

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

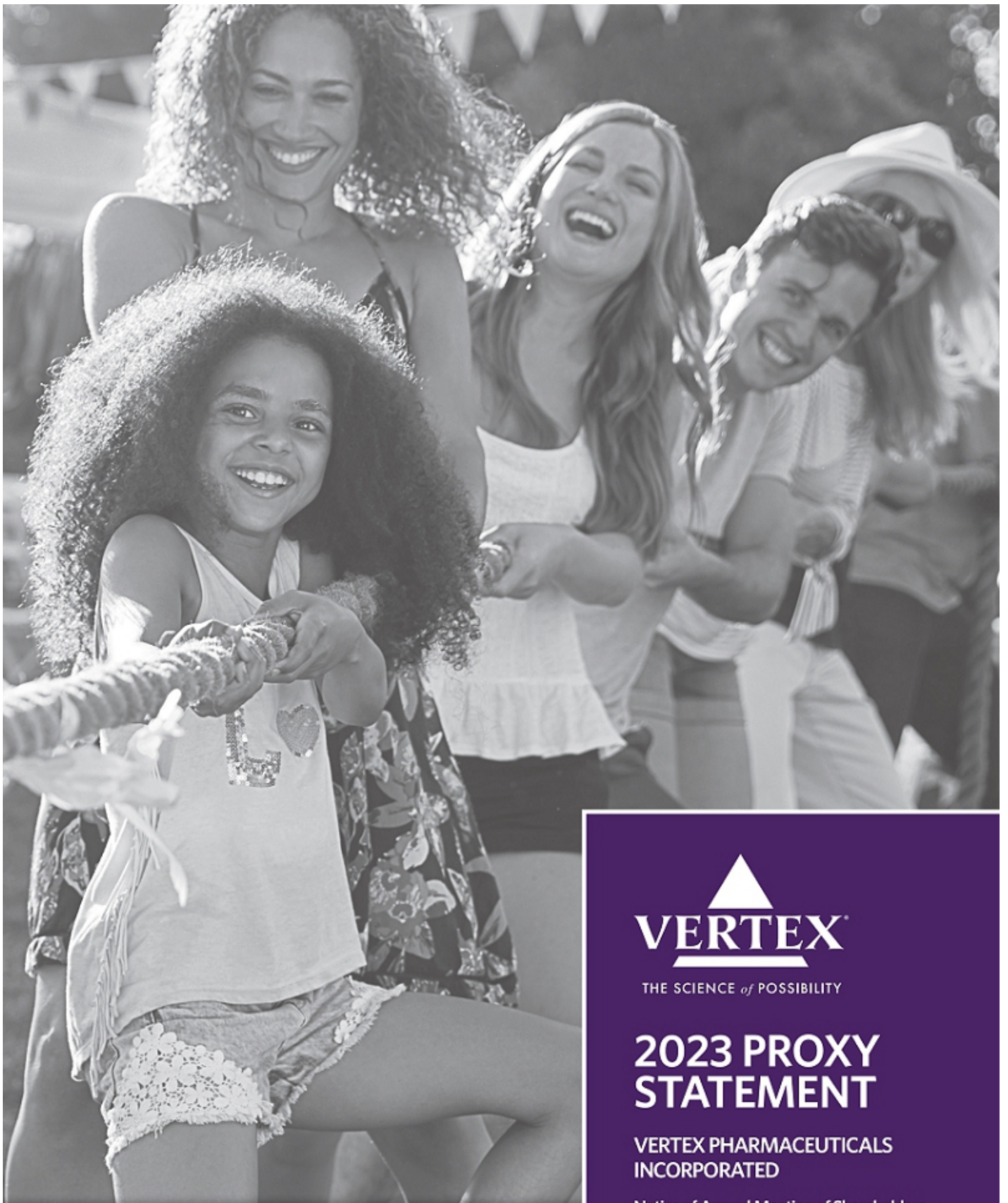


**VERTEX PHARMACEUTICALS INCORPORATED**

*(Name of Registrant as Specified In Its Charter)*

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.



  
**VERTEX**  
THE SCIENCE *of* POSSIBILITY

## 2023 PROXY STATEMENT

VERTEX PHARMACEUTICALS  
INCORPORATED

Notice of Annual Meeting of Shareholders  
to be held on May 17, 2023

## Dear Shareholders:

2022 was an outstanding year for Vertex. We secured more reimbursement agreements and served more people with cystic fibrosis (“CF”) than in any previous year. Our research and development (“R&D”) strategy, which focuses on validated targets that address causal human biology, predictive assays and biomarkers, rapid paths to approval, and product candidates with transformative potential, drove substantial advancement of our pipeline. We also continued to strengthen our financial profile. These important advances in 2022 lay the foundation for sustained leadership in CF, multiple near term global commercial launches outside of CF, and significant value creation for patients and shareholders for many years to come.

Net product revenues from our CF franchise grew to \$8.9 billion in 2022, representing an 18% increase from 2021, and a near tripling of revenues since 2018. We continued to invest significantly in both internal and external innovation in support of our differentiated R&D approach, which has leveraged serial innovation to produce four transformational medicines for patients with CF and has now delivered assets into the clinic across eight disease areas and multiple modalities. Numerous programs, including in CF, sickle cell disease, beta thalassemia, acute pain, APOL1-mediated kidney disease and type 1 diabetes, are past the proof-of-concept stage and multiple assets hold the potential for near-term commercialization.

Our CF franchise exemplifies the patient impact and financial success that can be achieved through our business model and R&D strategy. Broad reimbursement and access to our medicines is now available in over 40 countries and, in 2022, we treated more people with CF than ever before. We reached lower age groups with the successful launches of TRIKAFTA/KAFTRIO in Europe and Canada for children with CF aged 6 to 11 years and of ORKAMBI in the U.S. for children with CF aged 1 to 2 years, which helped generate another year of double-digit revenue growth. In addition, we submitted U.S. and European regulatory filings for TRIKAFTA/KAFTRIO in children with CF aged 2 to 5 years and for KALYDECO in 1- to 4-month-old infants with CF. We also continued our strategy of serial innovation by completing enrollment of the Phase 3 trials of our triple combination of vanzacaftor/tezacaftor/deutivacaftor; entering the clinic with a messenger RNA therapeutic designed for the estimated 5,000 people with CF who cannot benefit from our current medicines; and advancing multiple next generation potentiators and correctors that have the potential to deliver even greater benefits to people living with CF.

Beyond CF, our differentiated R&D strategy has delivered a broad, deep and advanced pipeline with multiple potentially transformative mid- and late-stage assets, each representing multi-billion dollar market opportunities.

- In sickle cell disease and transfusion dependent beta thalassemia, we completed the European Union and U.K. regulatory submissions for exa-cel, a one-time gene therapy that has the potential to be a functional cure for people living with these diseases. Both submissions have been validated by the respective regulatory agencies. We also initiated a rolling regulatory submission in the U.S., which we recently completed. In addition, our teams made meaningful progress in pre-launch preparation, and in establishing the infrastructure necessary to ensure patient access to this therapy.
  - In pain, we announced positive Phase 2 results for VX-548 in acute pain and initiated Phase 3 studies, while also initiating a Phase 2 study in chronic neuropathic pain. Pre-launch preparations for acute pain are underway.
  - In APOL1-mediated kidney disease, we commenced pivotal clinical development of inaxaplin and obtained breakthrough therapy and PRIME designations in the U.S. and European Union, respectively.
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- In type 1 diabetes, we achieved proof-of-concept for our VX-880 stem-cell-derived islet cell therapy program and continued to enroll patients in the ongoing Phase 1/2 clinical trial. In addition, we progressed our VX-264 program, in which the cells are encapsulated in an immunoprotective device, into the clinic, while also continuing pre-clinical development for our hypoimmune VX-880 cell program. Furthermore, we completed the acquisition of ViaCyte, Inc., a company focused on stem-cell-derived cell replacement therapies for type 1 diabetes with complementary assets, capabilities, and technologies that we believe will accelerate our current programs to bring forward a functional cure for the disease.
- In alpha-1 antitrypsin (“AAT”) deficiency, we initiated a first-in-human clinical trial for VX-634, the first in a series of next-wave AAT correctors with significantly improved potency and drug-like properties compared to our prior AAT correctors. We also initiated a second Phase 2 study of VX-864, a first-generation AAT corrector, to assess the impact of longer-term treatment on the liver and on levels of functional AAT in the plasma.

In addition to our focus on discovering transformative medicines and growing our business, we remained committed to supporting patients, our local communities and our workforce, and progressed our environmental, social, and governance practices. We advanced our progress in 2022 by continuing to integrate sustainability best practices in our operations, exceeding our environmental targets, and making a positive impact in the communities where we live and work. We also celebrated the 5<sup>th</sup> anniversary of the Vertex Foundation, which works to improve the lives of people with serious diseases and contribute to our local communities, with a focus on education, innovation, and health. In 2022, Vertex and the Vertex Foundation contributed nearly \$35 million in charitable giving to local communities globally. Our employees also continued to participate in community service throughout the year, with 57% of Vertexians participating in our global Day of Service, which resulted in more than 6,300 hours of volunteer work across 90 projects in 20 countries. We also continued to nurture our culture, focus on the well-being of our people, and develop our talent, all while successfully transitioning to a hybrid work environment.

As Executive Chairman and Chief Executive Officer, we are committed to the continued execution of our strategy of serial innovation that will be critical to our long-term success in bringing more transformative medicines to patients. Looking to the future, we are focused on sustaining and expanding our leadership in CF, preparing for multiple new product launches outside of CF, bringing the next wave of innovation to patients, and continuing to deliver revenue growth and industry-leading operating margins. We believe our focus on transforming and curing serious diseases, combined with the experience and passion of our workforce and our strong financial profile, will fuel our continued success for both patients and shareholders in 2023 and beyond.

Sincerely,



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



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

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# Notice of Annual Meeting of Shareholders

**Wednesday, May 17, 2023**

**9:00 a.m. (Eastern Time)**

<https://meetnow.global/MS2Z5F>

**Dear Shareholders:**

**You are invited to attend the Vertex Pharmaceuticals Incorporated 2023 Annual Meeting of Shareholders. At the annual meeting, shareholders will vote:**

- to elect the nine 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 2024 annual meeting of shareholders and until such person's successor has been duly elected and qualified;
- to ratify the selection of Ernst & Young LLP as our independent registered public accounting firm for 2023;
- to hold an advisory vote on our 2022 named executive officer compensation; and
- to hold an advisory vote on the frequency of future advisory votes on our executive compensation.

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, 2022 ("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:**

**THE ANNUAL MEETING WILL BE HELD VIRTUALLY VIA WEBCAST. A VIRTUAL 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/MS2Z5F](https://meetnow.global/MS2Z5F). THERE IS NO PHYSICAL LOCATION FOR THE ANNUAL MEETING.**

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 electronically 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](mailto: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 12, 2023. 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 9:00 a.m. (Eastern Time) on May 17, 2023.

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 23, 2023 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 6, 2023**

By Order of the Board of Directors,



**Joy Liu**  
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, 2022 are first being made available to holders of record of our common stock on or about April 6, 2023. These materials are available to holders of record of our common stock at [www.envisionreports.com/VRTX](http://www.envisionreports.com/VRTX) and to beneficial holders of our common stock at [www.edocumentview.com/VRTX](http://www.edocumentview.com/VRTX).



# SUMMARY

In 2022, we continued to execute on our strategy of investing in scientific innovation to create transformative medicines for people with serious diseases, with a focus on specialty markets. We delivered our medicines to more people with cystic fibrosis (“CF”) than ever before, made great strides in advancing our broad and diverse pipeline, prepared for potential near-term global commercial launches in multiple new disease areas, and further strengthened our financial profile.

Today, our medicines are collectively being used to treat more than two two-thirds of the approximately 88,000 people with CF in North America, Europe and Australia. These medicines are approved, have broad reimbursement and are accessible in more than 40 countries outside of the U.S. As we look to the future, we expect to grow our CF business through continued uptake of our medicines and label expansions of our commercialized medicines, as well as increases in the number of people living with CF. We also continue to serially innovate in CF, as demonstrated by the completion of enrollment in our Phase 3 clinical trials of our next-generation triple combination and the initiation of clinical trials for a messenger RNA (“mRNA”) therapeutic designed for people with CF who cannot benefit from our existing medicines.

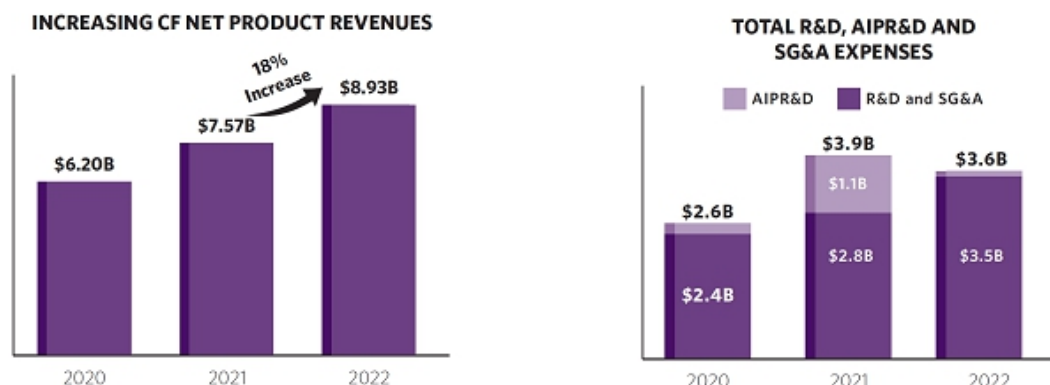
Beyond CF, our robust research and development (“R&D”) pipeline includes multiple mid- and late-stage clinical programs that have already achieved proof-of-concept, including sickle cell disease, beta thalassemia, acute pain, APOL1-mediated kidney disease, and type 1 diabetes, as well as earlier-stage programs in pre-clinical development in diseases such as Duchenne muscular dystrophy and myotonic dystrophy type 1.

In addition to significant R&D pipeline advancement, our outstanding financial performance in 2022 resulted in net product revenues of \$8.93 billion and strong operating margins. As a result, we are well-positioned to continue creating long-term value for both patients and shareholders with a portfolio of high-value medicines for CF, a broad and deep pipeline beyond CF, clinical programs in multiple therapeutic modalities that range from 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.

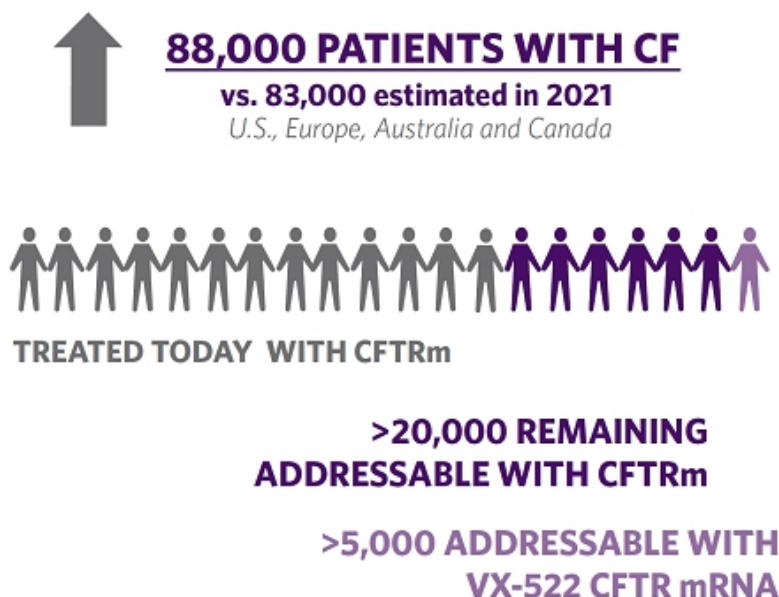
- Our CF net product revenues increased to \$8.93 billion in 2022, up 18% or approximately \$1.4 billion, from our 2021 net product revenues.
- Our total R&D, acquired in-process research and development (“AIPR&D”) and selling, general and administrative (“SG&A”) expenses decreased to \$3.6 billion compared to \$3.9 billion in 2021. The decrease was primarily due to lower AIPR&D as a result of the one-time \$900 million upfront payment to CRISPR Therapeutics AG (“CRISPR”) in 2021, partially offset by increased investment in support of multiple programs that have advanced to mid- and late-stage clinical development and the costs to support launches of Vertex’s therapies globally.



## Marketed Products

Our successful strategy of serial innovation has sustained and expanded our leadership position in CF and continues to propel us toward 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, expanding access to our medicines in additional geographies, and seeking improved treatment options for all patients with CF.

Our four approved medicines have broad reimbursement, are accessible in more than 40 countries, and are being used to treat more than two-thirds of the approximately 88,000 people with CF in North America, Europe, and Australia. Yet, as of the beginning of the year, there were more than 25,000 untreated patients in these geographies who could benefit from our therapies. We expect to grow our CF business with (i) continued uptake by patients in countries where we are early on the launch curve, such as those with recently achieved reimbursement agreements, (ii) label expansions, including into younger patient groups, (iii) the development of mRNA therapies for people with CF who are not eligible for our approved CFTR modulators, and (iv) growth in the number of people living with CF.



Since the beginning of 2022, notable progress includes:

- The European Commission and the Medicines and Healthcare products Regulatory Agency (“MHRA”) 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.
- Health Canada granted marketing authorization for TRIKAFTA for children with CF 6 through 11 years of age who have at least one F508del mutation.
- The U.S. Food and Drug Administration (“FDA”) approved the use of ORKAMBI for children with CF 12 to less than 24 months of age who are homozygous for the F508del mutation.
- We submitted global regulatory filings for TRIKAFTA/KAFTRIO in children with CF 2 through 5 years of age and for KALYDECO in children with CF from 1 month to less than 4 months of age.

## Potential Near-Term Launch Opportunities

We are preparing for the following near-term launches of new products:

- *Exa-cel* in severe sickle cell disease (“SCD”) and transfusion-dependent beta thalassemia (“TDT”). We completed European Union and U.K. regulatory submissions for exagamglogene autotemcel (“exa-cel”), an ex-vivo CRISPR gene-editing therapy, in the fourth quarter of 2022 and initiated a rolling submission in the U.S., which we recently completed. The European Medicines Agency (“EMA”) and MHRA have validated the exa-cel marketing authorization application (“MAA”) for their respective jurisdictions.
- *VX-548* in acute pain. We continue to enroll the Phase 3 pivotal program for VX-548 for the treatment of moderate to severe acute pain and expect to complete the pivotal program in late 2023 or early 2024.
- *Vanzacaftor/tezacaftor/deutivacaftor, the next-in-class triple combination, in CF.* We continued our strategy of serial innovation by completing enrollment of the Phase 3 trials of our once-daily triple combination of vanzacaftor/tezacaftor/deutivacaftor. Our clinical and preclinical data indicate that the vanzacaftor/tezacaftor/deutivacaftor triple combination has the potential to provide enhanced benefit beyond TRIKAFTA/KAFTRIO for people who have at least one mutation in their CFTR gene responsive to CFTR modulators. This regimen also has the benefit of once-daily dosing and has substantially decreased royalties compared with TRIKAFTA.



## 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 combines transformative advances in the understanding of human disease and the science of therapeutics to dramatically advance human health. This approach has yielded a broad and deep pipeline and increases the speed and likelihood of successfully bringing medicines to patients, as demonstrated by our success in moving novel product candidates into clinical trials and obtaining marketing approvals, including for TRIKAFTA/KAFTRIO, SYMDEKO/SYMKEVI, ORKAMBI, and KALYDECO for the treatment of CF. The strategy was designed to deliver transformative medicines for serious diseases at high rates of success, and it has delivered just that. Beyond CF, our approach to drug discovery has yielded clinical proof-of-concept in five additional disease areas: SCD and beta thalassemia with exa-cel, acute pain with VX-548, APOL1-mediated kidney disease (“AMKD”) with inaxaplin, and type 1 diabetes (“T1D”) with VX-880, a stem cell-derived islet cell therapy.

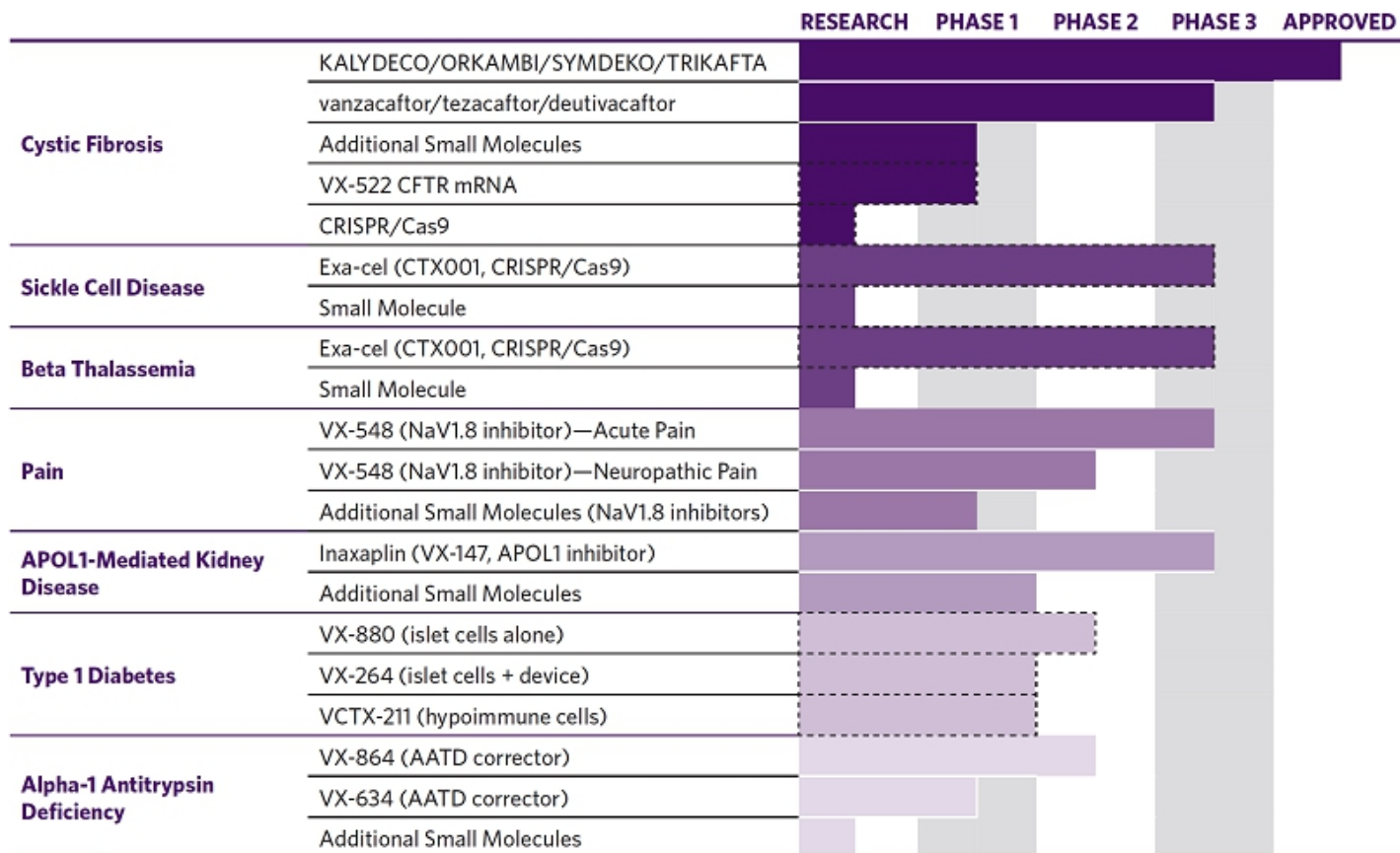
Our research and development approach also includes pursuing multiple modalities tailored to the specific disease area target under investigation, using biomarkers that translate from the bench to the bedside, and advancing multiple candidates into clinical trials with the goal of bringing first-in-class, followed by best-in-class, therapies to patients. In addition to expanding our small molecule programs, we have also advanced an industry-leading portfolio of programs in cell and gene therapies.

