clinical trials, pursuing multiple modalities, and evaluating clinical and non-clinical data to inform drug discovery and development, with the goal of bringing best-in-class therapies to patients. In 2022, we expect to have several small molecule programs in pivotal development (AMKD, CF, pain). In addition to expanding our small molecule programs during the last seven years, we have also assembled an industry-leading portfolio of programs in cell and gene therapies. In collaboration with our partner, CRISPR, we have developed the first human gene editing approach for two serious genetic diseases, SCD and beta thalassemia. Based on our acquisition of Semma Therapeutics, we have recently reported unprecedented clinical data for the first stem cell-derived therapy for T1D. We also continue to advance our late-stage pre-clinical gene editing program for DMD.

We are advancing programs across multiple disease areas and modalities, including:

- *Cystic Fibrosis*. We are evaluating in Phase 3 clinical trials a new, once-daily investigational triple combination of VX-121/tezacaftor/VX-561 (deutivacaftor). We also are researching mRNA therapies as well as gene-editing approaches to treat the remaining people with CF who are not expected to benefit from our small molecule medicines. We expect to submit an IND for our CF mRNA program in 2022.
- *Sickle Cell Disease and Beta Thalassemia*. We are evaluating in Phase 3 clinical trials CTX001, an investigational CRISPR/Cas9-based gene-editing therapy for severe sickle cell disease and transfusion-dependent beta thalassemia with CRISPR. Enrollment is complete, and we anticipate regulatory submissions for CTX001 in late 2022.
- *APOL1-Mediated Kidney Disease*. Based on positive Phase 2 data for VX-147, our small molecule for the treatment of APOL1-mediated focal segmental glomerulosclerosis, we advanced VX-147 into pivotal development in a broader population of people with AMKD in the first quarter of 2022.
- *Type 1 Diabetes*. We are evaluating VX-880, a stem-cell derived therapy involving the transplantation of fully differentiated pancreatic islet cells, for the treatment of T1D in a Phase 1/2 clinical trial, and announced positive Day 150 data for the first T1D patient in this clinical trial. Our trials in the U.S. and Canada are ongoing, and we continue to dose patients. We also are pursuing additional programs in T1D, in which the implanted islet cells are encapsulated in an immunoprotective device or modified to produce hypoimmune cells. We are conducting IND-enabling studies for the cells and device program and expect to submit an IND for this program in 2022.
- *Pain*. We recently announced positive Phase 2 data for VX-548, a NaV 1.8 inhibitor, for the non-opioid treatment of acute pain. We expect to advance VX-548 into pivotal development in the second half of 2022.
- *Alpha-1 Antitrypsin Deficiency*. We obtained proof-of-mechanism for VX-864 in a Phase 2 study of protein folding correction of the Z-AAT protein. We plan to advance into the clinic one or more novel small molecule correctors intended to address the lung and liver manifestations of AAT deficiency in 2022.
- *Duchenne muscular dystrophy and myotonic dystrophy type 1*. We are focused on advancing gene-editing therapies aimed at treating the underlying cause of DMD and DM1. We are also exploring potential small molecule approaches to address the underlying causal biology for DM1.
- In addition to the programs listed above, we have a number of early-stage research programs aimed at other targets that represent the causal human biology of serious diseases.

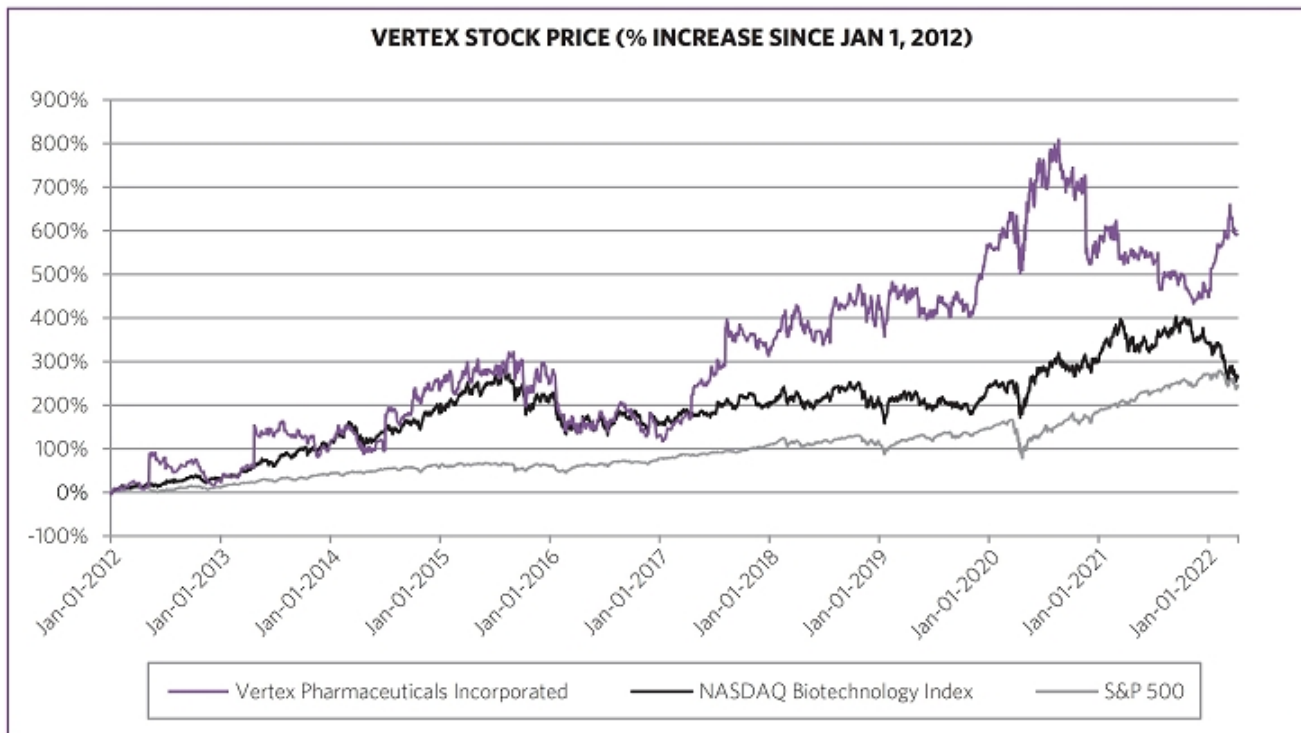
We plan to continue investing in our research and development programs and fostering scientific innovation by identifying additional product candidates through our internal research efforts and investing in business development transactions to access emerging technologies, products, and product candidates.

The following chart represents our pipeline programs by disease area, stage of development, and modality, for programs that have lead assets in the clinic.

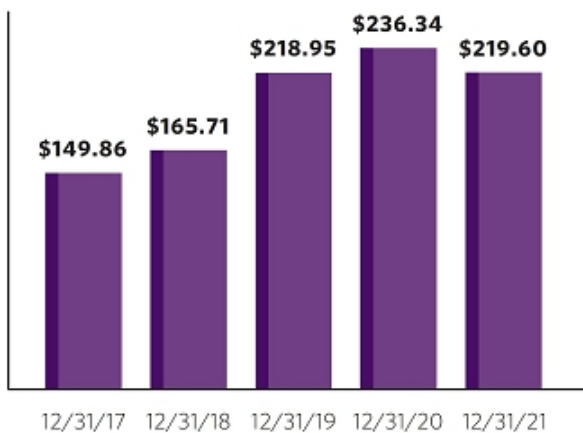


Increasing Shareholder Value

We believe that execution of our differentiated serial innovation strategy will continue to create shareholder value over the long term. The biotechnology sector is subject to short-term volatility and many biotechnology companies, including Vertex, experienced stock price fluctuations in 2021. Notwithstanding these short-term fluctuations, our executive team has outperformed on our CF business and successfully executed on our focused strategy, creating significant shareholder returns over the last several years. The following charts show our total shareholder return relative to the NBI and S&P 500 indices since the beginning of 2012, when KALYDECO was first approved, as well as our stock price performance over multiple periods.



STOCK PRICE



2021 Compensation Decisions and Pay-for Performance

In 2021, our executive compensation program received substantial support from our shareholders, approved by approximately 91% 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 short- and 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 more than 90% of our NEO compensation tied to performance.** Retention of our talented executives is critical, as their outstanding performance has led to the company's advancement and the creation of significant long-term shareholder value.

In 2021, 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:** In 2021, based on a comparative analysis of companies in our Peer Group (described below), we increased compensation for Dr. Kewalramani and Mr. Wagner, and we increased Mr. Arbuckle's compensation in connection with his promotion to Chief Operating Officer. Under his employment agreement, Dr. Leiden no longer receives a base salary for his role of Executive Chairman.
- **Annual Cash Bonus:** We increased the target cash bonus of Mr. Arbuckle to 90% of his base salary in connection with his promotion to Chief Operating Officer. We maintained the target cash bonus, which is a percentage of base salary, for our other NEOs, except for Dr. Leiden who does not receive an annual cash bonus pursuant to his employment agreement. The company's outstanding performance in 2021, as described above, resulted in the board determining that the company had achieved a leading rating (a company rating of 138 out of a potential 150) for 2021, with the payment of annual cash bonuses near the high end of the range for 2021. Please see "Overview of Company Performance Rating & Achievement in 2021."
- **Long-Term Equity Program:**
 - In 2021, based on a comparative analysis of companies in our Peer Group, we increased the target equity grant for Dr. Kewalramani and, in connection with his promotion to Chief Operating Officer, Mr. Arbuckle. We maintained the target equity grants for our other NEOs based on a comparative analysis with companies in our Peer Group and our expectations of their future impact on, and contributions to, our long-term objectives. For his second year as Executive Chairman, Dr. Leiden received equity grants of \$8.5 million pursuant to the terms of his employment agreement. Under his amended employment agreement, Dr. Leiden will continue to receive equity grants for the third and fourth years in his Executive Chairman role.
 - We maintained our mix of equity granted under our compensation program with 50% consisting of PSUs 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 and shareholder alignment 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.
 - We achieved all goals established for the 2019 non-financial based performance restricted stock unit awards and the 2021 financial-based PSU awards at the maximum level under these awards, resulting in a maximum payout under these awards in February 2022.
 - In early 2022, the MDCC granted new awards of PSUs and established the financial and non-financial metrics that will determine whether and to what extent these awards become earned and vested. Fifty percent of the PSUs, which vest annually in installments over three years, are tied to CF net product revenues in 2022, while the remaining fifty percent, which cliff vest after three years, 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 shareholders to solicit and understand a variety of perspectives and interests, and our practice has been to engage with our top shareholders regularly over the course of the year.

During 2021, we solicited feedback regarding our corporate governance practices from our top 40 shareholders representing approximately 60% of our outstanding shares. Our integrated outreach team included leaders from our Investor Relations, Human Resources, Corporate Responsibility, and Legal teams, and we discussed numerous topics of shareholder interest, including our business strategy, research and development, our diversity initiatives and metrics, employee engagement and development, political and lobbying disclosures, executive compensation, sustainability and climate change matters, and COVID-related impacts to our employees, patients, and our business.

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 incentive 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
Annual risk review	
Pay for performance sensitivity and emphasis	
Robust shareholder outreach	

Detailed Discussion and Analysis

Compensation Philosophy

Our MDCC regularly reviews the elements of the individual compensation packages for our executive officers to ensure that they continue to support the achievement of 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 company and individual 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 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 board 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 address several key objectives, including increasing revenues from our current products, achievement of research and development objectives, enhancing organizational capabilities, and maintaining financial strength. We believe this mix of goals provides an appropriate balance of near- and long-term objectives and financial and organizational development objectives. We believe this mix provides an appropriate balance between near- and long-term objectives and financial and organizational development objectives. 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, superior profitability, and ability to continue creating value over the long-term. Our MDCC and board expects to continue seeking balance in the use of financial metrics and research and development goals 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, and, most importantly, discovering, developing, and delivering transformative medicines for patients who can benefit from them.

Compensation Decision-Making Process

Role of MDCC and CEO in Setting Executive Compensation

The MDCC has responsibility for overseeing the design, development, and implementation of the compensation program for our CEO and other executive officers. The MDCC evaluates the performance of our CEO and other executive officers. Our CEO and our human resources group assist the MDCC in evaluating the performance of our other executive officers, including the NEOs other than the CEO. Our CEO 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 executive compensation to the independent directors of the board, who together make final compensation decisions for the CEO and other executive officers based on these performance 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 an independent compensation consultant to conduct an analysis of all elements of our executive officer compensation program compared to similar elements paid to similarly situated executives at companies in our Peer Group (as defined below) 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 2021, the MDCC continued its engagement with Pearl Meyer as its independent compensation consultant. Pearl Meyer is compensated for advice provided at the direction of the MDCC.

The MDCC reviews Pearl Meyer's independence in accordance with applicable Nasdaq and SEC rules. Based on this review, 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 (our "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 that revenue alone adequately indicates whether a company has 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 requires 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 approved the following comparator companies for 2021, which were the same comparator companies that were used in 2020. In 2022, we expect to replace Alexion Pharmaceuticals, Inc. ("Alexion") due to its acquisition by AstraZeneca PLC ("AstraZeneca").

