UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

SCHEDULE 14A

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

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

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

VERTEX
THE SCIENCE of POSSIBILITY

Vertex Pharmaceuticals Incorporated

(Name of Registrant as Specified In Its Charter)

Payment of Filing Fee (Check all boxes that apply):	
☒	**No fee required.**
☐	**Fee paid previously with preliminary materials.**
☐	**Fee computed on table in exhibit required by Item 25(b) per Exchange Act Rules 14a-6(i)(1) and 0-11.**

VERTEX®

2025 PROXY STATEMENT

Vertex Pharmaceuticals Incorporated

Notice of Annual Meeting of Shareholders
to be held on May 14, 2025

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A Letter from our Executive Chairman and Chief Executive Officer

Dear Shareholders:

2024 marked a year of tremendous growth for Vertex and excellent performance across the business, with our commercial, research & development, and business development functions leading the way. The important advances of 2024, combined with our continued strong financial performance, have ushered in a new era of commercial diversification for Vertex that we believe will benefit both patients and shareholders for many years to come.

Our portfolio of marketed therapies now consists of seven products across three disease areas. In cystic fibrosis ("CF"), we extended our leadership by reaching younger patients, patients in new geographies, and securing additional regulatory approvals. Importantly, we obtained U.S. and U.K. approval for ALYFTREK, our fifth cystic fibrosis transmembrane conductance regulator ("CFTR") modulator. ALYFTREK is a once-daily oral medicine proven to be non-inferior to TRIKAFTA on lung function and superior to TRIKAFTA in correcting CFTR protein function as measured by sweat chloride levels. ALYFTREK is approved to treat even more mutations than TRIKAFTA and its clinical profile may set a new bar in CF treatment. Beyond CF, we diversified our commercial footprint with the global launch of CASGEVY for severe sickle cell disease and transfusion-dependent beta thalassemia, having obtained approvals in the U.S., Europe, Canada, and the Middle East for this transformative, first-in-class CRISPR/Cas9 gene-edited cell therapy. In addition to the CASGEVY launch and the approval of ALYFTREK, we also filed for U.S. approval for JOURNAVX, the first new class of acute pain medicine and the first non-opioid for acute pain in more than two decades. In early 2025, JOURNAVX was approved in the U.S. with a broad indication for moderate-to-severe acute pain, and the commercial launch is now underway.

Our investment in research and development also continued to deliver in 2024. We advanced four programs into Phase 3 clinical development: inaxaplin for APOL-1-mediated kidney disease, suzetrigine for diabetic peripheral neuropathy, zimislecel for type 1 diabetes, and povetacicept for IgA nephropathy ("IgAN"). Our earlier stage pipeline also continued to make rapid progress, including our programs in CF, pain, autosomal dominant polycystic kidney disease and myotonic dystrophy type 1. In total, our clinical-stage pipeline includes over 10 disease areas and utilizes multiple modalities, including small molecules, biologics, and cell and genetic therapies. We believe these rapid advances will lead to multiple first-in-class and best-in-class medicines for patients and continue to drive increasing commercial diversification.

From a revenue perspective, we reached a new milestone in 2024, with net product revenue achieving just over $11 billion, representing a 12% increase from 2023 and our tenth consecutive year of double-digit revenue growth. We continue to invest significantly in innovation, both internal and external, to support our differentiated research and development approach. Significantly, in 2024 we acquired Alpine Immune Sciences, Inc. and its Phase-3-ready lead asset, povetacicept, which holds the promise to be a "pipeline-in-a-product" for multiple autoimmune diseases. Povetacicept has the potential to become a transformative medicine in IgAN and a number of other B cell-mediated autoimmune diseases.

As we advance our work to discover, develop and commercialize transformative medicines for people with serious diseases, we continue to support patients, our local communities, and our employees. Last year, Vertex celebrated its 16th annual service event with a global Week of Service, during which 70% of Vertexians participated, contributing more than 10,900 hours of volunteer work across more than 170 projects in 22 countries. In addition, Vertex and the Vertex Foundation provided more than $52 million in charitable donations towards education, innovation, health, and our local communities. We continue to focus on recruiting, retaining, and developing highly-qualified employees, promoting our employees' well-being and professional development, and nurturing our unique culture. Our strengths as an organization continue to be recognized externally and in 2024, Vertex was named to *Fortune* 100 Best Companies to Work For, *Time* 100 Most Influential Companies, *U.S. News & World Report* Best Companies to Work For, and *Forbes* America's Best Companies.

We are in a new and exciting era of commercial, geographic and pipeline diversification, fueled by the consistent execution of our corporate strategy and underpinned by our culture. We are poised to continue to deliver strong financial results and durable long-term growth. As Executive Chairman and Chief Executive Officer, we are excited about the opportunity to continue our work with the 6,000+ Vertexians across the globe to deliver on the promise of our marketed therapies and pipeline. We remain committed to continuing to execute on the serial innovation strategy that has been essential to Vertex's successes in delivering transformative medicines to patients who need them.

Sincerely,

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

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

VERTEX

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NOTICE OF ANNUAL MEETING OF SHAREHOLDERS

Wednesday, May 14, 2025

9:00 a.m. (Eastern Time)

https://meetnow.global/MXD5MZM

Dear Shareholders:

You are invited to attend the Vertex Pharmaceuticals Incorporated 2025 Annual Meeting of Shareholders. At the annual meeting, shareholders will vote:

- to elect the eleven 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 2026 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 2025;
- to hold an advisory vote on our 2024 named executive officer compensation; and
- on one proposal submitted by a shareholder, if properly presented at the meeting.

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

MEETING INFORMATION

PROXY MATERIALS:

We are using the "Notice and Access" method of providing proxy materials to you via the Internet. We are mailing to you a Notice of Internet Availability of Proxy Materials instead of paper copies of this notice, our proxy statement, and our Annual Report on Form 10-K for the year ended December 31, 2024 ("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 ANNUAL MEETING WILL FACILITATE SHAREHOLDER ATTENDANCE AND PARTICIPATION BY ENABLING SHAREHOLDERS TO PARTICIPATE FROM ANY LOCATION AND AT NO COST. YOU WILL BE ABLE TO PARTICIPATE IN THE MEETING ONLINE, VOTE YOUR SHARES ELECTRONICALLY, AND SUBMIT YOUR QUESTIONS DURING THE MEETING BY VISITING HTTPS://MEETNOW.GLOBAL/MXD5MZM. 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. 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 9, 2025. 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 14, 2025.

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 17, 2025 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 3, 2025

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, 2024 are first being made available to holders of record of our common stock on or about April 3, 2025. These materials are available to holders of record of our common stock at www.envisionreports.com/VRTX and to beneficial holders of our common stock at www.edocumentview.com/VRTX.

SUMMARY

2024 marked another year of tremendous growth for Vertex across research, development, and commercialization, along with excellent financial performance. Our strategy of investing in scientific innovation to create transformative medicines for people with serious diseases, with a focus on specialty markets, continued to deliver. We now have seven approved medicines: five that treat cystic fibrosis ("CF"), one that treats severe sickle cell disease ("SCD") and transfusion-dependent beta thalassemia ("TDT"), and one that treats moderate-to-severe acute pain. In 2024, we extended our leadership in CF through the approval of a new product, ALYFTREK, and by continuing to reach more people than ever before with our portfolio of CF medicines. We began to diversify our revenues through the global launch of CASGEVY, our gene-edited cell therapy for the treatment of SCD and TDT. And, we recently received a landmark approval in the U.S. for JOURNAVX, a first-in-class non-opioid treatment for moderate-to-severe acute pain. In addition, our broad and diverse pipeline continued to make significant progress, with four potentially transformative medicines advancing to pivotal development. Additionally, we acquired Alpine Immune Sciences, Inc. ("Alpine") and its Phase 3 ready lead asset, povetacicept, adding the promise of a "pipeline-in-a-product" for multiple autoimmune diseases to our robust clinical portfolio.

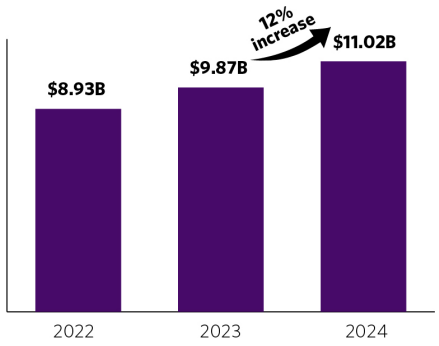
From a financial perspective, our outstanding performance in 2024 resulted in net product revenues of $11.02 billion, representing 12% growth versus 2023, our tenth consecutive year of double-digit growth, and the continued strength of our balance sheet, ending the year with $11.2 billion in cash and investments. In summary, we are well-positioned to continue to create long-term value for both patients and shareholders, with a marketed product portfolio of transformative medicines for CF, SCD, TDT, and acute pain, and a clinical pipeline spanning more than ten disease areas and multiple therapeutic modalities including small molecules, biologics, and genetic and cell therapies.

Financial Performance

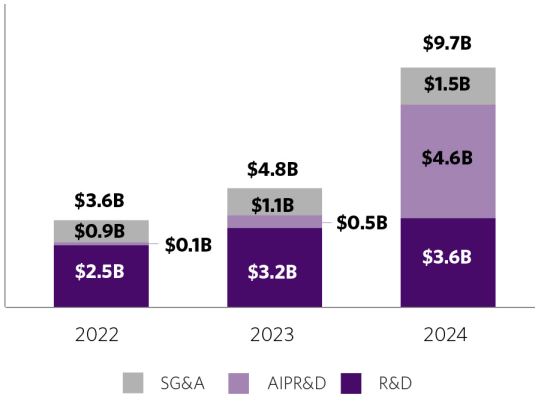
In 2024, sales of TRIKAFTA/KAFTRIO continued to drive our financial performance. We expect that our recently approved medicines, CASGEVY, ALYFTREK and JOURNAVX, will drive both continued revenue growth and diversification in 2025 and beyond.

- Our net product revenues increased to $11.02 billion in 2024, an increase of 12% or more than $1.1 billion, from our 2023 net product revenues.
- Our total research and development ("R&D"), acquired in-process research and development ("AIPR&D") and selling, general and administrative ("SG&A") expenses increased to $9.7 billion compared to $4.8 billion in 2023. This increase was primarily due to higher AIPR&D, including $4.4 billion related to our acquisition of Alpine, continued investment to support additional therapies in mid-to-late stage development, and increased commercial investments to support launches of our newly-approved therapies globally.

INCREASING NET PRODUCT REVENUES



TOTAL R&D, AIPR&D AND SG&A EXPENSES



Marketed Products

Our differentiated R&D strategy has delivered more than a decade of leadership in CF. It also delivered the historic, global approvals for CASGEVY, the first CRISPR-based gene-edited cell therapy to be approved for people with SCD or TDT. And more recently, U.S. approval of JOURNAVX, the first and only non-opioid pain signal inhibitor, representing the first new class of pain medicines approved in over 20 years.

Cystic Fibrosis

In CF, our goal for more than 20 years has been to address the underlying cause of the disease and to bring more people with the disease to normal levels of CFTR function. We have continued to serially innovate in the years since the 2012 approval of KALYDECO, which was first approved to treat a CF population of approximately 1,000 people in the U.S. Today, we have five approved CF medicines that treat nearly three-quarters of the approximately 94,000 people with CF in the U.S., Europe, Australia, and Canada. Additionally, we continue to secure formal reimbursement in multiple additional countries that collectively comprise approximately 15,000 additional people with CF. Approximately 10,000 of those additional people with CF are eligible for treatment with CFTR modulators. We previously served many of these markets through named patient sales.

Notable progress since the beginning of 2024 includes:

- In December 2024, the U.S. Food and Drug Administration (the "FDA") approved ALYFTREK (vanzacaftor/tezacaftor/deutivacaftor), our once-daily, “next generation 2.0” combination CFTR modulator for the treatment of people with CF 6 years of age and older who have at least one F508del mutation or another responsive mutation in the CFTR gene. In March 2025, the U.K. Medicines and Healthcare products Regulatory Agency (“MHRA”) also approved ALYFTREK.
- Regulatory submissions for ALYFTREK, which are currently under review in the European Union (“E.U.”), Canada, Switzerland, Australia, and New Zealand.
- In December 2024, the FDA approved the expanded use of TRIKAFTA for the treatment of people with CF with 94 additional non-F508del CFTR mutations. TRIKAFTA is now approved in the U.S. for a total of 272 CFTR mutations. In February 2025, the European Medicines Agency (“EMA”) adopted a positive Committee for Medicinal Products for Human Use (“CHMP”) opinion for the label expansion of KAFTRIO for the treatment of people with additional non-F508del CFTR mutations.
- We entered into an extended long-term reimbursement agreement with National Health Services (“NHS”) England providing access to KAFTRIO, SYMKEVI and ORKAMBI, and continued access to KALYDECO, for existing and future eligible CF patients in England. We have entered into similar reimbursement agreements in Wales, Northern Ireland and Scotland. These reimbursement agreements include access to any future license extensions of these medicines.
- KAFTRIO is now reimbursed in all 27 countries of the E.U.