Our advancements across multiple disease areas and modalities include:

- **Cystic Fibrosis.** We continue to pursue next-in-class, small molecule CFTR modulator therapies as well as genetic therapies for people with CF who do not make CFTR protein and, as a result, cannot benefit from our current CF medicines. In the past year, we significantly advanced our program for VX-522, a CF mRNA therapeutic designed to treat the underlying cause of CF in these people by enabling cells in the lungs to produce functional CFTR protein. The FDA cleared our investigational new drug (“IND”) application in December 2022 and we have initiated a clinical trial for VX-522 in people with CF; the trial is active and enrolling.
- **Sickle Cell Disease and Beta Thalassemia.** The Phase 3 studies of exa-cel in patients 12 years of age and older is ongoing, as is a long-term follow-up study. Two additional Phase 3 studies in pediatric patients continue to enroll.
- **Neuropathic Pain.** We have initiated a Phase 2 clinical trial of VX-548 in diabetic peripheral neuropathy, a common form of chronic peripheral neuropathic pain.
- **APOL-1 Mediated Kidney Disease.** We initiated pivotal development of inaxaplin and continue to enroll the Phase 2/3 adaptive clinical trial in patients with AMKD.
- **Type 1 Diabetes.** We are evaluating VX-880, an investigational stem-cell derived fully-differentiated islet cell therapy, for the treatment of T1D in a Phase 1/2 clinical trial in which patients receive immunosuppressive therapy to protect the islet cells from immune rejection. Our Clinical Trial Application (“CTA”) in Canada and our IND in the U.S. for our second program in T1D, VX-264, in which the implanted islet cells are encapsulated in an immunoprotective device, were authorized and we plan to begin screening, enrollment and dosing in both Canada and the U.S. in the coming months. We have also continued pre-clinical development of our hypoimmune program utilizing VX-880 cells, and our second hypoimmune program that we are developing in partnership with CRISPR is the subject of a Phase 1/2 study that is active and enrolling patients.
- **Alpha-1 Antitrypsin Deficiency (“AATD”).** We initiated a first-in-human clinical trial for VX-634, which is the first in a series of next-wave investigational small molecules with significantly improved potency and drug-like properties as compared to our previous alpha-1 antitrypsin (“AAT”) correctors. We also initiated a second Phase 2 clinical trial of VX-864, a first-generation AAT corrector, to assess the impact of longer-term treatment on the liver, as well as the levels of functional AAT in the plasma.
- **Duchenne muscular dystrophy (“DMD”).** We are conducting IND-enabling studies for our first in vivo gene-editing therapy for DMD, and we expect to submit an IND for this program in 2023.
- **Myotonic dystrophy type 1 (“DM1”).** We are exploring multiple approaches to address the underlying causal biology for DM1, and are collaborating with Entrada Therapeutics, Inc. (“Entrada”) on IND-enabling studies for an endosomal escape vehicle therapeutic.
- In addition to the programs listed above, we have several earlier-stage research programs aimed at diseases that fit our R&D strategy.

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.

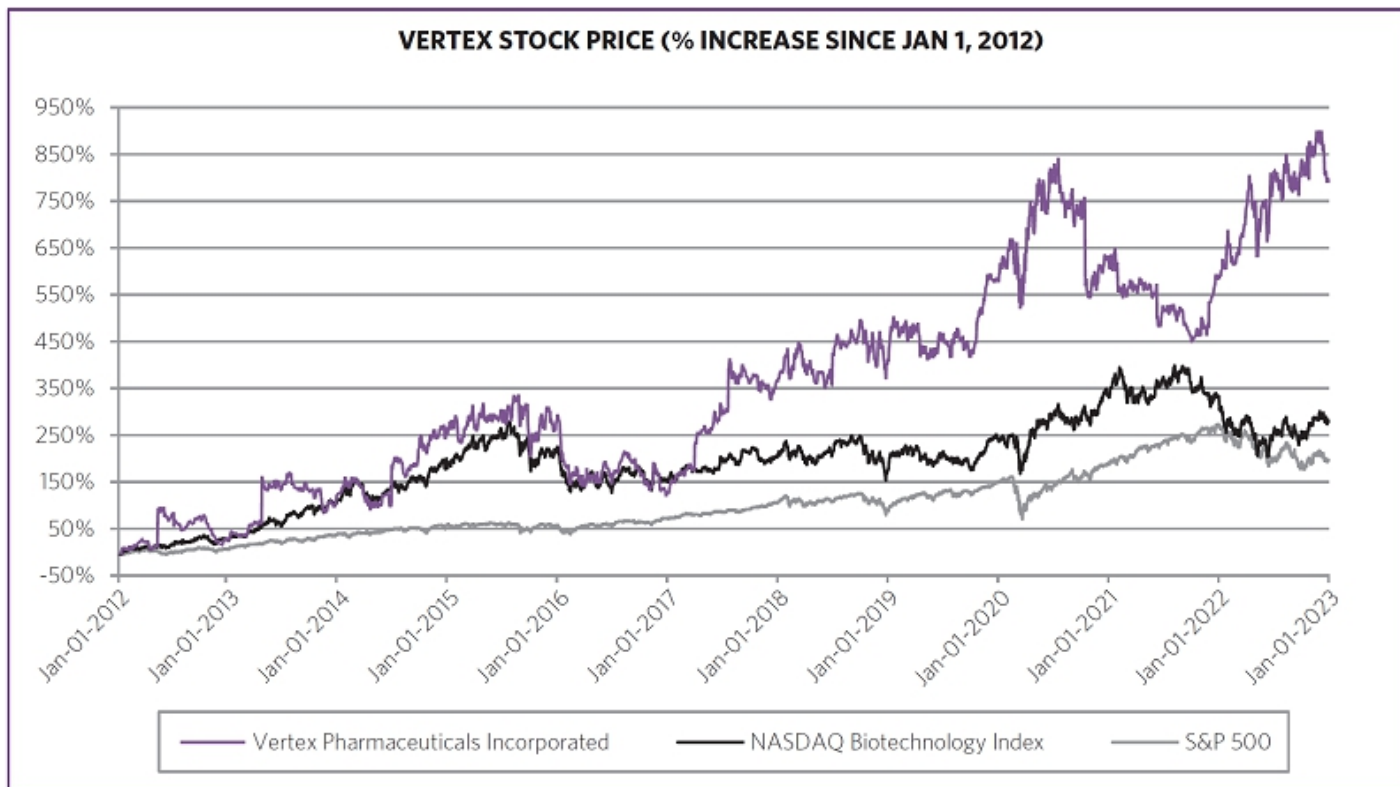
The following chart represents our clinical stage pipeline and all follow-on assets for those programs by disease area, stage of development, and modality; it does not include all preclinical programs.



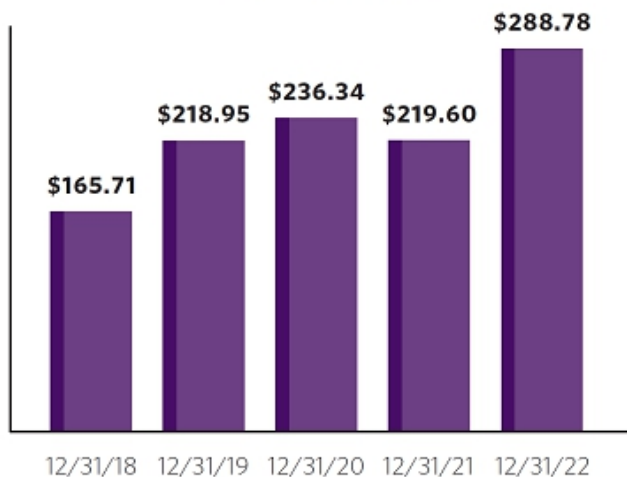
--- Cell therapy or nucleic acid therapy (mRNA, gene editing)

## Increasing Shareholder Value

Driven by our outstanding financial performance and pipeline successes, our stock price increased 31.5% from \$219.60 per share at the end of 2021 to \$288.78 per share at the end of 2022. While we are pleased with our stock performance in 2022, we believe biotechnology companies are best measured over the long term, as opposed to one-year or other shorter-term increments. The following charts show our total shareholder return relative to the Nasdaq Biotechnology Index (“NBI”) and S&P 500 index since the beginning of 2012, when KALYDECO was first approved, as well as our stock price performance over multiple periods. We believe the execution of our differentiated serial innovation strategy will continue to create shareholder value over the long term.






## STOCK PRICE



## Corporate Responsibility

We are a leading global biotechnology company that serially innovates to bring transformative medicines to people with serious diseases. We remain committed to corporate responsibility through robust programs and annual disclosures. Our progress and efforts in corporate responsibility, community engagement, and workplace practices were recognized broadly in 2022. A selection of awards and recognitions include Forbes' World's Best Employers, JUST Capital's list of the top 100 Companies Supporting Healthy Families and Communities, Newsweek's America's Most Responsible Companies, PEOPLE Magazine's 100 Companies That Care, Points of Light's Civic 50, Science Magazine's Top Employers, Seramount's 100 Best Companies, and many others.

	<b>Community</b>	Vertex and the Vertex Foundation contributed nearly \$35 million in charitable giving in 2022. The Vertex Foundation, a 501(c)(3) nonprofit 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 2022, it supported nearly 2,000 nonprofit organizations through Vertex Volunteers and the Vertex Foundation Matching Gift programs. In 2022, on our 14 <sup>th</sup> annual Day of Service, 57% of employees volunteered in their local communities around the globe.
	<b>Workplace</b>	Our commitment to inclusion, diversity, and equity on our board of directors and in our workforce is long-standing and deeply ingrained in our culture. Three of our nine director nominees, including our chief executive officer ("CEO"), are women, and four of our nine director nominees are from underrepresented ethnic and racial groups. As of December 31, 2022, women represented 54% of our global workforce and 39% of our global leadership (vice president and above). In the U.S., as of December 31, 2022, employees from underrepresented ethnic and racial groups represented approximately 40% of our workforce and 51% of new hires. We are pleased to have been recognized by numerous best workplace lists, including Seramount's 100 Best Companies & 100 Best Companies for Dads.
	<b>Environment</b>	We are committed to limiting our environmental impact and to operating our business in a sustainable manner. In 2022, our Scope 1 and Scope 2 absolute greenhouse gas ("GHG") emissions were 21.4% below our 2018 baseline. This exceeds our goal to reduce GHG emissions by 20% by the end of 2023. We performed well on the CDP Climate Change survey, obtaining a score of B, which demonstrates that we have addressed the environmental impacts of our business and have ensured good environmental management, and which was higher than the global average score of C. We continue to source 100% renewable electricity for our U.K. facilities. 83% of the square footage of our buildings globally are, or are expected to be, green certified by the end of 2023. We also have ongoing efforts 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 nine 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
<b>Jeffrey Leiden</b> Executive Chairman, Vertex Former CEO and President, Vertex	67	2009	No				
<b>Reshma Kewalramani</b> CEO and President, Vertex	50	2020	No				
<b>Sangeeta Bhatia</b> John J. and Dorothy Wilson Professor of Health Sciences & Technology/Electrical Engineering & Computer Science, MIT	54	2015	Yes			✓	Ⓜ
<b>Lloyd Carney</b> Former CEO, Brocade Communications	61	2019	Yes	✓	✓		
<b>Alan Garber</b> Provost, Harvard University	67	2017	Yes	✓			✓
<b>Terrence Kearney</b> Former Chief Operating Officer, Hospira	68	2011	Yes	Ⓜ	✓		
<b>Diana McKenzie</b> Former Chief Information Officer, Workday Former Chief Information Officer, Amgen	58	2020	Yes			✓	✓
<b>Bruce Sachs</b> General Partner, Charles River Ventures	63	1998	Yes		Ⓜ	✓	
<b>Suketu Upadhyay</b> Executive Vice President and Chief Financial Officer, Zimmer Biomet	54	2022	Yes	✓			

\* Margaret McGlynn currently serves as the Chair of the Corporate Governance and Nominating Committee ("CGNC"). Ms. McGlynn is not standing for re-election at the annual meeting. Following the annual meeting, Lloyd Carney is expected to become the Chair of our CGNC and we expect to make additional changes to the composition of our committees.

Ⓜ = Chair

## 2022 Compensation Decisions and Pay-for Performance

In 2022, our executive compensation program received substantial support, with approval by approximately 93% 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. Our management development and compensation committee ("MDCC") and our board of directors reviewed our compensation programs and made the following key decisions with respect to 2022 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, and maintained her target cash bonus as a percentage of base salary.
- We increased compensation for select named executive officers ("NEOs"), including Dr. David Altshuler and Mr. Charles Wagner, based on a comparative analysis of companies in our peer group.
- We extended Dr. Jeffrey Leiden's employment agreement by one year, until 2025. Under his amended employment agreement, Dr. Leiden continues to receive no 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 fourth and fifth years of service as Executive Chairman.
- Our outstanding performance in 2022 resulted in the board determining that we had achieved a leading rating for 2022 (145 out of a potential 150), with the payment of annual cash bonuses commensurate with this high level of performance.
- The MDCC approved special, one-time equity award grants for Mr. Stuart Arbuckle, our Chief Operating Officer ("COO"). These performance-based and time-based grants are intended to incentivize and retain Mr. Arbuckle, who is in a key commercialization role, during a critical period where we expect to launch multiple transformational therapies in disease areas outside of CF.
- We maintained the mix of equity granted to our NEOs with 50% consisting of performance stock units ("PSUs") that vest upon achievement of specific performance goals and 50% consisting of time-vesting restricted stock units ("RSUs"). This mix rewards stock price appreciation and incentivizes long-term tenure.

## Shareholder Engagement

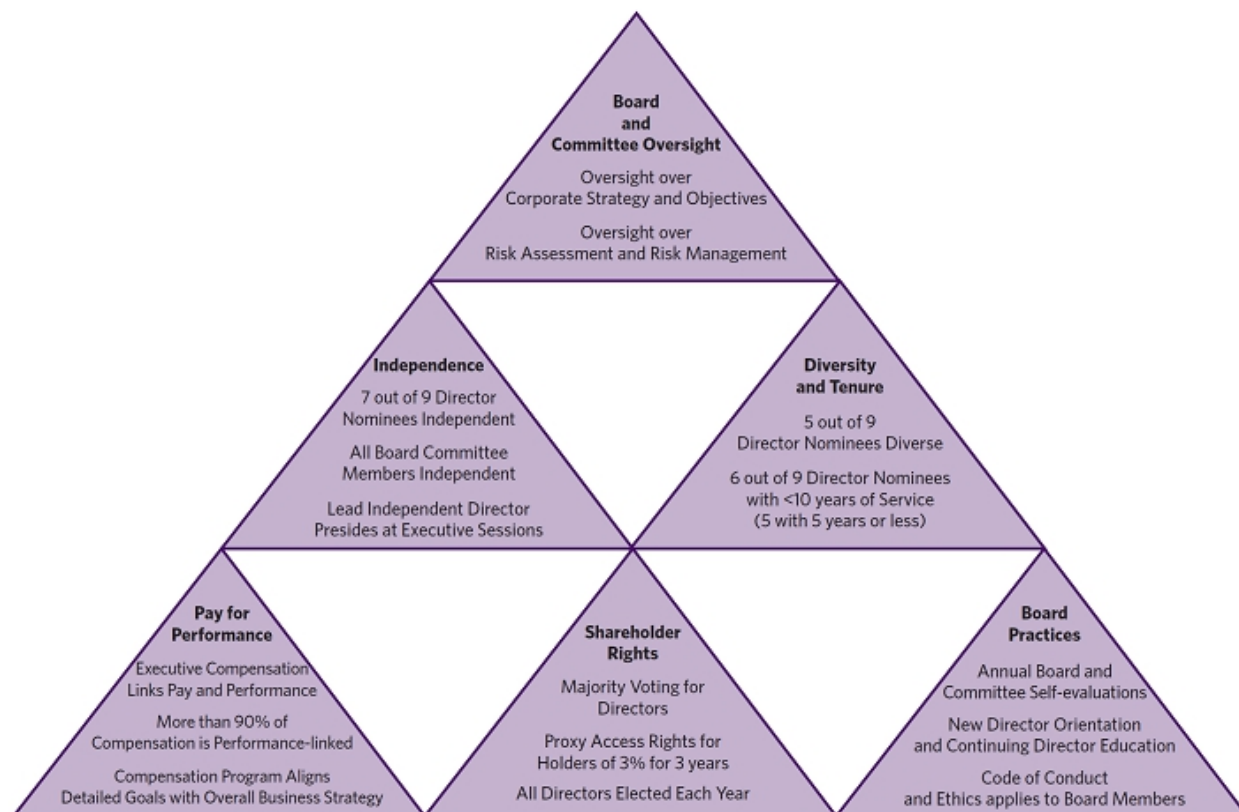
We believe that a robust shareholder outreach program is an important component of maintaining our strong corporate governance practices. We strive for a collaborative approach with shareholders to solicit and understand a variety of perspectives and interests, and our practice has been to engage with our shareholders regularly over the course of the year.

During 2022, we solicited feedback regarding our corporate governance practices from our top 40 shareholders representing approximately 65% 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, R&D approach, diversity initiatives and metrics, employee engagement and development, political and lobbying disclosures, executive compensation, and sustainability and climate change matters.



## 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

<b>Item 1:</b> Elect Each of the Director Nominees for One Year Term Expiring in 2024	<b>FOR</b> all Nominees
<b>Item 2:</b> Ratify Selection of Independent Auditor for 2023	<b>FOR</b>
<b>Item 3:</b> Approve, on an Advisory Basis, Our Named Executive Officer Compensation	<b>FOR</b>
<b>Item 4:</b> Approve, on an Advisory Basis, the Frequency of Future Advisory Votes on our Executive Compensation	<b>1 YEAR</b>

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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 2023 annual meeting of shareholders and at any postponement or adjournment thereof. The annual meeting will be held on Wednesday, May 17, 2023, at 9:00 a.m. (Eastern Time) as a virtual meeting conducted exclusively via live webcast at <https://meetnow.global/MS225F>. 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 has nominated the following current directors - Sangeeta Bhatia, Lloyd Carney, Alan Garber, Terrence Kearney, Reshma Kewalramani, Jeffrey Leiden, Diana McKenzie, Bruce Sachs, and Suketu Upadhyay for election at our 2023 annual meeting of shareholders to hold office until our 2024 annual meeting of shareholders. Yuchun Lee and Margaret McGlynn, both current directors, are not standing for re-election at 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 eleven members on our board and expect to have nine members of our board immediately following the 2023 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 such criteria.

## Director Criteria, Qualifications and Experience; Diversity

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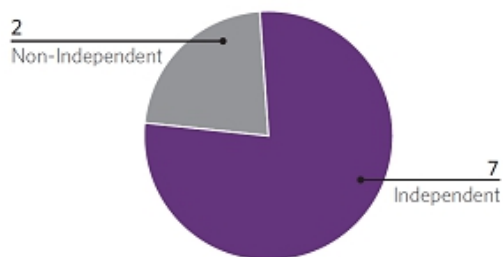
The CGNC seeks to recommend for nomination experienced directors who have substantive knowledge of our business and industry or who can bring to the board specific and valuable strategic or management capabilities acquired in other industries. The committee expects each of our directors to have proven leadership, sound judgment, the highest ethics and integrity, and a commitment to our success. It also seeks personal qualities that foster a respectful environment in which our directors listen to one another and engage in robust and constructive discussions. These goals for our board composition presuppose a diverse range of viewpoints, experiences, and specific expertise. The CGNC considers a nominee's personal characteristics and business experience relative to those of our existing board members, including the type of prior management experience, levels of expertise relevant to our business, prior board service, reputation in the business community, personal characteristics such as gender and race, and other factors that the committee believes to be important. When considering whether or not to re-nominate a director for board service, the CGNC also considers whether the director has served as a member of our board for more than 20 years and whether the director is over 72 years of age.