2021 Peer Group	
AbbVie Inc.	Gilead Sciences, Inc.
Alexion Pharmaceuticals, Inc.	Incyte Corporation
Alkermes plc	Jazz Pharmaceuticals plc
Amgen Inc.	Regeneron Pharmaceuticals, Inc.
Biogen Inc.	SeaGen Inc.
BioMarin Pharmaceuticals Inc.	United Therapeutics Corporation
Eli Lilly and Company	

Properties of Peer Group

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		Innovative and Importance of Medicines									
		R&D Expense ⁽¹⁾		Operational Focus		Orphan/Unmet Clinical Need	Breakthrough Therapy Designations ⁽²⁾	Innovative Approved Drugs in Last 10 Years ⁽³⁾	Uses Vertex as Peer	Market Position	
Company	Industry	\$ (millions)	% of Revenue	Global	Commercial					Nasdaq 100	S&P 500
AbbVie	Biotech	\$ 8,046	14%	✓	✓	✓	7	8		✓	
Alexion ⁽⁴⁾	Biotech	\$ 1,284	21%	✓	✓	✓	2	3	✓		
Alkermes	Biotech	\$ 407	35%	✓	✓	✓	—	3			
Amgen	Biotech	\$ 6,324	24%	✓	✓	✓	2	9		✓	
Biogen	Biotech	\$ 2,519	23%	✓	✓	✓	—	6	✓	✓	
BioMarin	Biotech	\$ 629	34%	✓	✓	✓	1	4	✓		
Eli Lilly	Pharma	\$ 7,901	28%	✓	✓	✓	3	10		✓	
Gilead	Biotech	\$ 5,540	20%	✓	✓	✓	4	8		✓	
Incyte	Biotech	\$ 1,488	50%	✓	✓	✓	1	4	✓	✓	
Jazz	Pharma	\$ 1,032	33%	✓	✓	✓	—	4	✓		
Regeneron	Biotech	\$ 2,908	18%	✓	✓	✓	6	7	✓	✓	
SeaGen	Biotech	\$ 1,229	78%	✓	✓	✓	4	3	✓	✓	
United Therapeutics	Biotech	\$ 540	32%	✓	✓	✓	—	3	✓		
Vertex	Biotech	\$ 3,051	40%	✓	✓	✓	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, 2021 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 nine years include: VIEKIRA PAK, IMBRUVICA, VENCLEXTA, ORLISSA, MAVYRET, RINVOQ, SKYRIZI and QULIPTA (AbbVie), STRENSIQ, ULTOMIRIS and KANUMA (Alexion), ARISTADA, VUMERITY, and LYBALVI (Alkermes), AIMOVIQ, BLINCYTO, XGEVA, PROLIA, KYPROLIS, PARSABIV, EVENITY, TEZSPIRE, and LUMAKRAS (Amgen), TECFIDERA, ALPROLIX, SPINRAZA, ELOCTATE, VUMERITY and ADUHELM (Biogen), BRINEURA, PALYNZIQ, VIMIZIM and VOXZOGO (BioMarin), CYRAMZA, EMGALITY, JARDIANCE, OLUMIANT, PORTRAZZA, RETEVMO, REYVOW, TALTZ, VERZENIO and BAMLANIVIMAB/ ETESEVIMAB (emergency use authorization) (Eli Lilly), YESCARTA, SOVALDI, HARVONI, VEMLIDY, CAYSTON, ZYDELIG, BIKTARVY and VEKLURY (Gilead), JAKAFI, OLUMIANT, PEMAZYRE and RUXOLITINIB (Incyte), VYXEOS, DEFITELIO, ZEPZELCA and RYLAZE (Jazz), DUPIXENT, LIBTAYO, PRALUENT, EYLEA, ZALTRAP, INMAZEB and EVKEEZA (Regeneron), PADCEV, TUKYSA and TIVDAK (Seagen) and REMODULIN, ORENITRAM and UNITUXIN (United Therapeutics).

(4) Alexion data reflects the trailing data for the most recent four quarters prior to Alexion's acquisition by AstraZeneca - financials reflect data as of March 31, 2021 per the S&P Capital IQ database.

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. 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.

In support of Stuart Arbuckle’s promotion to Chief Operating Officer and the low representation of the Chief Operating Officer role within the Peer Group, Pearl Meyer supplemented the Peer Group with broader life science industry companies for purposes of analyzing competitive compensation for this role. Pearl Meyer reviewed companies within the broader life sciences industry and included all companies who maintained a chief operating officer or similar role that also had greater than \$2 billion revenues and greater than \$10 billion market capitalization. The MDCC reviewed the compensation practices for the following Peer Group and broader life science industry companies when considering Mr. Arbuckle’s expanded role:

Peer Group Companies	Life Science Companies
Alkermes plc	Bio-Rad Laboratories, Inc.
Amgen Inc.	DexCom, Inc.
Jazz Pharmaceuticals plc	ResMed Inc.
United Therapeutics Corporation	Stryker Corporation
	Thermo Fisher Scientific Inc.
	Zimmer Biomet Holdings Inc.

Based on this discussion, for 2021, we increased Mr. Arbuckle’s base salary to \$900,000, his target cash bonus to 90% of his base salary, and his target equity grant to \$4.75 million.

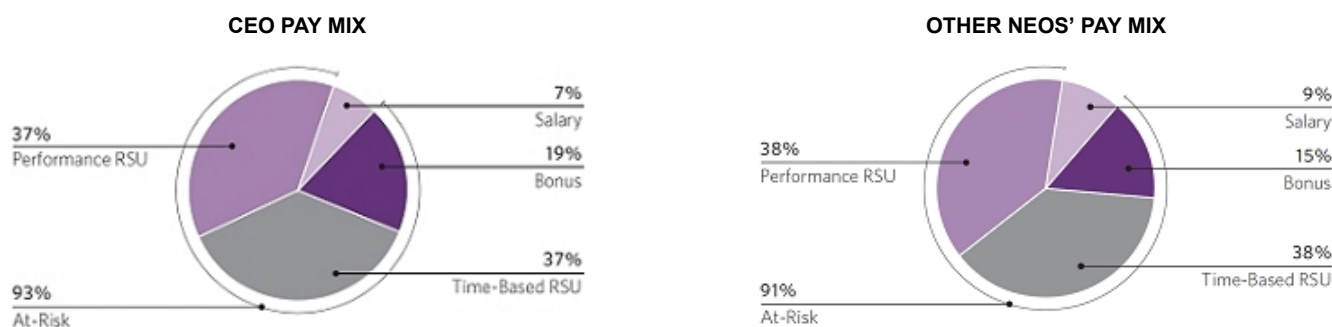
Elements of Annual Compensation

Our practice is to target total direct compensation including base salary, target annual cash incentives, and target long-term incentive awards 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 they are appropriately designed in light of our goals to align the program with our business strategy, the competitive environment and our shareholders’ interests.

Our executive compensation program emphasizes a mix of long-term equity compensation awards to incentivize and reward those individuals who make the greatest contribution to 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 2021 equity grants, we maintained our mix of equity awards, including performance restricted stock units and time-based restricted stock units.

Compensation Program

As shown in the following charts, our compensation program places significant weight on performance-based compensation, with more than 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. These charts exclude the compensation of our Executive Chairman.

Performance-Based Value-Based Program

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

Compensation Element	Performance Link
Annual Cash Bonus	Annual bonus dependent on both company and individual performance factors
Equity Awards	Grant date value of equity awards based on target award values by level with differentiation for 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	<ul style="list-style-type: none"> 50% of PSUs with range of shares issued 0% to 200% of target based on one year financial metrics (vesting in equal 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	<ul style="list-style-type: none"> Value of awards increases or decreases based on stock price over the three-year vesting period 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 as well as the resulting value dependent upon increases or decreases in our stock price over the three-year vesting period.

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. Fifty percent (50%) of the target number of PSUs are eligible to vest based on the achievement of financial goals and the remaining 50% of the target number of PSUs are eligible to vest based on the achievement of non-financial goals. The financial PSUs, if earned, vest in annual installments over a three-year period, and the non-financial PSUs, if earned, cliff vest after three years. The potential shares earned pursuant to these PSU awards range from 0% to 200% of the target number of shares, with the number of shares actually issued determined by the achievement of the financial and non-financial performance 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 short- and long-term strategic objectives and 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 that vest over a three-year period measured from the date of grant. With 50% of the annual long-term incentive award at risk pending successful execution of our strategic objectives pursuant to our PSUs, we believe that it is important to have the remaining half of the annual long-term equity 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.

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 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 Peer Group 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 or years, the MDCC recommends an appropriate base 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 our Peer Group companies.

Dr. Kewalramani's base salary for 2021, as our CEO and President, was increased to \$1.32 million based on multiple factors, including her contributions as CEO and President since April 1, 2020, expected future contributions, experience, and knowledge, and based on a comparative analysis of CEO compensation in our Peer Group.

In 2021, Stuart Arbuckle was promoted to Chief Operating Officer in recognition of his expanded responsibilities including global commercial operations, manufacturing supply chain, corporate communications, and human resources. Based on his expanded role and a comparative analysis of Chief Operating Officer compensation in our Peer Group and the broader life science industry, as described above under "Properties of Peer Group," we increased Mr. Arbuckle's base salary to \$900,000.

We also increased the base salary for Mr. Wagner to \$770,000 in recognition of his contributions since becoming Chief Financial Officer in April of 2019, expected future contributions, experience, and knowledge, and based on a comparative analysis of Chief Financial Officer compensation in our Peer Group. In 2021, we maintained Ms. Tatsis' base salary.

Name	2021 Base Salary
Reshma Kewalramani	\$1,320,000
Charles F. Wagner, Jr.	\$ 770,000
Stuart A. Arbuckle	\$ 900,000
Jeffrey M. Leiden ⁽¹⁾	\$ —
Nia Tatsis	\$ 550,000

(1) Pursuant to his employment agreement, Dr. Leiden's base salary was \$1.0 million for his first year as Executive Chairman (from April 1, 2020 through March 31, 2021). As of April 1, 2021, Dr. Leiden does not receive a base salary for his role as Executive Chairman.

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 2021

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 associated with these goals. The aggregate discretionary adjustment may not exceed 10% of the performance score and the total 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 2021, the board set company goals and assigned relative weights to such goals that reflected our operational, strategic, and financial objectives for the year and the importance of these goals in achieving short- and 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. We believe this mix of goals provides an appropriate balance between our near- and long-term objectives and between pipeline, financial, and organizational development objectives.

Our 2021 weighted goals and the year-end score achieved by the company as determined by the board are set forth in the following table:

Goal(s)	Maximum Score	Actual 2021 Performance Score
Marketed and Approval-Stage Products	55	52
<ul style="list-style-type: none"> ■ Achieve CF net product revenue goals through compliant marketing practices, including U.S. and ex-U.S. revenue goals ■ Achieve successful U.S. launch of TRIKAFTA for children with CF 6 to 11 years of age ■ Achieve commercial manufacturing milestones 		
Pipeline Growth	65	55
<ul style="list-style-type: none"> ■ Achieve proof-of-concept for two non-CF programs ■ Obtain approval in U.S. for TRIKAFTA for children with CF 6 to 11 years of age ■ Submit MAA in the E.U. for triple combination for children with CF 6 to 11 years of age ■ Advance multiple non-CF development programs ■ Advance multiple research programs, including CF and non-CF programs 		
Organizational Development and Capability	13	13
<ul style="list-style-type: none"> ■ 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 ■ Continue to grow and entrench Vertex corporate social responsibility programs 		
Financial Strength	17	17
<ul style="list-style-type: none"> ■ Continue to manage operating expenses and achieve financial targets 		
Additional Accomplishments and Shortcomings, Net (see page 59 of this proxy statement)		1
TOTAL	150	138

Our 2021 company performance score, as determined by the board, was 138 out of a potential of 150. We did not change or adjust our goals in light of the COVID-19 pandemic. Our 2022 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 (50 points), Pipeline Growth (63 points), Organizational Development and Capability (12 points), Financial Strength (15 points), and with the addition of a new category for 2022: Manufacturing, Quality and Operations (10 points).

Detailed Discussion of Company Performance Rating Factors and Achievements

Goals - Marketed and Approval-Stage Products

In 2021, we made significant progress with respect to our marketed and approval-stage products.

- CF net product revenues increased to \$7.57 billion, up 22% as compared to 2020. Our CF net product revenues exceeded the mid-point of our initial CF net product revenues guidance by approximately \$0.8 billion (\$7.57 billion actual as compared to the mid-point of our initial guidance of \$6.8 billion) as a result of the performance of TRIKAFTA in the U.S., including the launch for children with CF 6 to 11 years of age, and strong uptake of KAFTRIO in Europe.
- We achieved strong commercial execution for KAFTRIO in Europe driven by new regulatory approvals and reimbursement agreements and by continued uptake in eligible patients and successfully launched TRIKAFTA for children with CF 6 to 11 years of age in the U.S.
- We began execution of a long-term commercial manufacturing strategy and made advancements in our commercial manufacturing processes, including manufacturing partner discussions and selection.

For marketed and approval-stage products goals, our board assigned the company a score of 52 out of 55, due to exceeding goals with respect to total CF net product revenues, achieving the successful launch of TRIKAFTA for children with CF 6 to 11 years of age in the U.S., and achieving select commercial manufacturing milestones.

Goals - Pipeline Growth (Late and Early-Stage)

Since the beginning of 2021, we made significant progress advancing our CF medicines, including providing improved treatment for people who are already eligible for one of our medicines.

- We expanded the eligibility of TRIKAFTA in the U.S. to include children with CF 6 to 11 years of age.
- We submitted our MAA in the E.U. for approval of KAFTRIO for children with CF 6 to 11 years of age, and in January 2022, we obtained approval for this expanded indication in both the E.U. and the U.K.
- We initiated Phase 3 clinical trials evaluating a once-daily investigational triple combination of VX121/tezacaftor/VX-561 (deutivacaftor).
- We advanced our mRNA program designed to address the patients not currently eligible for any of our products, including conducting IND-enabling studies for our CF mRNA program, and we expect to submit an IND for this program in 2022.

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 2021, we have made important progress in activities supporting these efforts.

- We delivered proof of concept for VX-147, our small molecule inhibitor of APOL1 function for patients with APOL1-mediated focal segmental glomerulosclerosis.
- We completed enrollment in our pivotal studies for CTX-001 for patients with TDT and SCD.
- We initiated and have now completed two Phase 2 dose-ranging acute pain clinical trials evaluating VX-548, a selective small molecule inhibitor of Nav1.8, one following bunionectomy surgery and the other following abdominoplasty surgery.
- We initiated our first in human study for VX-880, our cell therapy designed to treat T1D and announced positive results for the first patient treated.
- We initiated IND-enabling studies for our T1D cells and device program.
- We initiated various first in human studies and delivered numerous preclinical candidates in our areas of therapeutic focus.

Partially offsetting these achievements were challenges advancing VX-864 into pivotal development, notwithstanding obtaining proof of mechanism for this therapy.

On the basis of the accomplishments in advancing our research and development programs and, in particular the achievement of proof-of-concept in AMKD, 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-864 for the treatment of AAT deficiency, our board assigned the company a score of 55 out of 65 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 all 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 continuing to adapt 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.

Corporate Social Responsibility

We continued to grow and make part of our culture our corporate social responsibility programs and enhance patient engagement and community affairs.

To reflect the improvements to our organizational structure, processes, and systems achieved in 2021, our board assigned the company a score of 13 out of 13 for our organizational development and capability goals.

Goals - Financial Strength

We exceeded our financial goals in 2021. We increased our net product revenues to \$7.57 billion, a 22% increase from 2020, and managed our operating expenses resulting in a GAAP operating margin of 37% and a non-GAAP operating margin of 57% (see *Appendix B for a reconciliation of non-GAAP figures*). As a result, we ended 2021 with cash, cash equivalents, and marketable securities of approximately \$7.5 billion, an increase of approximately \$0.9 billion from 2020.

As a result of our strong financial performance, including increasing revenues and managing operating expenses, our board assigned the company a score of 17 out of 17 for our financial strength goals.

Additional Factors (accomplishments and/or shortcomings)

In connection with determining our 2021 company rating, our board of directors made positive and negative adjustments based on factors not anticipated when the company's original goals for 2021 were established. By design, potential adjustments are capped at $\pm 10\%$ (or ± 15 points) and used by the board to address and highlight important achievements and or shortcomings. Positive adjustments were related to our success in significantly exceeding our forecasted net product revenue goal, advancing additional novel, non-CF molecules and therapies, and making additional progress with respect to T1D clinical development. Overall, the board of directors increased our company rating by five points for positive additional accomplishments, which was offset by four points related to a delay in the preclinical development in one therapeutic area and delays in select organizational initiatives. As a result, our final company rating was increased by one point to a total of 138 points.