Sickle Cell Disease and Transfusion-Dependent Beta Thalassemia

2024 was a foundational year for the commercial launch of CASGEVY, following approvals in the U.S., the E.U., the United Kingdom (the “U.K.”), the Kingdom of Saudi Arabia (“Saudi Arabia), the Kingdom of Bahrain (“Bahrain”), the United Arab Emirates (the “UAE”), Canada, and Switzerland. We estimate approximately 60,000 people with severe SCD or TDT are or could become eligible for CASGEVY in these jurisdictions. Our global launch for CASGEVY continues to focus on countries with high unmet medical need and infrastructure to support treatment with this CRISPR/Cas9-based gene-editing therapy, including the U.S., the Middle East, and major markets in Europe. We are working with authorized treatment centers (“ATCs”) to enable patient initiation, supporting the patient journey through infusion with CASGEVY, working with payors to secure broad and equitable access for patients and expanding our manufacturing and supply chain to meet growing patient demand. Our teams are also focused on educating patients, physicians and policymakers on the treatment journey and CASGEVY clinical data, as appropriate.

Notable progress since the beginning of 2024 includes:

- CASGEVY is now approved in the U.S., the E.U., the U.K., Saudi Arabia, Bahrain, the UAE, Canada and Switzerland for people 12 years of age and older with SCD or TDT.
- We have activated more than 50 authorized treatment centers globally, and more than 50 patients have initiated cell collection.
- In the U.S., we have broad coverage of CASGEVY with both private and public payers. In addition, we reached an agreement with the Centers for Medicare & Medicaid Services to participate in its cell and gene therapy access model, which may enable additional access mechanisms for states and authorized treatment centers.
- In the Middle East, we have reached hospital-based reimbursement for people with SCD or TDT in Saudi Arabia, and national reimbursement for eligible people in Bahrain. We are actively working to expand access to CASGEVY across Europe and the Middle East.
- We entered into a reimbursement agreement with NHS England for eligible people with SCD to access CASGEVY, consistent with the reimbursement agreement reached in August 2024 for eligible people with TDT.
- The Italian Medicines Agency has approved early access for CASGEVY, on a case-by-case basis, for the treatment of people with TDT and SCD.

Acute Pain

In January 2025, the FDA approved JOURNAVX for the treatment of moderate-to-severe acute pain in adults. JOURNAVX is a first-in-class, oral pain signal inhibitor that is highly selective for NaV1.8 voltage-gated sodium channels. Through this mechanism, JOURNAVX provides effective relief of pain without evidence of the limitations of other currently available therapies, including the addictive potential of opioids. Our launch strategy for JOURNAVX in the U.S. focuses on securing broad access for people with acute pain, educating patients and physicians on the clinical profile of JOURNAVX, and making investments to provide seamless treatment experiences for physicians and people with acute pain. We are engaging with payors and formulary decision-makers to secure reimbursement and access to JOURNAVX. We have secured broad stocking agreements at various national retail pharmacies as well as regional chains to facilitate broad availability of JOURNAVX. We have also established financial and co-pay assistance programs for patients that will support access to JOURNAVX.

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 advances in the understanding of human disease and the science of therapeutics to dramatically advance human health. This strategy was designed to deliver transformative medicines for serious diseases at high rates of speed and success, and it has delivered just that. 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 and/or best-in-class, therapies to patients. In addition to expanding our small molecule programs, we have also advanced an industry-leading portfolio of biologics, cell therapies and genetic therapy programs.

The advancement of novel candidates from the bench into clinical trials and successfully completing pivotal development and obtaining regulatory approvals reflects our strategy in action. It has yielded multiple commercial products including ALYFTREK, TRIKAFTA/KAFTRIO, SYMDEKO/SYMKEVI, ORKAMBI, and KALYDECO for CF, CASGEVY for SCD and TDT, and JOURNAVX for the treatment of moderate-to-severe acute pain. Our approach to drug discovery has also yielded therapies that have demonstrated clinical proof-of-concept in additional disease areas, including diabetic peripheral neuropathy with suzetrigine, AMKD with inaxaplin, and T1D with zimislecel. Furthermore, in 2024, we acquired Alpine and its lead asset, povetacicept, which has the potential to be a “pipeline-in-a-product” and a best-in-class approach to treat multiple B cell-mediated autoimmune diseases including IgA nephropathy (“IgAN”), where it has demonstrated positive proof-of-concept.

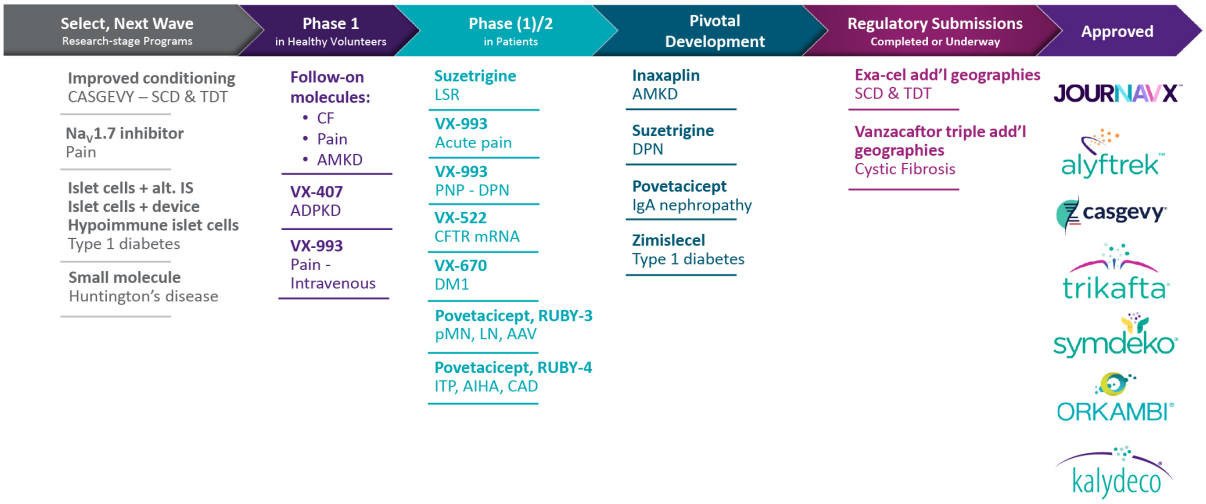
Our advancements across multiple disease areas and modalities since the beginning of 2024 include:

- *Cystic Fibrosis.* We are enrolling and dosing a Phase 3 clinical trial evaluating ALYFTREK in children with CF 2 to 5 years of age who have at least one F508del mutation or a mutation responsive to triple combination CFTR modulators. We continue to serially innovate in CF, raising the bar each time we do so, as we continue our mission to bring all patients with CF to normal levels of CFTR function. Our first “next-generation” triple combination of TRIKAFTA (NG 1.0) set a high bar for improvements in CFTR function, and ALYFTREK (NG 2.0) has improved upon TRIKAFTA. Our next triple combination regimen, NG 3.0, will consist of tezacaftor, VX-828 (a new CFTR corrector), and either VX-118 (a new CFTR potentiator) or deutivacaftor. We have completed Phase 1 clinical trials evaluating VX-118 and we are in the process of completing Phase 1 clinical trials with VX-828. We expect to enter clinical trials evaluating NG 3.0 in people with CF this year. We are also pursuing genetic therapies for people with CF who do not make full-length CFTR protein and, as a result, cannot benefit from our current CF medicines. For these more than 5,000 people, in collaboration with Moderna, we are developing VX-522, a CFTR 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 multiple ascending dose portion of the clinical trial for VX-522 in people with CF is ongoing and we expect to share data in the first half of 2025.
- *Sickle Cell Disease and Transfusion-Dependent Beta Thalassemia.* Two global Phase 3 clinical trials evaluating CASGEVY in children 5 to 11 years of age with severe SCD and TDT are ongoing. We have completed enrollment in these two clinical trials, and we expect to complete dosing in 2025. We are advancing preclinical assets for myeloablative conditioning agents with improved tolerability profiles, which could be used in connection with treatment with CASGEVY and significantly broaden the eligible SCD and TDT patient population. We are also investigating in vivo gene-editing approaches and small molecules for the potential treatment of SCD and TDT.
- *Acute Pain.* We are enrolling and dosing patients in a Phase 2 clinical trial evaluating an oral formulation of VX-993, our next-generation NaV1.8 pain signal inhibitor, for the treatment of moderate-to-severe acute pain. We are also enrolling and dosing healthy volunteers in a Phase 1 clinical trial evaluating an intravenous formulation of VX-993.
- *Neuropathic Pain.* The FDA has granted suzetrigine Breakthrough Therapy Designation in diabetic peripheral neuropathy and we are enrolling and dosing in the Phase 3 pivotal program evaluating suzetrigine in this population. In addition, we are enrolling and dosing patients in a Phase 2 diabetic peripheral neuropathy clinical trial of the oral formulation of VX-993. In December 2024, we announced results from a Phase 2 clinical trial evaluating suzetrigine in people with lumbosacral radiculopathy (“LSR”). The clinical trial met its primary endpoint, but the suzetrigine arm did not separate from the placebo reference arm. We hypothesize that a high placebo response in this clinical trial led to a lack of separation of the suzetrigine and placebo response curves. We believe we can innovate in pain clinical trial design to better control the placebo effect, and succeed in pivotal development with suzetrigine. Pending discussions with regulators, we plan to initiate a Phase 3 clinical trial of suzetrigine in LSR.

- *APOL-1 Mediated Kidney Disease*. Inaxaplin, our small molecule for the treatment of APOL1-mediated kidney disease ("AMKD") is in pivotal development. We continue to enroll and dose people with AMKD in the Phase 3 portion of the global Phase 2/3 clinical trial. We expect to complete enrollment in the interim analysis cohort in 2025. This cohort requires 48 weeks of follow-up, at which point the interim analysis will be conducted. If the interim analysis is positive, we will apply for potential accelerated approval in the U.S.
- *IgA Nephropathy*. Povetacicept, a dual inhibitor of the B cell activating factor ("BAFF") and a proliferation-inducing ligand ("APRIL") pathways, is a potentially best-in-class approach to treat IgAN and is in pivotal development. We are currently enrolling and dosing patients in the Phase 3 clinical trial and expect to complete enrollment in the interim analysis cohort this year. This cohort requires 36 weeks of follow-up, at which point the interim analysis will be conducted. If positive, we will apply for potential accelerated approval in the U.S. Povetacicept is also being studied in two Phase 2 basket trials of additional B cell-mediated autoimmune diseases: renal conditions in RUBY-3 and hematologic conditions in RUBY-4. We expect data in some of these conditions in 2025.
- *Type 1 Diabetes*. Zimislecel, formerly known as VX-880, is an allogeneic, stem-cell derived, fully differentiated islet cell therapy in pivotal development for the treatment of type 1 diabetes ("T1D"). We expect to complete enrollment and dosing in the Phase 3 portion of this Phase 1/2/3 clinical trial in 2025 and, assuming positive data, we expect to file for approval in 2026. In March 2025, we announced results from the Phase 1/2 clinical trial evaluating VX-264, our second clinical program in T1D, in which zimislecel is encapsulated in an immunoprotective device. VX-264 was generally safe and well-tolerated, however, efficacy data are not supportive of further clinical development. We plan to conduct further analyses of the VX-264 Phase 1/2 study, including explanted devices, to better understand these findings. In research, we are pursuing development of gentler approaches to immunosuppression for patients receiving zimislecel, as well as gene-editing approaches to develop hypoimmune stem cell-derived allogeneic cells.
- *Myotonic dystrophy type 1*. We are exploring multiple approaches to address the underlying causal biology for myotonic dystrophy type 1 ("DM1"), including small molecules and VX-670, an oligonucleotide-based approach in-licensed from Entrada Therapeutics, Inc. ("Entrada"). We completed the single ascending dose portion of the global Phase 1/2 clinical trial evaluating VX-670 in people with DM1 and we are currently enrolling and dosing the multiple ascending dose portion of the trial, which will evaluate the safety and efficacy of VX-670.
- *Autosomal Dominant Polycystic Kidney Disease*. We are nearing completion of a Phase 1 clinical trial in healthy volunteers evaluating VX-407, our first-in-class small molecule corrector that targets the underlying cause of autosomal dominant polycystic kidney disease ("ADPKD") in people with a subset of variants in the PKD1 gene. We expect to advance VX-407 into a Phase 2 proof-of-concept study in people with ADPKD in 2025.
- In addition to the programs listed above, we have several earlier-stage research programs aimed at diseases that fit our R&D strategy, as well as follow-on programs in diseases already in the clinic.

We will continue investing in scientific innovation through our internal research efforts and by accessing emerging technologies and product candidates through business development transactions.