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

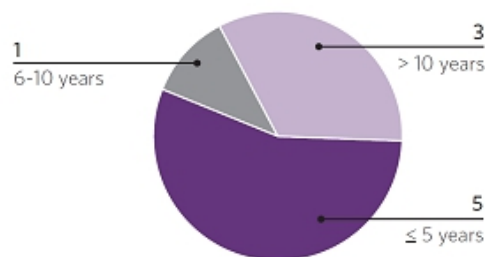
The following table and charts provide information regarding our director nominees:

	Bhatia	Carney	Garber	Kearney	Kewalramani	Leiden	McKenzie	Sachs	Upadhyay
<b>Leadership Experience.</b> We believe that directors who have held significant leadership positions over extended periods of time provide our company with special insights.	✓	✓	✓	✓	✓	✓	✓	✓	✓
<b>Industry Knowledge.</b> 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.	✓		✓	✓	✓	✓	✓		✓
<b>Financial Expertise.</b> 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.		✓	✓	✓	✓	✓	✓	✓	✓
<b>International Perspective.</b> We have significant operations outside the United States and value directors with experience in the operation of complex multinational organizations.		✓	✓	✓	✓	✓	✓	✓	✓
<b>Public Policy and Regulation.</b> We operate in a highly-regulated industry and seek directors who have experience in public policy and the regulation of medicines.			✓		✓	✓			
<b>Academic Experience or Technological Background.</b> 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.	✓	✓	✓		✓	✓	✓	✓	
<b>Commitment to Company Values and Goals.</b> 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.	✓	✓	✓	✓	✓	✓	✓	✓	✓
<b>Independence</b>	Y	Y	Y	Y	N	N	Y	Y	Y
<b>Age</b>	54	61	67	68	50	67	58	63	54
<b>Tenure on Board</b>	7	4	5	11	3	13	3	24	1
<b>Gender</b>	F	M	M	M	F	M	F	M	M
<b>Underrepresented Ethnic and Racial Groups</b>	✓	✓			✓				✓

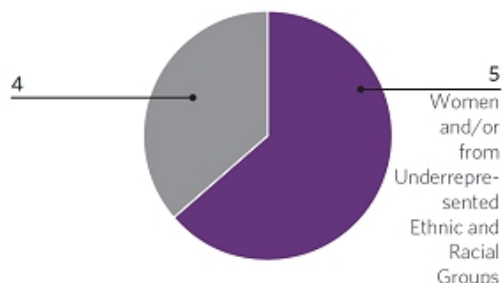
**NOMINEE INDEPENDENCE**



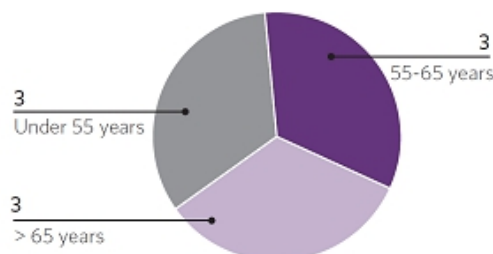
**NOMINEE TENURE**



**NOMINEE DIVERSITY**



**NOMINEE AGE**



## Board Diversity Matrix

Our commitment to diversity and inclusion is also demonstrated by the current composition of our board, which includes four women and five members from underrepresented ethnic and racial groups. 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 6, 2023**

Total Number of Directors	11			
	Female	Male	Non-Binary	Did Not Disclose Gender
<b>Part I: Gender Identity</b>				
Directors	4	7	0	0
<b>Part II: Demographic Background</b>				
African American or Black	0	1	0	0
Alaskan Native or Native American	0	0	0	0
Asian	2	2	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 the candidate 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 2024 annual meeting of shareholders using the procedures set forth in our by-laws, the shareholder must follow the procedures described in our by-laws and summarized in the section titled *Other Information—Shareholder Proposals and Nominations for Director for the 2024 Annual Meeting* on page 84 of this proxy statement. If a shareholder wishes to solicit proxies for a shareholder nominee for election to our board at the 2024 annual meeting of shareholders pursuant to Rule 14a-19 of the Securities Exchange Act of 1934, as amended (the “Exchange Act”), the shareholder must follow the procedures set forth in Rule 14a-19 of the Exchange Act and our by-laws.

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 voting shares continuously for at least 3 years.
Number of Board Nominees	Total number of proxy access nominees is capped at the greater of 20% of the existing number of board seats (or the closest whole number below 20%) and 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 2024 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 2024 Annual Meeting* on page 84 of this proxy statement.



## Majority Votes Cast Standard

Our by-laws provide for a majority votes cast 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 their 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:** 54

**Director Since:** 2015

#### **Board Committees:**

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

#### **Experience:**

- Professor at the Massachusetts Institute of Technology (“MIT”); John J. and Dorothy Wilson Professor of Health Sciences & Technology/Electrical Engineering & Computer Science, since 2005
- Co-founder of Port Therapeutics, a private company focused on thermal bioswitches in oncology, since 2022
- 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 provide 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:** 61

**Director Since:** 2019

### Board Committees:

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

### Other Public Company Boards:

- Visa Inc.
- Grid Dynamics Holdings Inc.

### Experience:

- Chief Acquisition Officer of Carney Technology Acquisition Corp. II, a special purpose acquisition corporation, from October 2020 until February 2023
- 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 2013 until it was acquired by Broadcom in 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, from 2003 until it was acquired by IBM in 2006
- 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.



## Alan Garber

**Age:** 67

**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 of 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. His expertise in health care policy and as an advisor to government agencies provides our board important insights and perspectives on the issues facing our company.



## Terrence Kearney

**Age:** 68

**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 2006 until 2011
- Senior Vice President, Finance, and Chief Financial Officer of Hospira from 2004 to 2006
- Vice President and Treasurer of Abbott Laboratories, from 2001 to 2004
- Divisional Vice President and Controller for Abbott's International Division, from 1996 until 2001
- Member of the following Boards of Directors of Levo Therapeutics, Inc., a biotechnology company focused on developing treatments for Prader-Willi Syndrome, from 2018 to June 2022; Acceleron Pharma Inc., a publicly traded biopharmaceutical company, from 2014 until it was acquired by Merck in November 2021; Innoviva (formerly known as Theravance, Inc.), a publicly traded royalty management company, from 2014 through 2016; and AveXis, Inc., a publicly traded gene therapy company, from 2016 until it was acquired by Novartis in 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," as defined by the Securities and Exchange Commission ("SEC"), with particular experience in pharmaceuticals.



## Reshma Kewalramani

**Age:** 50

**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 2018 through March 2020
- Senior Vice President, Late Development of Vertex from 2017 until 2018
- Served in roles of increasing responsibility at Amgen Inc. from 2004 to 2017, most recently as Vice President and Head of 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 possesses strong leadership qualities, industry experience, and research, development and commercialization expertise in drug development, demonstrated through her services as a senior executive in the biotechnology sector. She is a physician-executive with extensive industry knowledge garnered through her scientific and medical roles and experience 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:**

- None

### **Other Public Company Boards:**

- Ginkgo Bioworks Holdings, Inc.

**Jeffrey Leiden****Age:** 67**Position:****Director Since:** 2009

- 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 2012; previously served as lead independent director from 2010 through 2011
- Managing Director at Clarus Ventures, a life sciences venture capital firm, from 2006 to 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 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 2012; Chairman of Revolution Healthcare Acquisition Corp., a special purpose acquisition corporation, from April 2021 to December 2022

**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 our corporate strategy.

**Diana McKenzie****Age:** 58**Board Committees:****Director Since:** 2020

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

**Experience:**

- Chief Information Officer of Workday, Inc., a cloud-based financial and human capital management software company, from 2016 until April 2019
- Held roles of increasing responsibility at Amgen Inc., a biotechnology company, for 12 years, 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; Special Advisor to Brighton Park Capital
- Member of the Board of Directors of Change Healthcare, Inc., a publicly traded healthcare technology company, from August 2019 until it was acquired by United Health Group in October 2022
- 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 brings extensive experience growing, scaling, and transforming global businesses in the healthcare and software industries.

**Other Public Company Boards:**

- None

**Other Public Company Boards:**

- MetLife Inc.
- agilon health, inc.



## Bruce Sachs

**Age:** 63

**Director Since:** 1998

**Board Committees:**

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

**Other Public Company Boards:**

- None

**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.



## Suketu "Suky" Upadhyay

**Age:** 54

**Director Since:** 2022

**Board Committees:**

- Member – Audit and Finance Committee

**Other Public Company Boards:**

- None

**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 2016 to June 2019
- Executive Vice President and Chief Financial Officer of Endo International from 2013 to 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, hospital supply, and medical device industries provide him with multiple perspectives on our industry. His knowledge and expertise make him a valuable contributor to our board of directors and management.

## 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](http://www.vrtx.com) under “Investors—Corporate Governance—Governance Documents.”

## Director Independence

Our board of directors has determined that nine of our eleven current directors and seven of our nine director nominees qualify as “independent” under the definition of that term adopted by The Nasdaq Stock Market LLC (“Nasdaq”). Our independent director nominees are Dr. Bhatia, Mr. Carney, Dr. Garber, Mr. Kearney, Ms. McKenzie, Mr. Sachs, and Mr. Upadhyay. 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.

## Board Leadership Structure

Our board recognizes that one of its key responsibilities is to periodically evaluate the optimal leadership structure to ensure robust independent oversight of management and an engaged and effective board with complementary qualities, perspectives, and experiences. Given the dynamic and competitive environment in which we operate, the board believes that its optimal leadership structure may vary as circumstances warrant. The board values the flexibility to determine its optimal model for board leadership at any given time. As such, the board annually reviews its leadership structure and may choose a different leadership structure if circumstances should arise that lead it to believe that such structure would promote the long-term interests of our shareholders.

Our governing documents permit the roles of Chair of the board and CEO to be filled by the same or different individuals. To ensure robust independent leadership on the board, our corporate governance guidelines also require our independent directors to elect a Lead Independent Director if the Chair of the board is a member of management or does not otherwise qualify as independent under the company’s director independence standards.

Currently, the board believes it is in the best interests of the company and our shareholders for the roles of Chair of the board and CEO to be separated, supported by a Lead Independent Director who has oversight responsibilities. Separating these positions at this time allows our CEO to focus on strategic decisions and our day-to-day business operations and performance, allows the Chair, our former CEO, to drive organization and effectiveness of the board in addition to his specifically delineated executive responsibilities, and allows our Lead Independent Director to lead the board in its fundamental role of providing advice to and independent oversight of management, including promoting communication between management and our board and supporting our board’s oversight of risk and other key governance matters. The board believes that this structure provides our board with 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.

The board annually evaluates whether combining or separating the roles of Chair of the board and CEO is in the best interests of the company and our shareholders. In its evaluation, the board considers a number of factors, including: (1) the individuals currently in the roles of CEO, Chair and Lead Independent Director and their record of leadership and performance in their roles; (2) current composition of the board; (3) the effectiveness of the policies, practices, and people in place to help ensure strong, independent board oversight; (4) the company’s performance and the effect the leadership structure could have on its performance; (5) the board’s performance and the effect the leadership structure could have on the board’s performance; (6) the Chair and Lead Independent Director’s performance in their respective roles; and (7) the views of our shareholders. A change in any of these factors could lead the board to determine in the future that it is more appropriate to have a different board leadership structure. Any such changes to our board leadership structure would be communicated to our shareholders through our annual proxy statement and as otherwise required by law.

## Executive Chair of the Board

Since 2020, Dr. Leiden has served as our Executive Chairman. In this role, Dr. Leiden not only serves as the Chair of our board, but also continues to have executive responsibilities, as described below, with our corporate business development function, our cell and genetic therapy programs, and our external communications and government affairs activities. The board believes this leadership structure is currently in the best interest of shareholders because Dr. Leiden, as a long-time executive of the company, has a vast knowledge and deep understanding of the company and its strategic plans, people, and operations. This company-specific experience, along with Dr. Leiden’s extensive knowledge



of the industry and comparable organizations and broad involvement in drug discovery and development, as well as his distinguished tenure as Chair of the board since 2012 and wide-ranging experience in corporate governance and leadership, provide him with outstanding advising and oversight capabilities as Chair of the board. Dr. Leiden's specific responsibilities include:

- overseeing the corporate business development function;
- providing guidance on our cell and genetic therapy programs;
- supporting external communications, including with our shareholders;
- assisting the CEO with specific government affairs activities;
- collaborating with CGNC, the Lead Independent Director, and the CEO on the identification, evaluation, and recruitment of potential candidates for board membership and consideration of overall board composition;
- collaborating with CGNC and the Lead Independent Director on the recommendation to the board of individual directors to serve as members and chairs of each board committee;
- collaborating with CGNC and the Lead Independent Director on development and recommendation to the board of the annual self-evaluation process for the board and its committees; and
- collaborating with CGNC and the lead independent director on the oversight of the CEO succession planning process, including assistance in recruiting and identifying potential candidates for the CEO position.

## Lead Independent Director

Our board believes that strong, independent board leadership is a critical aspect of effective corporate governance. Our corporate governance guidelines require that if the Chair is not an independent director, the independent directors shall elect a Lead Independent Director. Since December 2011, Mr. Sachs has served as our Lead Independent Director or Co-Lead Independent Director. Mr. Sachs' extensive business leadership experience as a CEO, a venture capitalist, and a director of the company, combined with his financial expertise, strongly positions him to provide independent leadership of the board and its responsibility for identifying and assessing company risks and providing guidance on risk mitigation strategies.

The board recognizes the importance of appointing a strong Lead Independent Director to maintain a counterbalancing structure to ensure that the board functions in an appropriately independent manner and to hold management accountable for our continued success. As such, the responsibilities of the Lead Independent Director are designed to ensure that our independent directors are empowered to provide robust guidance to, and 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;
- facilitating discussion and open dialogue among the independent directors, including with respect to the consideration of company risks and risk mitigation strategies;
- presiding at executive sessions of the independent directors;
- reviewing the planned dates for regularly scheduled board meetings and the primary agenda items for each meeting, which allows the Lead Independent Director to provide input and direction with respect to the matters that come before the board, including risk matters;
- providing board leadership if the Chair of the board or CEO may be (or may be perceived to be) in conflict with the best interests of the company and its shareholders;
- representing the board in certain communications with shareholders when requested and as appropriate;
- collaborating with CGNC, the Chair of the board, and the CEO on the identification, evaluation, and recruitment of potential candidates for board membership and consideration of overall board composition;
- collaborating with CGNC and the Chair of the board on the recommendation to the board of individual directors to serve as members and chairs of each board committee;
- collaborating with CGNC and the Chair of the board on development and recommendation to the board of an annual self-evaluation process for the board and its committees; and
- collaborating with CGNC and the Chair of the board on the oversight of the CEO succession planning process, including assistance in recruiting and identifying potential candidates for the CEO position.

We believe our board structure provides consistent and strong independent oversight of management, while also facilitating a collaborative and collegial environment for board deliberations and decision-making.

## 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 30 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. 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.

### Audit and Finance Committee

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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, and review material tax matters, including tax structure and strategies;
- 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 39 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 board 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 2022, 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

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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

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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 66 of this proxy statement.

## Science and Technology Committee

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Our S&T committee assists our board of directors in its responsibilities relating to the oversight of our investment in pharmaceutical R&D. In furtherance of that oversight function, the S&T committee:

- reviews and assesses our current and planned R&D programs and technology initiatives from a scientific perspective;
- oversees risks related to our R&D 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.

## Compensation Committee Interlocks and Insider Participation

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Messrs. Carney, Kearney, Lee, and Sachs served on the MDCC during 2022. 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 2022 that would be required to be disclosed pursuant to Item 404(a) of Regulation S-K. During 2022, 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.

## Board Attendance, Committee Meetings, and Committee Membership

During 2022, our board of directors met seven times. Each of our incumbent directors attended 100% of the total meetings of the board and the board committees on which the director served that were held during the time that person was a director in 2022. All of our current directors attended our 2022 Annual Meeting of Shareholders.

The following table provides information regarding our current board of directors. We expect that in May 2023, (i) Mr. Carney will join the Corporate Governance and Nominating Committee as Chair, and (ii) we will make additional changes to our committee memberships resulting from the departures of Mr. Lee and Ms. McGlynn following the 2023 Annual Meeting of Shareholders.

Director	Independence	Board	Audit Committee	CGNC	MDCC	S&T Committee
Sangeeta N. Bhatia	✓	●●	●●	●●		●●
Lloyd Carney	✓	●●	●●		●●	
Alan Garber	✓	●●	●●			●●
Terrence C. Kearney	✓	●●	●●		●●	
Reshma Kewalramani		●●				
Yuchun Lee	✓	●●	●●		●●	
Jeffrey M. Leiden		●●				
Margaret G. McGlynn	✓	●●		●●		●●
Diana McKenzie	✓	●●		●●		●●
Bruce I. Sachs	✓	★		●●	●●	
Suketu Upadhyay	✓	●●	●●			
<b>2022 Meetings</b>		<b>7</b>	<b>8</b>	<b>5</b>	<b>6</b>	<b>5</b>

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

## Risk Management

Our board oversees an enterprise-wide approach to risk management, which is designed to support execution of our strategy and achievement of our goals to improve long-term operational and financial performance and generate long-term value for our shareholders. Our board believes that a fundamental part of risk management is understanding the risks that we face, adopting appropriate controls and mitigation activities for such risks, monitoring these risks, and responding to emerging developments with respect to such risks.

In performing its risk oversight responsibilities, the board relies, in part, upon the results and information gained through our annual Enterprise Risk Management (“ERM”) Program. The ERM Program is overseen by our Chief Risk & Compliance Officer, who reports to our Chief Legal Officer, and is designed to identify key enterprise risks and ensure appropriate monitoring of, and controls over, those risks. As part of our ERM Program, we obtain input from our senior management and relevant subject-matter experts, evaluate industry trends and benchmarks, and consult external advisors as appropriate to identify the risks associated with our business based on likelihood of occurrence and potential impact to the business, as well as root causes of those risks. The ERM Program also assigns members of management responsibility 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 by the board and regularly reviewed with senior management.

The board's role in our risk management process also includes reviewing regular reports and updates from senior management on both near-term, medium-term and long-term risks to the company. The board reviews and discusses strategic, operational, financial, compliance, legal, social (e.g., human capital management), environmental, governance, cybersecurity, and other risks. The board also receives updates from management regarding various enterprise risks related to our research, development, and commercialization plans, such as the competitive environment, manufacturing capabilities, and drug pricing and reimbursement. These activities enable the board to understand and assess our risk environment, risk management, and risk mitigation strategies.

Near- and medium-term enterprise risks are afforded significant attention by the board. The board and its committees have the opportunity to provide input and direction as to the management of those risks in a variety of manners, including through the ERM Program review, regular operational and financial updates and review of development programs, regular updates from our Chief Legal Officer, internal audit updates, talent reviews and succession planning, updates on cyber-security, healthcare compliance updates, reviews of executive compensation, budget

reviews, and reviews of significant transactions. Longer term risks are addressed by the board through the annual strategic planning process, during which the board discusses and reviews our long-term operating plans and overall corporate strategy. Other risks that do not rise to the level of enterprise risks also are regularly assessed, discussed, managed, and monitored, including discussion with the board, as appropriate.

Cross-functional members of management, including from our finance, accounting, investor relations, legal, compliance, information security, facilities, corporate communications, manufacturing, and disease strategy teams, work to ensure that material incidents and risks, including matters relating to significant actual or threatened litigation, significant regulatory matters and other matters that may have material financial, legal or reputational impacts on the Company are timely reported to the Board and senior management and disclosed to our shareholders, as appropriate. In addition, we disclose our significant environmental, social and governance progress, strategies, and commitments in our annual Corporate Responsibility Report.

While the board has the ultimate oversight responsibility for risk management, the board also manages risk through the division of responsibility within its committee structure, with each board committee being responsible for overseeing risk within its area of focus.

Board Committee	Area of Risk Oversight
Audit and Finance Committee	<ul style="list-style-type: none"> <li>■ Financial, accounting, disclosure, insurance, tax, investment, credit, disclosure controls and procedures, and other risks reviewed in its oversight of the internal audit function</li> <li>■ Cybersecurity</li> <li>■ Internal audit</li> <li>■ Compliance program</li> <li>■ Periodic reviews of relevant developments in disclosure requirements</li> </ul>
Management Development and Compensation Committee	<ul style="list-style-type: none"> <li>■ Executive compensation policies, practices, and goal setting, including whether such policies, practices, and goal setting balance risk-taking and rewards in an appropriate manner, align with shareholder interests, and are consistent with best practices</li> <li>■ Company incentive compensation plans and equity-based plans</li> <li>■ Stock ownership guidelines for executive officers and officers</li> </ul>
Corporate Governance and Nominating Committee	<ul style="list-style-type: none"> <li>■ Corporate governance</li> <li>■ Board organization, membership, and structure</li> <li>■ Board and CEO succession planning</li> <li>■ Director independence</li> </ul>
Science and Technology Committee	<ul style="list-style-type: none"> <li>■ Assessments of planned R&amp;D programs and technology initiatives</li> <li>■ Emerging science and technology issues and trends</li> </ul>

At each regular meeting, or more frequently as needed, the board receives and considers committee reports, and such reports may provide additional detail on risk management issues and management's response. The board and each committee also have the authority, in their sole discretion, to consult with and retain outside advisors and experts in connection with performance of its duties and responsibilities. Such outside advisors and experts are retained on a regular basis to assist the board and its committees in evaluating, managing, and anticipating risks, and include external auditors, legal counsel, compensation consultants, and business consultants, as appropriate. We have also established robust standards of business conduct that apply to all employees globally and provides numerous methods for employees to elevate risk concerns directly to management or through anonymous channels.

## 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](http://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.

## 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 update 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:	
	■	options that are fully-vested upon grant;
	■	restricted stock units that vest on the first anniversary of the date of grant; or
	■	a 50/50 mix of options and restricted stock units

Each of our non-employee directors is eligible to defer 50% or 100% of the cash and restricted stock unit portion of their 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 2022.



## 2022 Summary Compensation

Director	Fees Earned or Paid in Cash	Stock Awards <sup>(1)</sup>	Option Awards <sup>(1)</sup>	All Other Compensation <sup>(3)</sup>	Total
Sangeeta N. Bhatia	\$135,000	\$ 400,170	\$ —	\$ 15,000	\$ 550,170
Lloyd Carney	\$127,500	\$ 400,170	\$ —	\$ 25,000	\$ 552,670
Alan Garber	\$125,000	\$ —	\$ 400,018	\$ —	\$ 525,018
Terrence C. Kearney	\$142,500	\$ 200,223	\$ 200,009	\$ —	\$ 542,732
Yuchun Lee	\$127,500	\$ —	\$ 400,018	\$ 5,000	\$ 532,518
Margaret G. McGlynn	\$135,000	\$ —	\$ 400,018	\$ 25,000	\$ 560,018
Diana McKenzie <sup>(2)</sup>	\$115,001	\$ 400,170	\$ —	\$ 23,000	\$ 538,171
Bruce I. Sachs <sup>(2)</sup>	\$175,000	\$ —	\$ 400,018	\$ 25,000	\$ 600,018
Suketu Upadhyay <sup>(2)</sup>	\$ 69,588	\$ 400,001	\$ —	\$ —	\$ 469,589

(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 2022. Our methodology, including underlying estimates and assumptions, for calculating these values is set forth in Note O to our consolidated financial statements included in our 2022 Annual Report on Form 10-K, filed with the SEC on February 10, 2023.

(2) Ms. McKenzie, Mr. Sachs and Mr. Upadhyay 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 \$289.41, \$289.23, \$296.82 and \$298.42.

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

## 2022 Equity Grants

Grant	Date	Shares	Exercise Price	Grant-Date Fair Value
Annual Non-Employee Director - 100% Option Grants	May 1, 2022	4,462	\$ 276.17	\$ 400,018
Annual Non-Employee Director - 50% Option Grants	May 1, 2022	2,231	\$ 276.17	\$ 200,009
Annual Non-Employee Director - 100% Restricted Stock Unit Grants	May 1, 2022	1,449	—	\$ 400,170
Annual Non-Employee Director - 50% Restricted Stock Unit Grants	May 1, 2022	725	—	\$ 200,223
Initial Restricted Stock Unit Grant to Suketu Upadhyay	May 18, 2022	1,558	—	\$ 400,001

## Outstanding Equity

As of December 31, 2022, 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	1,449	—	1,938	1,938
Lloyd Carney	1,449	—	—	—
Alan Garber	—	—	24,672	24,672
Terrence C. Kearney	725	—	41,349	41,349
Yuchun Lee	—	1,801	77,312	77,312
Margaret G. McGlynn	—	5,609	37,016	37,016
Diana McKenzie	1,449	2,927	—	—
Bruce I. Sachs	—	14,122	82,312	82,312
Suketu Upadhyay	1,558	139	—	—

## 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. Our stock ownership guidelines exclude unexercised stock options. As of March 31, 2023, 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. Mr. Upadhyay joined our board of directors in May 2022 and has five years to satisfy the individual holding requirements.