2021 Individual Performance Ratings - Overview

The MDCC evaluates each executive's 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 "inconsistent demonstration," "living the values," or "exemplary demonstration." The possible individual performance ratings under this program are as set forth in the following table:

Annual Performance Ratings

		RESULTS EVALUATION			
		RESULTS - Not Building	RESULTS - Building	RESULTS - Strong	RESULTS - Leading
Values And Behaviors Evaluation	Exemplary Demonstration	Not Possible	Strong	Leading	Leading Exemplary
	Living the Values	Not Building	Building	Strong	Leading
	Inconsistent Demonstration	Not Building	Not Building	Building	Not Possible

The 2021 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 CEO 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 the recommendations of Dr. Kewalramani and Dr. Leiden, 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 is based on a similar assessment of individual performance by our MDCC and the independent directors. Individual performance can significantly affect an executive officer's cash and equity compensation.

In light of Dr. Leiden's employment agreement, which reduced his base salary and bonus to zero following his first year as Executive Chairman, the MDCC did not assign an individual performance rating for Dr. Leiden.

2021 Actual Individual Ratings for Named Executive Officers

Dr. Reshma Kewalramani	2021 Rating:	Leading
CEO and President	2021 Salary:	\$ 1,320,000
	2021 Bonus:	\$ 3,016,570
	LTI Equity Grants (Feb 2022):	\$ 14,187,500

On the basis of the MDCC's recommendation, our independent directors rated Dr. Kewalramani's overall performance for 2021 as "Leading," with an individual performance factor of 138%. 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 2021, including:

- Leadership in executing our corporate strategy to develop transformative medicines for serious diseases and achieving our business goals
- Leadership and execution in growing, transforming, and preparing the company for diversification in multiple new disease areas
- The substantial over-achievement of our financial goals, including significantly increasing CF net product revenues, strengthening our balance sheet, and continued delivery of strong operating margins
- The advancement of our CF programs, including indication expansions throughout the world, and progress with respect to the CF pipeline
- Leadership in the advancement of our non-CF pre-clinical and clinical development pipeline, including the progress in the CTX001, AMKD, T1D, and pain clinical programs, as well as the expansion of our pre-clinical pipeline
- Exhibiting outstanding leadership qualities and advancing Vertex's values, including exemplary management and coordination throughout the COVID-19 pandemic, successful recruitment of top-tier talent across the organization, including filling critical hires with superior and diverse talent, and fostering our values and culture of innovation

Charles F. Wagner, Jr.	2021 Rating:	Leading
EVP, Chief Financial Officer	2021 Salary:	\$ 770,000
	2021 Bonus:	\$ 1,078,539
	LTI Equity Grants (Feb 2022):	\$ 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 145%. Mr. Wagner's rating derived from his leadership of the finance, accounting, investor relations, and facilities and real estate functions, 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
- Leading the execution of an amended agreement with CRISPR, under which we now lead the worldwide development, manufacturing, and commercialization of CTX001
- Successfully completing the construction of our new cell and genetic therapy facility on time and within budget
- 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 our COVID Management Team

Stuart A. Arbuckle	2021 Rating:	Leading Exemplary
EVP, Chief Operating Officer	2021 Salary:	\$ 900,000
	2021 Bonus:	\$ 1,676,700
	LTI Equity Grants (Feb 2022):	\$ 7,125,000

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 global commercial operations, manufacturing supply chain, corporate communications, and human resources organizations, including the following:

- Delivering CF net product revenues of \$7.57 billion in 2021, an increase of 22% compared to 2020 and exceeding our initial revenue forecast by approximately \$0.8 billion
- Leading continued strong commercial execution across the entire portfolio, driven by new regulatory approvals, reimbursement agreements, and by continued uptake in eligible patients, including the successful launch of TRIKAFTA for children with CF 6 to 11 years of age in the U.S.
- Enhancement of the commercial manufacturing function, including progress with respect to the company's long-term commercial manufacturing strategy
- Successful evolution of the Human Resources organization to enable growth while sustaining our values and culture of innovation
- Successful leadership of the Corporate Communications team, including the company's Corporate Social Responsibility efforts

Ourania “Nia” Tatsis	2021 Rating:	Leading
EVP, Chief Regulatory and Quality Officer	2021 Salary:	\$ 550,000
	2021 Bonus:	\$ 743,820
	LTI Equity Grants (Feb 2022):	\$ 5,000,000

The MDCC recommended and the board adopted an overall rating of “Leading” for Ms. Tatsis based on a results-based rating of “leading” and a behaviors-based rating of “living the values” with an individual performance factor of 140%. Ms. Tatsis’ rating derived principally from her leadership of the regulatory and quality organizations, including the following:

- Successfully leading numerous approvals and label expansions for our CF portfolio globally, including the approval of TRIKAFTA for children with CF 6 to 11 years of age in the U.S.
- Completing numerous regulatory submissions for the company’s current and pipeline assets
- Significant and key efforts to obtain regulatory clearance for numerous clinical development programs, including T1D
- Leading key discussions with regulatory authorities across the globe regarding advancement of pipeline programs, including with respect to VX-147, VX-880, and CTX001
- Successful reorganization of the quality organization, including recruiting and developing multiple new senior members of the team

Annual Cash Bonus

The 2021 cash bonus for each NEO (referred to in the *Summary Compensation Table* on page 68 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:

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. For 2021, Dr. Kewalramani’s individual incentive target remained at 120% of her base salary while Mr. Arbuckle’s incentive target was increased to 90% of his base salary in connection with his promotion to Chief Operating Officer. The individual incentive target for each of our other NEOs remained at 70% of such other NEO’s base salary during 2021; Dr. Leiden does not receive an annual cash bonus pursuant to his employment agreement. The resulting target annual cash bonuses of our executives approximate the median target annual cash bonuses for comparable executives at our Peer Group 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 2021 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 MDCC recommended, and our independent directors approved, individual performance factors and annual bonus awards for each of the NEOs, on account of 2021 performance, as set forth in the table below.

Name	2021 Base Salary	Individual Incentive Target	2021 Target Bonus	Company Performance Factor	Individual Performance Factor	2021 Performance Cash Bonus
Reshma Kewalramani	\$ 1,320,000	x 120%	= \$ 1,584,000	x 138%	x 138%	= \$ 3,016,570
Charles F. Wagner, Jr.	\$ 770,000	x 70%	= \$ 539,000	x 138%	x 145%	= \$ 1,078,539
Stuart A. Arbuckle	\$ 900,000	x 90%	= \$ 810,000	x 138%	x 150%	= \$ 1,676,700
Jeffrey M. Leiden	\$ —	x —%	= \$ —	x —%	x —%	= \$ —
Nia Tatsis	\$ 550,000	x 70%	= \$ 385,000	x 138%	x 140%	= \$ 743,820

Annual Equity Awards

Value-Based Guidelines for Annual NEO Equity Grants

Under our compensation program, our CEO and EVPs were eligible for awards with the following target values based on 2021 performance:

	Performance Ratings				
	Not Building	Building	Strong (target)	Leading	Leading Exemplary
CEO	\$ —	\$ 6,250,000	\$ 12,500,000	\$ 14,187,500	\$ 15,875,000
COO	\$ —	\$ 2,375,000	\$ 4,750,000	\$ 5,937,500	\$ 7,125,000
EVP (excluding the COO)	\$ —	\$ 2,000,000	\$ 4,000,000	\$ 5,000,000	\$ 6,000,000

Based on a comparative analysis of our Peer Group companies, the MDCC set a target equity value for Dr. Kewalramani and Mr. Arbuckle of \$12.5 million and \$4.75 million, respectively, and maintained the target equity value of \$4.0 million for our other EVPs. The number of shares subject to the time-vested restricted stock units and PSUs is based on the fair value of our common stock on the date of grant (with the number of shares subject to PSUs determined at target). Pursuant to the terms of his employment agreement, Dr. Leiden received equity grants of \$8.5 million in the first quarter of 2022 and will receive annual equity grants of \$6.5 million in each of the first quarters of 2023 and 2024 for his role as Executive Chairman. With respect to these grants, fifty percent will be in the form of fully-vested common stock and fifty percent in the form of PSUs based on financial goals with a one-year performance period.

February 2022 Grants Based on 2021 Performance

In February 2022, upon the MDCC's recommendation, our independent directors approved individual performance factors and equity awards for 2021 performance for each of the NEOs as 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	\$ 7,093,750	\$ 7,093,750	\$ 14,187,500
Charles F. Wagner, Jr.	Leading	\$ 2,500,000	\$ 2,500,000	\$ 5,000,000
Stuart A. Arbuckle	Leading Exemplary	\$ 3,562,500	\$ 3,562,500	\$ 7,125,000
Nia Tatsis	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 to develop additional transformative medicines for serious diseases.

The final performance multipliers for our 2021 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 2022. The following chart shows the pre-established financial goals and the actual results for the financial-based performance restricted stock unit awards granted in 2021:

Award Year	Company Goal	Below Threshold	Threshold	Target	Max	Results	
		0% Payout	50% Payout	100% Payout	200% Payout	CF Revenue	Payout
2021	2021 CF Net Product Revenues	<\$6.595 billion	\$ 6.595 billion	\$ 6.770 to 6.840 billion	\$ 7.0 billion	\$ 7.57 billion	200.0%

Consistent with our philosophy of aligning compensation with performance, for 2021, 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 2019 non-financial PSUs were established in February 2019 and our performance against these goals was determined in the first quarter of 2022. 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%.

2019	CF Portfolio Milestone - Approval of triple combination in both the U.S. and E.U.	Achieved
	Complete a clinical trial that establishes proof-of-concept for a drug candidate in a disease area other than pain, cystic fibrosis, sickle cell disease, and beta-thalassemia	Achieved
	First subject is dosed in a pivotal clinical trial for a nucleic acid therapy	Achieved

The performance multiples for the 2020, 2021 and 2022 non-financial based performance restricted stock unit awards will be determined in the first quarter of 2023, 2024 and 2025, 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 2020, 2021 and 2022 are based on multiple clinical milestones, and 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 all of our eligible employees, including our NEOs, may 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 the contributions 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. Under his amended employment agreement, Dr. Leiden receives an annual cash payment intended to facilitate participation in the company's benefit plans.

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 an equity 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 February 2022, we extended Dr. Leiden's employment agreement by one year, until 2024. Under his amended employment agreement, Dr. Leiden will not receive any cash compensation for his role as Executive Chairman other than an annual cash payment intended to facilitate participation in the company's benefit plans, and he will continue to receive equity awards for his third and fourth years of service.

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 transaction 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

Under Section 162(m) of the Internal Revenue Code, publicly held corporations generally may not deduct compensation in excess of \$1 million paid to certain executive officers, subject to limited transition relief for certain arrangements in place as of November 2, 2017. 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 equity awards 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 of 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. We intend to update this policy once the clawback provisions of the Dodd-Frank Act are finalized.

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 32 of this proxy statement. The guidelines for our NEOs are set forth in the following table:

Employee	Minimum Shareholding Requirement
CEO	6X base salary
Executive Chairman	30% of annual equity grant
EVPs	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, 2022, 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 (a) short selling or hedging our securities, (b) purchasing or selling derivative securities based on our securities, and (c) 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 above under "Compensation Governance Practices."

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 diseases 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.

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 2022 annual meeting of shareholders and incorporated by reference into Vertex's Annual Report on Form 10-K for the year ended December 31, 2021. This report is provided by the following directors who comprise the Management Development and Compensation Committee:

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

COMPENSATION AND EQUITY TABLES

Summary Compensation Table

The following table provides summary information concerning the compensation for each of our NEOs for 2021, 2020, and 2019 (or such shorter period of the NEO's service, as applicable).

Name and Principal Position	Year	Salary	Bonus	Stock Awards ⁽¹⁾	Option Awards	Non-Equity Incentive Plan Compensation	All Other Compensation	Total
Reshma Kewalramani ⁽²⁾ CEO and President	2021	\$ 1,221,923	\$ —	\$ 10,924,599	\$ —	\$ 3,016,570	\$ 35,764	\$ 15,198,856
	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
Charles F. Wagner, Jr. ⁽³⁾ EVP & Chief Financial Officer	2021	\$ 729,615	\$ —	\$ 4,375,430	\$ —	\$ 1,078,539	\$ 40,348	\$ 6,223,932
	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
Stuart A. Arbuckle EVP & Chief Operating Officer	2021	\$ 842,308	\$ —	\$ 5,250,173	\$ —	\$ 1,676,700	\$ 40,960	\$ 7,810,141
	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
Jeffrey M. Leiden ⁽⁴⁾ Executive Chairman	2021	\$ 242,308	\$ —	\$ 7,875,259	\$ —	\$ —	\$ 39,672	\$ 8,157,239
	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
Nia Tatsis EVP & Chief Regulatory and Quality Officer	2021	\$ 550,000	\$ —	\$ 5,250,173	\$ —	\$ 743,820	\$ 40,035	\$ 6,584,028

(1) Pursuant to applicable SEC rules, the grant-date fair values of the equity awards granted in February 2021 for 2020 performance are included in 2021 compensation. Equity awards granted in February 2022 to Dr. Kewalramani, Mr. Wagner, Mr. Arbuckle, and Ms. Tatsis for 2021 performance and the equity awards granted in February 2022 to Dr. Leiden pursuant to his employment agreement are not reflected in the Summary Compensation Table above.

(2) Dr. Kewalramani was our EVP and Chief Medical Officer through March 2020.

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

(4) Dr. Leiden was our CEO and President through March 2020.

Bonus

Pursuant to applicable SEC rules, the annual cash bonuses earned by our NEOs are included under the caption "Non-Equity Incentive Plan Compensation." Other bonuses, such as sign-on bonuses, are included 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. In general, the equity awards reflected in the Summary Compensation Table for a specific year reflect equity grants made earlier 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 2021 in the table above is significantly affected by his or her performance during 2020. 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 in 2019, is set forth in Note N to our consolidated financial statements included in our 2021 Annual Report on Form 10-K filed with the SEC on February 9, 2022.

The "Stock Awards" for 2021, 2020, and 2019 consist of PSU awards and time-vested restricted stock unit awards granted in February of each year. In each of 2021, 2020, and 2019, the financial and non-financial PSU awards had grant-date values of 100% and 50% of the fair value of the target shares, respectively, in accordance with U.S. GAAP, based on the probable outcome of the performance conditions associated with these portions of the awards. If the grant-date fair value of the financial and non-financial PSU awards had been 200% of the fair value of the target shares, the table above would have included the following amounts:

	2021	2020	2019 ⁽¹⁾
Reshma Kewalramani	\$ 18,728,038	\$ 9,000,877	\$ 5,513,196
Charles F. Wagner, Jr.	\$ 7,500,890	\$ 7,501,175	\$ 2,100,794
Stuart A. Arbuckle	\$ 9,000,297	\$ 9,000,877	\$ 5,513,196
Jeffrey M. Leiden	\$ 13,500,444	\$ 22,860,288	\$ 16,002,311
Nia Tatsis	\$ 9,000,297	\$ —	\$ —

(1) 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.