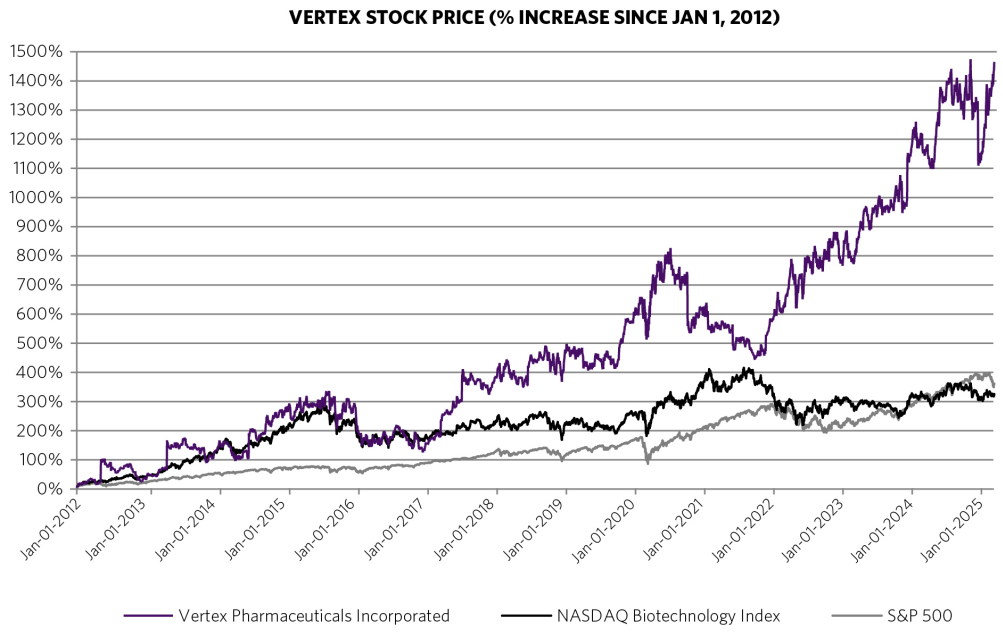
The following chart represents our approved medicines, clinical stage programs and select pre-clinical programs.



SCD: sickle cell disease; TDT: transfusion-dependent beta thalassemia; alt. IS: alternative immunosuppression; CF: cystic fibrosis; AMKD: APOL-1 mediated kidney disease; ADPKD: autosomal dominant polycystic kidney disease; LSR: lumbosacral radiculopathy; PNP: peripheral neuropathic pain; DPN: painful diabetic peripheral neuropathy; CFTR mRNA: cystic fibrosis transmembrane conductance regulator messenger RNA; DM1: myotonic dystrophy type 1; pMN: primary membranous nephropathy; LN: lupus nephritis; AAV: ANCA-associated vasculitides; ITP: idiopathic thrombocytopenia; AIHA: warm autoimmune hemolytic anemia; CAD: cold agglutin disease.

Increasing Shareholder Value

We expect that execution of our differentiated serial innovation strategy will continue to create shareholder value over the long-term. The biotechnology sector is subject to short-term volatility and many biotechnology companies experienced stock price fluctuations in 2024, including Vertex, where our stock price reached an all-time high of $519.88. We believe, however, that biotechnology companies are best measured over the long term as opposed to one-year or other shorter-term increments. The following chart shows our total shareholder return relative to the Nasdaq Biotechnology Index and S&P 500 index since 2012, when our first CF medicine was approved.



Corporate Responsibility

We are a leading global biotechnology company that serially innovates to bring transformative medicines to people with serious diseases. We are committed to operating our business responsibly and disclosing our progress to stakeholders on an annual basis. Our progress and efforts with respect to environmental, social, and governance topics, including community engagement and workplace practices, were recognized broadly in 2024. A selection of awards and recognitions include Forbes' America's Best Companies, Fortune 100 Best Companies to Work For® 2024, TIME 100 Most Influential Companies, U.S. News & World Report Best Companies to Work For, Points of Light's Civic 50, Science Magazine's Top Employers, Fast Company's 2024 World's 50 Most Innovative Companies list, TIME Magazine's Best Inventions of 2024 for CASGEVY, and many others.

Our corporate responsibility priorities relate to four objectives fundamental to our business: improving the lives of people with serious diseases; fostering a culture of innovation, integrity, and belonging; carefully managing our operations and environmental footprint; and making a positive impact in our communities.

Improve the lives of people with serious diseases	We are focused on discovering, developing and producing innovative medicines so that people with serious diseases can lead better lives. We invest significantly in research and development, with the majority of operating expenses and our workforce dedicated to that purpose. Once we discover transformative medicines, we then work to ensure patients have access to our medicines. We are deeply committed to understanding the challenges and unmet needs of patients and recognize the importance of partnering with, elevating, and empowering patient communities.
Foster a culture of innovation, integrity and belonging	We are focused on fostering a culture of innovation, integrity and belonging. Our culture of high ethical standards and integrity is one of the key components to our success. All of our directors, officers, employees and contractors are responsible for complying with our Code of Conduct and upholding and demonstrating ethics and integrity in our work every day. We are committed to building an outstanding, committed and passionate team. This involves not only recruiting, retaining and developing the most talented employees, but also investing to make sure they feel supported, valued and free to bring their unique perspectives to the table. To promote our employees' well-being and development, we also offer a variety of benefits and career development opportunities.
Carefully manage our operations and environmental footprint	We are committed to limiting our environmental impact and to operating our business in a sustainable manner. In 2023, we established a new target to reduce our Scope 1 and Scope 2 absolute greenhouse gas ("GHG") emissions. Approximately 50% of our global energy comes from renewable energy sources and we source approximately 98% renewable energy for our U.K.-based international headquarters and research facility. For our continued efforts, we received a score of B on the 2024 CDP Climate Change survey, demonstrating environmental management. We also continually improve standards and incorporate industry best practices with regards to important topics such as employee health and safety as well as our supply chain.
Make a positive impact in the communities where we are located	We continue to support our communities through collaborations, donations, and volunteering across the world. In 2024, Vertex and the Vertex Foundation contributed approximately $53 million in charitable giving. 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 we live and work through education, innovation and health. In 2024, it supported nearly 2,600 nonprofit organizations through the Vertex Foundation Matching Gift program. For our 16th annual Week of Service, a record 70% of employees volunteered in their local communities across 178 global opportunities.

Director Nominees

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

Name, Occupation or Experience	Age	Director Since	Independent	Committees			
				AC	MDCC	CGNC	S&T
Jeffrey Leiden Executive Chairman, Vertex	69	2009	No				
Reshma Kewalramani CEO and President, Vertex	52	2020	No				
Sangeeta Bhatia John J. and Dorothy Wilson Professor of Health Sciences & Technology/Electrical Engineering & Computer Science, MIT	56	2015	Yes			✔	C
Lloyd Carney Chief Executive Officer, Carney Global Ventures, LLC Former CEO, Brocade Communications	63	2019	Yes	✔		C	
Alan Garber President, Harvard University	69	2017	Yes			✔	✔
Michel Lagarde Executive Vice President and Chief Operating Officer, Thermo Fisher Scientific Inc.	51	2023	Yes	✔			
Diana McKenzie Former Chief Information Officer, Workday Former Chief Information Officer, Amgen	60	2020	Yes	✔	✔		
Bruce Sachs Partner Emeritus, Charles River Ventures	65	1998	Yes		C	✔	
Jennifer Schneider Co-Founder and CEO, Homeward Health Inc.	50	2024	Yes		✔		
Nancy Thornberry Former CEO, Kallyope, Inc.	68	2023	Yes				✔
Suketu Upadhyay Chief Financial Officer and Executive Vice President, Zimmer Biomet	56	2022	Yes	C	✔		

C = Chair

2024 Compensation Decisions and Pay-for-Performance

In 2024, our executive compensation program received substantial support, with approval by approximately 91% of the votes cast at the annual meeting. We believe this support is consistent with our shareholders' understanding of our business model, our pay-for-performance compensation philosophy, 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 2024 compensation:

- We increased the base salary and the target cash bonus as a percentage of base salary for Dr. Reshma Kewalramani, our CEO and President, based on a comparative analysis of companies in our peer group, and maintained her target equity level.
- Based on a comparative analysis of companies in our peer group, we increased the base salaries and target cash bonuses as a percentage of base salary for Dr. David Altshuler, Mr. Stuart Arbuckle, Dr. Nia Tatsis, and Mr. Charles Wagner, and maintained their target equity levels.
- Our outstanding performance in 2024 resulted in the MDCC determining that we had achieved a leading rating for 2024 (142 out of a total potential score of 150), with the payment of annual cash bonuses commensurate with this high level of performance.
- Our total revenue exceeded the board's pre-approved financial targets for 2024, resulting in maximum payout achievement for our 2024 financial-based performance stock units ("PSUs"). In addition, the MDCC determined that our non-financial PSUs with a three-year performance period ending December 31, 2024 achieved maximum payout based on achieving all three milestones associated with each award.
- We maintained the mix of equity granted to our named executive officers (each, a "NEO") with 50% of the awards consisting of PSUs that vest upon achievement of specific performance goals and 50% consisting of time-vesting restricted stock units ("RSUs"). This mix incentivizes both shorter-term financial accomplishments and longer-term strategic objectives, long-term tenure, and the creation of shareholder value.
- We extended the term of the employment agreement of our Executive Chairman, Dr. Jeffrey Leiden, until 2027. 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 service as Executive Chairman.

Executive Transitions

In February 2025, we announced the retirement of Mr. Arbuckle, our Chief Operating Officer, and the appointment of Mr. Wagner as Chief Operating Officer, each effective as of July 1, 2025. Mr. Wagner will remain our Chief Financial Officer following his appointment. We also announced the appointment of Duncan McKechnie as Chief Commercial Officer effective July 1, 2025. In connection with his appointment, we entered into a new employment agreement and a new change of control agreement with Mr. Wagner. Under his new employment agreement, Mr. Wagner will receive a base salary of $1,000,000 and a target annual bonus of 100% of his base salary effective July 1, 2025. In connection with his retirement, the MDCC considered Mr. Arbuckle as eligible for the retirement vesting provisions of his equity awards.

Shareholder Engagement

Shareholder Outreach and 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.

In 2024, we solicited feedback regarding our corporate governance practices from shareholders representing approximately 70% 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, human capital management, corporate governance, political and lobbying disclosures, executive compensation, shareholder proposals, and environmental sustainability matters.

Response to 2024 Shareholder Proposal

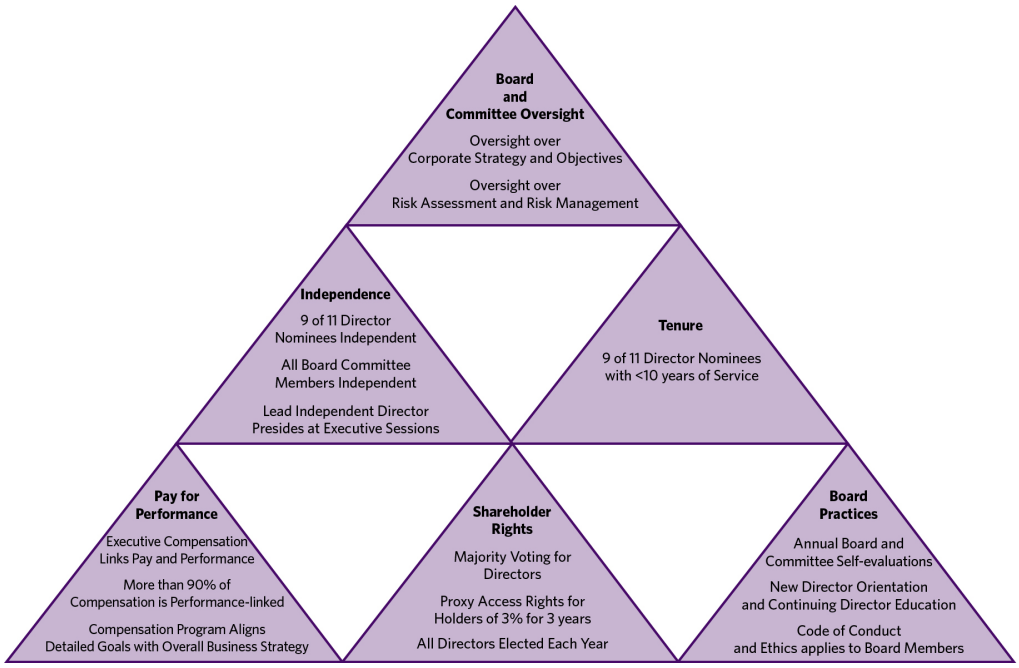
Among the topics our outreach team discussed with shareholders in 2024 was the advisory proposal (the “Advisory Proposal”) presented to shareholders at our 2024 annual meeting. The Advisory Proposal sought to lower the ownership threshold required to call a special shareholder meeting (such ownership threshold, the “Special Meeting Threshold”) from 40% to 10%. The Advisory Proposal was approved by holders of a majority of shares represented at the 2024 Annual Meeting.