# CORPORATE RESPONSIBILITY



## Community

We are a leading global biotechnology company that serially innovates to bring transformative medicines to people with serious diseases. We are committed to making a positive difference in the communities where we are located, including through a ten-year \$500 million corporate giving commitment previously announced by the company. Our progress and efforts in corporate responsibility, community engagement, and workplace practices were recognized broadly in 2022. A selection of awards and recognitions include JUST Capital's list of the top 100 Companies Supporting Healthy Families and Communities, Newsweek's America's Most Responsible Companies, PEOPLE Magazine's 100 Companies That Care, Points of Light's Civic 50, and many others.

Volunteering and giving back are core to our culture. In 2022, we supported nearly 2,000 nonprofit organizations in more than 25 countries through Vertex Volunteers and the Vertex Foundation Matching Gift Program.

The Vertex Foundation, a 501(c)(3) nonprofit 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 2022, the Vertex Foundation awarded \$8.4 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.

Throughout the year, we encourage our employees to participate in community service through the Vertex Volunteers program, including activities such as pro bono service conducted by members of our legal and compliance group and our 14<sup>th</sup> annual Day of Service. Last year, 57% of Vertex employees around the globe volunteered during Day of Service, contributing more than 6,300 volunteer hours to their local communities.

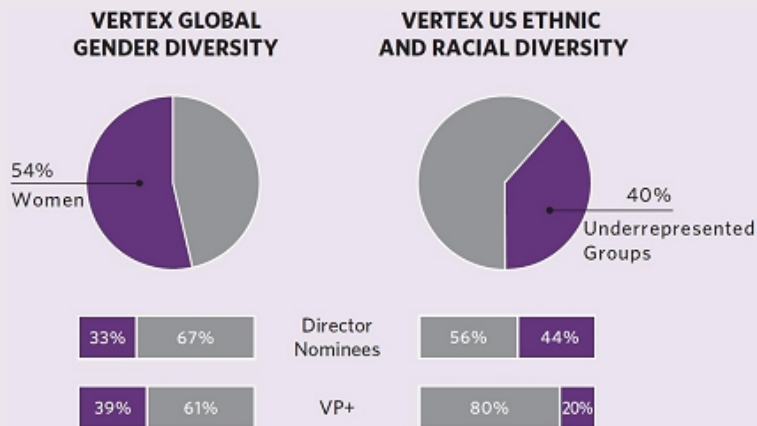
Our corporate giving extends and expands our long-term commitment to patients with serious diseases and our communities, with an on-going focus on STEAM education. In 2022, we continued to offer opportunities to scores of teachers and hundreds of students through our Learning Lab programs in Boston, San Diego, and Oxford, U.K., and the Vertex Foundation provided dozens of scholarships to people with CF and their family members who are pursuing higher education. The Vertex Foundation is also committed to supporting programs and initiatives in the countries in which we operate to nurture the next generation of innovators, enable innovative solutions to community challenges, and support the quality of life of families with members living with serious diseases.



## Workplace

We are committed to building an outstanding, dedicated, and passionate team at Vertex. Our ability to create transformative medicines for people with serious diseases relies on both the diversity of our people and an inclusive and equitable culture where all points of view are respected and heard. We are pleased to have been awarded listings on Seramount's 100 Best Companies & 100 Best Companies for Dads, Boston Globe's Top Places to Work, Forbes' World's Best Employers, Science Magazine's Top Employers, and San Diego Business Journal's Best Places to Work.

Five of our nine director nominees are women and/or from underrepresented ethnic and racial groups. As of December 31, 2022, women represented 54% of our global workforce. In the U.S., as of December 31, 2022, approximately 40% of our workforce and 51% of new hires were from underrepresented ethnic and racial groups. As of December 31, 2022, 39% of our global leadership (vice president and above) were women and 20% of U.S. leadership were from underrepresented ethnic and racial groups.



## Environment

We are committed to limiting our environmental impacts and to operating our business in a sustainable manner. We make strong local efforts to reduce our impact on the environment.

In 2022, our Scope 1 and Scope 2 absolute GHG emissions were 21.4% below our 2018 baseline. This exceeds our goal to reduce GHG emissions by 20% by the end of 2023. We performed well on the CDP Climate Change survey, obtaining a score of B, which demonstrates that we have addressed the environmental impacts of our business and have ensured good environmental management, and which was higher than the global average score of C. We continue to source 100% renewable electricity for our U.K. facilities. 83% of the square footage of our buildings globally are, or are expected to be, green certified by the end of 2023. We also have ongoing efforts to minimize waste across all of our sites through employee engagement initiatives, vendor takeback programs and improved product distribution processes.

# 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, 2023 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 2022 and 2021.

Service	2022	2021
Audit fees	\$ 4,652,200	\$ 3,989,000
Audit-related fees	—	—
Tax fees	2,936,000	4,650,000
All other fees	4,000	6,000
<b>TOTAL</b>	<b>\$ 7,592,200</b>	<b>\$ 8,645,000</b>

“**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 2022 and 2021 consisted of:

- tax compliance and preparation fees, including the preparation of original and amended tax returns and refund claims, and tax payment planning of \$1,806,000 and \$1,990,000, respectively; and
- tax advice and planning fees of \$1,130,000 and \$2,660,000, 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, 2023.

# 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 monitors 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, 2022 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, 2022 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**  
**Suketu Upadhyay**

# 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 2022, our annual advisory vote on executive compensation received support from approximately 93% 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 90% of our NEO compensation linked to performance. Our board and MDCC routinely review our compensation programs and made the following key decisions with respect to 2022 compensation:

- We increased the base salary and target equity level for Dr. Kewalramani, 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 2022.
- Based on a comparative analysis of companies in our peer group, we increased compensation for Dr. Altshuler and for Mr. Wagner.
- We extended Dr. Leiden's employment agreement by one year, until 2025. Under his amended employment agreement, Dr. Leiden continues to receive no 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 fourth and fifth years in his Executive Chairman role.
- Our outstanding performance in 2022 resulted in the board determining that we had achieved a leading rating for 2022 (145 out of a potential 150), with the payment of annual cash bonuses commensurate with this high level of performance.
- The MDCC approved special, one-time equity award grants for Mr. Arbuckle. These performance-based and time-based grants are intended to incentivize and retain Mr. Arbuckle, who is in a key commercialization role, during a critical period where we expect to launch multiple transformational therapies in disease areas outside of CF.
- We maintained the mix of equity granted to our NEOs with 50% consisting of performance stock units that vest upon achievement of specific performance goals and 50% consisting of time-vesting restricted stock units. This mix rewards stock price appreciation and incentivizes long-term tenure.

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

As required by Section 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.

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



# PROPOSAL NO. 4: ADVISORY VOTE ON THE FREQUENCY OF FUTURE ADVISORY VOTES ON EXECUTIVE COMPENSATION

In this proposal, we are asking our shareholders to vote on whether future advisory votes on executive compensation, similar to proposal 3 contained in this proxy statement, should occur every year, every two years, or every three years. While this say-on-pay frequency vote is advisory in nature and therefore will not bind us to adopt any particular frequency, our board of directors intends to consider carefully the shareholder vote resulting from this proposal in determining how frequently we will hold future “say-on-pay” votes.

Our board of directors has determined that an annual advisory vote on executive compensation will allow our shareholders to continue to provide timely, direct input on our executive compensation philosophy, policies and practices as disclosed in the proxy statement each year. In determining to recommend that shareholders vote for a frequency of once per year, our board of directors considered how an advisory vote at this frequency might over-emphasize short-term variations in compensation and business results, particularly in our industry, where a long-term focus for our executive compensation program is required because it can take 10-15 years to take a product from inception through to commercialization. On balance, however, our board of directors has determined that the advantages of receiving regular and prompt feedback from our shareholders on our executive compensation program continue to outweigh this concern at this time.

Our board of directors unanimously recommends that you vote **1 YEAR** for the proposal concerning the frequency of future advisory votes on our executive compensation program.

# 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, with a focus on specialty markets. 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 \$74 billion at the end of 2022.

We take seriously our role in the governance of compensation programs and the importance of 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 leadership, stability and operational excellence of our senior executive team.

2022 was a remarkable year for Vertex as the company continued to execute successfully on its business strategy. Vertex expanded its long-term leadership in CF in numerous ways and treated more people with CF than ever before. Vertex's medicines are collectively used by more than two-thirds of the approximately 88,000 people with CF in North America, Europe and Australia, and our medicines are now approved, broadly reimbursed and accessible in more than 40 countries outside of the U.S.

In 2022 the research and development team made significant progress in advancing multiple mid- and late-stage clinical programs, including those aimed to treat CF, sickle cell disease, beta thalassemia, acute and neuropathic pain, APOL1-mediated kidney disease, type 1 diabetes, and alpha-1 antitrypsin deficiency. With these advances, the company is positioned to sustain its leadership in CF and launch multiple new therapies in the near-term, thereby delivering increasing and meaningful value for patients and shareholders.

The company delivered outstanding financial performance in 2022, achieving CF net product revenues of \$8.93 billion, an 18% increase compared to 2021. This revenue growth drove significant growth in earnings and cash flow, and the company finished the year in a strong financial position with \$10.8 billion in cash, cash equivalents, and marketable securities. The senior management team additionally strengthened the company's organizational capabilities by recruiting and onboarding top-tier talent across the organization and filling critical hires with superior and diverse talent.

The company's successes in 2022 reflect both the company's excellent performance and the differentiated corporate strategy that its senior management team continues to champion. Consistent with these outstanding results, for 2022, 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 maintaining 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**

## Executive Summary

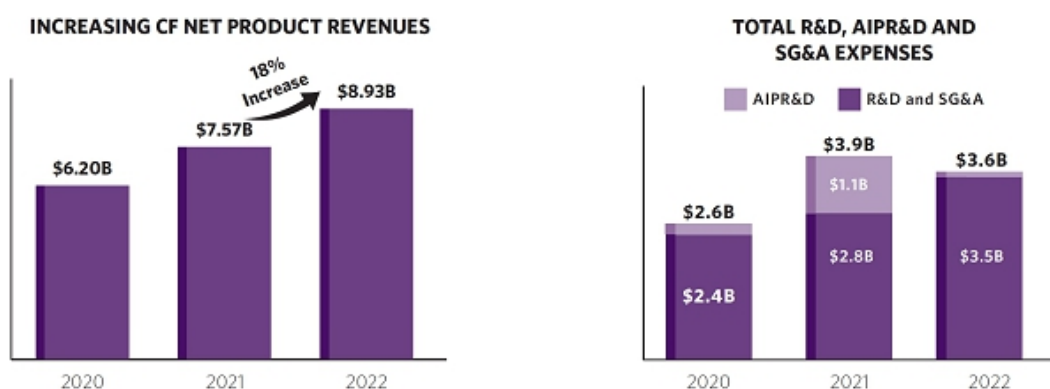
This section discusses the principles underlying our policies and decisions with respect to the compensation of our NEOs for 2022 and the factors we believe are relevant to an analysis of these policies and decisions. Our NEOs for 2022 are listed below.

Name	Position
Reshma Kewalramani	Chief Executive Officer and President
Charles F. Wagner, Jr.	Executive Vice President, Chief Financial Officer
David M. Altshuler	Executive Vice President, Global Research and Chief Scientific Officer
Stuart A. Arbuckle	Executive Vice President, Chief Operating Officer
Jeffrey M. Leiden	Executive Chairman

## 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.

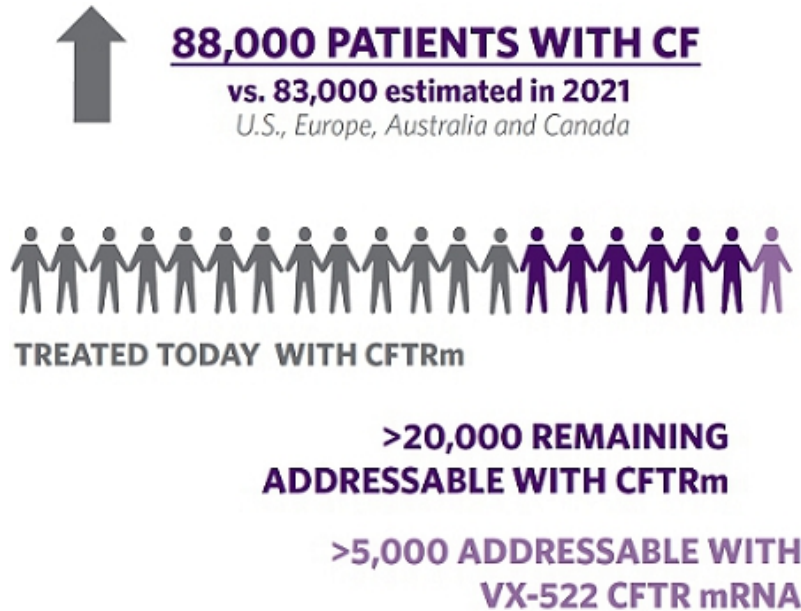
- Our CF net product revenues increased to \$8.93 billion in 2022, up 18% or approximately \$1.4 billion, from our 2021 net product revenues.
- Our total R&D, AIPR&D and SG&A expenses decreased to \$3.6 billion compared to \$3.9 billion in 2021. The decrease was primarily due to lower AIPR&D as a result of the one-time \$900 million upfront payment to CRISPR in 2021, partially offset by increased investment in support of multiple programs that have advanced to mid- and late-stage clinical development and the costs to support launches of Vertex's therapies globally.



## Marketed Products

Our successful strategy of serial innovation has sustained and expanded our leadership position in CF and continues to propel us toward 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, expanding access to our medicines in additional geographies, and seeking improved treatment options for all patients with CF.

Our four approved medicines have broad reimbursement, are accessible in more than 40 countries, and are being used to treat more than two-thirds of the approximately 88,000 people with CF in North America, Europe, and Australia. Yet, as of the beginning of the year, there were more than 25,000 untreated patients in these geographies who could benefit from our therapies. We expect to grow our CF business with (i) continued uptake by patients in countries where we are early on the launch curve, such as those with recently achieved reimbursement agreements, (ii) label expansions, including into younger patient groups, (iii) the development of mRNA therapies for people with CF who are not eligible for our approved CFTR modulators, and (iv) growth in the number of people living with CF.



Since the beginning of 2022, notable progress includes:

- The European Commission and the MHRA 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.
- Health Canada granted marketing authorization for TRIKAFTA for children with CF 6 through 11 years of age who have at least one F508del mutation.
- The FDA approved the use of ORKAMBI for children with CF 12 to less than 24 months of age who are homozygous for the F508del mutation.
- We submitted global regulatory filings for TRIKAFTA/KAFTRIO in children with CF 2 through 5 years of age and for KALYDECO in children with CF from 1 month to less than 4 months of age.

## Potential Near-Term Launch Opportunities

We are preparing for the following near-term launches of new products:

- *Exa-cel in SCD and TDT.* We completed European Union and U.K. regulatory submissions for exa-cel, an ex-vivo CRISPR gene-editing therapy, in the fourth quarter of 2022 and initiated a rolling submission in the U.S., which we recently completed. The EMA and MHRA have validated the exa-cel MAA for their respective jurisdictions.
- *VX-548 in acute pain.* We continue to enroll the Phase 3 pivotal program for VX-548 for the treatment of moderate to severe acute pain and expect to complete the pivotal program in late 2023 or early 2024.
- *Vanzacaftor/tezacaftor/deutivacaftor, the next-in-class triple combination, in CF.* We continued our strategy of serial innovation by completing enrollment of the Phase 3 trials of our once-daily triple combination of vanzacaftor/tezacaftor/deutivacaftor. Our clinical and preclinical data indicate that the vanzacaftor/tezacaftor/deutivacaftor triple combination has the potential to provide enhanced benefit beyond TRIKAFTA/ KAFTRIO for people who have at least one mutation in their CFTR gene responsive to CFTR modulators. This regimen also has the benefit of once-daily dosing and has substantially decreased royalties compared with TRIKAFTA.

## Research and Development

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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 combines transformative advances in the understanding of human disease and the science of therapeutics to dramatically advance human health. This approach has yielded a broad and deep pipeline and increases the speed and likelihood of successfully bringing medicines to patients, as demonstrated by our success in moving novel product candidates into clinical trials and obtaining marketing approvals, including for TRIKAFTA/KAFTRIO, SYMDECO/SYMKEVI, ORKAMBI, and KALYDECO for the treatment of CF. The strategy was designed to deliver transformative medicines for serious diseases at high rates of success, and it has delivered just that. Beyond CF, our approach to drug discovery has yielded clinical proof-of-concept in five additional disease areas: SCD and beta thalassemia with exa-cel, acute pain with VX-548, AMKD with inaxaplin, and T1D with VX-880, a stem cell-derived islet cell therapy.

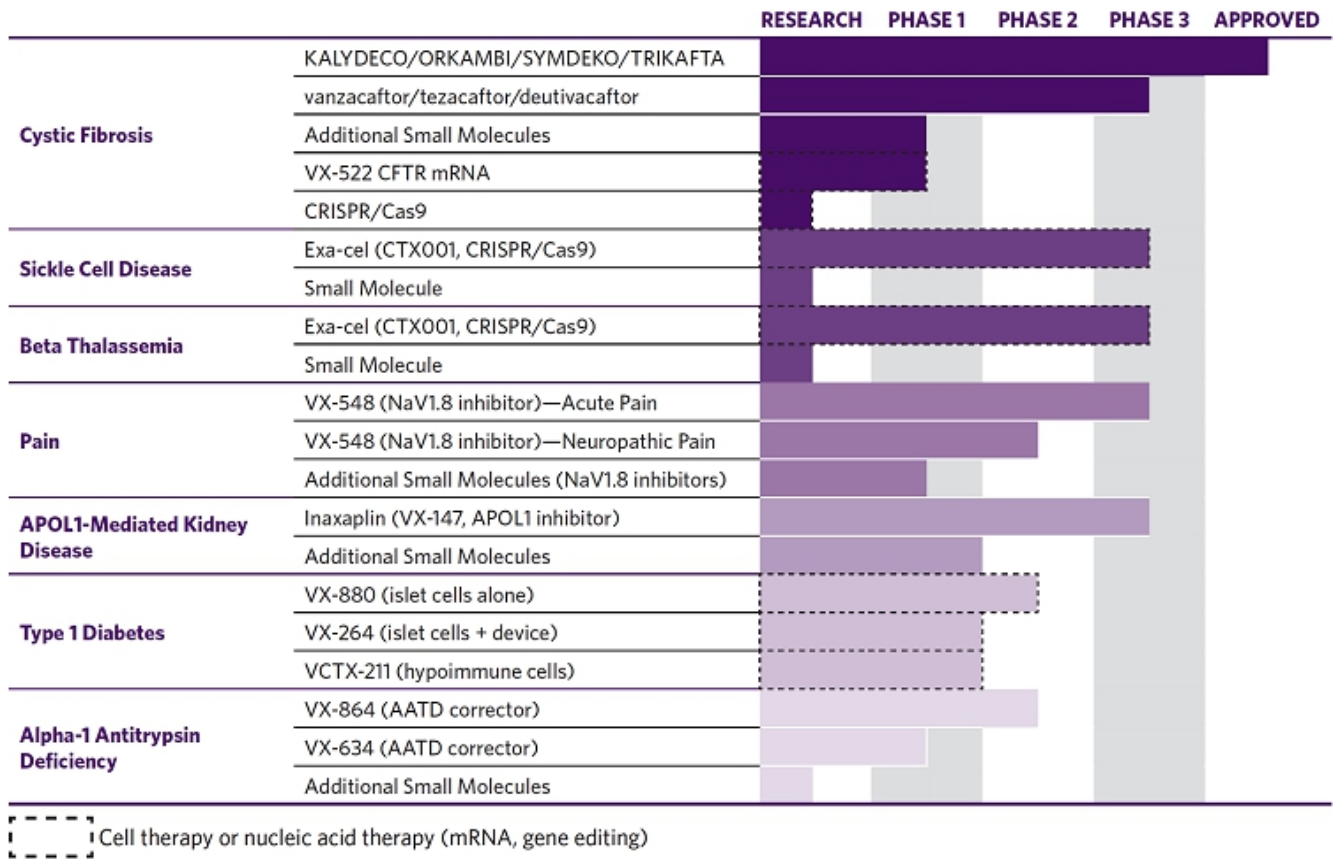
Our research and development approach also includes pursuing multiple modalities tailored to the specific disease area target under investigation, using biomarkers that translate from the bench to the bedside, and advancing multiple candidates into clinical trials with the goal of bringing first-in-class, followed by best-in-class, therapies to patients. In addition to expanding our small molecule programs, we have also advanced an industry-leading portfolio of programs in cell and gene therapies.

Our advancements across multiple disease areas and modalities include:

- *Cystic Fibrosis*. We continue to pursue next-in-class, small molecule CFTR modulator therapies as well as genetic therapies for people with CF who do not make CFTR protein and, as a result, cannot benefit from our current CF medicines. In the past year, we significantly advanced our program for VX-522, a CF mRNA therapeutic designed to treat the underlying cause of CF in these people by enabling cells in the lungs to produce functional CFTR protein. The FDA cleared our IND application in December 2022 and we have initiated a clinical trial for VX-522 in people with CF; the trial is active and enrolling.
- *Sickle Cell Disease and Beta Thalassemia*. The Phase 3 studies of exa-cel in patients 12 years of age and older is ongoing, as is a long-term follow-up study. Two additional Phase 3 studies in pediatric patients continue to enroll.
- *Neuropathic Pain*. We have initiated a Phase 2 clinical trial of VX-548 in diabetic peripheral neuropathy, a common form of chronic peripheral neuropathic pain.
- *APOL1-Mediated Kidney Disease*. We initiated pivotal development of inaxaplin and continue to enroll the Phase 2/3 adaptive clinical trial in patients with AMKD.
- *Type 1 Diabetes*. We are evaluating VX-880, an investigational stem-cell derived fully-differentiated islet cell therapy, for the treatment of T1D in a Phase 1/2 clinical trial in which patients receive immunosuppressive therapy to protect the islet cells from immune rejection. Our CTA in Canada and our IND in the U.S. for our second program in T1D, VX-264, in which the implanted islet cells are encapsulated in an immunoprotective device, were authorized and we plan to begin screening, enrollment and dosing in both Canada and the U.S. in the coming months. We have also continued pre-clinical development of our hypoimmune program utilizing VX-880 cells, and our second hypoimmune program that we are developing in partnership with CRISPR is the subject of a Phase 1/2 study that is active and enrolling patients.
- *Alpha-1 Antitrypsin Deficiency*. We initiated a first-in-human clinical trial for VX-634, which is the first in a series of next-wave investigational small molecules with significantly improved potency and drug-like properties as compared to our previous AAT correctors. We also initiated a second Phase 2 clinical trial of VX-864, a first-generation AAT corrector, to assess the impact of longer-term treatment on the liver, as well as the levels of functional AAT in the plasma.
- *Duchenne muscular dystrophy*. We are conducting IND-enabling studies for our first in vivo gene-editing therapy for DMD, and we expect to submit an IND for this program in 2023.
- *Myotonic dystrophy type 1*. We are exploring multiple approaches to address the underlying causal biology for DM1, and are collaborating with Entrada on IND-enabling studies for an endosomal escape vehicle therapeutic.
- In addition to the programs listed above, we have several of earlier-stage research programs aimed at diseases that fit our R&D strategy.