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 2021, 2020 and 2019, performance, each of which was paid in the first quarter of the subsequent year. The cash bonus awards to the NEOs for 2021 performance were determined as follows:

Name	Base Salary	Individual Incentive Target	2021 Target Bonus	Company Performance Factor	Individual Performance Factor	2021 Performance Cash Bonus
Reshma Kewalramani	\$ 1,320,000	x 120%	= \$ 1,584,000	x 138%	x 138%	= \$ 3,016,570
Charles F. Wagner, Jr.	\$ 770,000	x 70%	= \$ 539,000	x 138%	x 145%	= \$ 1,078,539
Stuart A. Arbuckle	\$ 900,000	x 90%	= \$ 810,000	x 138%	x 150%	= \$ 1,676,700
Jeffrey M. Leiden	\$ —	x —%	= \$ —	x —%	x —%	= \$ —
Nia Tatsis	\$ 550,000	x 70%	= \$ 385,000	x 138%	x 140%	= \$ 743,820

All Other Compensation

The amounts set forth under the caption "All Other Compensation" in the table for 2021 consist of:

Name	401(k) Match	Life Insurance Premiums	Matching Gift Program	Other	Total
Reshma Kewalramani	\$ 13,050	\$ 1,810	\$ 20,168	\$ 736 ⁽¹⁾	\$ 35,764
Charles F. Wagner, Jr.	\$ 13,050	\$ 1,247	\$ 25,000	\$ 1,051 ⁽¹⁾	\$ 40,348
Stuart A. Arbuckle	\$ 13,050	\$ 1,372	\$ 25,000	\$ 1,538 ⁽¹⁾	\$ 40,960
Jeffrey M. Leiden	\$ 13,050	\$ 1,622	\$ 25,000	\$ — ⁽¹⁾	\$ 39,672
Nia Tatsis	\$ 13,050	\$ 1,060	\$ 25,000	\$ 925 ⁽¹⁾	\$ 40,035

(1) Tax reimbursements.

Grants of Plan-Based Awards During 2021

The following table provides information with respect to grants of awards to each of our NEOs during 2021. Pursuant to SEC rules, (i) the threshold, target and maximum amounts payable pursuant to our 2021 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 2021 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 2021 is set forth under “All Other Stock Awards: Number of Shares of Stock or Units.”

Name	Grant Date	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 (\$)
		Threshold (\$)	Target (\$)	Maximum (\$)	Threshold (#)	Target (#)	Maximum (#)		
Reshma Kewalramani	(1)	\$ 0	\$ 1,584,000	\$ 3,564,000					
	(2a)	2/3/2021			—	14,516	29,032		\$ 3,121,375
	(2b)	2/3/2021			—	14,516	29,032		\$ 1,560,688
	(3)	2/3/2021						29,031	\$ 6,242,536
Charles F. Wagner, Jr.	(1)	\$ 0	\$ 539,000	\$ 1,212,750					
	(2a)	2/3/2021			—	5,814	11,628		\$ 1,250,184
	(2b)	2/3/2021			—	5,814	11,628		\$ 625,092
	(3)	2/3/2021						11,627	\$ 2,500,154
Stuart A. Arbuckle	(1)	\$ 0	\$ 810,000	\$ 1,822,500					
	(2a)	2/3/2021			—	6,976	13,952		\$ 1,500,049
	(2b)	2/3/2021			—	6,976	13,952		\$ 750,025
	(3)	2/3/2021						13,952	\$ 3,000,099
Jeffrey M. Leiden	(1)	\$ 0	\$ —	\$ —					
	(2a)	2/3/2021			—	10,464	20,928		\$ 2,250,074
	(2b)	2/3/2021			—	10,464	20,928		\$ 1,125,037
	(3)	2/3/2021						20,928	\$ 4,500,148
Nia Tatsis	(1)	\$ 0	\$ 385,000	\$ 866,250					
	(2a)	2/3/2021			—	6,976	13,952		\$ 1,500,049
	(2b)	2/3/2021			—	6,976	13,952		\$ 750,025
	(3)	2/3/2021						13,952	\$ 3,000,099

(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 to earn pursuant to our 2021 annual cash bonus program. Actual amounts paid to each of the NEOs under this program for 2021 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 number of shares that could be earned and vest pursuant to PSUs granted in 2021. 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 2021. 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 2021* 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 2021, 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*.

Outstanding Equity Awards at Fiscal Year-End for 2021

The following table provides information with respect to outstanding equity awards held by each of our NEOs on December 31, 2021, based on the closing price of \$219.60 per share of our common stock on December 31, 2021:

Name	Option Awards					Stock Awards			
	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								
					3,267 ⁽²⁾	\$ 717,433			
					8,258 ⁽³⁾	\$ 1,813,457			
					29,031 ⁽⁴⁾	\$ 6,375,208			
	Performance-based RSU								
					3,268 ⁽⁵⁾	\$ 717,653			
					8,260 ⁽⁶⁾	\$ 1,813,896			
					9,800 ⁽⁷⁾	\$ 2,152,080			
					29,032 ⁽⁸⁾	\$ 6,375,427			
							6,194 ⁽⁹⁾	\$ 1,360,202	
						14,516 ⁽¹⁰⁾	\$ 3,187,714		
	Stock Options								
	2,548	510	\$ 155.57	2/5/2028					
	7,821	7,821	\$ 187.53	2/5/2029					
Charles F. Wagner	Time-based RSU								
					1,233 ⁽²⁾	\$ 270,767			
					6,882 ⁽³⁾	\$ 1,511,287			
					11,627 ⁽⁴⁾	\$ 2,553,289			
	Performance-based RSU								
					1,234 ⁽⁵⁾	\$ 270,986			
					6,884 ⁽⁶⁾	\$ 1,511,726			
					3,698 ⁽⁷⁾	\$ 812,081			
					11,628 ⁽⁸⁾	\$ 2,553,509	5,162 ⁽⁹⁾	\$ 1,133,575	
							5,814 ⁽¹⁰⁾	\$ 1,276,754	
	Stock Options								
	5,957	3,575	\$ 189.38	4/9/2029					
Stuart A. Arbuckle	Time-based RSU								
					3,267 ⁽²⁾	\$ 717,433			
					8,258 ⁽³⁾	\$ 1,813,457			
					13,952 ⁽⁴⁾	\$ 3,063,859			
	Performance-based RSU								
					3,268 ⁽⁵⁾	\$ 717,653			
					8,260 ⁽⁶⁾	\$ 1,813,896			
					9,800 ⁽⁷⁾	\$ 2,152,080			
					13,952 ⁽⁸⁾	\$ 3,063,859	6,194 ⁽⁹⁾	\$ 1,360,202	
							6,976 ⁽¹⁰⁾	\$ 1,531,930	
	Stock Options								
	7,338	1,223	\$ 155.57	2/5/2028					
	9,385	7,821	\$ 187.53	2/5/2029					
Jeffrey M. Leiden	Performance-based RSU								
					28,444 ⁽⁷⁾	\$ 6,246,302			
					20,928 ⁽⁸⁾	\$ 4,595,789			
							15,731 ⁽⁹⁾	\$ 3,454,528	
							10,464 ⁽¹⁰⁾	\$ 2,297,894	
	Stock Options								
	93,866	0	\$ 91.05	2/1/2026					
	103,550	0	\$ 86.52	2/2/2027					

Name	Option Awards				Stock Awards			
	Number of Securities Underlying Unexercised Options (shares) ⁽¹⁾	Number of Securities Underlying Unexercised Options (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
Nia Tatsis	Time-based RSU							
					1,167 ⁽²⁾	\$ 256,273		
					4,130 ⁽³⁾	\$ 906,948		
					13,952 ⁽⁴⁾	\$ 3,063,859		
	Performance-based RSU							
					1,168 ⁽⁵⁾	\$ 256,493		
					4,130 ⁽⁶⁾	\$ 906,948		
					3,500 ⁽⁷⁾	\$ 768,600		
					13,952 ⁽⁸⁾	\$ 3,063,859		
							3,097 ⁽⁹⁾	\$ 680,101
						6,976 ⁽¹⁰⁾	\$ 1,531,930	
	Stock Options							
	2,446	408	\$ 155.57	2/5/2028				
	3,351	2,794	\$ 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 24, 2022.
- (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 10, 2022 and are scheduled to vest February 10, 2023, 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 17, 2022, and are scheduled to vest in two remaining annual installments on February 17, 2023 and 2024.
- (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 2019. In February 2020, 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 24, 2020, 2021 and 2022. The shares listed on the table above represent the final installment of the earned shares, which vested on February 24, 2022.
- (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 2020, with vesting of the earned shares in three equal installments on 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. The shares listed on the table above represent the second and third installments of earned shares, which vested on February 10, 2022 and are scheduled to vest on February 10, 2023, respectively.
- (7) This performance stock unit award is based on the achievement of three-year non-financial performance metrics. The performance conditions associated with the awards consist of multiple clinical and research milestones, with a payout range of zero to 200%. In February 2022, our MDCC certified as to the level of performance at 200% of the number of target shares, with the number and value of shares reported above reflected as such. The earned shares vested on February 24, 2022.
- (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 2021, with vesting of the earned shares generally occurring in three equal installments scheduled for each of February 17, 2022, 2023 and 2024. In February 2022, our MDCC certified as to the level of performance at 200% of the number of target shares, with the number and value of shares reported above reflected as such.
- (9) This performance stock unit award is based on the achievement of three-year non-financial performance metrics, with the number and value of shares reported assuming target performance (100%). The performance conditions associated with the awards consist of 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.
- (10) This performance stock unit award is based on the achievement of three-year non-financial performance metrics, with the number and value of shares reported assuming target performance (100%). The performance conditions associated with the awards consist of 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 2024.

Option Exercises and Stock Vested for 2021

The following table sets forth the value realized by our NEOs from options to purchase common stock exercised by the NEOs during 2021 and shares of stock that vested during 2021. 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.

Name	Option Awards		Stock Awards	
	Number of Shares Acquired on Exercise	Value Realized on Exercise	Number of Shares Acquired on Vesting	Value Realized on Vesting
Reshma Kewalramani	—	\$ —	19,477	\$ 4,182,170
Charles F. Wagner, Jr.	—	\$ —	9,345	\$ 2,009,284
Stuart A. Arbuckle	1,554	\$ 197,693	28,854	\$ 6,167,750
Jeffrey M. Leiden	—	\$ —	83,888	\$ 17,907,751
Nia Tatsis	—	\$ —	11,151	\$ 2,384,751

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, 2021 and/or a change of control of the company had occurred on such date.

	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	\$ —	\$ 7,392,000	\$ 10,266,960	\$ 1,584,000	\$ 1,584,000
Continuation of Employee Benefits	—	45,756	45,756	—	—
Accelerated Vesting of Stock Options	—	233,285	283,475	283,475	283,475
Accelerated Vesting of Restricted Stock Units	—	7,512,443	20,249,316	20,249,316	20,249,316
TOTAL	\$ —	\$ 15,183,484	\$ 30,845,507	\$ 22,116,791	\$ 22,116,791
Charles F. Wagner, Jr.					
Cash Severance Benefits	\$ —	\$ 1,309,000	\$ 1,848,000	\$ —	\$ —
Continuation of Employee Benefits	—	27,579	27,579	—	—
Accelerated Vesting of Stock Options	—	—	108,037	108,037	108,037
Accelerated Vesting of Restricted Stock Units	—	—	10,211,178	10,211,178	10,211,178
TOTAL	\$ —	\$ 1,336,579	\$ 12,194,794	\$ 10,319,215	\$ 10,319,215
Stuart A. Arbuckle					
Cash Severance Benefits	\$ —	\$ 1,710,000	\$ 2,520,000	\$ —	\$ —
Continuation of Employee Benefits	—	30,504	30,504	—	—
Accelerated Vesting of Stock Options	—	—	329,128	329,128	329,128
Accelerated Vesting of Restricted Stock Units	—	—	13,626,399	13,626,399	13,626,399
TOTAL	\$ —	\$ 1,740,504	\$ 16,506,031	\$ 13,955,527	\$ 13,955,527
Jeffrey M. Leiden					
Cash Severance Benefits	\$ —	\$ 15,000,000	\$ 15,000,000	\$ 8,500,000	\$ 8,500,000
Continuation of Employee Benefits	—	30,747	30,747	—	—
Accelerated Vesting of Stock Options	—	—	—	—	—
Accelerated Vesting of Restricted Stock Units	—	—	—	—	—
TOTAL	\$ —	\$ 15,030,747	\$ 15,030,747	\$ 8,500,000	\$ 8,500,000
Nia Tatsis					
Cash Severance Benefits	\$ —	\$ 935,000	\$ 1,320,000	\$ —	\$ —
Continuation of Employee Benefits	—	19,559	19,559	—	—
Accelerated Vesting of Stock Options	—	—	115,728	115,728	115,728
Accelerated Vesting of Restricted Stock Units	—	—	9,518,781	9,518,781	9,518,781
TOTAL	\$ —	\$ 954,559	\$ 10,974,068	\$ 9,634,509	\$ 9,634,509

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 \$219.60 per share (the closing price on the last trading day of 2021), 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 \$219.60 per share (the closing price on the last trading day of 2021). The value of any PSUs that have not been certified as to the level of performance by the MDCC as of December 31, 2021 are reported above assuming target performance (100%).
- 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 2021 individual and company performance ratings on December 31, 2021 as they assigned in the first quarter of 2022.
- PSUs granted to Dr. Leiden while in his role as CEO, as well as his current role as Executive Chairman, are not subject to service-based vesting conditions and will remain eligible to vest following certification of the corresponding performance criteria.
- No NEO who has met the age and service requirements for retirement has provided the required notice for a termination of employment to qualify as a retirement as of December 31, 2021.

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.

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 NEO’s employment is terminated due to disability, he or she 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, she would be entitled to receive:

- a pro-rated bonus for the year of employment termination;
- for equity awards not covered by the company-wide equity program described above, vesting of any options then unvested at the time of termination.

Agreement with Jeffrey Leiden

Dr. Leiden's amended employment agreement has a four-year term that commenced on April 1, 2020 and provides for (i) annual equity grants over the four-year term, and (ii) eligibility to receive the other benefits generally made available to our executives. In February 2022, Dr. Leiden's employment agreement was amended to provide for an annual payment of \$65,000 in each of February 2022, 2023, and 2024 to facilitate his participation in the company's benefit plans. 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) 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 (ii) 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 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 CEO 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, as well as his current role as Executive Chairman, are not subject to service-based vesting conditions and will remain eligible to vest following certification of the corresponding performance criteria.