We asked shareholders for their perspectives about the appropriate Special Meeting Threshold. Shareholders representing approximately 60% of our outstanding shares responded, including those who voted for and against the Advisory Proposal. Some investors shared their concerns that a 10% Special Meeting Threshold would be too low, allowing a small number of shareholders to call a special meeting. This would potentially allow holders of a small minority of outstanding shares of the company to advance their own special interests at the expense of other shareholders while also distracting directors and management to the detriment of the company. Other investors indicated that, while they supported the Advisory Proposal when the Special Meeting Threshold was at 40%, they would be supportive of an alternative Special Meeting Threshold higher than 10% and lower than 40%. More than half of respondents expressed the view that a 25% Special Meeting Threshold would be appropriate.

After careful consideration of the views expressed during our shareholder outreach, in February 2025, our board amended our by-laws to reduce the Special Meeting Threshold from 40% to 25%. Consistent with the feedback we received from many of the shareholders with whom we engaged, our board believes that a 25% Special Meeting Threshold is a reasonable threshold that strikes an appropriate balance between ensuring that shareholders have a meaningful right to call a shareholder meeting and protecting against the risk that a small minority of shareholders could trigger a special meeting that is not in the best interest of all shareholders, requiring significant corporate resources and disrupting our business.

Corporate Governance

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



Voting Roadmap

Item 1: Elect Each of the Director Nominees for One Year Term Expiring in 2026	**FOR** all Nominees
Item 2: Ratify Selection of Independent Auditor for 2025	**FOR**
Item 3: Approve, on an Advisory Basis, Our Named Executive Officer Compensation	**FOR**
Item 4: Shareholder Proposal Regarding Excessive Golden Parachutes	**AGAINST**

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PROXY STATEMENT

This proxy statement is being made available to shareholders of Vertex Pharmaceuticals Incorporated in connection with the solicitation by our board of directors of proxies to be voted at our 2025 annual meeting of shareholders and at any postponement or adjournment thereof. The annual meeting will be held on Wednesday, May 14, 2025, at 9:00 a.m. (Eastern Time) as a virtual meeting conducted exclusively via live webcast at https://meetnow.global/MXD5MZM. 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, Reshma Kewalramani, Michel Lagarde, Jeffrey Leiden, Diana McKenzie, Bruce Sachs, Jennifer Schneider, Nancy Thornberry, and Suketu Upadhyay - for election at our 2025 annual meeting of shareholders to hold office until our 2026 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 eleven members of our board immediately following the 2025 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.

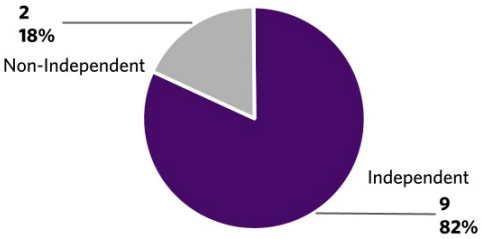
Director Criteria, Qualifications and Experience

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 broad 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, and other factors that the committee believes to be important. When considering whether 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.

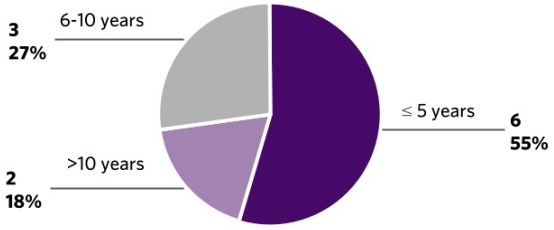
The following table and charts provide information regarding our director nominees:

	BHATIA	CARNEY	GARBER	KEWALRAMANI	LAGARDE	LEIDEN	MCKENZIE	SACHS	SCHNEIDER	THORNBERRY	UPADHYAY
Leadership Experience. We believe that directors who have held significant leadership positions over extended periods of time provide our company with special insights.	✔	✔	✔	✔	✔	✔	✔	✔	✔	✔	✔
Industry Knowledge. We seek directors with substantive knowledge of the healthcare and biotechnology industries to successfully advise and oversee the strategic development and direction of our company.	✔		✔	✔	✔	✔	✔		✔	✔	✔
Financial Expertise. We believe that an understanding of finance is important for members of our board, and our budgeting processes and financial and strategic transactions require our directors to be financially knowledgeable.		✔	✔	✔	✔	✔	✔	✔	✔	✔	✔
International Perspective. We have significant operations outside the United States and value directors with experience in the operation of complex multinational organizations.		✔	✔	✔	✔	✔	✔	✔			✔
Public Policy and Regulation. We operate in a highly-regulated industry and seek directors who have experience in public policy and the regulation of medicines.			✔	✔		✔				✔	
Academic Experience or Technological Background. As a biotechnology company that seeks to develop transformative medicines for patients with serious diseases, we look for directors with backgrounds in academia, science and technology and, in particular, the research and development of pharmaceutical products.	✔	✔	✔	✔		✔	✔	✔	✔	✔	
Commitment to Company Values and Goals. We seek directors who are committed to our company and its values and goals and who value the contributions that can be provided by individuals who believe in our company and its prospects for success.	✔	✔	✔	✔	✔	✔	✔	✔	✔	✔	✔
Independence	Y	Y	Y	N	Y	N	Y	Y	Y	Y	Y
Age	56	63	69	52	51	69	60	65	50	68	56
Tenure on Board	9	6	7	5	1	15	5	26	1	1	3

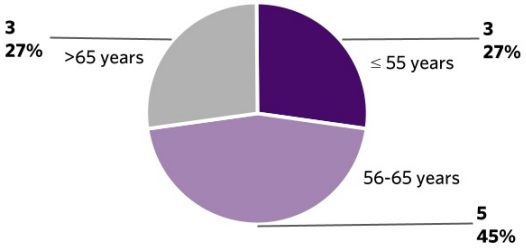
NOMINEE INDEPENDENCE



NOMINEE TENURE



NOMINEE AGE



Shareholder-Recommended Director Candidates

The CGNC will consider director candidates recommended by shareholders using the same criteria for director selection described above under *Director Criteria, Qualifications and Experience*. 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 2026 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 2026 Annual Meeting* on page 94 of this proxy statement. If a shareholder wishes to solicit proxies for a shareholder nominee for election to our board at the 2026 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.

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: 56

Director Since: 2015

Board Committees:
- Chair – Science and Technology Committee
- Member – Corporate Governance and Nominating Committee

Other Public Company Boards:
- None

Experience:
- John J. and Dorothy Wilson Professor of Health Sciences & Technology/Electrical Engineering & Computer Science at the Massachusetts Institute of Technology ("MIT") since 2005; Director of the Marble Center for Cancer Nanomedicine at the Koch Institute for Integrative Cancer Research at MIT since 2016; Investigator of the Howard Hughes Medical Institute at MIT since 2008
- Co-Founder of Ropirio Therapeutics, a private biotechnology company focused on lymphatic medicine, since 2023
- Co-Founder of Amplifyer Bio, a private biotechnology company focused on oncology diagnostics, since 2023
- Co-Founder of Matrisome Bio, a private biotechnology company, since 2023
- 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, from 2018 until it was acquired by Sunbird Bio, Inc. in August 2023
- Professor of bioengineering and medicine at the University of California at San Diego, from 1998 through 2005
- Member of the Department of Medicine at Brigham and Women's Hospital and member of the Broad Institute
- 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.

Lloyd Carney

Age: 63

Director Since: 2019

Board Committees:
- Chair – Corporate Governance and Nominating Committee
- Member – Audit and Finance Committee

Other Public Company Boards:
- Visa Inc.
- Grid Dynamics Holdings Inc.

Experience:
- Chief Executive Officer and Chairman, Carney Global Ventures, LLC, an early round investor, since March 2007
- 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 and Director 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, from 2008 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
- Ambassador/Special Investment Envoy for Technology Jamaica, since May 2023
- Chancellor for the University of Technology, Jamaica, a public university in Jamaica, since August 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, a Honorary Doctorate degree in Engineering from Wentworth Institute of Technology and a Honorary Doctorate degree in Technology from University of Technology Jamaica

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. As Chief Executive Officer of multiple technology companies, Mr. Carney has extensive experience in operations, strategic planning, finance, information technology and cybersecurity, and risk management.

Alan Garber

Age: 69

Director Since: 2017

Board Committees:

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

Other Public Company Boards:

- None

Experience:

- President of Harvard University since August 2024 after serving as Interim President from January to August 2024; Provost of Harvard University and the Mallinckrodt Professor of Health Care Policy at Harvard Medical School, a Professor of Economics in the Faculty of Arts and Sciences, Professor of Public Policy in the Harvard Kennedy School of Government, and Professor in the Department of Health Policy and Management in the Harvard T.H. Chan School of Public Health, from September 2011 to August 2024
- 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
- Member of the board of Directors of Exelixis, Inc., a genomics-based drug-discovery company, from January 2005 to May 2024
- Fellow of the American Association for the Advancement of Science, the American College of Physicians, and the Royal College of Physicians
- Current 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 with important insights and perspectives on the issues facing our company.

Reshma Kewalramani

Age: 52

Director Since: 2020

Position:

- Chief Executive Officer and President

Other Public Company Boards:

- None

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
- Member of the Board of Directors of Ginkgo Bioworks Holdings, Inc., a publicly traded biotechnology company, from 2021 to 2024
- 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 is an alumna of the Harvard Business School, having completed the General Management Program

Key Skills and Qualifications:

Dr. Kewalramani possesses strong leadership qualities, significant experience overseeing and scaling the operations of a global enterprise, deep expertise in drug development, and wide-ranging experience in policy matters, 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.

Michel Lagarde

Age: 51

Director Since: 2023

Board Committees:

- Member – Audit and Finance Committee

Other Public Company Boards:

- None

Experience:

- Executive Vice President and Chief Operating Officer at Thermo Fisher Scientific Inc. (“Thermo Fisher”), a supplier of analytical instruments, life sciences solutions, specialty diagnostics, laboratory, pharmaceutical and biotechnology services, since January 2022; Thermo Fisher is a supplier to Vertex
- Executive Vice President at Thermo Fisher from 2019 through 2021
- Senior Vice President and President, Pharma Services at Thermo Fisher from 2017 to 2019, joining Thermo Fisher as Senior Vice President, as a result of its acquisition of Patheon N.V., a pharma services company, in 2017
- President and Chief Operating Officer of Patheon N.V. from 2016 to 2017
- Managing Director of JLL Partners, a private equity firm focused on healthcare, from 2008 to 2016
- Holds a bachelor’s degree in business administration from European University in Antwerp and an executive master’s degree in finance and control from the University of Maastricht and University of Amsterdam

Key Skills and Qualifications:

Mr. Lagarde has deep experience across numerous segments of the health care industry and markets around the world, as well as a successful track record of growing and scaling profitable businesses. He brings to our board of directors strong leadership experience in biotechnology and pharmaceutical development and commercial manufacturing services, as well as financial expertise across several international markets.

Jeffrey Leiden

Age: 69

Director Since: 2009

Position:

- Executive Chairman

Other Public Company Boards:

- None

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 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
- Dr. Leiden received his M.D., Ph.D. and B.A. degrees from the University of Chicago

Key Skills and Qualifications:

Dr. Leiden possesses strong leadership qualities, demonstrated through his service as a senior executive in the biotechnology and pharmaceutical industries and as a life sciences venture capitalist. He 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: 60

Director Since: 2020

Board Committees:
- Member – Audit and Finance Committee
- Member – Management Development and Compensation Committee

Other Public Company Boards:
- MetLife Inc.
- agilon health, inc.

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 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. In addition, Ms. McKenzie is a proven technology leader who brings extensive digital, technology, and cybersecurity knowledge and perspective based on nearly three decades of experience in the space.

Bruce Sachs

Age: 65

Director Since: 1998

Position:
- Lead Independent Director

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

Other Public Company Boards:
- None

Experience:
- Partner Emeritus at Charles River Ventures ("CRV"), a venture capital firm; General Partner at CRV for more than 20 years, including more than 10 years as the Managing Partner
- 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 until it was acquired by Ascend Communications in 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 until it was acquired by Bay Networks in 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 exceptionally strong business judgment to our board, honed through his experience developing business strategy as a senior executive and in venture capital. Mr. Sachs has an incomparable understanding of our business, gained through his service on the board of directors of the Company, and of the global business environment. In addition, Mr. Sachs has significant business leadership experience, financial expertise, and knowledge with respect to information technology and security, having served as a technology company CEO and as a board member of several computer networking companies.