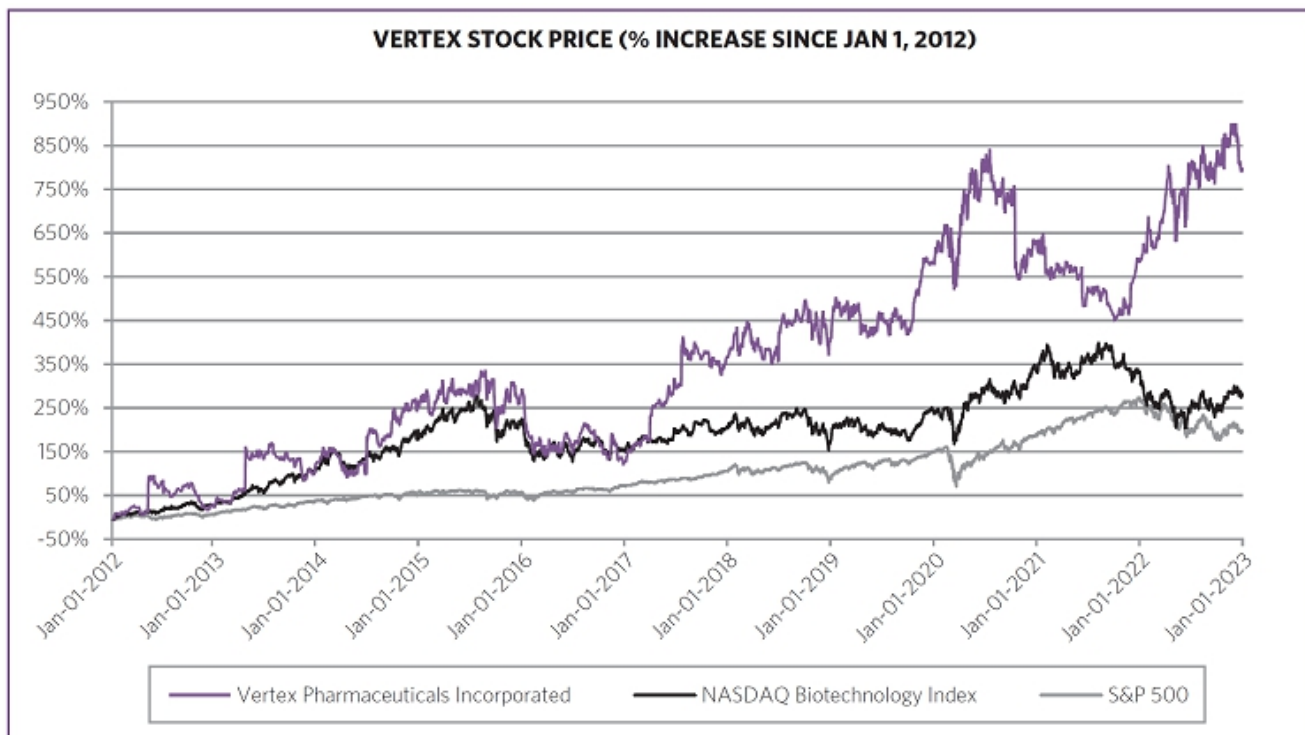
We will continue investing in our research and development programs and fostering scientific innovation by identifying additional product candidates through our internal research efforts and investing in business development transactions to access emerging technologies, products, and product candidates.

The following chart represents our clinical stage pipeline and all follow-on assets for those programs by disease area, stage of development, and modality; it does not include all preclinical programs.



## Increasing Shareholder Value

Driven by our outstanding financial performance and pipeline successes, our stock price increased 31.5% from \$219.60 per share at the end of 2021 to \$288.78 per share at the end of 2022. While we are pleased with our stock performance in 2022, we believe biotechnology companies are best measured over the long term, as opposed to one-year or other shorter-term increments. The following charts show our total shareholder return relative to the NBI and S&P 500 index since the beginning of 2012, when KALYDECO was first approved, as well as our stock price performance over multiple periods. We believe the execution of our differentiated serial innovation strategy will continue to create shareholder value over the long term.





## 2022 Compensation Decisions and Pay-for Performance

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In 2022, our executive compensation program received substantial support from our shareholders, with approval by approximately 93% 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 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 2022, 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 2022, based on a comparative analysis of companies in our Peer Group (described below), we increased base salary compensation for Dr. Kewalramani, Dr. Altshuler and Mr. Wagner and maintained base salary compensation for Mr. Arbuckle. Under his employment agreement, Dr. Leiden no longer receives a base salary for his role of Executive Chairman.
- **Annual Cash Bonus:** We maintained the target cash bonus, which is a percentage of base salary, for all of our NEOs. Dr. Leiden does not receive an annual cash bonus pursuant to his employment agreement. The company's outstanding performance in 2022, as described above, resulted in the board determining that the company had achieved a leading rating for 2022 (a rating of 145 out of a potential 150), and the payment of above-target annual cash bonuses. Please see *Overview of Company Performance Rating & Achievement in 2022*.
- **Long-Term Equity Program:**
  - In 2022, based in part on a comparative analysis of companies in our Peer Group, we increased the target equity grant for Dr. Kewalramani and we maintained the target equity grants for our other NEOs. For his third year as Executive Chairman, Dr. Leiden received equity grants of \$6.5 million pursuant to the terms of his employment agreement. Under his employment agreement, as extended in February 2023, Dr. Leiden will continue to receive equity grants for the fourth and fifth 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 specific performance goals and 50% consisting of time-vesting RSUs. This mix rewards stock price appreciation and incentivizes long-term tenure at the company. The number of RSUs 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 2020 non-financial based PSU awards and the 2022 financial-based PSU awards at the maximum level under these awards, resulting in a maximum payout under these awards in February 2023.
  - The MDCC approved special, one-time equity award grants for Mr. Arbuckle, our COO. These performance-based and time-based grants are intended to incentivize and retain Mr. Arbuckle, who is in a key commercialization role, during a critical period where we expect to launch multiple transformational therapies in disease areas outside of CF.
  - In early 2023, 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. 50% of the PSUs, which vest annually in installments over three years, are tied to CF net product revenues in 2023, while the remaining 50%, which cliff vest after three years, are tied to specific clinical and research milestones over a three-year period.

## Shareholder Engagement

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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 shareholders regularly over the course of the year.

During 2022, we solicited feedback regarding our corporate governance practices from our top 40 shareholders representing approximately 65% 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, R&D approach, our diversity initiatives and metrics, employee engagement and development, political and lobbying disclosures, executive compensation, sustainability and climate change matters.

## 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	Excessive executive perquisites
Multiple performance factors	Supplemental pension benefits for executives
Range of awards; not all or nothing	Single-trigger vesting in connection with a change-in-control for equity awards
Compensation recoupment (clawback) policy	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)	Re-pricing of stock options without shareholder approval
Executive and Non-Employee Director Stock Ownership Guidelines	Payment of dividends on unvested performance shares or units
Independent compensation consultant	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 leadership, 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 used in our equity awards. Our company goals address several key objectives, including increasing revenues from our current products, achievement of commercial manufacturing and R&D objectives, enhancing organizational capabilities, and maintaining financial strength. 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 MDCC and 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 R&D 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, Executive Chairman, 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, our Executive Chairman, 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 recommendations.

## 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 2022, 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 both within and outside the U.S.
Commercial operations	Marketing and selling approved medicines
Significant R&D investment	Greater than \$1.5B or 25% of revenue
Number of employees	Greater than 950 employees
Market capitalization and significance to broader economy	Market cap at least ¼ our size and/or inclusion in 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. 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 R&D. 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 the importance of medicines to patients and society as we believe these are the key drivers of our business model. On a regular basis, we review and revise the list of companies with the goal of maintaining a group of comparators comprised of at least twelve companies.

As a result of this analysis, and on the basis of the criteria listed above, the MDCC selected the following comparator companies for 2022. The peer group was modified in 2022 from 2021 to include three new companies (Alnylam Pharmaceuticals, Bristol-Myers Squibb Company and Moderna, Inc.) to replace three prior peer companies (Alexion, Alkermes and United Therapeutics). We replaced Alexion Pharmaceuticals, Inc. ("Alexion") due to its acquisition by AstraZeneca PLC and Alkermes and United Therapeutics because of diminishing business model similarity.

2022 Peer Group	
AbbVie Inc.	Gilead Sciences, Inc.
Alnylam Pharmaceuticals	Incyte Corporation
Amgen, Inc.	Jazz Pharmaceuticals plc
Biogen, Inc.	Moderna, Inc.
BioMarin Pharmaceuticals, Inc.	Regeneron Pharmaceuticals, Inc.
Bristol-Myers Squibb Company	Seagen Inc.
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		R&D Expense <sup>(1)</sup>		Operational Focus		Innovative and Importance of Medicines					
		\$ (millions)	% of Revenue			Orphan/Unmet Clinical Need	Breakthrough Therapy Designations <sup>(2)</sup>	Innovative Approved Drugs in Last 12 Years <sup>(3)</sup>	Uses Vertex as Peer	Market Position Nasdaq 100	S&P 500
AbbVie	Biotech	\$ 7,207	12%	✓	✓	✓	7	8			✓
Alnylam	Biotech	\$ 883	85%	✓	✓	✓	3	2			
Amgen	Biotech	\$ 4,434	17%	✓	✓	✓	2	9		✓	✓
Biogen	Biotech	\$ 2,231	22%	✓	✓	✓	—	6	✓	✓	✓
BioMarin	Biotech	\$ 650	31%	✓	✓	✓	1	4	✓		
Bristol-Myers	Pharma	\$ 10,324	22%	✓	✓	✓	12	15			✓
Eli Lilly	Pharma	\$ 8,099	28%	✓	✓	✓	4	10			✓
Gilead	Biotech	\$ 8,621	32%	✓	✓	✓	6	9	✓	✓	✓
Incyte	Biotech	\$ 1,638	48%	✓	✓	✓	2	4	✓		✓
Jazz	Pharma	\$ 1,634	45%	✓	✓	✓	—	4	✓		
Moderna	Biotech	\$ 3,295	17%	✓	✓	✓	—	1	✓	✓	✓
Regeneron	Biotech	\$ 3,593	30%	✓	✓	✓	8	7	✓	✓	✓
Seagen	Biotech	\$ 1,344	69%	✓	✓	✓	4	3	✓	✓	✓
Vertex	Biotech	\$ 2,540	28%	✓	✓	✓	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, 2022 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 twelve years include: VIEKIRA PAK, IMBRUVICA, VENCLEXTA, ORILISSA, MAVYRET, RINVOQ, SKYRIZI and QULIPTA (AbbVie), ONPATTRO and GIVLAARI (Alnylam), AIMOVIG, BLINCYTO, XGEVA, PROLIA, KYPROLIS, PARSABIV, EVENITY, TEZSPIRE, and LUMAKRAS (Amgen), TECFIDERA, ALPROLIX, SPINRAZA, ELOCTATE, VUMERITY and ADUHELM (Biogen), BRINEURA, PALYNZIQ, VIMIZIM and VOXZOGO (BioMarin), ABECMA, BREYANZI, SOTYKTU, CAMZYOS, ZESPOSIA, ONUREG, REBLOZYL, INREBIC, IDHIFA, EVOTAZ, OPDIVO, POMALYST, ELIQUIS, YERVOY and OPDUALAG (Bristol-Myers), CYRAMZA, EMGALITY, JARDIANCE, OLUMIANT, PORTRAZZA, RETEVMO, REYVOW, TALTZ, VERZENIO, and MOUNJARO (Eli Lilly), YESCARTA, SOVALDI, HARVONI, VEMLIDY, CAYSTON, ZYDELIG, BIKTARVY, VEKLURY and SUNLENCA (Gilead), JAKAFI, OLUMIANT, PEMAZYRE and RUXOLITINIB (Incyte), VYXEOS, DEFITELIO, ZEPZELCA and RYLAZE (Jazz), SPIKEVAX (Moderna), DUPIXENT, LIBTAYO, PRALUENT, EYLEA, ZALTRAP, INMAZEB and EVKEEZA (Regeneron), and PADCEV, TUKYSA and TIVDAK (Seagen).

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.

Due to 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 broader life science industry companies when considering compensation for Mr. Arbuckle:

Peer Group Companies	Life Science Companies
Amgen, Inc.	Baxter International Inc
Jazz Pharmaceuticals plc	Bio-Rad Laboratories, Inc
	ResMed, Inc.
	Thermo Fisher Scientific Inc.
	Zimmer Biomet Holdings Inc.

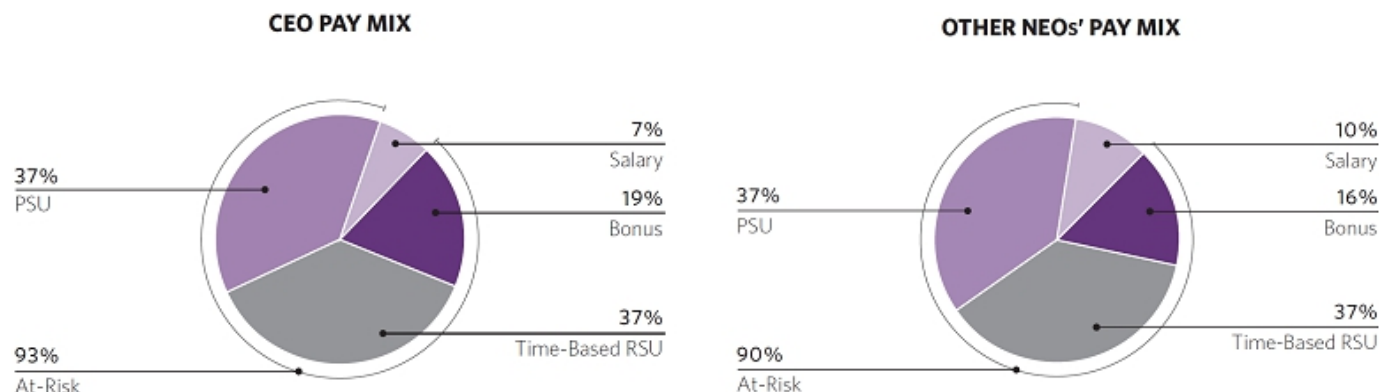
## Elements of Annual Compensation

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 executive compensation. Each year we review the mix 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 2022 equity grants, we maintained our mix of equity awards, including PSUs and time-based RSUs.

## 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 and special, one-time equity award grants to Mr. Arbuckle in 2022.

## 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	<ul style="list-style-type: none"> <li>Annual bonus dependent on both company and individual performance factors</li> </ul>
Equity Awards	<ul style="list-style-type: none"> <li>Grant date value of equity awards based on target award values by level with differentiation for individual performance</li> <li>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</li> </ul>
PSU Awards	<ul style="list-style-type: none"> <li>50% of PSUs with range of shares issued <b>0% to 200%</b> of target based on one year financial metrics (vesting in equal installments over a three year period)</li> <li>50% of PSUs with range of shares issued <b>0% to 200%</b> of target based on three-year non-financial metrics (cliff-vesting after three years)</li> </ul>
Time-Based RSUs	<ul style="list-style-type: none"> <li>Value of awards increases or decreases based on stock price over the three-year vesting period</li> <li>We consider our time-vesting RSU awards to be performance-based awards because the target number of RSUs 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</li> </ul>

### More specifically:

- PSU Awards.** Our CEO and executive vice presidents ("EVPs") receive 50% of their annual equity compensation in the form of PSUs. 50% of the number of PSUs are eligible to vest based on the achievement of financial goals and the remaining 50% of the 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 RSUs.** Our CEO and EVPs receive 50% of their annual equity compensation in the form of time-based RSUs 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 RSUs 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. The MDCC does not strictly benchmark to a particular level of compensation relative to compensation levels at the Peer Group companies. Instead, the MDCC's 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 the executive's 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 2022 was increased to \$1.50 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 2022, we increased the base salary of Dr. Altshuler from \$800,000 to \$825,000 in recognition of his contributions since becoming Chief Scientific Officer, expected future contributions, experience and knowledge, and based on a comparative analysis of compensation in our Peer Group.



We also increased the base salary for Mr. Wagner from \$770,000 to \$825,000 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 2022, we maintained Mr. Arbuckle's base salary.

Name	2022 Base Salary
Reshma Kewalramani	\$ 1,500,000
Charles F. Wagner, Jr.	\$ 825,000
David M. Altshuler	\$ 825,000
Stuart A. Arbuckle	\$ 900,000
Jeffrey M. Leiden <sup>(1)</sup>	\$ —

(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.

## 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 47% fewer shares of common stock in 2022 as compared to 2018 and reduced our "gross burn rate" from 1.7% in 2018 to 0.9% in 2022.

	2018	2019	2020	2021	2022	% Change 2018 to 2022
	(in thousands, except percentages and employee numbers)					
Total Shares Granted Subject to Equity Awards	4,391	3,687	1,814	2,908	2,338	(47)%
Gross Burn Rate <sup>(1)</sup>	1.7%	1.4%	0.7%	1.1%	0.9%	
Awards Canceled, Forfeited or Expired	826	886	432	646	311	
Net Dilution	3,565	2,801	1,382	2,262	2,027	(43)%
Net Burn Rate	1.4%	1.1%	0.5%	0.9%	0.8%	
Average # of Employees During Fiscal Year <sup>(2)</sup>	2,398	2,668	3,113	3,655	4,280	

(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.

## 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 2022

At the beginning of each year, our MDCC and 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 in assessing our corporate performance, our MDCC and board consider 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 2022, the MDCC recommended and 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. Our commercial manufacturing, quality and operations goals were designed to incentivize supply chain resilience, efficiency in delivery of our CF medicines and commercial manufacturing readiness for medicines in our pipeline. Our pipeline goals and our budgets were established with the expectation that we would invest with discipline in R&D 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 2022 weighted goals and the year-end score achieved by the company as recommended by the MDCC and approved by the board are set forth in the following table:

Goal(s)	Maximum Score	Actual 2022 Performance Score
<b>Marketed and Approval-Stage Products</b>	<b>50</b>	<b>50</b>
<ul style="list-style-type: none"> <li>Achieve CF net product revenue goals through compliant marketing practices, including U.S. and ex-U.S. revenue goals</li> <li>Execute successful global launches of CF medicines into younger patient populations</li> <li>Advance cross-functional readiness for anticipated launch of exa-cel</li> </ul>		
<b>Pipeline Growth</b>	<b>63</b>	<b>56.5</b>
<ul style="list-style-type: none"> <li>Complete enrollment in Phase 3 trials for vanzacaftor/tezacaftor/deutivacaftor</li> <li>Advance CF mRNA therapy program</li> <li>Advance multiple non-CF development programs</li> <li>Advance multiple research programs, including CF and non-CF programs</li> </ul>		
<b>Manufacturing, Quality &amp; Operations</b>	<b>10</b>	<b>8</b>
<ul style="list-style-type: none"> <li>Complete multiple manufacturing readiness processes for exa-cel launch</li> <li>Enhance CF supply chain resiliency</li> <li>Advance manufacturing plans for pipeline products</li> </ul>		
<b>Organizational Development and Capability</b>	<b>12</b>	<b>12</b>
<ul style="list-style-type: none"> <li>Successful transition to hybrid working, while sustaining our culture and values and continuing to foster a diverse and inclusive environment</li> <li>Continue to build the organization, expand capabilities, and grow internal talent for leadership positions</li> <li>Drive enterprise risk management functions to match increasing scale and complexity</li> </ul>		
<b>Financial Strength</b>	<b>15</b>	<b>15</b>
<ul style="list-style-type: none"> <li>Continue to manage operating expenses and achieve financial targets</li> </ul>		
<b>Additional Accomplishments and Shortcomings, Net (see page 57 of this proxy statement)</b>		<b>3</b>
<b>TOTAL (FINAL SCORING ROUNDED TO WHOLE NUMBER)</b>	<b>150</b>	<b>145</b>

Our 2022 company performance score, as determined by the board, was 145 out of a potential of 150. Our 2023 company performance will be evaluated against the broad categories set forth above, but with slightly different weighting with respect to Pipeline Growth (59 points), Manufacturing, Quality and Operations (13 points), and Organizational Development and Capability (13 points).

## Detailed Discussion of Company Performance Rating Factors and Achievements

### Goals - Marketed and Approval-Stage Products

In 2022, we made significant progress with respect to our marketed and approval-stage products.

- CF net product revenues increased to \$8.93 billion, up 18% as compared to 2021. Our CF net product revenues exceeded the mid-point of our initial CF net product revenues guidance by approximately \$400 million (\$8.93 billion actual as compared to the mid-point of our initial guidance of \$8.5 billion) as a result of strong uptake of TRIKAFTA/KAFTRIO in multiple countries internationally and the continued steady performance of TRIKAFTA in the U.S. for children with CF 6 to 11 years of age.
- We executed strong commercial launches of KAFTRIO in multiple countries outside of the U.S.
- We advanced our cross-functional commercial readiness in advance of the anticipated launch of exa-cel, including with respect to critical hires, activation of treatment centers, and engagement with policymakers, payers and patient advocacy groups.

*For marketed and approval-stage products goals, our board assigned the company a score of 50 out of 50, due to exceeding goals with respect to total CF net product revenues, successfully launching our CF medicines in younger age groups, and making meaningful progress in commercial launch preparation.*

## Goals - Pipeline Growth (Late and Early-Stage)

In 2022, we made significant progress advancing our pipeline of CF and non-CF medicines.