Agreements with Mr. Arbuckle, Ms. Tatsis, and Mr. Wagner

Employment Agreements

The terms and conditions of Mr. Arbuckle's, Ms. Tatsis' 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 or 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, each officer has agreed not to engage in specified competitive activities for a period of one year after the termination of his or her employment with us.

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

Severance Payment:	The sum of his or her (i) base salary at the time of termination and (ii) target bonus for the year in which his or her 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 Mr. Arbuckle, Ms. Tatsis and Mr. Wagner that was 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 or her 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 or she would be entitled to receive:

Severance Payment:	A) The sum of his or her (i) base salary at the time of termination and (ii) target bonus for the year in which his or her employment is terminated B) A pro rata portion of his or her 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. Based on these requirements, the median employee may be identified once every three years if there is no significant impact to the pay ratio disclosure during the fiscal year.

We have determined that the pay ratio calculated using the same median employee identified in 2020 (the "Median Employee") best represents the ratio in effect for our 2021 fiscal year. We believe there has been no significant change during 2021 to our employee population or employee compensation arrangements that would significantly affect the pay ratio disclosure. In 2021, the Median Employee's compensation included recognition awards consistent with awards made to similar employees; however, there were no changes to the Median Employee's compensation arrangements that would significantly affect the pay ratio disclosure.

In 2020, we identified the 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

The methodology included all 3,388 company employees as of October 1, 2020, and included employees in 21 countries.

We calculated the median employee's annual total compensation using the same methodology used to calculate Dr. Kewalramani's annual total compensation for the Summary Compensation Table. In 2021, the total annual compensation for the Median Employee equaled \$234,107.

In 2021, Dr. Kewalramani's total annual compensation was \$15,198,856. The ratio of total annual compensation for Dr. Kewalramani to our median employee's total annual compensation was 65:1.

SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT

The following table sets forth information regarding beneficial ownership of our common stock as of March 24, 2022, 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 and our director nominee;
- 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	23,944,931	9.4%
The Vanguard Group ⁽⁴⁾ 100 Vanguard Blvd. Malvern, Pennsylvania 19355	20,155,842	7.9%
Sangeeta N. Bhatia ⁽⁵⁾	9,036	*
Lloyd Carney ⁽⁵⁾	5,401	*
Alan Garber ⁽⁵⁾	26,100	*
Terrence C. Kearney ⁽⁵⁾	44,929	*
Reshma Kewalramani ⁽⁵⁾	60,763	*
Yuchun Lee ⁽⁵⁾	96,526	*
Jeffrey M. Leiden ⁽⁵⁾	287,805	*
Margaret G. McGlynn ⁽⁵⁾	48,341	*
Diana McKenzie ⁽⁵⁾	4,278	*
Bruce I. Sachs ⁽⁵⁾	132,732	*
Suketu Upadhyay ⁽⁵⁾	—	*
Stuart A. Arbuckle ⁽⁵⁾	44,794	*
Nia Tatsis ⁽⁵⁾	21,682	*
Charles F. Wagner, Jr. ⁽⁵⁾	20,702	*
All directors and executive officers as a group (18 persons) ⁽⁵⁾	955,927	0.4%

* 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 2022.
- (2) Percentage ownership is based on 255,533,949 shares of our common stock outstanding on March 24, 2022.
- (3) Reflects shares beneficially owned by BlackRock Life Limited, BlackRock International Limited, BlackRock Advisors, LLC, Aperio Group, LLC, BlackRock Capital Management, Inc., BlackRock (Netherlands) B.V., BlackRock Institutional Trust Company, National Association, BlackRock Asset Management Ireland Limited, BlackRock Financial Management, Inc., BlackRock Japan Co., Ltd., BlackRock Asset Management Schweiz AG, BlackRock Investment Management, LLC, FutureAdvisor, Inc., BlackRock Investment Management (UK) Limited, BlackRock Asset Management Canada Limited, BlackRock Asset Management Deutschland AG, BlackRock (Luxembourg) S.A., BlackRock Investment Management (Australia) Limited, BlackRock Advisors (UK) Limited, BlackRock Fund Advisors, BlackRock Asset Management North Asia Limited, BlackRock (Singapore) Limited, BlackRock Fund Managers Ltd, each of which is a wholly-owned subsidiary of BlackRock, Inc. BlackRock, Inc. has sole voting power with respect to 21,372,207 shares and sole dispositive power with respect to 23,944,931 shares.
- (4) Includes shares beneficially owned by clients of one or more investment advisers directly or indirectly owned by the Vanguard Group, Inc. The Vanguard Group, Inc. has sole voting power with respect to 0 shares, shared voting power with respect to 417,081 shares, sole dispositive power with respect to 19,111,242 shares, and shared dispositive power with respect to 1,044,600 shares.

- (5) Includes shares that may be acquired upon the exercise of options exercisable within 60 days after March 24, 2022, unvested restricted stock units vesting within 60 days of March 24, 2022 and deferred stock units as of March 24, 2022 issued pursuant to our Non-Employee Director Deferred Compensation Plan, as follows:

	Stock Options Exercisable Within 60 Days of March 24, 2022	Unvested Restricted Stock Units Vesting Within 60 Days of March 24, 2022	Deferred Stock Units as of March 24, 2022
Sangeeta N. Bhatia	3,845	1,842	—
Lloyd Carney	—	1,842	—
Alan Garber	20,210	—	—
Terrence C. Kearney	39,118	—	—
Reshma Kewalramani	14,007	—	—
Yuchun Lee	92,850	—	1,801
Jeffrey M. Leiden	197,416	—	—
Margaret G. McGlynn	42,554	—	5,609
Diana McKenzie	—	—	2,636
Bruce I. Sachs	77,850	—	13,672
Suketu "Suky" Upadhyay	—	—	—
Stuart A. Arbuckle	21,074	—	—
Nia Tatsis	7,323	—	—
Charles F. Wagner, Jr.	7,149	1,233	—
All directors and executive officers as a group (18 persons)	609,765	9,673	23,718

Delinquent Section 16(a) Reports

Section 16(a) of the Exchange Act requires directors, officers and persons who are beneficial owners of more than 10% of our common stock to file with the SEC reports of their ownership of our securities and of changes in that ownership. We assist our directors and officers by monitoring transactions and completing and filing these reports on their behalf. Based solely on a review of the copies of such forms in our possession and on written representations from reporting persons, we believe that all of our executive officers and directors filed the required reports on a timely basis during 2021 with the exception of Charles Wagner and Bastiano Sanna. Due to an administrative error, one Form 4 was filed late for each of Mr. Wagner and Mr. Sanna to report shares withheld by the company to satisfy tax withholding obligations in connection with the vesting of restricted stock units on April 30, 2021.

OTHER INFORMATION

Other Matters

The 2022 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 2022 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 and Nominations for Director for the 2023 Annual Meeting

In order to be considered for inclusion in the proxy statement for our 2023 annual meeting of shareholders, shareholder proposals must be received by us no later than December 8, 2022. If we do not receive notice of a matter to be considered for presentation at the 2023 annual meeting of shareholders by February 21, 2023, 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 2023 annual meeting of shareholders, but is not eligible or does not elect to have such candidate included in the proxy statement for our 2023 annual meeting of shareholders, such nomination may be submitted to our corporate secretary no later than February 17, 2023, 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 2023 annual meeting of shareholders, and is eligible and elects to have such candidate included in the proxy statement for our 2023 annual meeting of shareholders pursuant to our proxy access by-law, such nomination must be submitted to our corporate secretary no later than February 17, 2023 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.

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 products and product 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 data from preclinical testing or 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, 2021 and available through the company’s website at www.vrtx.com. You should not place undue reliance on these statements, or any data presented. 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.

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 2021 named executive officer compensation; and
- The approval of an amendment and restatement of our 2013 Stock and Option Plan to increase the number of shares authorized for issuance under this plan by 13.5 million shares.

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 7, 2022, 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, 2021 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 continued concerns related to the 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 <https://meetnow.global/MYNFZZ5> to attend and submit questions during the meeting. No physical meeting will be held this year.

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.

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

If you are a registered shareholder (i.e., you hold your shares through our transfer agent, Computershare), 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 through an intermediary, such as a bank or broker, 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 13, 2022. 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.

What if I have Trouble Accessing the Virtual Annual Meeting?

The virtual meeting platform is fully supported across browsers (MS Edge, Firefox, Chrome and Safari) and devices (desktops, laptops, tablets and cell phones) running the most up-to-date version of applicable software and plugins. Please note that Internet Explorer is not a supported browser. 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. For further assistance should you need it you may call 1-888-724-2416.

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.

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 <https://meetnow.global/MYNFZZ5>. 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 24, 2022 and was established by our board of directors. On the record date, there were 255,533,949 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, 2022;
- FOR our 2021 named executive officer compensation;
- FOR the approval of an amendment and restatement of our 2013 Stock and Option Plan to increase the number of shares authorized for issuance under this plan by 13.5 million shares.

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 on certain matters 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 approval of an amendment and restatement of our 2013 Stock and Option plan are considered not 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 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: Approval of an Amendment and Restatement of our 2013 Stock and Option Plan

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

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.

APPENDIX A VERTEX PHARMACEUTICALS INCORPORATED AMENDED AND RESTATED 2013 STOCK AND OPTION PLAN

1. Definitions

Unless otherwise specified or unless the context otherwise requires, the following terms, as used in this Vertex Pharmaceuticals Incorporated Amended and Restated 2013 Stock and Option Plan, have the following meanings:

Accounting Rules means Financial Accounting Standards Board Accounting Standards Codification Topic 718, or any successor provision.

Administrator means the Board of Directors and/or a committee of the Board of Directors to which the Board of Directors has delegated power to act on its behalf in administering this Plan in whole or in part.

Affiliate means a corporation that, for purposes of Section 424 of the Code, is a parent or subsidiary of the Company, direct or indirect.

Board of Directors means the Board of Directors of the Company.

Code means the United States Internal Revenue Code of 1986, as amended.

Common Stock means shares of the Company's common stock, \$.01 par value.

Company means Vertex Pharmaceuticals Incorporated, a Massachusetts corporation.

Disability means a disability entitling the Participant to benefits under the Company's long-term disability program, as in effect from time to time. With regard to any payment considered to be nonqualified deferred compensation under Section 409A of the Code, to the extent applicable, that is payable upon a Termination of Service due to Disability, to avoid the imposition of an additional tax, interest or penalty under Section 409A of the Code, no amount will be payable unless such Disability constitutes a disability or becoming disabled within the meaning of Section 1.409A-3(i)(4) of the Treasury Regulations.

Employee means an employee of the Company or of an Affiliate (including, without limitation, an employee who is also serving as an officer or director of the Company or of an Affiliate), who is designated by the Administrator to be eligible to be granted one or more Stock Rights under the Plan.

Exchange Act means the Securities Exchange Act of 1934, as amended.

Fair Market Value of a share of Common Stock on a particular date shall be the mean between the highest and lowest quoted selling prices on such date (the "valuation date") on the securities market where the Common Stock is traded, or if there were no sales on the valuation date, on the next preceding date within a reasonable period (as determined in the sole discretion of the Administrator) on which there were sales. If there were no sales in such a market within a reasonable period, the Fair Market Value shall be as determined in good faith by the Administrator in its sole discretion. The Fair Market Value as determined in this paragraph shall be rounded down to the next lower whole cent if the foregoing calculation results in fractional cents.

Full Value Award means any Stock Grant or Stock-Based Award other than Options and Stock Appreciation Rights.

ISO means an option entitling the holder to acquire Shares upon payment of the exercise price that is intended to qualify as an incentive stock option under Section 422 of the Code.

Non-Employee Director means a member of the Board of Directors who is not an employee of the Company or any Affiliate.

Non-Qualified Option means an option entitling the holder to acquire Shares upon payment of the exercise price that is not an ISO.

Option means an ISO or Non-Qualified Option.

Participant means an Employee, Non-Employee Director, consultant or advisor of the Company or an Affiliate to whom one or more Stock Rights are granted under the Plan. As used herein, "Participant" shall include "Participant's Survivors" and a Participant's permitted transferees where the context requires.

Participant's Survivors means a deceased Participant's legal representatives and/or any person or persons who acquires the Participant's rights to a Stock Right by will or by the laws of descent and distribution.

Plan means this Vertex Pharmaceuticals Incorporated Amended and Restated 2013 Stock and Option Plan, as amended from time to time.

Restricted Stock Units means an unfunded and unsecured promise, denominated in shares of Common Stock, to deliver Common Stock or cash measured by the value of Common Stock in the future, subject to the satisfaction of specified performance or other vesting conditions.

Shares means shares of the Common Stock as to which Stock Rights have been or may be granted under the Plan or any shares of capital stock into which the Shares are changed or for which they are exchanged within the provisions of the Plan.

Stock Agreement means an agreement between the Company and a Participant delivered pursuant to the Plan with respect to a Stock Right, in such form as the Administrator shall approve.

Stock Appreciation Right means a right entitling the holder upon exercise to receive an amount (payable in cash or in shares of Common Stock of equivalent value) equal to the excess of the Fair Market Value of the shares of Common Stock subject to the right over the base value (i.e., the exercise price) from which appreciation under the Stock Appreciation Right is to be measured.

Stock-Based Award means Restricted Stock Units, Stock Appreciation Rights or any other grant by the Company under the Plan of an equity award, equity-based award or other award that is convertible into Common Stock that is not an Option or Stock Grant.

Stock Grant means a grant by the Company of Shares under the Plan that may or may not be subject to restrictions requiring that the Shares underlying the Stock Grant be redelivered or offered for sale to the Company if specified service or performance-based conditions are not satisfied.

Stock Right means an Option (including an ISO or a Non-Qualified Stock Option), Stock Grant, or Stock-Based Award.

Substitute Stock Rights means Stock Rights issued under the Plan in substitution for equity awards of an acquired company that are converted, replaced or adjusted in connection with the acquisition.

Termination of Service means that a Participant ceases to be an Employee, Non-Employee Director, consultant or advisor with the Company and its Affiliates (for any reason other than death). A change in a Participant's form of service (e.g., from Employee to Non-Employee Director, consultant or advisor) shall not be a Termination of Service hereunder. Notwithstanding the foregoing, in construing the provisions applicable to any Stock Right relating to the payment of "nonqualified deferred compensation" (subject to Section 409A of the Code) upon a termination or cessation of employment or service, references to termination or cessation of employment or service, separation from service, retirement or similar or correlative terms will be construed to require a "separation from service" (as that term is defined in Section 1.409A-1(h) of the Treasury Regulations, after giving effect to the presumptions contained therein) from the Company and from all other corporations and trades or businesses, if any, that would be treated as a single "service recipient" with the Company under Section 1.409A-1(h) (3) of the Treasury Regulations.

2. Purposes of the Plan

The Plan is intended to encourage ownership of Shares by Employees, Non-Employee Directors and certain consultants and advisors to the Company in order to attract such persons, to induce them to work for the benefit of the Company or of an Affiliate and to provide additional incentive for them to promote the success of the Company or of an Affiliate. The Plan provides for the granting of Stock Rights to Employees, Non-Employee Directors, consultants and advisors of the Company.