Jennifer Schneider

Age: 50

Director Since: **2024**

Board Committees:

- Member - Management Development and Compensation Committee

Other Public Company Boards:

- None

Experience:

- Co-Founder and Chief Executive Officer of Homeward Health Inc., a company committed to rearchitecting the delivery of health and care in rural America in partnership with communities, since 2022
- President of Livongo Health, a biotechnology company, from December 2018 to October 2020, and served as the Chief Medical Officer from September 2015 to December 2018
- Served in multiple leadership roles at Castlight Health, Inc., a healthcare navigation company, from 2010 to 2015, most recently as Chief Medical Officer
- Member of the board of directors at Revolution Healthcare Acquisition Corp., a special purpose acquisition company, from March 2021 to December 2022
- Member of the board of directors at Health Assurance Acquisition Corp., a special purpose acquisition company, from September 2020 until it liquidated in November 2022
- Holds a B.S. in Biology from the College of the Holy Cross, an M.D. from Johns Hopkins School of Medicine, and an M.S. in Health Services Research from Stanford University

Key Skills and Qualifications:

Dr. Schneider has deep knowledge and expertise in healthcare and technology. She has led or held senior leadership roles in multiple companies focused on delivering innovative solutions in healthcare management. At Livongo, Dr. Schneider led the company through the largest consumer digital health initial public offering in history as well as its merger with Teladoc Health, the industry's largest ever merger. Dr. Schneider brings extensive experience as a practicing physician and as a leader building healthcare companies that use technology to provide access to clinical services.

Nancy Thornberry

Age: 68

Director Since: 2023

Board Committees:
- Member – Science and Technology Committee

Other Public Company Boards:
- Denali Therapeutics
- Schrödinger Inc.

Experience:
- Founder and Chief Executive Officer of Kallyope, Inc. ("Kallyope"), a private biotechnology company, from November 2015 to October 2021, and served as Chair of Research and Development through December 2023
- Self-employed as a consultant to companies in the biotechnology and pharmaceutical industries from August 2013 to October 2015
- Served in roles of increasing responsibility at Merck & Co., Inc., a pharmaceutical company, for more than 30 years, most recently as Senior Vice President and Franchise Head, Diabetes and Endocrinology
- Holds a B.S. in Chemistry and Biology from Muhlenberg College

Key Skills and Qualifications:

Ms. Thornberry has over 30 years of experience in the pharmaceutical and biotechnology industries and her scientific leadership has spanned across drug discovery, research & development, and business development. She brings to our board of directors leadership experience in critical scientific roles that drove innovation at both public and private companies. Her industry experience, scientific acumen and strategic thinking brings great value to our board of directors.

Suketu Upadhyay

Age: 56

Director Since: 2022

Board Committees:
- Chair – Audit and Finance Committee
- Member - Management Development and Compensation Committee

Other Public Company Boards:
- None

Experience:
- Chief Financial Officer and Executive Vice President - Finance, Operations and Supply Chain 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.

For all of the above reasons, our board of directors unanimously recommends that you vote FOR each of the nominees.

CORPORATE GOVERNANCE AND RISK MANAGEMENT

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

Director Independence

Our board of directors has determined that nine of our eleven 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. Lagarde, Ms. McKenzie, Mr. Sachs, Dr. Schneider, Ms. Thornberry, 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) the 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 with our corporate business development function, our cell and genetic therapy programs, and our external communications and government affairs activities, as described below. 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 34 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

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 financial and accounting systems, accounting policies and investment strategies, internal audit function, and cybersecurity;
- oversee 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. Upadhyay, chair of our audit committee, and Messrs. Lagarde and Carney, members of the audit committee, each qualify as an "audit committee financial expert" as that term is defined in applicable rules and regulations of the SEC, and each is independent according to the applicable listing standards of Nasdaq and SEC rules. The report of the audit committee appears on page 46 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 2024, we had one transaction considered to be a related party transaction pursuant to Item 404(a) of Regulation S-K: our Chief Financial Officer's daughter is employed by the Company in a non-executive position and received approximately $127,000 in total compensation in 2024. In addition, she participated in our employee benefit plans on the same basis as other similarly situated employees in 2024.

Corporate Governance and Nominating Committee

The primary purposes of the CGNC are to:

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

Management Development and Compensation Committee

The primary purposes of the MDCC are to:

- assess the overall compensation programs of the company and adopt a written statement of compensation philosophy and objectives;
- oversee and make recommendations to the board regarding compensation for our CEO;
- oversee and approve compensation for our other executives;
- approve (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;
- review and make recommendations to the board regarding new equity plans; and
- oversee and approve the adoption, amendment, administration, and termination of any recoupment policy of the company.

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 77 of this proxy statement.

Science and Technology Committee

Our S&T committee assists our board of directors in its responsibilities relating to the oversight of our investment in pharmaceutical 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;
- 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

Messrs. Carney, Sachs, and Upadhyay, Ms. McKenzie, and Dr. Schneider served on the MDCC during 2024. Terrence Kearney, a former member of our board of directors, also served on the MDCC for part of 2024. 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 2024 that would be required to be disclosed pursuant to Item 404(a) of Regulation S-K. During 2024, 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 2024, our board of directors met 8 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 2024. All of our current directors attended our 2024 annual meeting of shareholders.

The following table provides information regarding our current board of directors.

Director	Independence	Board	Audit Committee	CGNC	MDCC	S&T Committee
Sangeeta N. Bhatia	✔	●		●		C
Lloyd Carney	✔	●	●	C		
Alan Garber	✔	●		●		●
Reshma Kewalramani		●				
Michel Lagarde	✔	●	●			
Jeffrey M. Leiden		C				
Diana McKenzie	✔	●	●		●	
Bruce I. Sachs	✔	★		●	C	
Jennifer Schneider	✔	●			●	
Nancy Thornberry	✔	●				●
Suketu Upadhyay	✔	●	C		●	
2024 Meetings		**8**	**9**	**5**	**6**	**5**

● = Member

C = 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 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 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, product safety and quality, 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	• Financial, accounting, disclosure, insurance, tax, investment, credit, disclosure controls and procedures, and other risks reviewed in its oversight of the internal audit function • Cybersecurity • Internal audit • Compliance program • Periodic reviews of relevant developments in disclosure requirements
Management Development and Compensation Committee	• 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 • Company incentive compensation plans and equity-based plans • Stock ownership guidelines for executive officers and officers
Corporate Governance and Nominating Committee	• Corporate governance • Board organization, membership, and structure • Board and CEO succession planning • Director independence
Science and Technology Committee	• Assessments of planned R&D programs and technology initiatives • Emerging science and technology issues and trends

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 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.

Insider Trading Policy

We have adopted insider trading policies and procedures governing the purchase, sale and/or other dispositions of our securities by directors, officers and employees, or the company itself, that are reasonably designed to promote compliance with insider trading laws, rules and regulations and any listing standards applicable to us. A copy of our Insider Trading Policy is incorporated by reference to our Annual Report on Form 10-K for the fiscal year ended December 31, 2024.

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		$ 55,000
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. In 2024, Dr. Leiden received $70,000 to facilitate his participation in the Company's benefit plans, and $6.5 million of equity awards (determined based on grant date fair value, with PSUs determined based on target) consisting of $3.250 million in PSUs for which earned shares are based on one-year financial metrics (the same one-year financial metrics underlying the awards granted to the other NEOs) and $3.250 million in immediately vested RSUs.

We annually review the compensation program for our non-employee directors. In the second half of 2024, based upon a market assessment of the board compensation of our Peer Group (described below) and the advice of the MDCC's independent compensation consultant, we modified the non-employee director compensation program to increase the Annual Lead Independent Director Retainer from $40,000 to $55,000.

2024 Director Compensation

Director[1]	Fees Earned or Paid in Cash	Stock Awards[2]	Option Awards[2]	All Other Compensation	Total
Sangeeta N. Bhatia	$ 135,000	$ 400,110	$ —	$ 15,000 (3)	$ 550,110
Lloyd Carney	$ 139,073	$ 400,110	$ —	$ 25,000 (3)	$ 564,183
Alan Garber	$ 121,854	$ —	$ 400,008	$ —	$ 521,862
Terrence C. Kearney[4]	$ 47,287	$ —	$ 400,008	$ 14,971 (5)	$ 462,266
Michel Lagarde	$ 113,516	$ —	$ 400,008	$ 25,000 (3)	$ 538,524
Diana McKenzie	$ 129,354	$ 400,110	$ —	$ 20,500 (3)	$ 549,964
Bruce I. Sachs[6]	$ 178,179	$ —	$ 400,008	$ 25,000 (3)	$ 603,187
Jennifer Schneider[7]	$ 70,776	$ 400,093	$ —	$ 25,000 (3)	$ 495,869
Nancy Thornberry	$ 109,011	$ 200,255	$ 200,004	$ 10,000 (3)	$ 519,270
Suketu Upadhyay	$ 137,864	$ 400,110	$ —	$ 25,000 (3)	$ 562,974

(1) For Dr. Jeffrey Leiden's service as the Executive Chairman in 2024, he received (1) $3.25 million of immediately vested RSUs (based on grant date fair value): (2) $3.25 million of PSUs (based on grant date fair value, assuming target performance) for which earned shares cliff vest in approximately one year, subject to meeting 2024 financial targets: and (3) $70,000 in an annual cash payment to facilitate his participation in the Company's benefits plans, all of which are provided under the terms of his amended employment agreement.

(2) 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 2024. The grant-date fair value of each option granted during 2024 was $127.31 utilizing the Black-Scholes option pricing model. See Note N to the Consolidated Financial Statements included in the company's Annual Report on Form 10-K filed for the year ended December 31, 2024.

(3) Amounts represent participation in the Vertex Foundation Matching Gift Program.

(4) Mr. Kearney served on the Board of Directors until May 15, 2024.

(5) Amount represents company gifts Mr. Kearney received in connection with the end of his service as a board member, and travel expenses for Mr. Kearney's spouse in connection with a board meeting.

(6) Mr. Sachs elected to defer his quarterly cash retainers, which were paid in deferred stock units, on each of the quarterly payment dates occurring on the 15th of the month following the quarter end in an amount equal to the dollar value of the cash amount that would have been paid on such date divided by the fair market value of a share of common stock on each such date. The per share fair market values of our common stock on each of those dates was $399.58, $490.12, $484.39 and $420.31.

(7) Dr. Schneider joined the Board of Directors on May 15, 2024.

2024 Equity Grants

Grant	Date	Shares	Exercise Price	Grant-Date Fair Value
Annual Non-Employee Director - 100% Option Grants	May 1, 2024	3,142	$ 399.71	$ 400,008
Annual Non-Employee Director - 50% Option Grants	May 1, 2024	1,571	$ 399.71	$ 200,004
Annual Non-Employee Director - 100% Restricted Stock Unit Grants	May 1, 2024	1,001	—	$ 400,110
Annual Non-Employee Director - 50% Restricted Stock Unit Grants	May 1, 2024	501	—	$ 200,255
Initial Restricted Stock Unit Grant to Jennifer Schneider	May 15, 2024	922	—	$ 400,093

Outstanding Equity

As of December 31, 2024, our non-employee directors had outstanding restricted stock units, deferred stock units and options to purchase our common stock as follows:

Director	Outstanding Restricted Stock Units	Outstanding Deferred Stock Units	Outstanding Options (All Exercisable)
Sangeeta N. Bhatia	1,001	—	—
Lloyd Carney	1,001	—	—
Alan Garber	—	—	29,555
Michel Lagarde	—	—	3,142
Diana McKenzie	1,001	5,990	—
Bruce I. Sachs	—	15,033	31,567
Jennifer Schneider	922	—	—
Nancy Thornberry	501	—	1,571
Suketu Upadhyay	1,001	1,403	—

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 17, 2025, 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. Dr. Schneider joined our board of directors in May 2024 and has five years from the date of her initial appointment to satisfy the individual holding requirements.

CORPORATE RESPONSIBILITY

We are committed to operating our business responsibly and disclosing our progress to stakeholders on an annual basis. Our progress and efforts with respect to environmental, social, and governance topics, including community engagement and workplace practices, were recognized broadly in 2024. A selection of awards and recognitions include Forbes' America's Best Companies, Fortune 100 Best Companies to Work For® 2024, TIME 100 Most Influential Companies, U.S. News & World Report Best Companies to Work For, Points of Light's Civic 50, Science Magazine's Top Employers, Fast Company's 2024 World's 50 Most Innovative Companies list, TIME Magazine's Best Inventions of 2024 for CASGEVY, and many others.

Our corporate responsibility priorities relate to four objectives fundamental to our business: improving the lives of people with serious diseases, fostering a culture of innovation, integrity, and belonging; carefully managing our operations and environmental footprint; and making a positive impact in our communities.

Improve the Lives of People with Serious Diseases

We are relentless in our pursuit to create transformative medicines for people with serious diseases. This has been our singular purpose for more than 30 years. We involve the voices of people living with the diseases early in our drug discovery and development processes. We listen, learn and incorporate the patient voice in our decisions and our R&D, every step of the way.