- We completed enrollment in Phase 3 clinical trials evaluating our once-daily investigational triple combination of vanzacaftor/tezacaftor/deutivacaftor.
- We advanced our CF mRNA program designed to address the patients not currently eligible for any of our products. In December 2022, the FDA cleared our IND for VX-522 and we have initiated a clinical trial in people with CF.
- We expanded the eligibility of our medicines to younger age groups in the U.S., Europe, Australia, and Canada and submitted regulatory filings for approval in younger age groups across the portfolio.
- We made significant progress advancing a broad pipeline of potentially transformative small molecule, cell, and genetic therapies aimed at treating serious diseases.
- We completed regulatory submissions in the European Union and U.K. for exa-cel for SCD and TDT, and initiated U.S. regulatory submissions. We also initiated two additional Phase 3 trials evaluating exa-cel in pediatric patients with SCD and TDT.
- We announced positive Phase 2 data for VX-548, a selective small molecule, non-opioid inhibitor of NaV1.8, for the treatment of acute pain and have initiated three Phase 3 trials. We have also initiated a Phase 2 clinical trial of VX-548 in peripheral neuropathic pain.
- We initiated pivotal development of inaxaplin, our small molecule inhibitor of APOL1 function for patients with AMKD.
- We achieved proof-of-concept for VX-880, our cell therapy designed to treat T1D, and achieved clearance to begin clinical trials in Canada for our second program in T1D, VX-264, our cells and device program.
- We initiated various first in human studies and delivered numerous preclinical candidates in our areas of therapeutic focus.

***On the basis of the accomplishments in advancing our R&D programs and, in particular the completion of European Union and U.K. regulatory submissions for exa-cel, achievement of proof-of-concept for VX-548 and VX-880, advancements of other clinical trials, and advancement of multiple pre-clinical candidates across multiple modalities, and also taking into account the challenges experienced with certain clinical trials, our board assigned the company a score of 56.5 out of 63 for our pipeline growth goal.***

## Goals - Manufacturing, Quality and Operations

- We advanced execution of a long-term commercial manufacturing strategy and made advancements in our commercial manufacturing processes, including manufacturing partner discussions and selection for pipeline products.
- We enhanced the resiliency of our CF supply chain by meeting stock targets, advancing commercial supply plans for critical materials, and achieving successful inspection results.

***In recognition of achieving manufacturing milestones, including the advancement of the commercial manufacturing strategy for pipeline programs and strengthening of our CF supply chain, the board assigned the company a score of 8 out of 10 for our manufacturing, quality and operations goal.***

## Goals - Organizational Development and Capability

### ***Flexible and Inclusive Work Environment***

With emphasis on sustaining our values and culture of innovation, in 2022 we thoughtfully transitioned our employees to a hybrid work environment and we continued to foster an inclusive and equitable culture that enables all people with different backgrounds to thrive, with particular focus on attracting and retaining a diverse employee base.

### ***Talent and expertise***

We strengthened our organizational capabilities by attracting and retaining the key talent necessary to operate our business, including filling all critical hires and developing our internal talent base for leadership roles.

### ***Ethics and Compliance***

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

### ***Systems and Infrastructure***

We continued to prioritize our infrastructure to support an increasingly complex organization, including enhancing policies and programs, technology solutions and security, and business processes.

## Corporate Social Responsibility

We continued to focus on transforming the lives of people with serious diseases, fostering an environment that embraces inclusion, diversity, and equity, carefully managing our environmental footprint, and making a positive impact in communities where we live and work.

***To reflect the improvements to our organizational structure, processes, and systems achieved in 2022, our board assigned the company a score of 12 out of 12 for our organizational development and capability goals.***

### Goals - Financial Strength

We exceeded our financial goals in 2022. We increased our net product revenues to \$8.93 billion, an 18% increase from 2021, reached our target adjusted non-GAAP EBITDA, and managed our operating expenses, resulting in a GAAP operating margin of 48% and a non-GAAP operating margin of 54% (see Appendix A for a reconciliation of non-GAAP operating margin). As a result, we ended 2022 with cash, cash equivalents, and marketable securities of approximately \$10.8 billion, an increase of approximately \$3.3 billion from 2021.

***As a result of our strong financial performance, including increasing revenues and managing operating expenses, our board assigned the company a score of 15 out of 15 for our financial strength goals.***

### Additional Factors (accomplishments and/or shortcomings)

In connection with determining our 2022 company rating, our board of directors made positive and negative adjustments based on factors not anticipated when the company's original goals for 2022 were established. By design, potential adjustments are capped at  $\pm 10\%$  (or  $\pm 15$  points) and used by the board to address and highlight important achievements and or shortcomings. Positive adjustments were related to advancing additional novel, non-CF molecules and therapies, making additional progress with respect to T1D manufacturing, and acceleration of our acute pain program. Overall, the board of directors increased our company rating by four points for positive additional accomplishments, which was offset by a one point reduction related to delays in one therapeutic area. As a result, our final company rating was increased by three points to a total of 145 points (rounded).

## 2022 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 their 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 MDCC and 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 2022 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 their 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.

## 2022 Actual Individual Ratings for Named Executive Officers

<b>Dr. Reshma Kewalramani</b> CEO and President	2022 Rating:	Leading Exemplary
	2022 Salary:	\$ 1,500,000
	2022 Bonus:	\$ 3,784,500
	LTI Equity Grants (Feb 2023):	\$17,145,000

On the basis of the MDCC's recommendation, our independent directors rated Dr. Kewalramani's overall performance for 2022 as "Leading Exemplary," with an individual performance factor of 145%. The performance rating for Dr. Kewalramani combined a "leading" results-based rating with an "exemplary demonstration" behaviors-based rating. Dr. Kewalramani's rating derived from her leadership of our executive team in 2022, 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, utilizing multiple therapeutic modalities with increasing complexity, while ensuring that quality and compliance remain paramount
- The 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 approvals for younger age groups around the world, completion of enrollment of the vanzacaftor/tezacaftor/deutivacaftor Phase 3 studies, and initiation of the VX-522 clinical trial
- Leadership in the advancement of our non-CF pipeline, including the progress in the exa-cel, pain, AMKD, and T1D programs, as well as the expansion our pre-clinical pipeline
- Overseeing business development transactions that have enhanced the company's capabilities in various therapeutic areas and modalities
- Exhibiting outstanding leadership qualities in advancing Vertex's culture and values, transitioning our workforce to a hybrid environment, and recruiting, retaining and developing top-tier talent across the organization
- Building an excellent relationship with the board based on trust, transparency, clear communication and responsiveness

<b>Charles F. Wagner, Jr.</b> EVP, Chief Financial Officer	2022 Rating:	Leading Exemplary
	2022 Salary:	\$ 825,000
	2022 Bonus:	\$ 1,239,315
	LTI Equity Grants (Feb 2023):	\$ 6,000,000

The MDCC recommended and the board adopted an overall rating of "Leading Exemplary" for Mr. Wagner based on a results-based rating of "leading" and a behaviors-based rating of "exemplary demonstration" with an individual performance factor of 148%. 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 our business development group, whose numerous successes included:
  - The acquisition of ViaCyte to accelerate our T1D portfolio
  - The establishment of a collaboration with Entrada focused on discovering and developing therapies for DM1
  - The acquisition of a portfolio of protease medicines from Catalyst Biosciences, Inc. to further broaden our pipeline
- Exemplary leadership of the finance, accounting, business development, investor relations and facilities organizations and successfully recruiting, developing, and mentoring key talent

<b>David M. Altshuler</b> EVP, Global Research and Chief Scientific Officer	2022 Rating:	Leading
	2022 Salary:	\$ 825,000
	2022 Bonus:	\$ 1,172,325
	LTI Equity Grants (Feb 2023):	\$ 5,000,000

The MDCC recommended and the board adopted an overall rating of "Leading" for Dr. Altshuler based on a results-based rating of "leading" and a behaviors-based rating of "living the values" with an individual performance factor of 140%. Dr. Altshuler's rating derived from his leadership of the global research, preclinical sciences, external innovation, data science, and data technology and engineering organizations, including the following:

- Advancing R&D of multiple next-generation CFTR potentiator and corrector compounds and enabling advancement of our mRNA program into the clinic
- Leadership in the advancement of our pipeline, including by exceeding goals for the delivery of preclinical product candidates
- Supporting business development efforts through our acquisition of ViaCyte, acquisition of assets from Catalyst Biosciences, and strategic collaboration with Entrada Therapeutics
- Leading the data science and the data, technology and engineering organizations, which enhanced operational excellence, implemented innovative data analytics and process automation solutions, and further improved information security

<b>Stuart A. Arbuckle</b>	2022 Rating:	Leading Exemplary
EVP, Chief Operating Officer	2022 Salary:	\$ 900,000
	2022 Bonus:	\$ 1,761,750
	LTI Equity Grants (Feb 2023):	\$ 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 \$8.93 billion in 2022, an increase of 18% compared to 2021 and exceeding our initial revenue forecast by approximately \$400 million
- Leading continued strong commercial execution across the entire portfolio, driven by new regulatory approvals, reimbursement agreements, and continued and rapid uptake in eligible patients
- Enhancement of the commercial manufacturing function, including progress with respect to the company’s long-term commercial manufacturing strategy, and increased resiliency of our CF supply chain
- Leadership of the activities surrounding commercialization of exa-cel and other potentially near term launches in disease areas outside of CF
- Leadership of the human resources function, including its continued nurturing of our culture, development of our workforce, and focus on diversity, equity, and inclusion
- Leadership of the corporate communications function, which generated significant external awareness and recognition of our differentiated R&D strategy, our clinical successes, and our impact on patients’ lives

## Annual Cash Bonus

The 2022 cash bonus for each NEO (referred to in the *Summary Compensation Table* on page 67 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 (as supplemented for Mr. Arbuckle, as described above). For 2022, Dr. Kewalramani’s individual incentive target remained at 120% of her base salary and Mr. Arbuckle’s individual incentive target remained at 90% of his base salary. The individual incentive target for Mr. Wagner and Dr. Altshuler remained at 70% of his respective base salary during 2022; 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 (as supplemented for Mr. Arbuckle, as described above).

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 2022 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 2022 performance, as set forth in the table below.

Name	2022 Base Salary		Individual Incentive Target	=	2022 Target Bonus		Company Performance Factor	x	Individual Performance Factor	=	2022 Performance Cash Bonus
Reshma Kewalramani	\$ 1,500,000	x	120%	=	\$ 1,800,000	x	145%	x	145%	=	\$ 3,784,500
Charles F. Wagner, Jr.	\$ 825,000	x	70%	=	\$ 577,500	x	145%	x	148%	=	\$ 1,239,315
David M. Altshuler	\$ 825,000	x	70%	=	\$ 577,500	x	145%	x	140%	=	\$ 1,172,325
Stuart A. Arbuckle	\$ 900,000	x	90%	=	\$ 810,000	x	145%	x	150%	=	\$ 1,761,750
Jeffrey M. Leiden	\$ —	x	—%	=	\$ —	x	—%	x	—%	=	\$ —



## 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 2022 performance:

	Performance Ratings				
	Not Building	Building	Strong (target)	Leading	Leading Exemplary
CEO	\$ —	\$ 6,750,000	\$ 13,500,000	\$ 15,322,500	\$ 17,145,000
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 of \$13.5 million, and maintained the target equity value for Mr. Arbuckle and our other EVPs of \$4.75 million and \$4.0 million, respectively. The equity values for Leading and Leading Exemplary were selected based on award values approximating the 75<sup>th</sup> and mid upper quartile percentiles of peer executives. The number of shares granted pursuant to the time-vested RSU award and PSU award was 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 \$6.5 million in the first quarter of 2023 and will receive an annual equity grant of \$6.5 million in each of the first quarters of 2024 and 2025 for his role as Executive Chairman. With respect to these grants, 50% will be in the form of fully-vested common stock and 50% in the form of PSUs based on financial goals with a one-year performance period.

### February 2023 Grants Based on 2022 Performance

In February 2023, upon the MDCC's recommendation, our independent directors approved individual performance factors and equity awards for 2022 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 Exemplary	\$ 8,572,500	\$ 8,572,500	\$ 17,145,000
Charles F. Wagner, Jr.	Leading Exemplary	\$ 3,000,000	\$ 3,000,000	\$ 6,000,000
David M. Altshuler	Leading	\$ 2,500,000	\$ 2,500,000	\$ 5,000,000
Stuart A. Arbuckle	Leading Exemplary	\$ 3,562,500	\$ 3,562,500	\$ 7,125,000

### Performance Units Results Table

We annually grant one-year financial-based PSU awards and three-year non-financial based PSU 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 R&D to develop additional transformative medicines for serious diseases.

The final performance multipliers for our 2022 financial-based PSU 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 2023. The following chart shows the pre-established financial goals and the actual results for the financial-based PSU awards granted in 2022:

Award Year	Company Goal	Below Threshold	Threshold	Target	Max	Results	
		0% Payout	50% Payout	100% Payout	200% Payout	CF Revenue	Payout
2022	2022 CF Net Product Revenues	<\$8.345 billion	\$ 8.345 billion	\$ 8.520 to \$ 8.620 billion	\$ 8.820 billion	\$ 8.93 billion	200.0%

Consistent with our philosophy of aligning compensation with performance, for 2022, 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 2020 non-financial PSUs were established in February 2020 and our performance against these goals was determined in the first quarter of 2023. 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%.

2020	CF Portfolio Milestone - Approval of triple combination in U.S. for patients six years of age or older and submission of an NDA or sNDA for triple combination in the U.S. for patients two to five years of age	Achieved
	Establish proof-of-concept for a drug candidate in a disease area other than cystic fibrosis, sickle cell disease, and beta-thalassemia, and VX-150	Achieved
	First subject is dosed in a pivotal clinical trial for a nucleic acid therapy or cell-based therapy	Achieved

The performance multiples for the 2021, 2022 and 2023 non-financial based PSU awards will be determined in the first quarter of 2024, 2025 and 2026, respectively, based on performance over the relevant three-year performance period. The non-financial goals contained in our three-year PSU awards for 2021, 2022 and 2023 are based on multiple clinical milestones, and are not disclosed for competitive reasons and because the relevant performance periods are ongoing.

## Special One-Time Equity Award

The MDCC approved special grants to retain Mr. Arbuckle, our COO, during a critical period where we expect to commercialize multiple transformational therapies in disease areas outside of CF and to incentivize him to achieve these important company goals. Specifically, in December 2022, the MDCC approved one-time equity award grants for Mr. Arbuckle consisting of a time-vested RSU award having a grant date value of \$4.0 million and a PSU having a target grant date value of \$5.9 million. The number of shares granted pursuant to this time-vested RSU award and PSU award was 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). The RSU award vests in full on July 1, 2025, subject to continued employment, and the PSU vests based on the achievement of certain commercial milestone objectives that are different from the objectives used in our annual PSU award program. The awards do not partially vest, nor are they eligible for accelerated retirement vesting as described in *Employment Agreements and Post-Termination Compensation and Benefits*. The MDCC determined that it was appropriate to provide these grants because they encourage retention in the case of RSUs, and, in the case of PSUs, they utilize performance goals that are separate from those that are applicable to our outstanding PSUs, thereby incentivizing performance in a manner that is not currently contemplated by our existing performance programs.

## 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 2023, we extended Dr. Leiden's amended employment agreement by one year, until 2025. 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 fourth and fifth years of service as Executive Chairman.

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 their 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 (1) who is at least age 55, (2) has completed at least five full years of service, (3) whose age plus full years of service is 65 or greater, and (4) who has completed a mandatory transitional period of employment with the company following notice of their 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

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### 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. In October 2022, the SEC adopted final rules implementing the clawback provisions of the Dodd-Frank Act and we will update our policy in accordance with Nasdaq's updated listing standards, as required by the final rules.

## 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 34 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 RSUs, and (c) shares held through our 401(k) plan count toward meeting these guidelines; unexercised stock options do not count toward meeting these guidelines. As of March 31, 2023, 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 the 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 R&D 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 2023 annual meeting of shareholders and incorporated by reference into Vertex's Annual Report on Form 10-K for the year ended December 31, 2022. 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 2022, 2021, and 2020.

Name and Principal Position	Year	Salary	Bonus	Stock Awards <sup>(1)</sup>	Option Awards	Non-Equity Incentive Plan Compensation	All Other Compensation	Total
<b>Reshma Kewalramani<sup>(2)</sup></b> CEO and President	2022	\$ 1,396,154	\$ —	\$ 10,640,784	\$ —	\$ 3,784,500	\$ 43,059	\$ 15,864,497
	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
<b>Charles F. Wagner, Jr.</b> EVP & Chief Financial Officer	2022	\$ 793,269	\$ —	\$ 3,750,197	\$ —	\$ 1,239,315	\$ 28,830	\$ 5,811,611
	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
<b>David M. Altshuler</b> EVP & Global Research and Chief Scientific Officer	2022	\$ 810,577	\$ —	\$ 4,500,090	\$ —	\$ 1,172,325	\$ 42,137	\$ 6,525,129
	2021	\$ 756,731	\$ —	\$ 4,375,430	\$ —	\$ 1,159,200	\$ 39,976	\$ 6,331,337
	2020	\$ 752,885	\$ —	\$ 5,250,411	\$ —	\$ 1,015,508	\$ 41,780	\$ 7,060,584
<b>Stuart A. Arbuckle</b> EVP & Chief Operating Officer	2022	\$ 900,000	\$ —	\$ 12,294,259	\$ —	\$ 1,761,750	\$ 43,097	\$ 14,999,106
	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
<b>Jeffrey M. Leiden<sup>(3)</sup></b> Executive Chairman	2022	\$ —	\$ —	\$ 8,500,250	\$ —	\$ —	\$ 92,930	\$ 8,593,180
	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

(1) Pursuant to applicable SEC rules, the grant-date fair values of the equity awards granted in February 2022 for 2021 performance are included in 2022 compensation. Also included in 2022 compensation is the grant-date fair value of the one-time equity awards granted in December 2022 to Mr. Arbuckle. The equity awards granted in February 2023 to Dr. Kewalramani, Mr. Wagner, Dr. Altshuler and Mr. Arbuckle for 2022 performance and the equity awards granted in February 2023 to Dr. Leiden pursuant to his employment agreement, in each case that are discussed in the *Compensation Discussion and Analysis* section above, are not reflected in the Summary Compensation Table above.

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

(3) 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.”

## Stock Awards

The amounts set forth under the caption “Stock 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 executive compensation is in the form of equity awards, the total compensation reflected in each executive’s compensation for 2022 in the table above is significantly affected by such executive’s performance during 2021. Our methodology for determining the grant-date fair value of equity awards is set forth in Note O to our consolidated financial statements included in our 2022 Annual Report on Form 10-K filed with the SEC on February 10, 2023.

The “Stock Awards” for 2022, 2021, and 2020 consist of PSU awards and time-vested RSU awards (or, in the case of Dr. Leiden for 2021 and 2022, fully vested common stock) granted in February of each year. In each of 2022, 2021, and 2020, the financial PSU awards had grant-date values of 100% of the fair value of the target shares, respectively, in accordance with U.S. GAAP. In 2022, 2021, and 2020, the non-financial PSU awards had grant-date values of 0%, 50% and 50%, of the fair value of the target shares, respectively, in accordance with U.S. GAAP. Additionally, the special, one-time PSU award granted to Mr. Arbuckle in December 2022 had a grant-date value of 50% of the fair value of the target shares in accordance with U.S. GAAP. For each of these awards, the grant-date fair values were based on the probable outcome of the performance conditions associated with 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:

Name	2022	2021	2020
Reshma Kewalramani	\$ 21,281,812	\$ 18,728,038	\$ 9,000,877
Charles F. Wagner, Jr.	\$ 7,500,393	\$ 7,500,890	\$ 7,501,175
David M. Altshuler	\$ 9,000,180	\$ 7,500,890	\$ 9,000,877
Stuart A. Arbuckle	\$ 26,488,914	\$ 9,000,297	\$ 9,000,877
Jeffrey M. Leiden	\$ 12,750,376	\$ 13,500,444	\$ 22,860,288

## 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 2022, 2021 and 2020 performance, each of which was paid in the first quarter of the subsequent year. The cash bonus awards to the NEOs for 2022 performance were determined as follows:

Name	Base Salary	Individual Incentive Target	2022 Target Bonus	Company Performance Factor	Individual Performance Factor	2022 Performance Cash Bonus
Reshma Kewalramani	\$ 1,500,000	x 120%	= \$ 1,800,000	x 145%	x 145%	= \$ 3,784,500
Charles F. Wagner, Jr.	\$ 825,000	x 70%	= \$ 577,500	x 145%	x 148%	= \$ 1,239,315
David M. Altshuler	\$ 825,000	x 70%	= \$ 577,500	x 145%	x 140%	= \$ 1,172,325
Stuart A. Arbuckle	\$ 900,000	x 90%	= \$ 810,000	x 145%	x 150%	= \$ 1,761,750
Jeffrey M. Leiden	\$ —	x —%	= \$ —	x —%	x —%	= \$ —

## All Other Compensation

The amounts set forth under the caption “All Other Compensation” in the table for 2022 consist of:

Name	401(k) Match	Life Insurance Premiums	Matching Gift Program	Other	Total
Reshma Kewalramani	\$ 13,725	\$ 2,202	\$ 25,000	\$ 2,132 <sup>(1)</sup>	\$ 43,059
Charles F. Wagner, Jr.	\$ 13,725	\$ 1,515	\$ 11,800	\$ 1,790 <sup>(1)</sup>	\$ 28,830
David M. Altshuler	\$ 13,725	\$ 1,666	\$ 25,000	\$ 1,746 <sup>(1)</sup>	\$ 42,137
Stuart A. Arbuckle	\$ 13,725	\$ 1,677	\$ 25,000	\$ 2,695 <sup>(1)</sup>	\$ 43,097
Jeffrey M. Leiden	\$ 2,925	\$ 5	\$ 25,000	\$ 65,000 <sup>(2)</sup>	\$ 92,930

(1) Tax reimbursements.

(2) Includes annual cash payment made to Mr. Leiden in order to facilitate his participation in the company’s benefits plans.