3. Shares Subject to the Plan

The number of Shares subject to this Plan as to which Stock Rights may be granted from time to time shall be equal to the sum of:

- a. 54,375,861 shares of Common Stock; and
- b. the number of shares subject to awards granted under the Company's Amended and Restated 2006 Stock and Option Plan (the "2006 Plan") which expire, terminate or are otherwise surrendered, cancelled, forfeited or repurchased by the Company at their original issuance price pursuant to a contractual repurchase right (subject, however, in the case of ISOs, to any limitations under the Code), or the equivalent of such number of Shares after the Administrator, in its sole discretion, has interpreted the effect of any stock split, stock dividend, combination, recapitalization or similar transaction in accordance with Section 17 of this Plan. Subject to Section 17 of this Plan, and the provisions of the second paragraph of this Section 3, the number of Shares remaining subject to this Plan shall be reduced by (i) one Share for each Share subject to a Stock Right granted under this Plan that is not a Full Value Award and (ii) 1.66 Shares for each Share (each, a "Full-Value Award Share") subject to a Stock Right granted under this Plan that is a Full Value Award.

If an Option granted hereunder ceases to be outstanding, in whole or in part (other than by exercise), or if the Company shall reacquire (at no more than its original issuance price) any Shares issued pursuant to a Stock Grant, or if any Stock Right expires or is forfeited, cancelled or otherwise terminated or results in any Shares not being issued, the unissued Shares that were subject to such Stock Right shall again be available for issuance from time to time pursuant to this Plan; provided, however, that, the following Shares may not again be made available for issuance under the Plan: (i) Shares that are not issued or delivered because they are applied to the payment of the exercise or purchase price of any Stock Right or to satisfy the tax withholding requirements with respect to any Stock Right, (ii) the full number of Shares underlying any Stock Appreciation Right any portion of which is settled in Shares (and not only the number of Shares delivered in settlement of the Stock Right) and (iii) any Shares that have been repurchased by the Company using proceeds directly attributable to the exercise of Options. To the extent that Shares are returned to the Plan pursuant to this Section 3, (i) 1.66 Shares, for each Full Value Award Share granted under this Plan, and (ii) one Share, for all other Shares (including Shares returned from the 2006 Plan in accordance with clause (b) above), shall again be available for issuance from time to time pursuant to this Plan. The maximum number of Shares that may be issued in satisfaction of ISOs is 27,875,861 Shares.

The Administrator may grant Substitute Stock Rights under the Plan. To the extent consistent with the requirements of Section 422 of the Code and the regulations thereunder (if applicable) and other applicable legal requirements (including applicable stock exchange requirements), Common Stock issued under Substitute Stock Rights will be in addition to and will not reduce the number of Shares available for Stock Rights under the Plan set forth in this Section 3, but, notwithstanding anything in this Section 3 to the contrary, if any Substitute Stock Right is settled in cash or expires, becomes unexercisable, terminates or is forfeited to or repurchased by the Company without the issuance of Common Stock, the Shares previously subject to such Stock Right will not be available for future grants under the Plan. The Administrator will determine the extent to which the terms and conditions of the Plan apply to Substitute Stock Rights, if at all, provided, however, that Substitute Stock Rights will not be subject to the last sentence of Section 6.1 or the per-Participant annual limits on grants of Stock Rights described in Section 13 below.

4. Administration of the Plan

The Administrator shall administer the Plan. Subject to the provisions of the Plan, the Administrator is authorized to:

- a. Interpret the provisions of the Plan and of any Stock Right or Stock Agreement and to make all rules and determinations that it deems necessary or desirable for the administration of the Plan;
- b. Determine which Employees, Non-Employee Directors, consultants and advisors of the Company and its Affiliates shall be granted Stock Rights;
- c. Determine the number of Shares and exercise price for which a Stock Right shall be granted;
- d. Specify the terms and conditions upon which a Stock Right or Stock Rights may be granted;
- e. In its discretion, accelerate:
 - i. the date of exercise of any installment of any Option; or
 - ii. the date or dates of vesting of Shares, or lapsing of Company repurchase rights with respect to any Shares, under any Stock Rights; and
- f. In its discretion, extend the period during which an Option may be exercised (but not beyond the earlier of the expiration date of the Option and the 10th anniversary of the date the Option was granted);

provided, however, that all such interpretations, rules, determinations, terms and conditions shall be made and prescribed in the context of preserving the tax status under Section 422 of the Code of those Options which are designated as ISOs (unless the holder of any such Option otherwise agrees). Subject to the foregoing, the interpretation and construction by the Administrator of any provisions of the Plan or of any Stock Right granted under it shall be final.

The Administrator may employ attorneys, consultants, accountants or other persons, and the Administrator, the Company and its officers and directors shall be entitled to rely upon the advice, opinions or valuations of such persons. All actions taken and all interpretations and determinations made by the Administrator in good faith shall be final and binding upon the Company, all Participants, and all other interested persons. Neither the Administrator, nor the Company, nor any person acting on behalf of the Administrator or the Company shall be personally liable for any action, determination, or interpretation made in good faith with respect to this Plan or grants hereunder or for any acceleration of income or additional tax (including interest and penalties) asserted by reason of the failure of a Stock Right to satisfy the requirements of Section 422 of the Code, Section 409A of the Code or by reason of Section 4999 of the Code, or otherwise with respect to a Stock Right. Each member of the Administrator shall be indemnified and held harmless by the Company against any cost or expense (including counsel fees) reasonably incurred by him or her or any liability (including any sum paid in settlement of a claim with the approval of the Company) arising out of any act or omission to act in connection with this Plan unless arising out of such member's own fraud or bad faith. Such indemnification shall be in addition to any rights of indemnification the members of the Administrator may have as directors or otherwise under the by-laws of the Company, or any agreement, vote of shareholders or disinterested directors, or otherwise.

5. Eligibility for Participation

The Administrator shall, in its sole discretion, select the individuals to be the Participants in the Plan; provided, however, that each Participant must be an Employee, Non-Employee Director, consultant or advisor of the Company or of an Affiliate at the time a Stock Right is granted. Notwithstanding the foregoing, the Administrator may authorize the grant of a Stock Right to a person not then an Employee, Non-Employee Director, consultant or advisor of the Company or of an Affiliate; provided, however, that the actual grant of such Stock Right shall not be effective until such person becomes eligible to be a Participant. ISOs may be granted only to Employees. The granting of any Stock Right to any individual shall neither entitle that individual to, nor disqualify him or her from, participation in other grants of Stock Rights.

6. Terms and Conditions of Options

6.1 General

Each Option shall be set forth in writing in a Stock Agreement, duly executed by the Company and, to the extent required by law or requested by the Company, by the Participant. The Administrator may provide that Options be granted subject to such terms and conditions, consistent with the terms and conditions specifically required under this Plan, as the Administrator may deem appropriate including, without limitation, subsequent approval by the shareholders of the Company of this Plan or any amendments thereto. Each Stock Agreement shall state the exercise price (per share) of the Shares covered by each Option, the number of Shares to which it pertains, the date or dates on which it first is exercisable and the date after which it may no longer be exercised (subject to Sections 11 and 12 of this Plan). Options may vest or become exercisable in installments over a period of time, or upon the achievement of certain conditions or the attainment of stated goals or events. The exercise price per share of Shares covered by an Option (including both ISOs and Non-Qualified Options) shall not be less than one hundred percent (100%) of the Fair Market Value per share of the Common Stock on the date of grant.

6.2 ISOs

Each Option intended to be an ISO shall be issued only to an Employee. In addition to the provisions set forth in Section 6.1, ISOs shall be subject to the following terms and conditions, with such additional restrictions or changes as the Administrator determines are appropriate but not in conflict with Section 422 of the Code and relevant regulations and rulings of the Internal Revenue Service:

6.2.1 ISO Exercise Price

In addition to the limitation set forth in Section 6.1, the exercise price per share of the Shares covered by each ISO granted to a Participant who owns, directly or by reason of the applicable attribution rules in Section 424(d) of the Code, more than ten percent (10%) of the total combined voting power of all classes of stock of the Company or an Affiliate shall not be less than one hundred ten percent (110%) of the Fair Market Value on the date of grant.

6.2.2 Term of ISO

Each ISO shall expire not more than ten (10) years from the date of grant; provided, however, that an ISO granted to a Participant who owns, directly or by reason of the applicable attribution rules in Section 424(d) of the Code, more than ten percent (10%) of the total combined voting power of all classes of stock of the Company or an Affiliate shall expire not more than five (5) years from the date of grant.

6.2.3 Annual Limit on Incentive Stock Options

To the extent required for "incentive stock option" treatment under Section 422 of the Code, the aggregate Fair Market Value (determined as of the time of grant) of the Shares with respect to which ISOs granted under this Plan and any other plan of the Company or its Affiliate become exercisable for the first time by a Participant during any calendar year shall not exceed the aggregate threshold for ISOs established by the Code (\$100,000 as of January 1, 2018). To the extent that any Option exceeds this limit, it shall constitute a Non-Qualified Option.

6.3 Non-Employee Directors' Options

Each Non-Employee Director, upon first being elected or appointed to the Board of Directors, shall, in addition to any other Stock Rights as may be determined by the Board of Directors, be granted a Non-Qualified Option to purchase that number of Shares as shall be established for such Option grants from time to time by the Board of Directors. In addition, unless otherwise determined by the Board of Directors, on June 1 of each year, each Non-Employee Director shall, in addition to any other Stock Rights as may be determined by the Board of Directors, be granted a Non-Qualified Option to purchase that number of Shares as shall be established for such Option grants from time to time by the Board of Directors. If a Non-Employee Director ceases to be any of an Employee, Non-Employee Director, consultant or advisor of the Company, Options granted under this Section 6.3 shall remain exercisable to the extent such Options are exercisable on the date of such Termination of Service, for their full term, and the provisions of Sections 11 and 12 below shall not apply to any such Options.

6.4 Term of Options

No Option will be granted with a term in excess of ten (10) years.

7. Terms and Conditions of Stock Grants

Each Stock Grant shall be set forth in a Stock Agreement, duly executed by the Company and, to the extent required by law or requested by the Company, by the Participant. The Stock Agreement shall be in the form approved by the Administrator, with such changes and modifications to such form as the Administrator, in its discretion, shall approve with respect to any particular Participant or Participants. The Stock Agreement shall contain terms and conditions that the Administrator determines to be appropriate. Each Stock Agreement shall state the number of Shares to which the Stock Grant pertains and the terms of any right of the Company to reacquire the Shares subject to the Stock Grant, including the time and events upon which such rights shall accrue and the purchase price therefor, and any restrictions on the transferability of such Shares.

8. Terms and Conditions of Stock-Based Awards

The Administrator shall have the right to grant Stock-Based Awards having such terms and conditions as the Administrator may determine, including, without limitation, the grant of Shares based upon certain conditions, the grant of securities convertible into Shares and the grant of Stock Appreciation Rights or Restricted Stock Units. The principal terms of each Stock-Based Award shall be set forth in a Stock Agreement, duly executed by the Company and, to the extent required by law or requested by the Company, by the Participant. The Stock Agreement shall be in a form approved by the Administrator and shall contain terms and conditions that the Administrator determines to be appropriate. No Stock Appreciation Right will be granted with a term in excess of ten (10) years. The base value (i.e., exercise price) of any Stock Appreciation Right shall not be less than one hundred percent (100%) of the Fair Market Value per share of the Common Stock on the date of grant.

9. Exercise of Options and Stock Appreciation Rights and Issuance of Shares

Options and Stock Appreciation Rights (or any part or installment thereof) shall be exercised by delivery to the Company, or its designee, of a notice of exercise in any form (which may be electronic) approved by the Company, together, in the case of an Option, with provision for payment of the full purchase price in accordance with this Section for the Shares as to which the Option is being exercised, and upon compliance with any other condition(s) set forth in the Stock Agreement. Payment of the exercise price for the Shares as to which such Option is being exercised shall be made (a) in cash or by check acceptable to the Administrator, or (b) at the discretion of the Administrator, (i) through delivery of shares of Common Stock not subject to any restriction under any plan and having a Fair Market Value equal as of the date of exercise to the exercise price of the Option, (ii) in accordance with a cashless exercise program established with a securities brokerage firm, and approved by the Company, (iii) by any other means (excluding, however, delivery of a promissory note of the Participant) that the Administrator determines to be consistent with the purpose of this Plan and applicable law, or (iv) by any combination of the foregoing. Notwithstanding the foregoing, the Administrator shall accept only such payment on exercise of an ISO as is permitted by Section 422 of the Code.

Subject to the last paragraph of Section 13, if on the date the term of a Non-Qualified Option expires or on the last date such Non-Qualified Option is exercisable in accordance with Section 11 or Section 12, the Fair Market Value of a share of Common Stock exceeds the exercise price per share of the Non-Qualified Option, then the Non-Qualified Option shall automatically be exercised with respect to all then vested Shares underlying such Non-Qualified Option and, upon such automatic exercise, such Non-Qualified Option shall immediately terminate. Payment of the exercise price for the Shares as to which such Non-Qualified Option is being exercised and all tax withholding requirements shall be satisfied by a "net exercise," as a result of which the Participant shall receive (i) the number of shares underlying the portion of the Non-Qualified Option so being exercised, less (ii) such whole number of shares (rounded up to the nearest share) that is equal to (A) the aggregate exercise price for the portion of the Non-Qualified Option that is so being exercised plus the amount of all applicable tax withholdings associated with such exercise divided by (B) the Fair Market Value of a share of Common Stock on the date of exercise. For the avoidance of doubt, this paragraph shall not apply to any Non-Qualified Stock Options that were granted to "covered employees" (within the meaning of Section 162(m) of the Code) or to the Company's Chief Financial Officer, in each case, that were outstanding on November 2, 2017.

Following the exercise of an Option or Stock Appreciation Right, and, in the case of an Option, the payment of the exercise price, in each case in accordance with this Section 9, and the satisfaction of any tax withholding as contemplated by Section 21, the Company shall, as soon as is reasonably practicable, deliver the Shares as to which such Option or Stock Appreciation Right was exercised to the Participant (or to the Participant's Survivors, as the case may be). It is expressly understood that the Company may delay the delivery of the Shares in order to comply with any law or regulation that requires the Company to take any action with respect to the Shares prior to their issuance. The Shares shall, upon delivery, be fully paid, non-assessable Shares.