Our unique approach to building drug discovery programs has led to the development of five medicines that treat the underlying cause of CF, and the first-ever approved CRISPR-based gene edited cell therapy for SCD and TDT, and the first new class of pain medicine approved in more than twenty years. Our CF medicines are accessible to patients in more than 60 countries, and are currently being used to treat nearly three-quarters of the approximately 94,000 people living with CF in the U.S., Europe, Australia, and Canada. In the U.S., more than 99 percent of eligible patients have access to TRIKAFTA through public and private insurance. We also have initiated a pilot donation program in lower-income countries to provide TRIKAFTA to eligible people with CF. In the geographies where CASGEVY is approved, we are actively working with key commercial and government payers and policymakers with the goal of securing rapid access for eligible patients with severe SCD and TDT. Similarly, we are actively working to make JOURNAVX available to patients in the U.S. by securing national retail distribution, engaging with payors and formulary decision-makers to secure reimbursement and access, and facilitating financial and co-pay assistance programs for patients.

We recognize the importance of going beyond R&D to engage in patient advocacy, disease awareness, and community support and are deeply committed to understanding the challenges and unmet needs of patients. We use the tenets outlined in Our Patient Commitment to guide our engagement, meeting each community where they are. In 2024, we sponsored numerous programs and initiatives, including the Bonnell Foundation's "Living with CF" podcast series, multiple conferences supporting CF, Sickle Cell Consortium, the American Kidney Fund's APOL1 Education Campaign, IgA Nephropathy Foundation's SPARK event, Breakthrough T1D's Clinical Trials Connection program, and U.S. Pain Foundation programming.

Foster a Culture of Innovation, Integrity, and Belonging

Our success depends on nurturing a workplace culture and team that values innovation, integrity and belonging. Our culture of high ethical standards and integrity is one of the key components to our success, and each employee is responsible for upholding and demonstrating ethics and integrity in our work every day. Our Code of Conduct, anonymous compliance hotline, and robust investigation process are in place to help ensure that we are adhering to the highest standards of ethics and accountability.

We also are committed to building an outstanding, dedicated, and passionate team. We believe that each employee brings unique perspectives and strengths, and by embracing these strengths, we can do our best work for patients. This involves not only recruiting, retaining and developing the most talented employees, but also investing in our employees to make sure they feel supported, valued and free to bring their unique perspectives to the table.

In the same way we invest in developing transformative treatments for patients, we invest in our employees through a highly competitive suite of compensation and benefits. This “Total Rewards” package is competitive, inspires exceptional performance, recognizes great work, promotes employee well-being and facilitates opportunities for growth.

We also provide our employees with career development and advancement opportunities, including job rotations, mentoring, and managerial training. We are committed to identifying and developing our next generation of leaders and have developed programs focused on manager excellence, talent and succession for critical roles in our organization.

Carefully Managing Our Operations and Environmental Footprint

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 2023, we established a new target to reduce our Scope 1 and Scope 2 GHG emissions by 42% by 2032 from a 2022 baseline. In 2024, we reduced absolute GHG emissions by approximately 2% compared to the prior year. Approximately 50% of our global energy comes from renewable energy sources and we source approximately 98% renewable electricity for our U.K.-based international headquarters and research facility. 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. Many of our facilities around the world are highly efficient, sustainable buildings. We received a score of B on the 2024 CDP Climate Change survey, demonstrating environmental management.

We strive to offer our employees, contractors and visitors a healthy and safe work environment and continually seek ways to improve our practices. We invest in safety programs and incorporate industry best practices to ensure that employees, contractors and visitors experience a healthy and safe work environment.

We also focus on the safety and security of our supply chain to protect our products and patients. Our medicines meet the highest safety, ethical and environmental standards and our teams work to prevent, detect and respond to instances of product diversion, tampering and counterfeiting, and to maintain the quality of our products for the patients who rely on them.

Making a Positive Impact in Our Communities

We are committed to making a positive difference in the patient communities we serve and where we live and work.

We support our communities through collaborations, grants and donations, and volunteering across the world. In 2024, Vertex and the Vertex Foundation contributed approximately $53 million in charitable giving. The Vertex Foundation, a 501(c)(3) nonprofit organization, seeks to improve the lives of people with serious diseases and contribute to our communities through education, innovation and health. In 2024, we and the Vertex Foundation provided grants in support of STEAM education, healthy families, and social innovation. For example, in 2024, we offered opportunities to more than 4,200 students through our Learning Lab and STEAM education programs in Boston, San Diego, and Oxford, U.K., and, through the Vertex Foundation, provided 88 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 designed 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.

Volunteering and giving back are core to our culture. 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 16th annual Week of Service. Last year, 70% of Vertex employees around the globe volunteered during Week of Service, contributing nearly 11,000 volunteer hours to their local communities. Additionally, in 2024, we supported nearly 2,600 nonprofit organizations through the Vertex Foundation Matching Gift Program, which matches employee donations 1:1 to thousands of eligible nonprofit organizations.

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, 2025 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. That evaluation 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. Our lead audit partner completed his fifth year during the 2024 audit cycle. After undertaking its review, our audit and finance committee decided to retain Ernst & Young LLP as our independent registered public accounting firm for the 2025 audit and, together with management, identified the new lead audit partner for the 2025 audit.

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 2024 and 2023.

Service	2024	2023
Audit fees	$ 5,905,000	$ 4,650,000
Audit-related fees	—	—
Tax fees	1,326,000	1,160,000
All other fees	7,000	7,000
TOTAL	**$ 7,238,000**	**$ 5,817,000**

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

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

"Tax fees" consisted of fees related to tax compliance, worldwide tax planning, and tax advice. The tax fees for 2024 and 2023 consisted of:

- tax compliance and preparation fees, including the preparation of original and amended tax returns and refund claims, and tax payment planning of $976,000 and $896,000, respectively; and
- tax advice and planning fees of $350,000 and $264,000, 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, 2025.

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, 2024 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, 2024 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:

Suketu Upadhyay *(Chair)*
Lloyd Carney
Michel Lagarde
Diana McKenzie

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 employees, including 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 2024, our annual advisory vote on executive compensation received support from approximately 91% of the votes cast at the annual meeting of shareholders. We believe this support is consistent with our shareholders' understanding of our business model, our pay-for-performance compensation philosophy and the long-term value we are creating. We plan to continue a high level of shareholder engagement regarding our executive compensation program.

Our focus is and continues to be maintaining the strong link between our compensation programs and our ability to continue to develop transformative medicines while delivering sustained company performance, with more than 90% of our NEO compensation linked to performance. Our board and MDCC routinely review our compensation programs and made the following key decisions with respect to 2024 compensation:

- We increased the base salary and the target cash bonus as a percentage of base salary for Dr. Kewalramani, our CEO, based on a comparative analysis of companies in our peer group, and maintained her target equity level.
- Based on a comparative analysis of companies in our peer group, we increased the base salaries and target cash bonuses as a percentage of base salary for Dr. Altshuler, Mr. Arbuckle, Dr. Tatsis and Mr. Wagner, and maintained their target equity levels.
- Our outstanding performance in 2024 resulted in the MDCC determining that we had achieved a leading rating for 2024 (142 out of a total potential score of 150), with the payment of annual cash bonuses commensurate with this high level of performance.
- Our total revenue exceeded the board's pre-approved financial targets for 2024, resulting in maximum payout achievement for our 2024 financial based PSUs. In addition, the board determined that our non-financial PSUs with a three-year performance period ending December 31, 2024 achieved maximum payout based on meeting all three milestones approved by the board in 2022 for the three-year performance period associated with these awards.
- We maintained the mix of equity granted to our NEOs with 50% of the awards consisting of performance stock units that vest over time but only upon achievement of specific performance goals and 50% consisting of time-vesting restricted stock units. This mix incentivizes both shorter-term financial accomplishments and longer-term strategic objectives as well as retention and the creation of shareholder value.
- We extended the term of the employment agreement of our Executive Chairman, Dr. Jeffrey Leiden, until 2027. 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 service as Executive Chairman.

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 51 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: SHAREHOLDER PROPOSAL REGARDING EXCESSIVE GOLDEN PARACHUTES

We expect the following shareholder proposal will be presented for consideration at the 2025 annual meeting of shareholders. The shareholder proposal will be voted on at the 2025 annual meeting of shareholders only if properly presented by or on behalf of the proponent. Our board of directors unanimously recommends a vote AGAINST this shareholder proposal for the reasons set forth following the proposal.

Vertex is not responsible for the content of this shareholder proposal or supporting statement.

The Shareholder Proposal

John Chevedden, 2215 Nelson Avenue, No. 205, Redondo Beach, California 90278, an owner of at least $2,000 worth of shares of our common stock as of December 6, 2024, has given notice that they intend to present the following proposal for action at our 2025 annual meeting of shareholders.

Supporting Statement

Proposal 4 — Shareholder Vote regarding Excessive Golden Parachutes

Shareholders request that the Board seek shareholder approval of any senior manager's new or renewed pay package that provides for severance or termination payments with an estimated value exceeding 2.99 times the sum of the executive's base salary plus target short-term bonus. This proposal only applies to the Named Executive Officers. This provision shall at least be included in the Governess Guidelines of the Company or similar document and be readily accessible on the Company website.

"Severance or termination payments" include cash, equity or other pay that is paid or vests due to a senior executive's termination for any reason. Payments include those provided under employment agreements, severance plans, and change-in-control clauses in long-term equity plans, but not life insurance, pension benefits, or deferred compensation earned and vested prior to termination.

"Estimated total value" includes: lump-sum payments; payments offsetting tax liabilities, prerequisites or benefits not vested under a plan generally available to management employees, post-employment consulting fees or office expense and equity awards if vesting is accelerated, or a performance condition waived, due to termination.

The Board shall retain the option to seek shareholder approval after material terms are agreed upon.

Unfortunately some companies only limit cash golden parachutes to the 2.99 figure which means that there is no limit on non-cash golden parachutes for which shareholders have no voting power.

This proposal is relevant even if there are current golden parachute limits. A limit on golden parachutes is like a speed limit. A speed limit by itself does not guarantee that the speed limit will never be exceeded. Like this proposal the rules associated with a speed limit provide consequences if the limit is exceeded. With this proposal the consequences are a non-binding shareholder vote is required for unreasonably rich golden parachutes.

This proposal places no limit on long-term equity pay or any other type pay. This proposal thus has no impact on the ability to attract executive talent and does not discourage the use of long-term equity pay because it places no limit on golden parachutes. It simply requires that overly rich golden parachutes be subject to a non-binding shareholder vote at a shareholder meeting already scheduled for other matters.

This proposal is relevant because the annual say on executive pay vote does not have a separate section for approving or rejecting golden parachutes.

This proposal topic also received between 51% and 65% support at:
FedEx (FDX)
Spirit AeroSystems (SPR)
Alaska Air (ALK)
AbbVie (ABBV)
Fiserv (FISV)

Please vote yes:
Shareholder Vote regarding Excessive Golden Parachutes — **Proposal 4**

Board of Directors' Statement in Opposition

The board has carefully considered this proposal and, for the reasons described below, has found it not in the best interest of the company or its shareholders and recommends that you vote **AGAINST** Proposal 4.

- The proposal is unnecessary because the company's severance practices, including the treatment of equity upon termination of employment, are aligned with market practices and are not excessive.
- Shareholders already have substantial opportunity to provide input on our executive programs through annual "Say on Pay" votes and our extensive shareholder outreach.
- Our executive compensation program effectively aligns the interests of our executives and shareholders when taken as a whole; addressing one element in isolation risks creating an imbalance and unintended consequences.
- Adoption of this proposal could prevent us from effectively recruiting, motivating and retaining the highest quality executives which would be contrary to the best interests of shareholders.

The company's existing cash severance practices are below the proposal's 2.99 limit (under all termination scenarios other than for our chief executive officer following change in control) and the treatment of equity upon termination aligns with market practice

As described under *Employment Contracts and Change of Control Arrangements* on page 85, Vertex's named executive officers each have employment agreements with severance provisions. The severance provisions for our named executive officers other than our chief executive officer provide for cash payments equal to one times the sum of base salary plus target bonus for terminations without cause or for good reason. Following a change of control and in alignment with market practice, a terminated named executive officer is also eligible to receive a pro-rata portion of their target annual bonus for the year of termination based on the number of days actively employed.

All named executive officers are entitled to receive full accelerated vesting of equity incentive awards upon a termination without cause or for good reason following a change in control.

Our chief executive officer also has an employment agreement with severance provisions for termination without cause or for good reason providing for cash payments equal to two times the sum of base salary plus target bonus, eligibility for a pro-rata portion of target bonus, and partial accelerated vesting of equity awards for any outstanding awards that would have vested during the 12-month period immediately following the date of termination. For a qualifying termination following a change of control, our chief executive officer's severance provisions provide for cash payments equal to 2.99 times the sum of base salary plus target bonus, eligibility for a pro-rata portion of target bonus for the year of termination based on the number of days actively employed and full accelerated vesting of equity incentive awards.

Under our existing company-wide policy, our named executives are eligible to receive accelerated vesting of equity incentive awards upon a termination by reason of death or disability or in connection with a qualified retirement as described herein under the *Employment Agreements and Post-Termination Compensation and Benefits* section on page 74. The acceleration of outstanding equity upon death, disability and qualified retirement is a common practice in our industry.