## Grants of Plan-Based Awards During 2022

The following table provides information with respect to grants of awards to each of our NEOs during 2022. Pursuant to SEC rules, (i) the threshold, target and maximum amounts payable pursuant to our 2022 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 2022 are set forth in columns under "Estimated Future Payouts under Equity Incentive Plan Awards," and (iii) the number of shares granted pursuant to other RSU awards in 2022 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)	\$ —	\$ 1,800,000	\$ 4,050,000					
	(2a) 2/1/2022				—	14,559	29,118		\$ 3,547,009
	(2b) 2/1/2022				—	14,559	29,118		\$ 0
	(3) 2/1/2022							29,117	\$ 7,093,775
Charles F. Wagner, Jr.	(1)	\$ —	\$ 577,500	\$ 1,299,375					
	(2a) 2/1/2022				—	5,131	10,262		\$ 1,250,066
	(2b) 2/1/2022				—	5,131	10,262		\$ 0
	(3) 2/1/2022							10,262	\$ 2,500,131
David M. Altshuler	(1)	\$ —	\$ 577,500	\$ 1,299,375					
	(2a) 2/1/2022				—	6,157	12,314		\$ 1,500,030
	(2b) 2/1/2022				—	6,157	12,314		\$ 0
	(3) 2/1/2022							12,314	\$ 3,000,060
Stuart A. Arbuckle	(1)	\$ —	\$ 810,000	\$ 1,822,500					
	(2a) 2/1/2022				—	7,312	14,624		\$ 1,781,423
	(2b) 2/1/2022				—	7,312	14,624		\$ 0
	(3) 2/1/2022							14,623	\$ 3,562,601
	(4) 12/6/2022				—	18,811	37,622		\$ 2,950,129
	(5) 12/6/2022							12,753	\$ 4,000,106
Jeffrey M. Leiden	(1)	\$ —	\$ —	\$ —					
	(2a) 2/1/2022				—	17,445	34,890		\$ 4,250,125
	(2b) 2/1/2022				—	—	—		\$ —
	(3) 2/1/2022							17,445	\$ 4,250,125

**(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 2022 annual cash bonus program. Actual amounts paid to each of the NEOs under this program for 2022 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 2022. 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 a fair value of 0% of the target shares in 2022. 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 2022* below.

**(3) Time-Based RSUs.** The amounts in the "All Other Stock Awards: Number of Shares of Stock or Units" column represent the number of time-based RSUs granted to the NEOs in 2022, which (other than with respect to Dr. Leiden) generally vest annually over three years.

**(4) Special One-Time 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 the special, one-time PSU award granted to Mr. Arbuckle in December 2022. Pursuant to U.S. GAAP, the grant date value of the special, one-time PSU award was based on 50% of the fair value of the target shares. This award vests if, and only if, performance objectives are achieved, as described in the footnotes to the table *Outstanding Equity Awards at Fiscal Year-End for 2022* below.

**(5) Special One-Time RSU.** The amounts in the "All Other Stock Awards: Number of Shares of Stock or Units" column represent the number of time-based RSUs granted to Mr. Arbuckle in December 2022 pursuant to a special, one-time equity award, of which 100% of the award vests in July 2025 generally subject to his continued employment.

## 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 2022

The following table provides information with respect to outstanding equity awards held by each of our NEOs on December 31, 2022, based on the closing price of \$288.78 per share of our common stock on December 30, 2022:

Name	Option Awards					Stock Awards		
	Number of Securities Underlying Unexercised Options Exercisable (shares) <sup>(1)</sup>	Number of Securities Underlying Unexercised Options (shares) <sup>(1)</sup>	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							
					4,129 <sup>(2)</sup>	\$ 1,192,373		
					19,354 <sup>(3)</sup>	\$ 5,589,048		
					29,117 <sup>(4)</sup>	\$ 8,408,407		
	Performance-based RSU							
					4,130 <sup>(5)</sup>	\$ 1,192,661		
					19,356 <sup>(6)</sup>	\$ 5,589,626		
					12,388 <sup>(7)</sup>	\$ 3,577,407		
					29,118 <sup>(8)</sup>	\$ 8,408,696		
							14,516 <sup>(9)</sup>	\$ 4,191,930
						14,559 <sup>(10)</sup>	\$ 4,204,348	
	Stock Options							
	3,058	0	\$ 155.57	2/5/2028				
	14,077	1,565	\$ 187.53	2/5/2029				
Charles F. Wagner, Jr.	Time-based RSU							
					3,441 <sup>(2)</sup>	\$ 993,692		
					7,752 <sup>(3)</sup>	\$ 2,238,623		
					10,262 <sup>(4)</sup>	\$ 2,963,460		
	Performance-based RSU							
					3,442 <sup>(5)</sup>	\$ 993,981		
					7,752 <sup>(6)</sup>	\$ 2,238,623		
					10,324 <sup>(7)</sup>	\$ 2,981,365		
					10,262 <sup>(8)</sup>	\$ 2,963,460	5,814 <sup>(9)</sup>	\$ 1,678,967
							5,131 <sup>(10)</sup>	\$ 1,481,730
	Stock Options							
	8,340	1,192	\$ 189.38	4/9/2029				
David M. Altshuler	Time-based RSU							
					4,129 <sup>(2)</sup>	\$ 1,192,373		
					7,752 <sup>(3)</sup>	\$ 2,238,623		
					12,314 <sup>(4)</sup>	\$ 3,556,037		
	Performance-based RSU							
					4,130 <sup>(5)</sup>	\$ 1,192,661		
					7,752 <sup>(6)</sup>	\$ 2,238,623		
					12,388 <sup>(7)</sup>	\$ 3,577,407		
					12,314 <sup>(8)</sup>	\$ 3,556,037	5,814 <sup>(9)</sup>	\$ 1,678,967
							6,157 <sup>(10)</sup>	\$ 1,778,018
	Stock Options							
	0	1,304	\$ 187.53	2/5/2029				

Name	Option Awards				Stock Awards			
	Number of Securities Underlying Unexercised Options Exercisable (shares) <sup>(1)</sup>	Number of Securities Underlying Unexercised Options (shares) <sup>(1)</sup>	Option Exercise Price (per share)	Option Expiration Date	Number of Shares or Units of Stock That Have Not Vested (shares)	Market Value of Shares or Units of Stock That Have Not Vested	Equity Incentive Plan Awards: Number of Unearned Shares, Units or Other Rights That Have Not Vested (shares)	Equity Incentive Plan Awards: Market or Payout Value of Unearned Shares, Units or Other Rights That Have Not Vested
Stuart A. Arbuckle	Time-based RSU							
					4,129 <sup>(2)</sup>	\$ 1,192,373		
					9,302 <sup>(3)</sup>	\$ 2,686,232		
					14,623 <sup>(4)</sup>	\$ 4,222,830		
					12,753 <sup>(11)</sup>	\$ 3,682,811		
	Performance-based RSU							
					4,130 <sup>(5)</sup>	\$ 1,192,661		
					9,302 <sup>(6)</sup>	\$ 2,686,232		
					12,388 <sup>(7)</sup>	\$ 3,577,407		
					14,624 <sup>(8)</sup>	\$ 4,223,119		
							6,976 <sup>(9)</sup>	\$ 2,014,529
							7,312 <sup>(10)</sup>	\$ 2,111,559
						18,811 <sup>(12)</sup>	\$ 5,432,241	
	Stock Options							
	15,641	1,565	\$ 187.53	2/5/2029				
Jeffrey M. Leiden	Performance-based RSU							
					31,462 <sup>(7)</sup>	\$ 9,085,596		
					34,890 <sup>(8)</sup>	\$ 10,075,534		
							10,464 <sup>(9)</sup>	\$ 3,021,794
	Stock Options							
	33,524	0	\$ 91.05	2/1/2026				
	103,550	0	\$ 86.52	2/2/2027				

- (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 RSU awards vest in three annual installments. The shares listed on the table above represent the third annual installment, which vested on February 10, 2023.
- (3) These time-based RSU awards vest in three annual installments. The shares listed on the table above represent the second and third annual installments, which vested on February 17, 2023 and are scheduled to vest February 17, 2024, respectively.
- (4) These time-based RSU awards vest in three annual installments. The shares listed on the table above represent the three annual installments, the first of which vested on February 24, 2023, and are scheduled to vest in two remaining annual installments on February 24, 2024 and 2025.
- (5) This PSU 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. In February 2021, 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 10, 2021, 2022 and 2023. The shares listed on the table above represent the final installment of the earned shares, which vested on February 10, 2023.
- (6) This PSU 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 in three equal installments on 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. The shares listed on the table above represent the second and third installments of earned shares, which vested on February 17, 2023 and are scheduled to vest on February 17, 2024, respectively.
- (7) This PSU 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 2023, our MDCC certified as to the level of performance at 200% of the number of target shares, with the number of shares reported above reflected as such. The earned shares vested on February 10, 2023.
- (8) This PSU 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 2022, with vesting of the earned shares generally occurring in three equal installments scheduled for each of February 24, 2023, 2024 and 2025. In February 2023, our MDCC certified as to the level of performance at 200% of the number of target shares, with the number of shares reported above reflected as such.
- (9) This PSU 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.
- (10) This PSU award is based on the achievement of three-year non-financial performance metrics, with the number 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 2025.
- (11) This special, one-time time-based RSU award was granted to Mr. Arbuckle in December 2022 and will cliff vest on July 1, 2025.
- (12) This special, one-time PSU award was awarded to Mr. Arbuckle in December 2022 and is based on the achievement of certain commercial milestone objectives that are different from the objectives used in our annual performance stock unit award program. The number of shares reported assumes target performance (100%). The performance conditions associated with the awards consist of multiple commercial milestones, with a payout range of zero to 200%. The specific commercial milestones are not disclosed for competitive reasons. Performance against these goals will be certified by our MDCC in July 2025.

## Option Exercises and Stock Vested for 2022

The following table sets forth the value realized by our NEOs from options to purchase common stock exercised by the NEOs during 2022 and shares of stock that vested during 2022. 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	—	\$ —	43,947	\$ 10,185,354
Charles F. Wagner, Jr.	—	\$ —	20,799	\$ 4,902,873
David M. Altshuler	25,032	\$ 3,087,009	29,620	\$ 6,866,854
Stuart A. Arbuckle	8,561	\$ 1,263,175	33,894	\$ 7,847,931
Jeffrey M. Leiden	60,342	\$ 11,485,170	66,817	\$ 15,597,344

# 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, 2022 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
<b>Reshma Kewalramani</b>					
Cash Severance Benefits	\$ —	\$ 8,400,000	\$ 11,667,000	\$ 1,800,000	\$ 1,800,000
Continuation of Employee Benefits	—	43,899	43,899	—	—
Accelerated Vesting of Stock Options	—	158,456	158,456	158,456	158,456
Accelerated Vesting of Restricted Stock Units	—	13,967,326	36,361,444	36,361,444	36,361,444
<b>TOTAL</b>	<b>\$ —</b>	<b>\$ 22,569,681</b>	<b>\$ 48,230,799</b>	<b>\$ 38,319,900</b>	<b>\$ 38,319,900</b>
<b>Charles F. Wagner, Jr.</b>					
Cash Severance Benefits	\$ —	\$ 1,402,500	\$ 1,980,000	\$ —	\$ —
Continuation of Employee Benefits	—	26,243	26,243	—	—
Accelerated Vesting of Stock Options	—	—	118,485	118,485	118,485
Accelerated Vesting of Restricted Stock Units	—	—	15,561,488	15,561,488	15,561,488
<b>TOTAL</b>	<b>\$ —</b>	<b>\$ 1,428,743</b>	<b>\$ 17,686,216</b>	<b>\$ 15,679,973</b>	<b>\$ 15,679,973</b>
<b>David M. Altshuler</b>					
Cash Severance Benefits	\$ —	\$ 1,402,500	\$ 1,980,000	\$ —	\$ —
Continuation of Employee Benefits	—	29,266	29,266	—	—
Accelerated Vesting of Stock Options	—	—	132,030	132,030	132,030
Accelerated Vesting of Restricted Stock Units	—	—	17,442,023	17,442,023	17,442,023
<b>TOTAL</b>	<b>\$ —</b>	<b>\$ 1,431,766</b>	<b>\$ 19,583,319</b>	<b>\$ 17,574,053</b>	<b>\$ 17,574,053</b>
<b>Stuart A. Arbuckle</b>					
Cash Severance Benefits	\$ —	\$ 1,710,000	\$ 2,520,000	\$ —	\$ —
Continuation of Employee Benefits	—	29,266	29,266	—	—
Accelerated Vesting of Stock Options	—	—	158,456	158,456	158,456
Accelerated Vesting of Restricted Stock Units	—	—	29,121,730	29,121,730	29,121,730
<b>TOTAL</b>	<b>\$ —</b>	<b>\$ 1,739,266</b>	<b>\$ 31,829,452</b>	<b>\$ 29,280,186</b>	<b>\$ 29,280,186</b>
<b>Jeffrey M. Leiden</b>					
Cash Severance Benefits	\$ —	\$ 13,000,000	\$ 13,000,000	\$ 6,500,000	\$ 6,500,000
Continuation of Employee Benefits	—	29,397	29,397	—	—
Accelerated Vesting of Stock Options	—	—	—	—	—
Accelerated Vesting of Restricted Stock Units	—	—	—	—	—
<b>TOTAL</b>	<b>\$ —</b>	<b>\$ 13,029,397</b>	<b>\$ 13,029,397</b>	<b>\$ 6,500,000</b>	<b>\$ 6,500,000</b>

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 \$288.78 per share (the closing price on the last trading day of 2022), 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 \$288.78 per share (the closing price on the last trading day of 2022). The value of any PSUs that have not been certified as to the level of performance by the MDCC as of December 31, 2022 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 2022 individual and company performance ratings on December 31, 2022 as they assigned in the first quarter of 2023.
- 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, 2022.

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 an NEO dies while an employee, their estate and/or beneficiaries would receive full acceleration of all outstanding equity awards, and if an NEO’s employment is terminated due to disability, they 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.

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 RSUs 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 five-year term that commenced on April 1, 2020 and provides for (i) annual equity grants over the five-year term, and (ii) eligibility to receive other benefits generally made available to our executives. Dr. Leiden's amended employment agreement provides for an annual cash payment in order to facilitate his participation in the company's benefits plans. Pursuant to his amended agreement, Dr. Leiden received \$65,000 in February 2022, received \$67,000 in February 2023, and will receive an amount to be determined by the Board or MDCC in each of 2024 and 2025. 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 the 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. Wagner, Dr. Altshuler, and Mr. Arbuckle

### Employment Agreements

The terms and conditions of Mr. Wagner's, Dr. Altshuler's, and Mr. Arbuckle'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 agreements provides that he is entitled to receive compensation as determined by our board of directors and is eligible to receive the benefits generally made available to our executives. In addition, each officer has agreed not to engage in specified competitive activities for a period of one year after the termination of his employment with us.

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

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

### Change of Control Agreements

We have a change of control agreement with each of Dr. Altshuler, Mr. Arbuckle, 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 employment within 30 days of an event giving rise to a right to terminate for good reason, subject to notice and cure provisions, and the event occurs on a date within the 90 days prior to or the 12 months after a change of control, he would be entitled to receive:

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

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

# PAY RATIO

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.

In 2022, Dr. Kewalramani's annual total compensation, as reported in the Summary Compensation Table, was \$15,864,497 and the median of the annual total compensation of all employees of the Company (other than our Chief Executive Officer) was \$238,818. The ratio of annual total compensation for Dr. Kewalramani to that of our median employee's annual total compensation was approximately 66:1.

Due to growth in our employee population, we identified a new median employee using target total annual compensation in 2022. 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, 2022) and includes:

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

The methodology included all 4,514 company employees across 21 countries as of October 1, 2022.

This pay ratio is a reasonable estimate calculated in a manner consistent with SEC rules based on our payroll and employment records and the methodology described above. Because the SEC rules for identifying the median compensated employee and calculating the pay ratio based on that employee's annual total compensation allow companies to adopt a variety of methodologies, to apply certain exclusions, and to make reasonable estimates and assumptions that reflect their compensation practices, the pay ratio reported by other companies may not be comparable to the pay ratio reported above, as other companies may have different employment and compensation practices and may utilize different methodologies, exclusions, estimates and assumptions in calculating their own pay ratios.

# PAY VERSUS PERFORMANCE

Pursuant to Item 402(v) of Regulation S-K, we are presenting information that describes the relationship between compensation actually paid, as computed under the rules prescribed by Item 402(v), to our NEOs and certain financial performance measures for the company's five most recently completed fiscal years. For more information about our executive compensation program, refer to the *Compensation Discussion and Analysis* section of this proxy statement starting on page 42.

Year	Summary Compensation Table Total for CEO <sup>(1)</sup>	Summary Compensation Table Total for CEO <sup>(2)</sup>	Compensation Actually Paid to CEO <sup>(1)(3)</sup>	Compensation Actually Paid to CEO <sup>(2)(4)</sup>	Average Summary Compensation Table Total for Non-CEO NEOs <sup>(5)</sup>	Average Compensation Actually Paid to Non-CEO NEOs <sup>(6)</sup>	Total Shareholder Return (Value of Initial Fixed \$100 Investment)		Net Income <sup>(9)</sup>	Net Product Revenue <sup>(10)</sup>
							VRTX TSR <sup>(7)</sup>	NBI TSR <sup>(8)</sup>		
2022	\$ 15,864,497	N/A	\$ 29,529,089	N/A	\$ 8,982,257	\$ 18,263,330	\$ 192.70	\$ 129.59	\$3.3 Billion	\$ 8.9 Billion
2021	\$ 15,198,856	N/A	\$ 18,341,489	N/A	\$ 7,193,835	\$ 8,969,051	\$ 146.54	\$ 144.18	\$2.3 Billion	\$ 7.6 Billion
2020	\$ 9,111,359	\$ 16,473,245	\$ 12,172,454	\$ 31,319,824	\$ 6,697,408	\$ 10,584,384	\$ 157.71	\$ 144.15	\$2.7 Billion	\$ 6.2 Billion
2019	N/A	\$ 18,789,985	N/A	\$ 37,124,321	\$ 4,668,405	\$ 7,828,475	\$ 146.10	\$ 114.02	\$1.2 Billion	\$ 4.2 Billion
2018	N/A	\$ 18,799,147	N/A	\$ 27,646,261	\$ 4,943,084	\$ 7,193,181	\$ 110.58	\$ 91.14	\$2.1 Billion	\$ 3.0 Billion

(1) This column reflects the amounts reported in the "Total" column of the Summary Compensation Table for Reshma Kewalramani, our CEO for a portion of 2020 (effective April 1, 2020), and for 2021 and 2022.

(2) This column reflects the amounts reported in the "Total" column of the Summary Compensation Table for Jeffrey Leiden, our CEO for 2018, 2019 and a portion of 2020 (until April 1, 2020).

(3) The amounts in this column reflect the Compensation Actually Paid for Reshma Kewalramani, our CEO for a portion of 2020 (effective April 1, 2020), and for 2021 and 2022. The amounts in the following table reflect the adjustments (additions/deductions) to the Summary Compensation Table Total to determine Compensation Actually Paid. Adjustments (additions/deductions) are not listed for Qualified Deferred Compensation because we do not offer these plans.

Year	Summary Compensation Table Total	Amounts Deducted from Grant Date Value of Annual Equity	Amounts Added for the Fair Value of Awards Granted During Fiscal Year	Amounts Added for Awards Granted & Vested During Fiscal Year	Amounts Add/ Deducted for Awards that Vested During Fiscal Year	Amounts Added/ Deducted for the Change in Fair Value of Awards Outstanding at Fiscal Year End <sup>(a)</sup>	Compensation Actually Paid
2022	\$ 15,864,497	\$ (10,640,784)	\$ 16,817,103	\$ —	\$ 768,712	\$ 6,719,561	\$ 29,529,089
2021	\$ 15,198,856	\$ (10,924,599)	\$ 14,344,492	\$ —	\$ (659,323)	\$ 382,063	\$ 18,341,489
2020	\$ 9,111,359	\$ (5,250,411)	\$ 6,587,268	\$ —	\$ 345,685	\$ 1,378,553	\$ 12,172,454

(a) Pursuant to applicable SEC rules, the fair values at the end of each fiscal year for the financial PSU awards were valued at 200% as of December 31, 2022, 2021, 2020 and 2019; and, the non-financial PSU award for 2020 was valued at 200%, 50% and 50% as of December 31, 2022, 2021 and 2020, respectively; the non-financial PSU award for 2021 was valued at 50% as of December 31, 2022 and 2021, respectively; the non-financial PSU award for 2022 was valued at 0% as of December 31, 2022.

(4) This amounts in this column reflect the Compensation Actually Paid for Jeffrey Leiden, our CEO for 2018, 2019 and a portion of 2020 (until April 1, 2020). The amounts in the following table reflect the adjustments to the Summary Compensation Table Total to determine Compensation Actually Paid.

Year	Summary Compensation Table Total	Amounts Deducted from Grant Date Value of Annual Equity	Amounts Added for Awards Granted During Fiscal Year	Amounts Added for Awards Granted & Vested During Fiscal Year	Amounts Add/ Deducted for Awards that Vested During Fiscal Year	Amounts Added/ Deducted for the Change in Fair Value of Awards Outstanding at Fiscal Year End <sup>(a)</sup>	Compensation Actually Paid
2020	\$ 16,473,245	\$ (13,335,168)	\$ 9,294,661	\$ 7,362,423	\$ 5,724,395	\$ 5,800,268	\$ 31,319,824
2019	\$ 18,789,985	\$ (13,906,720)	\$ 17,220,100	\$ 509,338	\$ 4,201,319	\$ 10,310,299	\$ 37,124,321
2018	\$ 18,799,147	\$ (14,044,261)	\$ 15,925,396	\$ 541,085	\$ 1,872,780	\$ 4,552,114	\$ 27,646,261

(a) Pursuant to applicable SEC rules, the fair values at the end of each fiscal year for the financial PSU awards were valued at 200% as of December 31, 2020, 2019, 2018 and 2017; and, the non-financial PSU award for 2016 was valued at 200% as of December 31, 2018 and 2017; the non-financial PSU award for 2017 was valued at 200% as of December 31, 2019, 2018 and 2017, respectively; the non-financial PSU award for 2018 was valued at 200%, 100% and 100% as of December 31, 2020, 2019 and 2018, respectively; the non-financial PSU award for 2019 was valued at 100% and 50% as of December 31, 2020 and 2019, respectively; the non-financial PSU award for 2020 was valued at 50% as of December 31, 2020.

(5) This column reflects the average of the amounts reported in the "Total" column of the Summary Compensation Table for our NEOs as a group (excluding our CEO or CEOs, in the case of 2020) for each of the periods presented. The NEOs included for purposes of computing the amounts in this column were as follows: for 2022, Mr. Wagner, Dr. Altshuler, Mr. Arbuckle, and Dr. Leiden; for 2021, Mr. Wagner, Mr. Arbuckle, Dr. Leiden, and Nia Tatsis; for 2020, Mr. Wagner, Dr. Altshuler, Mr. Arbuckle, and Michael Parini; for 2019, Ms. Kewalramani, Mr. Wagner, Mr. Arbuckle, Amit Sachdev, Paul Silva and Ian Smith; and for 2018, Mr. Arbuckle, Mr. Parini, Mr. Sachdev, Jeffrey Chodakewitz, Thomas Graney, and Mr. Smith.

(6) This column reflects the average of the Compensation Actually Paid for our NEOs as a group (excluding our CEO or CEOs, in the case of 2020) for each of the periods presented. The amounts in the following table reflect the adjustments to the Summary Compensation Table Total to determine Compensation Actually Paid. The NEOs included for purposes of computing the amounts in this column are listed in footnote (5) above.