10. Assignability and Transferability of Stock Rights

By its terms, a Stock Right granted to a Participant shall not be transferable by the Participant other than by will or by the laws of descent and distribution or pursuant to a domestic relations order as defined by the Code or Title I of the Employee Retirement Income Security Act or the rules thereunder or as approved by the Administrator in its discretion and set forth in the applicable Stock Agreement; provided, however, that the Administrator shall not approve any transfer of a Stock Right for consideration. Except as provided in the preceding sentence or as otherwise

permitted under a Stock Agreement, a Stock Right shall be exercisable, during the Participant's lifetime only by such Participant (or by his or her legal representative), and shall not be assigned, pledged or hypothecated in any way (whether by operation of law or otherwise) and shall not be subject to execution, attachment or similar process. Any attempted transfer, assignment, pledge, hypothecation or other disposition of any Stock Right or of any rights granted thereunder contrary to the provisions of this Plan, or the levy of any attachment or similar process upon a Stock Right, shall be null and void.

11. Effect on Stock Rights of Termination of Service

- 11.1 Except as otherwise provided in the applicable Stock Agreement or as otherwise provided in Section 12, all Options and Stock Appreciation Rights held by a Participant, if any, immediately prior to the Participant's Termination of Service, to the extent then exercisable, will remain exercisable for ninety (90) days after the date of the Participant's Termination of Service, unless otherwise provided in the applicable Stock Agreement, but in no event after the expiration of the term of the Stock Right.
- 11.2 The provisions of this Section, and not the provisions of Section 12, shall apply to a Participant who subsequently dies after the Termination of Service. In the event of the death of a Participant within ninety (90) days after the Participant's Termination of Service, all Options and Stock Appreciation Rights held by the Participant, if any, immediately prior to such death, to the extent then exercisable, will remain exercisable for one (1) year after the date of the Participant's death, but in no event after the expiration of the term of the Stock Right.
- 11.3 Absence from work with the Company or an Affiliate because of temporary disability or a leave of absence for any purpose, shall not, during the period of any such absence in accordance with Company policies, be deemed, by virtue of such absence alone, a Termination of Service, except as the Administrator may otherwise expressly provide or except as otherwise provided by law.
- 11.4 Except as required by law or as set forth in a Participant's Stock Agreement and, in the case of any Stock Right that constitutes "non-qualified deferred compensation" subject to Section 409A of the Code, only to the extent consistent with Section 409A of the Code, Stock Rights granted under the Plan shall not be affected by any change of a Participant's status within or among the Company and any Affiliates, so long as the Participant continues to be an Employee, Non-Employee Director, consultant or advisor of the Company or any Affiliate.

12. Effect on Stock Rights of Death or Disability While an Employee, Director, Consultant or Advisor

Except as otherwise provided in a Participant's Stock Agreement, in the event (a) of the death of a Participant while the Participant is an Employee, Non-Employee Director, consultant or advisor of the Company or of an Affiliate, or (b) that a Participant's employment or service with the Company or an Affiliate is terminated by the Company due to his or her Disability, then in the case of each of clauses (a) and (b), (i) vesting of all unvested Shares subject to outstanding Stock Rights (other than ISOs) shall be accelerated and (ii) all Non-Qualified Options and Stock Appreciation Rights held by the Participant, if any, immediately prior to such death or termination due to Disability, to the extent then exercisable, will remain exercisable for a period of one (1) year after the date of death or Termination of Service by the Company due to Disability, as applicable, of the Participant but in no event after the date of expiration of the term of the Stock Right. Notwithstanding the foregoing, clause (b) above shall not apply to any Stock Rights that were granted to "covered employees" (within the meaning of Section 162(m) of the Code) or to the Company's Chief Financial Officer, in each case, that were outstanding on November 2, 2017.

13. Annual Limits on Stock Rights; Performance Awards

13.1 Annual Limits

Notwithstanding anything in this Plan to the contrary, no Participant shall be granted Stock Rights under this Plan in any calendar year for more than an aggregate of 1,000,000 Shares (subject to adjustment pursuant to Section 17 to the extent consistent with Section 162(m) of the Code). For purposes of the foregoing limitation, each Share subject to a Stock Right shall be counted as one Share of Common Stock (including each Share subject to a Full-Value Award). To the extent applicable, the foregoing provisions will be construed in a manner consistent with Section 162(m) of the Code, including, without limitation, where applicable, the rules under Section 162(m) of the Code pertaining to permissible deferrals of exempt awards.

13.2 Performance Awards

Stock Grants and Stock-Based Awards may be made subject to the achievement of performance goals pursuant to this Section 13.2 ("Performance Awards"). Grants of Performance Awards intended to qualify as "performance-based compensation" under Section 162(m) of the Code ("Performance-Based Compensation") shall be made only by a "Committee" comprised solely of two or more directors eligible to serve on a committee making awards intended to qualify as "performance-based compensation" under Section 162(m) of the Code. For any Performance Award that is intended to qualify as Performance-Based Compensation, the Committee shall specify that the degree of granting, vesting and/ or payout of the Performance Award shall be based on the relative or absolute attainment of one or any combination of the following objective

performance measures: (i) revenue targets or revenue growth targets, (ii) achievement of specified milestones in the discovery, development or regulatory approval of one or more of the Company's drug candidates, (iii) achievement of specified milestones in the commercialization of one or more of the Company's products, (iv) achievement of specified milestones in the manufacturing of one or more of the Company's products, (v) cost reduction or other expense control targets, (vi) personal management objectives, (vii) stock price targets (including, but not limited to, growth measures), (viii) total shareholder return, (ix) income per share, (x) operating efficiency measures, (xi) operating margin, (xii) gross margin, (xiii) return measures (including, but not limited to, return on assets, capital, equity or sales), (xiv) net or total revenue levels, (xv) productivity ratios, (xvi) operating income, (xvii) net operating profit, (xviii) net earnings or net income (before or after taxes), (xix) cash flow (including, but not limited to, operating cash flow, free cash flow and cash flow return on capital), (xx) earnings or operating income before interest, taxes, depreciation, amortization and/or stock-based compensation expense, (xxi) mergers, acquisitions or divestitures objectives, (xxii) market share, (xxiii) customer satisfaction, (xxiv) working capital targets, (xxv) budget objectives and (xxvi) achievement of other balance sheet or statement of operations objectives.

Each objective performance measure that is a financial measure may be determined pursuant to generally accepted accounting principles ("GAAP") or on a non-GAAP basis, as determined by the Committee. Such objective performance measures may reflect absolute entity or business unit performance or a relative comparison to the performance of a peer group of entities, an index or indices or other external measure of the selected performance criteria and may be absolute in their terms or measured against or in relationship to other companies comparably, similarly or otherwise situated. The objective performance measures and any targets with respect thereto need not be based on an increase, a positive or improved result or the avoidance of loss.

The Committee may specify that such performance measures shall be adjusted to exclude or provide for appropriate adjustment for one or more of the following items: (A) asset impairments or write-downs; (B) litigation and governmental investigation expenses and judgments, verdicts or claim settlements; (C) the effect of changes in tax law, accounting principles or other laws, regulations or provisions affecting reported results; (D) the effect of exchange rates for non-U.S. dollar denominated net sales or goals based on operating profit, earnings or income; (E) accruals for reorganization and restructuring programs; (F) any non-GAAP adjustments as described in the Company's earnings releases or in the management's discussion and analysis of financial condition and results of operations appearing in the Company's periodic reports; (G) items of income, gain, loss or expense attributable to the operations of any business acquired by the Company or any parent or subsidiary or of any joint venture established by the Company or any parent or subsidiary; (H) costs and expenses incurred in connection with mergers and acquisitions; (I) items of income, gain, loss or expense attributable to one or more business operations divested by the Company or any parent or subsidiary or the gain or loss realized upon the sale of any such divested business or the assets thereof; or (J) the effect of any change in the outstanding shares of Common Stock effected by reason of a stock split, stock dividend, stock repurchase, reorganization, recapitalization, merger, consolidation, spin-off, combination or exchange of shares or other similar corporate change or any distributions to the Company's shareholders other than regular cash dividends.

Such performance measures: (1) may vary by Participant and may be different for different Stock Rights; (2) may be particular to a Participant or the department, branch, line of business, subsidiary or other unit in which a Participant works and may cover such performance period as may be specified by the Committee; and (3) shall be set by the Committee within the time period prescribed by, and shall otherwise comply with the requirements of, Section 162(m) of the Code.

With respect to any Performance Award that is intended to qualify as Performance-Based Compensation, the Committee may adjust downwards, but not upwards, the number of shares payable pursuant to such Performance Award, and the Committee may not waive the achievement of the applicable performance measures except in the case of the death or disability of the Participant or a change in control of the Company or as otherwise determined by the Committee.

The Committee shall have the power to impose such other restrictions on Performance Awards as it may deem necessary or appropriate to ensure that such Performance Awards satisfy all requirements for Performance-Based Compensation.

Notwithstanding anything to the contrary in the Plan, except as otherwise determined by the Administrator or as permitted by Internal Revenue Service guidance, the provisions of this 13.2 that relate to Performance-Based Compensation shall not apply to Stock Rights granted on or after May 17, 2018 (the "May Amendment Date"), provided, however, that the terms of this Section 13.2 and the terms of the Plan, as in effect on November 2, 2017, which were those same terms in effect as of immediately prior to the May Amendment Date, shall continue to govern the terms of any Performance Awards and Stock Options granted prior to the May Amendment Date. It is the intent of the Company that the amendment and restatement of the Plan on the May Amendment Date not constitute a "material modification" of the Plan or Stock Rights granted under it prior to the May Amendment Date within the meaning of Section 162(m) of the Code (and any Internal Revenue Service guidance issued thereunder) and the Plan shall be interpreted in accordance with the foregoing intent. In furtherance of the foregoing, the terms of the Plan, as amended and restated as of the May Amendment Date, shall only apply to Stock Rights granted after the May Amendment Date. Other than with respect to the second sentence of this paragraph, references to "Section 162(m) of the Code" in this Section 13 shall refer to Section 162(m) of the Code as in effect prior to December 22, 2017, including the regulations thereunder and other applicable Internal Revenue Service guidance, whether promulgated or issued before or after December 22, 2017.

14. Rights as a Shareholder

No Participant to whom a Stock Right (other than a Stock Grant) has been granted shall have rights as a shareholder with respect to any Shares covered by such Stock Right, except as to Shares actually issued under the Plan.

15. Employment or Other Relationship

Nothing in this Plan or any Stock Agreement shall be deemed to prevent the Company or an Affiliate from terminating the employment, consultancy or director status of a Participant, or to prevent a Participant from terminating his or her own employment, consultancy or director status or to give any Participant a right to be retained in employment or other service by the Company or any Affiliate for any period of time. The loss of existing or potential profit from a Stock Right will not constitute an element of damages in the event of a termination of employment or service for any reason, even if the termination is in violation of an obligation of the Company or any Affiliate.

16. Dissolution or Liquidation of the Company

Upon the dissolution or liquidation of the Company (other than in connection with a transaction subject to the provisions of Section 17.2), all Stock Rights granted under this Plan which as of such date have not been exercised will terminate and become null and void; provided, however, that if the rights of a Participant or a Participant's Survivors have not otherwise terminated and expired, the Participant or Participant's Survivors will have the right immediately prior to such dissolution or liquidation to exercise any Stock Right to the extent that such Stock Right is exercisable as of the date immediately prior to such dissolution or liquidation. Upon the dissolution or liquidation of the Company, any outstanding Stock Rights shall immediately terminate unless otherwise determined by the Administrator or specifically provided in the applicable Stock Agreement.

17. Adjustments

Upon the occurrence of any of the following events, a Participant's rights with respect to any outstanding Stock Right shall be adjusted as hereinafter provided, unless otherwise specifically provided in the Stock Agreement or in any employment agreement between a Participant and the Company or an Affiliate:

17.1 Stock Dividends and Stock Splits

If the shares of Common Stock shall be subdivided or combined into a greater or smaller number of shares or if the Company shall issue any shares of Common Stock as a stock dividend on its outstanding Common Stock, the number of shares of Common Stock subject to or deliverable upon the vesting or exercise of a Stock Right shall be appropriately increased or decreased, and appropriate adjustments shall be made in the purchase or exercise price per Share to reflect such event. The number of Shares subject to the limitation in Section 13.1 shall also be adjusted upon the occurrence of such events.

17.2 Consolidations or Mergers

In the event of a consolidation or merger in which the Company is not the surviving corporation or which results in the acquisition of substantially all the Company's outstanding stock by a single person or entity or by a group of persons and/or entities acting in concert, or in the event of the sale or transfer of substantially all the Company's assets (any of the foregoing, an "Acquisition"), all then outstanding Stock Rights (excluding any Shares subject to Stock Grants as to which all Company repurchase rights shall have lapsed) shall terminate unless assumed pursuant to clause (i) below; provided that either (i) the Administrator shall provide for the surviving or acquiring entity or an affiliate thereof to assume the outstanding Stock Rights or grant replacement Stock Rights in lieu thereof, any such replacement to be upon an equitable basis as determined by the Administrator, or (ii) if there is no such assumption or substitution, all outstanding Stock Rights shall become immediately and fully exercisable and all Company repurchase rights with respect to Stock Rights shall lapse, in each case immediately prior to the Acquisition, notwithstanding any restrictions or vesting conditions set forth therein.

17.3 Recapitalization or Reorganization

In the event of a recapitalization or reorganization of the Company (other than a transaction described in Section 17.2 above) pursuant to which securities of the Company or of another corporation are issued with respect to the outstanding shares of Common Stock, a Participant upon exercising a Stock Right shall be entitled to receive for the purchase price paid upon such exercise the securities he or she would have received if he or she had exercised such Stock Right immediately prior to such recapitalization or reorganization.

17.4 Adjustments to Shares, Stock Grants and Stock-Based Awards

Upon the happening of any of the events described in Sections 17.1, 17.2 or 17.3, or other change in the Company's capital structure that constitutes an equity restructuring within the meaning of the Accounting Rules, the maximum number of Shares specified in Section 3, the number of Shares subject to the limits in Section 13.1, any exercise price per Share of any Stock Right, any outstanding Stock-Based Award and the Shares subject to any Stock Grant, vested or unvested, shall be appropriately adjusted by the Administrator to reflect such events. The Administrator may also make adjustments of the type described above to take into account distributions to stockholders other than those provided for in Sections 17.1,

17.2 or 17.3, or any other event, if the Administrator determines that adjustments are appropriate to avoid distortion in the operation of the Plan. The Administrator shall determine the specific adjustments to be made under this Section 17.4. References in the Plan to Shares will be construed to include any stock or securities resulting from an adjustment pursuant to this Section 17.4.

17.5 Modification of ISOs.

Notwithstanding the foregoing, any adjustments made pursuant to Section 17.1, 17.2 or 17.3 with respect to ISOs shall be made only after the Administrator determines whether such adjustments would constitute a “modification” of such ISOs (as that term is defined in Section 424(h) of the Code) or would cause any adverse tax consequences for the holders of such ISOs. If the Administrator determines that such adjustments made with respect to ISOs would constitute a modification of such ISOs, it may refrain from making such adjustments, unless the holder of an ISO specifically consents in writing to such adjustment be made and such writing indicates that the holder has full knowledge of the consequences of such “modification” on his or her income tax treatment with respect to the ISO.