Because our existing severance terms with the named executive officer agreements are already within market practice and generally limit cash severance to below 2.99 times the sum of base salary plus target annual bonus, and the equity treatment upon termination we provide aligns with market practice with full acceleration only occurring in limited situations (i.e., death, disability, qualified retirement and termination following a change in control), the consent requirement contained within this shareholder proposal is unnecessary.

Shareholders already have substantial opportunity to express their approval or disapproval of our post-termination compensation policies

Vertex's shareholders can effectively express their views on our executive compensation program through the annual "Say on Pay" advisory vote. In 2024, holders of 91% of the shares present and entitled to vote at the annual meeting indicated their support for Vertex's executive compensation program by voting to approve the compensation of the named executive officers. In fact, at the company's last five Annual Meetings of Shareholders, our executive compensation programs were approved on average by more than 91% of votes cast.

We also have a robust year-round shareholder engagement program focused on proactive outreach on a variety of topics, including our executive compensation design and practices. As described, under “Shareholder Engagement” in this proxy statement, following our 2024 Annual Meeting of Shareholders, we conducted extensive shareholder outreach to request feedback on our executive compensation program and to discuss vote results, corporate governance, human capital management, and compensation program design. We reached out to shareholders representing approximately 70% of our outstanding shares. On these calls, none of our shareholders raised the topic of our executive severance practices as an area of concern.

This proposal’s request for a shareholder vote on a specific component of Vertex’s executive compensation program is unnecessary in light of the existing opportunities shareholders have to provide input on our executive compensation program and practices.

Vertex’s executive compensation program effectively aligns the interests of our executives’ and shareholders’ interests when taken as a whole; addressing one element in isolation risks creating an imbalance and unintended consequences

The company operates in a global, highly competitive market for 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. Our executive compensation program is designed to attract, retain and motivate talented and experienced executives across all areas of our business and align the interests of our executives with the interests of our shareholders as we seek to create value through the discovery, development and commercialization of transformative medicines. The MDCC takes seriously its role in the development and administration of an effective executive compensation program, including one that aligns executive pay and performance. In 2024, approximately 90% of our named executive officer pay was linked to performance.

Over the last ten years, we have evolved from a company focused on a single disease area with one marketed medicine to a company with a diversified pipeline and marketed medicines for multiple disease areas, including being the first to receive FDA approval for a CRISPR gene-editing therapy (CASGEVY) and more recently for the first oral non-opioid pain signal inhibitor and new class of pain medicine in over 20 years (JOURNAVX). As a result, as shown on page 8, our stock price has appreciated well over a 1000% since the beginning of 2012. We expect that execution of our differentiated serial innovation strategy will continue to create shareholder value over the long term.

Our executives have been critical to our success and the compensation program that Vertex has established for our executives and other key employees ties their compensation to company performance. This pay-for-performance philosophy has received strong shareholder support through our annual “Say on Pay” vote. Addressing one design element of a comprehensive program designed with specific intentions risks creating an imbalance and unintended consequences. If implemented, the shareholder proposal could hinder our ability to execute on the intended design of our carefully structured executive compensation program.

Adoption of this proposal could prevent us from effectively recruiting, motivating and retaining the highest quality executives in a competitive talent market, which would be contrary to the best interests of our shareholders

The company relies on equity awards and carefully designed severance terms to motivate and retain our employees, and we believe that these awards and severance terms are necessary for us to remain competitive in attracting and retaining highly qualified individuals who are critical to the ongoing success of the company. Because the proposal is inconsistent with market practice, its restrictions on cash payments in addition to the limitations on acceleration of outstanding equity awards upon a termination event could undermine our ability to recruit and retain top talent. Similarly, requesting shareholder approval, which is often expensive and impractical, in order for certain executive officers to realize the full value of their equity awards upon a qualifying termination such as retirement or in the event of an executive officer’s death or disability effectively reduces the recruitment and retention value of long-term equity incentive awards and could disadvantage our ability to recruit and retain qualified executives and undermine the purpose of our executive compensation program. Furthermore, the uncertainty from seeking shareholder approval in these circumstances would severely impact our ability to recruit talented executives. Applying a one-size-fits-all approach to each termination event is too rigid and does not reflect the complex world in which a company like Vertex operates.

The Board believes the concerns raised by the proponent are already and more appropriately addressed by the reasonableness of our existing cash severance arrangements and our carefully managed executive compensation program that has received above 91% shareholder support over the last five years than the overly broad policy sought by this proposal. Further, adopting the policy requested by the proponent would be unduly restrictive on the company’s ability to recruit and retain its most critical employees, would undermine the purpose of an important part of the company’s executive compensation program, and is not in the best interests of Vertex or its shareholders.

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

COMPENSATION DISCUSSION AND ANALYSIS

Letter from Management Development and Compensation Committee to Our Shareholders

Dear Fellow Shareholders,

The Management Development and Compensation Committee's stewardship of Vertex's compensation programs is guided by Vertex's mission of developing transformative medicines for people with serious diseases and, by so doing, creating value for our shareholders. We take seriously our role in the oversight and administration of compensation programs and the importance of recruiting, motivating, and retaining highly capable and 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.

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, including the company's leadership position in CF, its historic global regulatory approvals of CASGEVY, the first CRISPR-based gene therapy to be approved in the world, and, more recently, the landmark FDA approval of JOURNAVX in the U.S., a non-opioid treatment for acute pain in adults. Throughout this period, Vertex maintained a strong financial position with significant growth in revenues, continued delivery of strong operating margins and cash flows, and accelerated the advancement of its clinical-stage pipeline across multiple disease areas and modalities.

2024 was a breakthrough year as Vertex entered into a new era of commercial diversification through the launch of CASGEVY across multiple regions, the approval of ALYFTREK, Vertex's fifth CFTR modulator and the January 2025 U.S. approval of JOURNAVX, a medicine that can provide effective relief of pain without evidence of the limitations of other currently available therapies, including the addictive potential of opioids. Beyond commercial diversification, the company further diversified its geographic footprint clinical pipeline and therapeutic modalities.

These accomplishments have been recognized by the company's shareholders and have been reflected in the increasing value attributed to the company. Vertex's market capitalization has increased from approximately $7 billion in early 2012 to approximately $103 billion at the end of 2024.

It was also a remarkable year for Vertex as the company continued to successfully execute its business strategy. The research and development team made significant progress in advancing multiple programs into pivotal development, including those designed to treat APOL1-mediated kidney disease, diabetic peripheral neuropathy, type 1 diabetes, and IgA nephropathy ("IgAN"). Furthermore, the company is progressing several earlier stage programs in CF, pain, autosomal dominant polycystic kidney disease, and myotonic dystrophy type 1. With these advancements, Vertex's research and development strategy is continuing to deliver a broad and deep pipeline of potentially transformative therapies, and thereby providing the opportunity for creating additional meaningful value for patients and shareholders.

Furthermore, in 2024, the company acquired Alpine Immune Sciences, Inc. ("Alpine") and its Phase 3 ready lead asset, povetacicept, which has the potential to be a "pipeline-in-a-product," a best-in-class approach to treat multiple B cell-mediated autoimmune diseases including IgAN. Since the acquisition, Vertex has advanced povetacicept into a Phase 3 trial in IgAN in addition to advancing povetacicept in multiple clinical trials in additional indications while successfully integrating the Alpine business into the company.

The company delivered outstanding financial performance in 2024, achieving net product revenues of $11.02 billion, a 12% increase compared to 2023 and representing a decade of consecutive years of double-digit growth. The company finished the year in a strong financial position with $11.2 billion in total cash and investments. The senior management team additionally strengthened the company's organizational capabilities by recruiting and onboarding top-tier talent across the organization and filling critical positions with superior talent.

The company's comprehensive success in 2024 reflects the execution of our differentiated corporate strategy championed by our senior management team. Consistent with these outstanding results, for 2024, our executives received above-target cash bonuses and payouts on performance stock unit awards based both on one-year financial goals and three-year milestone goals. We believe these outcomes are aligned with our commitment to directly link pay to performance. Looking ahead, we will continue to focus on the strong link between Vertex's compensation programs and the 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)*
Diana McKenzie
Jennifer Schneider
Suketu Upadhyay

Executive Summary

This section discusses the principles underlying our policies and decisions with respect to the compensation of our NEOs for 2024 and the factors we believe are relevant to an analysis of these policies and decisions. Our NEOs for 2024 are listed below.

Name	Position
Reshma Kewalramani	Chief Executive Officer and President
Charles F. Wagner, Jr.	Executive Vice President, Chief Financial Officer(1)
David M. Altshuler	Executive Vice President, Chief Scientific Officer
Stuart A. Arbuckle	Executive Vice President, Chief Operating Officer(1)
Nia Tatsis	Executive Vice President, Chief Regulatory and Quality Officer

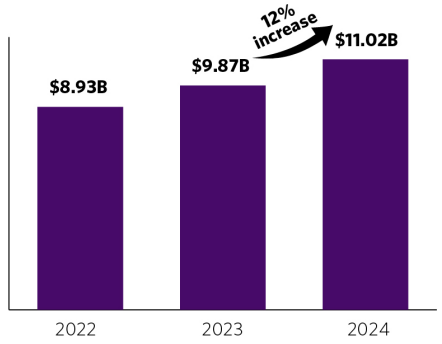
(1) As previously announced, effective July 1, 2025, Mr. Arbuckle will retire and Mr. Wagner will be appointed our Chief Operating Officer. Mr. Wagner will remain our Executive Vice President and Chief Financial Officer following his appointment.

Financial Performance

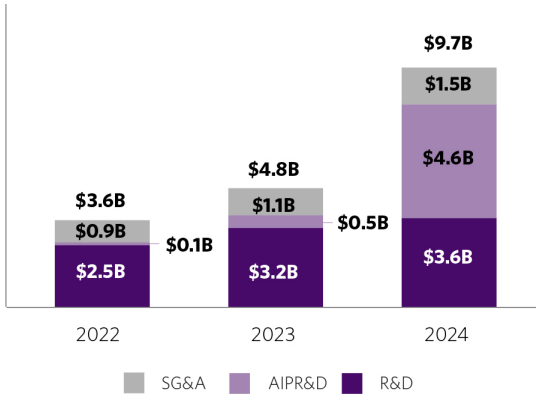
In 2024, sales of TRIKAFTA/KAFTRIO continued to drive our financial performance. We expect that our recently approved medicines, CASGEVY, ALYFTREK and JOURNAVX, will drive both continued revenue growth and diversification in 2025 and beyond.

- Our net product revenues increased to $11.02 billion in 2024, an increase of 12% or more than $1.1 billion, from our 2023 net product revenues.
- Our total R&D, AIPR&D and SG&A expenses increased to $9.7 billion compared to $4.8 billion in 2023. This increase was primarily due to higher AIPR&D, including $4.4 billion related to our acquisition of Alpine, continued investment to support additional therapies in mid-to-late stage development, and increased commercial investments to support launches of our newly-approved therapies globally.

INCREASING NET PRODUCT REVENUES



TOTAL R&D, AIPR&D AND SG&A EXPENSES



Marketed Products

Our differentiated R&D strategy has delivered more than a decade of leadership in CF. It also delivered the historic, global approvals for CASGEVY, the first CRISPR-based gene-edited cell therapy to be approved for people with SCD or TDT. And more recently, U.S. approval of JOURNAVX, the first and only non-opioid pain signal inhibitor, representing the first new class of pain medicines approved in over 20 years.

Cystic Fibrosis

In CF, our goal for more than 20 years has been to address the underlying cause of the disease and to bring more people with the disease to normal levels of CFTR function. We have continued to serially innovate in the years since the 2012 approval of KALYDECO, which was first approved to treat a CF population of approximately 1,000 people in the U.S. Today, we have five approved CF medicines that treat nearly three-quarters of the approximately 94,000 people with CF in the U.S., Europe, Australia, and Canada. Additionally, we continue to secure formal reimbursement in multiple additional countries that collectively comprise approximately 15,000 additional people with CF. Approximately 10,000 of those additional people with CF are eligible for treatment with CFTR modulators. We previously served many of these markets through named patient sales.

Notable progress since the beginning of 2024 includes:

- In December 2024, the FDA approved ALYFTREK, our once-daily, “next generation 2.0” combination CFTR modulator for the treatment of people with CF 6 years of age and older who have at least one F508del mutation or another responsive mutation in the CFTR gene. In March 2025, the MHRA also approved ALYFTREK in the U.K.
- Regulatory submissions for ALYFTREK, which are currently under review in the E.U., Canada, Switzerland, Australia, and New Zealand.
- In December 2024, the FDA approved the expanded use of TRIKAFTA for the treatment of people with CF with 94 additional non-F508del CFTR mutations. TRIKAFTA is now approved in the U.S. for a total of 272 CFTR mutations. In February 2025, the EMA adopted a positive CHMP opinion for the label expansion of KAFTRIO for the treatment of people with additional non-F508del CFTR mutations.
- We entered into an extended long-term reimbursement agreement with NHS England providing access to KAFTRIO, SYMKEVI and ORKAMBI, and continued access to KALYDECO, for existing and future eligible CF patients in England. We have entered into similar reimbursement agreements in Wales, Northern Ireland and Scotland. These reimbursement agreements include access to any future license extensions of these medicines.
- KAFTRIO is now reimbursed in all 27 countries of the E.U.