Year	Summary Compensation Table Total	Amounts Deducted from Grant Date Value of Annual Equity	Amounts Added for the Fair Value of Awards Granted During Fiscal Year	Amounts Added for Awards Granted & Vested During Fiscal Year	Amounts Add/Deducted for Awards that Vested During Fiscal Year	Amounts Added/Deducted for Change in Fair Value of Awards Outstanding at Fiscal Year End <sup>(a)</sup>	Compensation Actually Paid
2022	\$ 8,982,257	\$ (7,261,199)	\$ 9,489,852	\$ 1,062,531	\$ 538,093	\$ 5,451,796	\$ 18,263,330
2021	\$ 7,193,835	\$ (5,687,759)	\$ 6,319,320	\$ 1,125,037	\$ (778,741)	\$ 797,359	\$ 8,969,051
2020	\$ 6,697,408	\$ (4,812,998)	\$ 6,038,487	\$ —	\$ 1,048,920	\$ 1,612,567	\$ 10,584,384
2019	\$ 4,668,405	\$ (3,093,700)	\$ 4,011,590	\$ 103,204	\$ 866,837	\$ 1,272,139	\$ 7,828,475
2018	\$ 4,943,084	\$ (3,720,284)	\$ 4,253,936	\$ 143,306	\$ 474,492	\$ 1,098,647	\$ 7,193,181

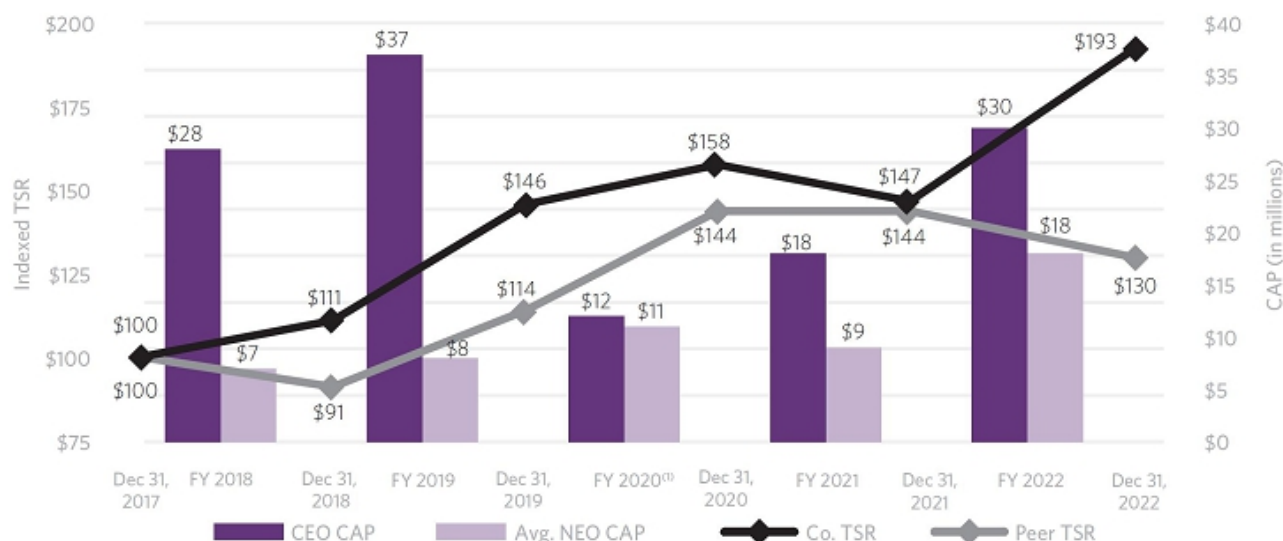
(a) Pursuant to applicable SEC rules, the fair values at the end of each fiscal year for the financial PSU awards were valued at 200% as of December 31, 2022, 2021, 2020, 2019, 2018 and 2017; and, the non-financial PSU award for 2016 was valued at 200% as of December 31, 2018 and 2017; the non-financial PSU award for 2017 was valued at 200% as of December 31, 2019, 2018 and 2017, respectively; the non-financial PSU award for 2018 was valued at 200%, 100% and 100% as of December 31, 2020, 2019 and 2018, respectively; the non-financial PSU award for 2019 was valued at 200%, 100% and 50% as of December 31, 2021, 2020 and 2019; the non-financial PSU award for 2020 was valued at 200%, 50% and 50% as of December 31, 2022, 2021 and 2020; the non-financial PSU award for 2021 was valued at 50% as of December 31, 2022 and 2021; the non-financial PSU award for 2022 was valued at 50% as of December 31, 2022.

- (7) This column represents our cumulative total shareholder return ("TSR") under SEC rules from December 29, 2017, the last trading day before the start of 2018, through the last trading day for the applicable fiscal year in the table. TSR is calculated by dividing the sum of the cumulative amount of dividends for the measurement period, assuming dividend reinvestment, and the difference between our share price at the end and the beginning of the measurement period by our share price at the beginning of the measurement period.
- (8) This column represents the TSR of the NBI, our selected peer group as discussed above, under SEC rules from December 29, 2017, the last trading day before the start of 2018, through the last trading day for the applicable fiscal year in the table, assuming reinvestment of dividends and weighted according to the respective companies' stock market capitalization at the beginning of each period for which a return is indicated.
- (9) This column reflects net income as reported for each year in our Annual Report on Form 10-K.
- (10) This column reflects net product revenue as reported for each year in our Annual Report on Form 10-K. For purposes of the table above, we have selected net product revenue as the financial performance measure representing the most important financial performance measure used to link executive compensation actually paid to our financial performance in the most recently completed fiscal year. Please see the *Compensation Discussion and Analysis* section beginning on page 42 of this proxy statement for additional information.

## Relationship Between Pay and Performance

The relationships between certain specified measures in the pay-versus-performance table over the five most recently completed fiscal years are provided below.

### Compensation Actually Paid vs TSR



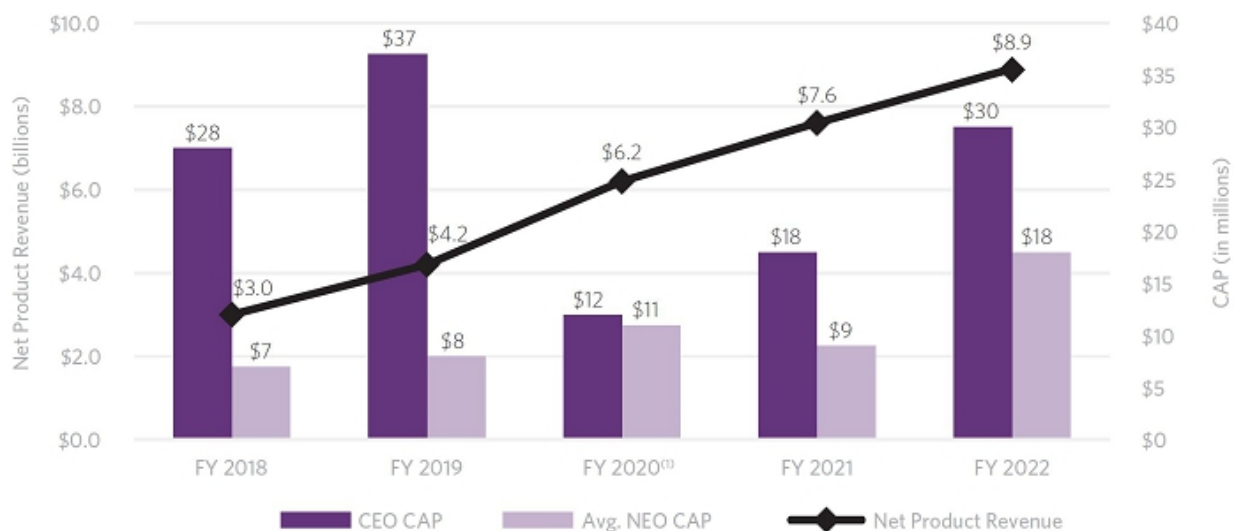
(1) 2020 Compensation Actually Paid represented here reflects 2020 compensation of Reshma Kewalramani, our current CEO, and excludes 2020 compensation paid to Jeffrey Leiden, our former CEO.

### Compensation Actually Paid vs Net Income



(1) 2020 Compensation Actually Paid represented here reflects 2020 compensation of Reshma Kewalramani, our current CEO, and excludes 2020 compensation paid to Jeffrey Leiden, our former CEO.

### Compensation Actually Paid vs Net Product Revenue



(1) 2020 Compensation Actually Paid represented here reflects 2020 compensation of Reshma Kewalramani, our current CEO, and excludes 2020 compensation paid to Jeffrey Leiden, our former CEO.

## List of Performance Measures

The tabular list below includes the three financial and non-financial performance measures that represent the most important performance measures used to link compensation actually paid to company performance in 2022. The performance measures included in this list are not ranked by relative importance.

### Performance Measures Used to Link Executive Compensation Actually Paid to Company Performance for the Most Recently Completed Fiscal Year

Net Product Revenue
Pipeline Progression <sup>(1)</sup>
Adjusted Non-GAAP EBITDA <sup>(2)</sup>

(1) Pipeline progression is a non-financial performance measure used to link executive compensation to company performance, as described in *Goals – Pipeline Growth (Late and Early Stage)* and *Performance Units Results Table*.

(2) Adjusted non-GAAP EBITDA is a financial performance measure used to link compensation actually paid to company financial performance, as described in *Goals – Financial Strength*. We calculated adjusted non-GAAP EBITDA by excluding interest, taxes, depreciation and amortization expenses, as well as AIPR&D, from net income, as well as excluding each of our non-GAAP adjustments to pre-tax income included in our "Reconciliation of GAAP to Non-GAAP Net Income" in our quarterly earnings release filed on February 7, 2023 for the twelve months ended December 31, 2022.

# SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT

The following table sets forth information regarding beneficial ownership of our common stock as of March 23, 2023, by:

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

Name and Address	Shares Beneficially Owned <sup>(1)</sup>	Percentage of Total <sup>(2)</sup>
<b>BlackRock, Inc.</b> <sup>(3)</sup> 55 East 52nd Street New York, New York 10055	24,241,437	9.4%
<b>The Vanguard Group</b> <sup>(4)</sup> 100 Vanguard Blvd. Malvern, Pennsylvania 19355	21,546,903	8.4%
<b>FRM LLC</b> <sup>(5)</sup> 245 Summer Street Boston, Massachusetts 02210	17,876,774	6.9%
<b>Capital World Investors</b> <sup>(6)</sup> 333 South Hope Street, 55th Floor Los Angeles, California 90071	12,939,319	5.0%
<b>Sangeeta N. Bhatia</b> <sup>(7)</sup>	5,978	*
<b>Lloyd Carney</b> <sup>(7)</sup>	4,150	*
<b>Alan Garber</b> <sup>(7)</sup>	30,562	*
<b>Terrence C. Kearney</b> <sup>(7)</sup>	47,885	*
<b>Reshma Kewalramani</b> <sup>(7)</sup>	63,518	*
<b>Yuchun Lee</b> <sup>(7)</sup>	60,988	*
<b>Jeffrey M. Leiden</b> <sup>(7)</sup>	185,863	*
<b>Margaret G. McGlynn</b> <sup>(7)</sup>	42,803	*
<b>Diana McKenzie</b> <sup>(7)</sup>	6,118	*
<b>Bruce I. Sachs</b> <sup>(7)</sup>	136,591	*
<b>Suketu Upadhyay</b> <sup>(7)</sup>	1,793	*
<b>David M. Altshuler</b> <sup>(7)</sup>	—	
<b>Stuart A. Arbuckle</b> <sup>(7)</sup>	21,138	*
<b>Charles F. Wagner, Jr.</b> <sup>(7)</sup>	30,035	*
<b>All directors and executive officers as a group (19 persons)</b> <sup>(7)</sup>	827,137	0.3%

\* Less than 1%

(1) Beneficial ownership of shares for purposes of this proxy statement is determined in accordance with applicable SEC rules and includes shares of common stock as to which a person has or shares voting power and/or investment power, including dispositive power. The persons and entities named in the table have sole voting and investment power with respect to all shares shown as beneficially owned by them, except as noted below. Information with respect to persons other than directors and executive officers is based solely upon Schedules 13G and amendments thereto filed with the SEC in the first quarter of 2023.

(2) Percentage ownership is based on 257,589,373 shares of our common stock outstanding on March 23, 2023.

(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 22,090,153 shares and sole dispositive power with respect to 24,241,437 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 381,939 shares, sole dispositive power with respect to 20,471,142 shares, and shared dispositive power with respect to 1,075,761 shares.



- (5) Includes shares beneficially owned by clients of one or more investment advisers directly or indirectly owned by FMR LLC, certain of its subsidiaries and affiliates, and other companies. FMR LLC has sole voting power with respect to 16,928,505 shares and sole dispositive power with respect to 17,876,774 shares.
- (6) Includes shares beneficially owned by clients of one or more investment advisers directly or indirectly owned by Capital World Investors, certain of its subsidiaries and affiliates, and other companies. Capital World Investors has sole voting power with respect to 12,893,656 shares and sole dispositive power with respect to 12,939,319 shares.
- (7) Includes shares that may be acquired upon the exercise of options exercisable within 60 days after March 23, 2023, unvested RSUs vesting within 60 days of March 23, 2023 and deferred stock units as of March 23, 2023 issued pursuant to our Non-Employee Director Deferred Compensation Plan, as follows:

	<b>Stock Options Exercisable Within 60 Days of March 23, 2023</b>	<b>Unvested Restricted Stock Units Vesting Within 60 Days of March 23, 2023</b>	<b>Deferred Stock Units as of March 23, 2023</b>
Sangeeta N. Bhatia	1,938	1,449	—
Lloyd Carney	—	1,449	—
Alan Garber	24,672	—	—
Terrence C. Kearney	41,349	725	—
Reshma Kewalramani	18,700	—	—
Yuchun Lee	57,312	—	1,801
Jeffrey M. Leiden	137,074	—	—
Margaret G. McGlynn	37,016	—	5,609
Diana McKenzie	—	—	4,476
Bruce I. Sachs	81,112	—	14,269
Suketu Upadhyay	—	1,558	235
David Altshuler	—	—	—
Stuart A. Arbuckle	17,206	—	—
Charles F. Wagner, Jr.	9,532	—	—
All directors and executive officers as a group (19 persons)	488,844	8,212	26,390

# OTHER INFORMATION

## Other Matters

The 2023 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 2023 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 2024 Annual Meeting

**Shareholder Proposals.** In order to submit a shareholder proposal to be considered for inclusion in our proxy statement for our 2024 annual meeting of shareholders, a shareholder must submit the proposal in accordance with Rule 14a-8 of the Exchange Act and such proposal must be received by our corporate secretary by no later than December 8, 2023. To introduce a proposal for presentation at the 2024 annual meeting of shareholders (other than a shareholder proposal included in the proxy statement in accordance with Rule 14a-8 of the Exchange Act), our by-laws require that a shareholder must provide advanced written notice of such proposal so that our corporate secretary receives such proposal no earlier than January 18, 2024 and no later than February 16, 2024. Proposals should be sent to the attention of our corporate secretary at our offices at 50 Northern Avenue, Boston, Massachusetts 02210.

**Director Nominations at the 2024 Annual Meeting.** If a shareholder wishes to nominate a candidate for election to our board of directors at the 2024 annual meeting of shareholders, but is not eligible or does not elect to have such candidate included in the proxy statement for our 2024 annual meeting of shareholders, such nomination may be submitted to our corporate secretary no earlier than January 18, 2024 and no later than February 16, 2024, and must include the information required under our by-laws including but not limited to:

- 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 personally 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 2024 annual meeting of shareholders, and is eligible and elects to have such candidate included in the proxy statement for our 2024 annual meeting of shareholders pursuant to our proxy access by-law, such nomination must be submitted to our corporate secretary no earlier than January 18, 2024 and no later than February 16, 2024, and must include, in addition to the information set forth above for other shareholder nominees, the information set forth in Sections 13 and 14 of Article I and Section 8 of Article II of our by-laws.

If a shareholder wishes to solicit proxies for a shareholder nominee for election to our board at the 2024 annual meeting of shareholders pursuant to Rule 14a-19 of the Exchange Act, notice must be submitted to our corporate secretary no later than March 18, 2024. Such solicitation and notice must comply with the requirements of Rule 14a-19 of the Exchange Act and our by-laws.

**Discretionary Voting Authority.** If we do not receive notice of a matter to be considered for presentation at the 2024 annual meeting of shareholders by the dates specified in our advanced notice provisions applicable to such matter (or, in the absence of such a provision, by February 21, 2024), our proxy holders will have the right to exercise discretionary voting authority with respect to such matter without including such matter in our proxy materials.

## Shareholder Communications to the Board

Any shareholder who wishes to address questions regarding our business directly with our board of directors, or any individual director(s), should direct such questions, in writing, in care of our corporate secretary, to our offices at 50 Northern Avenue, Boston, Massachusetts 02210. All substantive communications shall be reviewed by our corporate secretary and forwarded or reported to the chair of the CGNC, the lead independent director 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 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, as amended, including, without limitation, statements regarding our marketed products and pipeline therapies, particularly with respect to benefits and safety, potential regulatory submissions and approvals, expected clinical development plans and timing, and expectations regarding commercialization of certain pipeline therapies 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 therapies. 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, 2022 and available through the company’s website at [www.vrtx.com](http://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.

## Equity Compensation Plan Information

As of February 28, 2023, there were 17,106,396 shares remaining available for award under our Amended and Restated 2013 Stock and Option Plan (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, 2023, under our equity plans:

- Stock options covering 2,345,537 shares of our common stock, with a weighted average exercise price of \$149.62 and a weighted average remaining term of 4.7 years, were outstanding; and
- Unvested PSUs and RSUs covering 4,322,848 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, 2022. 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, 2022. Accordingly, the figures in the table below do not reflect the equity grants made to our employees under the 2013 Plan, since December 31, 2022.

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)
<b>Equity Compensation Plans Approved by Shareholders<sup>(1)</sup></b>	6,666,806 <sup>(2)</sup>	\$ 146.11 <sup>(3)</sup>	21,211,177 <sup>(4)</sup>
Equity Compensation Plans Not Approved by Shareholders	—	—	—
<b>TOTAL</b>	<b>6,666,806</b>		<b>21,211,177</b>

(1) These plans consist of the 2013 Plan, the Amended and Restated 2006 Stock and Option 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, RSUs, PSUs, and deferred stock units granted under shareholder approved plans, as of December 31, 2022, and includes 2,413,233 options granted under the 2013 Plan, 2,888,430 RSUs granted under the 2013 Plan, 1,226,960 PSUs (assuming the maximum number of PSUs will be earned) granted under the 2013 Plan, 24,598 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 113,585 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 RSUs, 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 19,695,337 shares available for future issuance under the 2013 Plan and 1,515,840 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, 2023.

# FREQUENTLY ASKED QUESTIONS REGARDING THE ANNUAL MEETING

## What is the Purpose of the Annual Meeting?

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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;
- To hold an advisory vote on our 2022 named executive officer compensation; and
- To hold an advisory vote on the frequency of future advisory votes on our executive compensation.

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?

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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, Jonathan Biller, and Joy Liu to serve as proxies at the annual meeting.

## What is a Proxy Statement?

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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?

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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 6, 2023, 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, 2022 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?

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**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?

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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/MS22Z5F> 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.

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.

The meeting webcast will begin promptly at 9:00 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.

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

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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. 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 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](mailto: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 12, 2023. 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 annual meeting virtually.

## What if I have Trouble Accessing the Virtual Annual Meeting?

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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?

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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?

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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](http://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/MS2Z5F>. 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?

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The record date for the annual meeting is March 23, 2023 and was established by our board of directors. On the record date, there were 257,589,373 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?

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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](http://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?

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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, 2023;
- FOR our 2022 named executive officer compensation;
- 1 YEAR for frequency of future advisory votes on our named executive compensation program.

## Are My Shares Voted if I Do Not Provide a Proxy?

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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 advisory vote with respect to the frequency of advisory votes on our named executive compensation program 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?

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### 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" their 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 personally 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 personally 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: Advisory Vote on the Frequency of Future Advisory Votes on Executive Compensation

To be approved, this proposal must receive an affirmative vote from shareholders present personally 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?

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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](http://sec.gov/spotlight/proxymatters.shtml).

# APPENDIX A NON-GAAP FINANCIAL MEASURES

In this proxy statement, our financial results are provided in accordance with accounting principles generally accepted in the United States (GAAP). We also include non-GAAP operating margin. Our non-GAAP operating income for 2022 excluded (i) stock-based compensation expense, (ii) a decrease in the fair value of contingent consideration, (iii) acquisition-related costs, and (iv) an intangible asset impairment charge. 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, 2022</u>
	(in millions, except percentages)
<b>Net product revenues</b>	\$8,930.7
<b>GAAP operating income</b>	\$4,307.4
Stock-based compensation expense	491.3
Decrease in fair value of contingent consideration	(57.5)
Intangible asset impairment charge	13.0
Acquisition-related costs	38.8
<b>Non-GAAP operating income</b>	\$4,793.0
<b>GAAP operating margin</b>	48%
<b>Non-GAAP operating margin</b>	54%

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 helps 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.



[www.vrtx.com](http://www.vrtx.com)

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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](http://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/MS225F>

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 listed below.

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 - Jeffrey Leiden	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
07 - Diana McKenzie	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	08 - Bruce Sachs	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	09 - Suketu Upadhyay	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>



### The Board of Directors recommends a vote FOR Proposals 2 and 3, and 1 YEAR for Proposal 4.

2. Ratification of Ernst & Young LLP as independent Registered Public Accounting firm for the year ending December 31, 2023.  For  Against  Abstain
3. Advisory vote to approve named executive office compensation.  For  Against  Abstain
4. Advisory vote on the frequency of future advisory votes on executive compensation.  1 Year  2 Years  3 Years  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 P C F



The 2023 Annual Meeting of Shareholders of Vertex Pharmaceuticals Incorporated  
will be held on  
May 17, 2023, at 9:00 a.m. Eastern Time  
virtually via the Internet at  
<https://meetnow.global/MS225F>

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 17, 2023:  
The Notice of Annual Meeting of Shareholders, Proxy Statement and Annual Report are available at  
<http://www.envisionreports.com/vrtx>

	<b>Small steps make an impact.</b> Help the environment by consenting to receive electronic delivery. Sign up at <a href="http://www.envisionreports.com/VRTX">www.envisionreports.com/VRTX</a>	
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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 17, 2023**

**THIS PROXY IS SOLICITED ON BEHALF OF THE BOARD OF DIRECTORS**

The undersigned does hereby constitute and appoint Jeffrey Leiden, Reshma Kewalramani, Jonathan Biller and Joy Liu, 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 17, 2023, at 9:00 A.M. Eastern Time, via live audio webcast available at <https://meetnow.global/MS225F> 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 Director Nominees in proposal 1, FOR proposals 2 and 3, and 1 YEAR for proposal 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.