18. Issuances of Securities

Except as expressly provided herein, no issuance by the Company of shares of stock of any class, or securities convertible into shares of stock of any class, shall affect, and no adjustment by reason thereof shall be made with respect to, the number or price of Shares subject to Stock Rights. Except as expressly provided herein, no adjustments shall be made for dividends paid in cash or in property (including without limitation, securities) of the Company.

19. Fractional Shares

No fractional share shall be issued under the Plan and the person exercising any Stock Right shall receive from the Company cash in lieu of any such fractional share equal to the Fair Market Value thereof.

20. Dividend Equivalents

The Administrator may provide for the payment of amounts (on terms and subject to conditions established by the Administrator, including providing for the reinvestment of such amounts in the form of additional Stock Rights) in lieu of cash dividends or other cash distributions with respect to Common Stock subject to a Stock Right whether or not the holder of such Stock Right is otherwise entitled to share in the actual dividend or distribution in respect of such Stock Right; provided, however, that notwithstanding anything to the contrary in the Plan (a) any dividends or dividend equivalents relating to a Stock Right (other than an Option or Stock Appreciation Right) that, at the dividend payment date, remains subject to a risk of forfeiture (whether service-based or performance-based) shall be subject to the same risk of forfeiture as applies to the underlying Stock Right and (b) except as contemplated by Section 17, no dividends or dividend equivalents shall be payable with respect to Options or Stock Appreciation Rights unless and until such Options or Stock Appreciation Rights have vested and been exercised in accordance with their terms.

21. Withholding

The delivery, vesting and retention of Shares, cash or other property under a Stock Right are conditioned upon full satisfaction by the Participant of all tax withholding requirements with respect to the Stock Right. The Administrator shall prescribe such rules for the withholding of taxes with respect to any Stock Right as it deems necessary. The Administrator may withhold from the Participant’s compensation or require that the Participant advance cash to the Company or an Affiliate the amount of such withholding and may hold back Shares from a Stock Right or permit a Participant to tender previously owned Shares in satisfaction of tax withholding requirements (but not in excess of the maximum withholding amount consistent with the award being subject to equity accounting treatment under the Accounting Rules). For purposes hereof, the Fair Market Value of any shares withheld for purposes of payroll withholding shall be determined in the manner provided in Section 1 above, as of the most recent practicable date prior to the date of grant, vesting, exercise or the date of a Disqualifying Disposition. If the Fair Market Value of the shares withheld is less than the amount of payroll withholdings required, the Participant may be required to pay the difference in cash to the Company or the Affiliate employer.

22. Notice to Company of Disqualifying Disposition

Each Employee who receives an ISO must agree to notify the Company in writing immediately after the Employee makes a “Disqualifying Disposition” of any Shares acquired pursuant to the exercise of an ISO. A Disqualifying Disposition is any disposition (as defined in Section 424(c) of the Code) of such Shares before the later of (a) two years from the date the Employee was granted the ISO, or (b) one year after the date the Employee acquired Shares by exercising the ISO. If the Employee has died before such Shares are sold, the notice provisions of this Section 22 shall not apply.

23. Effective Date; Termination of the Plan

This Plan was amended and restated by the Board on April 13, 2017 and April 2, 2018, in each case subject to the approval of the Plan by the shareholders of the Company, and was further amended and restated on October 16, 2018. The Plan, as amended and restated hereby, shall be effective as of June 5, 2019. The Plan will terminate on April 12, 2027. The Plan also may be terminated at an earlier date by vote of the Board of Directors. Termination of this Plan will not affect any Stock Rights granted or Stock Agreements executed prior to the effective date of such termination.

24. Amendment of the Plan; Amendment of Stock Rights

The Plan may be amended by the Board of Directors or the Administrator, including, without limitation, to the extent necessary to qualify any or all outstanding Stock Rights granted under the Plan or Stock Rights to be granted under the Plan for favorable federal income tax treatment (including deferral of taxation upon exercise) as may be afforded incentive stock options under Section 422 of the Code, and to the extent necessary to qualify the shares issuable upon exercise of any outstanding Stock Rights granted, or Stock Rights to be granted, under the Plan for listing on any national securities exchange or quotation in any national automated quotation system of securities dealers. Any amendments to the Plan will be conditioned upon stockholder approval only to the extent, if any, such approval is required by law (including the Code) or applicable stock exchange requirements, as determined by the Administrator. No modification or amendment of the Plan shall adversely and materially affect a Participant's rights under a Stock Right previously granted to the Participant, without such Participant's consent.

In its discretion, the Administrator may amend any term or condition of any outstanding Stock Right, provided: (i) such term or condition is not prohibited by the Plan; (ii) if the amendment is materially adverse to the Participant, such amendment shall be made only with the consent of the Participant or the Participant's Survivors, as the case may be; and (iii) any such amendment of any ISO shall be made only after the Administrator determines whether such amendment would constitute a "modification" of any Stock Right which is an ISO (as that term is defined in Section 424(h) of the Code) or would cause any adverse tax consequences for the holder of such ISO (in which case, the Participant's or Participant's Survivors' consent to such amendment shall be required). Notwithstanding the foregoing, unless such action is approved by the Company's shareholders, the Company may not (except for adjustments permitted under Section 17 of this Plan) (1) amend any outstanding Option or Stock Appreciation Right granted under the Plan to provide an exercise price per share that is lower than the then-current exercise price per share of such outstanding Option or Stock Appreciation Right; (2) cancel any outstanding Option or Stock Appreciation Right (whether or not granted under the Plan) and grant in substitution therefor new Stock Rights under the Plan covering the same or a different number of shares of Common Stock and having an exercise price per share lower than the then-current exercise price per share of the cancelled option or Stock Appreciation Right; or (3) cancel in exchange for a cash payment any outstanding Option or Stock Appreciation Right with an exercise price per share above the then-current Fair Market Value.

25. Recovery of Compensation

The Administrator may provide in any case that outstanding Stock Rights (whether or not vested or exercisable) and the proceeds from the exercise or disposition of Stock Rights or Common Stock acquired under Stock Rights will be subject to forfeiture and disgorgement to the Company, with interest and other related earnings, if the Participant to whom the Stock Right was granted violates (i) a non-competition, non-solicitation, confidentiality or other restrictive covenant by which he or she is bound, or (ii) any Company policy applicable to the Participant that provides for forfeiture or disgorgement with respect to incentive compensation that includes Stock Rights under the Plan. In addition, the Administrator may require forfeiture and disgorgement to the Company of outstanding Stock Rights and the proceeds from the exercise or disposition of Stock Rights or Common Stock acquired under Stock Rights, with interest and other related earnings, to the extent required by law or applicable stock exchange listing standards, including, without limitation, Section 10D of the Exchange Act, and any applicable Company policy. Each Participant, by accepting or being deemed to have accepted a Stock Right under the Plan, agrees to cooperate fully with the Administrator, and to cause any and all permitted transferees of the Participant to cooperate fully with the Administrator, to effectuate any forfeiture or disgorgement required hereunder. Neither the Administrator nor the Company nor any other person, other than the Participant and his or her permitted transferees, if any, will be responsible for any adverse tax or other consequences to a Participant or his or her permitted transferees, if any, that may arise in connection with this Section 25.

26. Compliance with Section 409a of the Code

Without limiting the generality of Section 4 hereof, each Stock Right will contain such terms as the Administrator determines and will be construed and administered, such that the Stock Right either qualifies for an exemption from the requirements of Section 409A of the Code or satisfies such requirements.

Notwithstanding Section 24 hereof or any other provision of this Plan or any Stock Agreement to the contrary, the Administrator may unilaterally amend, modify or terminate the Plan or any outstanding Stock Right, including but not limited to changing the form of the Stock Right, if the Administrator determines that such amendment, modification or termination is necessary or advisable to avoid the imposition of an additional

tax, interest or penalty under Section 409A of the Code. To the extent that a provision of this Plan is amended to provide for the accelerated payment or settlement of a Stock Right, no such amendment will be given effect if it would result in the imposition of an additional tax, interest or penalty under Section 409A of the Code.

If a Participant is deemed on the date of the Participant's Termination of Service to be a "specified employee" within the meaning of that term under Section 409A(a)(2)(B) of the Code, then, with regard to any payment that is considered nonqualified deferred compensation under Section 409A of the Code, to the extent applicable, payable on account of a "separation from service", such payment will be made or provided on the date that is the earlier of (i) the expiration of the six-month period measured from the date of such "separation from service" and (ii) the date of the Participant's death (the "Delay Period"). Upon the expiration of the Delay Period, all payments delayed pursuant to this Section 26 (whether they would have otherwise been payable in a single lump sum or in installments in the absence of such delay) will be paid on the first business day following the expiration of the Delay Period in a lump sum and any remaining payments due under the Stock Right will be paid in accordance with the normal payment dates specified for them in the applicable Stock Agreement.

For purposes of Section 409A of the Code, each payment made under this Plan will be treated as a separate payment.

With regard to any payment considered to be nonqualified deferred compensation under Section 409A of the Code, to the extent applicable, that is payable upon a change in control of the Company or other similar event, to avoid the imposition of an additional tax, interest or penalty under Section 409A of the Code, no amount will be payable unless such change in control constitutes a "change in control event" within the meaning of Section 1.409A-3(i)(5) of the Treasury Regulations.

27. Authorization of Sub-Plans

The Board of Directors may from time to time establish one or more sub-plans under the Plan for purposes of satisfying applicable securities, tax or other laws of various jurisdictions. The Board of Directors shall establish such sub-plans by adopting supplements to the Plan containing (i) such limitations on the Board of Director's discretion under the Plan as the Board of Directors deems necessary or desirable or (ii) such additional terms and conditions not otherwise inconsistent with the Plan as the Board of Directors shall deem necessary or desirable. All supplements adopted by the Board of Directors shall be deemed to be part of the Plan, but each supplement shall apply only to Participants within the affected jurisdiction and the Company shall not be required to provide copies of any supplement to Participants in any jurisdiction that is not the subject of such supplement.

28. Governing Law

This Plan, Stock Rights under the Plan and all claims or disputes arising out of or based upon the Plan or Stock Rights under the Plan or relating to the subject matter hereof or thereof shall be construed and enforced in accordance with the laws of The Commonwealth of Massachusetts without giving effect to any choice or conflict of laws provision or rule that would cause the application of the domestic substantive laws of any other jurisdiction.

By accepting or being deemed to have accepted a Stock Right under the Plan, each Participant will be deemed to (a) have submitted irrevocably and unconditionally to the jurisdiction of the federal and state courts located within the geographic boundaries of the United States District Court for the District of Massachusetts for the purpose of any suit, action or other proceeding arising out of or based upon the Plan or any Stock Right; (b) agree not to commence any suit, action or other proceeding arising out of or based upon the Plan or a Stock Right, except in the federal and state courts located within the geographic boundaries of the United States District Court for the District of Massachusetts; and (c) waive, and agree not to assert, by way of motion as a defense or otherwise, in any such suit, action or proceeding, any claim that he or she is not subject personally to the jurisdiction of the above-named courts that his or her property is exempt or immune from attachment or execution, that the suit, action or proceeding is brought in an inconvenient forum, that the venue of the suit, action or proceeding is improper or that the Plan or a Stock Right or the subject matter thereof may not be enforced in or by such court.

By accepting or being deemed to have accepted a Stock Right under the Plan, to the maximum extent permitted by applicable law, each Participant waives any right to a trial by jury in any action, proceeding or counterclaim concerning any rights under the Plan and any Stock Right, or under any amendment, waiver, consent, instrument, document or other agreement delivered or which in the future may be delivered in connection therewith, and agrees that any such action, proceedings or counterclaim will be tried before a court and not before a jury. By accepting or being deemed to have accepted a Stock Right under the Plan, each Participant certifies that no officer, representative, or attorney of the Company has represented, expressly or otherwise, that the Company would not, in the event of any action, proceeding or counterclaim, seek to enforce the foregoing waivers. Notwithstanding anything to the contrary in the Plan, nothing herein is to be construed as limiting the ability of the Company and a Participant to agree to submit disputes arising under the terms of the Plan or any Stock Right made hereunder to binding arbitration or as limiting the ability of the Company to require any eligible individual to agree to submit such disputes to binding arbitration as a condition of receiving a Stock Right hereunder.

APPENDIX B 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 operating margin. Our non-GAAP operating income for 2021 excluded (i) stock-based compensation expense, (ii) a decrease in the fair value of contingent consideration, (iii) revenues and expenses related to collaborative upfront and milestone payments, including the \$900 million upfront payment to CRISPR Therapeutics AG, and certain other business development activities, and (iv) acquisition-related costs. A reconciliation of GAAP operating income to non-GAAP operating income is included below.

GAAP AND NON-GAAP OPERATING INCOME

	<u>Twelve months ended December 31, 2021</u>
	(in millions, except percentages)
Net product revenues	\$7,573.4
GAAP operating income	\$2,782.1
Stock-based compensation expense	441.4
Decrease in fair value of contingent consideration	(3.1)
Collaborative revenues and expenses	1,112.3
Acquisition-related costs	11.3
Non-GAAP operating income	\$4,344.0
GAAP operating margin	37%
Non-GAAP operating margin	57%

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 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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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 <https://meetnow.global/MYNFZ25>

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 and FOR Proposals 2, 3, and 4.

1. Election of Directors:

	For	Against	Abstain		For	Against	Abstain		For	Against	Abstain
01 - Sangeeta Bhatia	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	02 - Lloyd Carney	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	03 - Alan Garber	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
04 - Terrence Kearney	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	05 - Reshma Kewalramani	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	06 - Yuchun Lee	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
07 - Jeffrey Leiden	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	08 - Margaret McGlynn	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	09 - Diana McKenzie	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
10 - Bruce Sachs	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	11 - Suketu Upadhyay	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>				



2. Ratification of Ernst & Young LLP as independent Registered Public Accounting firm for the year ending December 31, 2022. For Against Abstain

3. Advisory vote to approve named executive office compensation. For Against Abstain

4. Approval of an amendment and restatement of our 2013 Stock and Option Plan to increase the number of shares authorized for issuance under this plan by 13.5 million shares. For Against Abstain

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.





1 U P X



The 2022 Annual Meeting of Shareholders of Vertex Pharmaceuticals Incorporated
will be held on
May 18, 2022, at 9:30 a.m. Eastern Time
virtually via the Internet at
<https://meetnow.global/MYNFZZ5>.

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.

Important Notice Regarding the Availability of Proxy Materials for the Shareholder Meeting to be held on May 18, 2022:
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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▼ IF VOTING BY MAIL, SIGN, DETACH AND RETURN THE BOTTOM PORTION IN THE ENCLOSED ENVELOPE. ▼



Proxy – Vertex Pharmaceuticals Incorporated

ANNUAL MEETING OF SHAREHOLDERS – May 18, 2022

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 18, 2022, at 9:30 A.M. Eastern Time, via live audio webcast available at <https://meetnow.global/MYNFZZ5> 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, 3 and 4 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.