Sickle Cell Disease and Transfusion-Dependent Beta Thalassemia

2024 was a foundational year for the commercial launch of CASGEVY, following approvals in the U.S., the E.U., the U.K., Saudi Arabia, Bahrain, the UAE, Canada, and Switzerland. We estimate approximately 60,000 people with severe SCD or TDT are or could become eligible for CASGEVY in these jurisdictions. Our global launch for CASGEVY continues to focus on countries with high unmet medical need and infrastructure to support treatment with this CRISPR/Cas9-based gene-editing therapy, including the U.S., the Middle East, and major markets in Europe. We are working with ATCs to enable patient initiation, supporting the patient journey through infusion with CASGEVY, working with payors to secure broad and equitable access for patients and expanding our manufacturing and supply chain to meet growing patient demand. Our teams are also focused on educating patients, physicians and policymakers on the treatment journey and CASGEVY clinical data, as appropriate.

Notable progress since the beginning of 2024 includes:

- CASGEVY is now approved in the U.S., the E.U., the U.K., Saudi Arabia, Bahrain, the UAE, Canada and Switzerland for people 12 years of age and older with SCD or TDT.
- We have activated more than 50 authorized treatment centers globally, and more than 50 patients have initiated cell collection.
- In the U.S., we have broad coverage of CASGEVY with both private and public payers. In addition, we reached an agreement with the Centers for Medicare & Medicaid Services to participate in its cell and gene therapy access model, which may enable additional access mechanisms for states and authorized treatment centers.
- In the Middle East, we have reached hospital-based reimbursement for people with SCD or TDT in Saudi Arabia, and national reimbursement for eligible people in Bahrain. We are actively working to expand access to CASGEVY across Europe and the Middle East.
- We entered into a reimbursement agreement with NHS England for eligible people with SCD to access CASGEVY, consistent with the reimbursement agreement reached in August 2024 for eligible people with TDT.
- The Italian Medicines Agency has approved early access for CASGEVY, on a case-by-case basis, for the treatment of people with TDT and SCD.

Acute Pain

In January 2025, the FDA approved JOURNAVX for the treatment of moderate-to-severe acute pain in adults. JOURNAVX is a first-in-class, oral pain signal inhibitor that is highly selective for NaV1.8 voltage-gated sodium channels. Through this mechanism, JOURNAVX provides effective relief of pain without evidence of the limitations of other currently available therapies, including the addictive potential of opioids. Our launch strategy for JOURNAVX in the U.S. focuses on securing broad access for people with acute pain, educating patients and physicians on the clinical profile of JOURNAVX, and making investments to provide seamless treatment experiences for physicians and people with acute pain. We are engaging with payors and formulary decision-makers to secure reimbursement and access to JOURNAVX. We have secured broad stocking agreements at various national retail pharmacies as well as regional chains to facilitate broad availability of JOURNAVX. We have also established financial and co-pay assistance programs for patients that will support access to JOURNAVX.

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 advances in the understanding of human disease and the science of therapeutics to dramatically advance human health. This strategy was designed to deliver transformative medicines for serious diseases at high rates of speed and success, and it has delivered just that. 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 and/or best-in-class, therapies to patients. In addition to expanding our small molecule programs, we have also advanced an industry-leading portfolio of biologics, cell therapies and genetic therapy programs.

The advancement of novel candidates from the bench into clinical trials and successfully completing pivotal development and obtaining regulatory approvals reflects our strategy in action. It has yielded multiple commercial products including ALYFTREK, TRIKAFTA/KAFTRIO, SYMDEKO/SYMKEVI, ORKAMBI, and KALYDECO for CF, CASGEVY for SCD and TDT, and JOURNAVX for the treatment of moderate-to-severe acute pain. Our approach to drug discovery has also yielded therapies that have demonstrated clinical proof-of-concept in additional disease areas, including diabetic peripheral neuropathy with suzetrigine, AMKD with inaxaplin, and T1D with zimislecel. Furthermore, in 2024, we acquired Alpine and its lead asset, povetacicept, which has the potential to be a “pipeline-in-a-product” and a best-in-class approach to treat multiple B cell-mediated autoimmune diseases including IgAN, where it has demonstrated positive proof-of-concept.

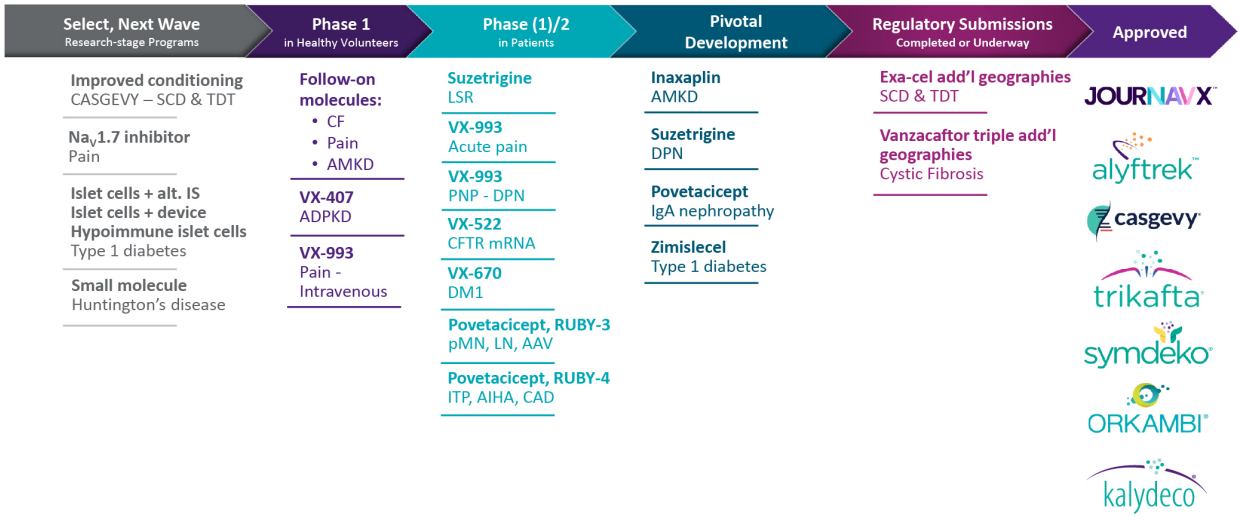
Our advancements across multiple disease areas and modalities since the beginning of 2024 include:

- *Cystic Fibrosis.* We are enrolling and dosing a Phase 3 clinical trial evaluating ALYFTREK in children with CF 2 to 5 years of age who have at least one F508del mutation or a mutation responsive to triple combination CFTR modulators. We continue to serially innovate in CF, raising the bar each time we do so, as we continue our mission to bring all patients with CF to normal levels of CFTR function. Our first “next-generation” triple combination of TRIKAFTA (NG 1.0) set a high bar for improvements in CFTR function, and ALYFTREK (NG 2.0) has improved upon TRIKAFTA. Our next triple combination regimen, NG 3.0, will consist of tezacaftor, VX-828 (a new CFTR corrector), and either VX-118 (a new CFTR potentiator) or deutivacaftor. We have completed Phase 1 clinical trials evaluating VX-118 and we are in the process of completing Phase 1 clinical trials with VX-828. We expect to enter clinical trials evaluating NG 3.0 in people with CF this year. We are also pursuing genetic therapies for people with CF who do not make full-length CFTR protein and, as a result, cannot benefit from our current CF medicines. For these more than 5,000 people, in collaboration with Moderna, we are developing VX-522, a CFTR 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 multiple ascending dose portion of the clinical trial for VX-522 in people with CF is ongoing and we expect to share data in the first half of 2025.
- *Sickle Cell Disease and Transfusion-Dependent Beta Thalassemia.* Two global Phase 3 clinical trials evaluating CASGEVY in children 5 to 11 years of age with severe SCD and TDT are ongoing. We have completed enrollment in these two clinical trials, and we expect to complete dosing in 2025. We are advancing preclinical assets for myeloablative conditioning agents with improved tolerability profiles, which could be used in connection with treatment with CASGEVY and significantly broaden the eligible SCD and TDT patient population. We are also investigating in vivo gene-editing approaches and small molecules for the potential treatment of SCD and TDT.
- *Acute Pain.* We are enrolling and dosing patients in a Phase 2 clinical trial evaluating an oral formulation of VX-993, our next-generation NaV1.8 pain signal inhibitor, for the treatment of moderate-to-severe acute pain. We are also enrolling and dosing healthy volunteers in a Phase 1 clinical trial evaluating an intravenous formulation of VX-993.
- *Neuropathic Pain.* The FDA has granted suzetrigine Breakthrough Therapy Designation in diabetic peripheral neuropathy and we are enrolling and dosing in the Phase 3 pivotal program evaluating suzetrigine in this population. In addition, we are enrolling and dosing patients in a Phase 2 diabetic peripheral neuropathy clinical trial of the oral formulation of VX-993. In December 2024, we announced results from a Phase 2 clinical trial evaluating suzetrigine in people with lumbosacral radiculopathy (“LSR”). The clinical trial met its primary endpoint, but the suzetrigine arm did not separate from the placebo reference arm. We hypothesize that a high placebo response in this clinical trial led to a lack of separation of the suzetrigine and placebo response curves. We believe we can innovate in pain clinical trial design to better control the placebo effect, and succeed in pivotal development with suzetrigine. Pending discussions with regulators, we plan to initiate a Phase 3 clinical trial of suzetrigine in LSR.

- *APOL-1 Mediated Kidney Disease*. Inaxaplin, our small molecule for the treatment of AMKD, is in pivotal development. We continue to enroll and dose people with AMKD in the Phase 3 portion of the global Phase 2/3 clinical trial. We expect to complete enrollment in the interim analysis cohort in 2025. This cohort requires 48 weeks of follow-up, at which point the interim analysis will be conducted. If the interim analysis is positive, we will apply for potential accelerated approval in the U.S.
- *IgA Nephropathy*. Povetacicept, a dual inhibitor of the BAFF and APRIL pathways, is a potentially best-in-class approach to treat IgAN and is in pivotal development. We are currently enrolling and dosing patients in the Phase 3 clinical trial and expect to complete enrollment in the interim analysis cohort this year. This cohort requires 36 weeks of follow-up, at which point the interim analysis will be conducted. If positive, we will apply for potential accelerated approval in the U.S. Povetacicept is also being studied in two Phase 2 basket trials of additional B cell-mediated autoimmune diseases: renal conditions in RUBY-3 and hematologic conditions in RUBY-4. We expect data in some of these conditions in 2025.
- *Type 1 Diabetes*. Zimislecel, formerly known as VX-880, is an allogeneic stem-cell derived, fully differentiated islet cell therapy in pivotal development for the treatment of T1D. We expect to complete enrollment and dosing in the Phase 3 portion of this Phase 1/2/3 clinical trial in 2025 and, assuming positive data, we expect to file for approval in 2026. In March 2025, we announced results from the Phase 1/2 clinical trial evaluating VX-264, our second clinical program in T1D, in which zimislecel is encapsulated in an immunoprotective device. VX-264 was generally safe and well-tolerated, however, efficacy data are not supportive of further clinical development. We plan to conduct further analyses of the VX-264 Phase 1/2 study, including explanted devices, to better understand these findings. In research, we are pursuing development of gentler approaches to immunosuppression for patients receiving zimislecel, as well as gene-editing approaches to develop hypoimmune stem cell-derived allogeneic islet cells.
- *Myotonic dystrophy type 1*. We are exploring multiple approaches to address the underlying causal biology for DM1, including small molecules and VX-670, an oligonucleotide-based approach in-licensed from Entrada. We completed the single ascending dose portion of the global Phase 1/2 clinical trial evaluating VX-670 in people with DM1 and we are currently enrolling and dosing the multiple ascending dose portion of the trial, which will evaluate the safety and efficacy of VX-670.
- *Autosomal Dominant Polycystic Kidney Disease*. We are nearing completion of a Phase 1 clinical trial in healthy volunteers evaluating VX-407, our first-in-class small molecule corrector that targets the underlying cause of ADPKD in people with a subset of variants in the PKD1 gene. We expect to advance VX-407 into a Phase 2 proof-of-concept study in people with ADPKD in 2025.
- In addition to the programs listed above, we have several earlier-stage research programs aimed at diseases that fit our R&D strategy, as well as follow-on programs in diseases already in the clinic.

We will continue investing in scientific innovation through our internal research efforts and by accessing emerging technologies and product candidates through business development transactions.

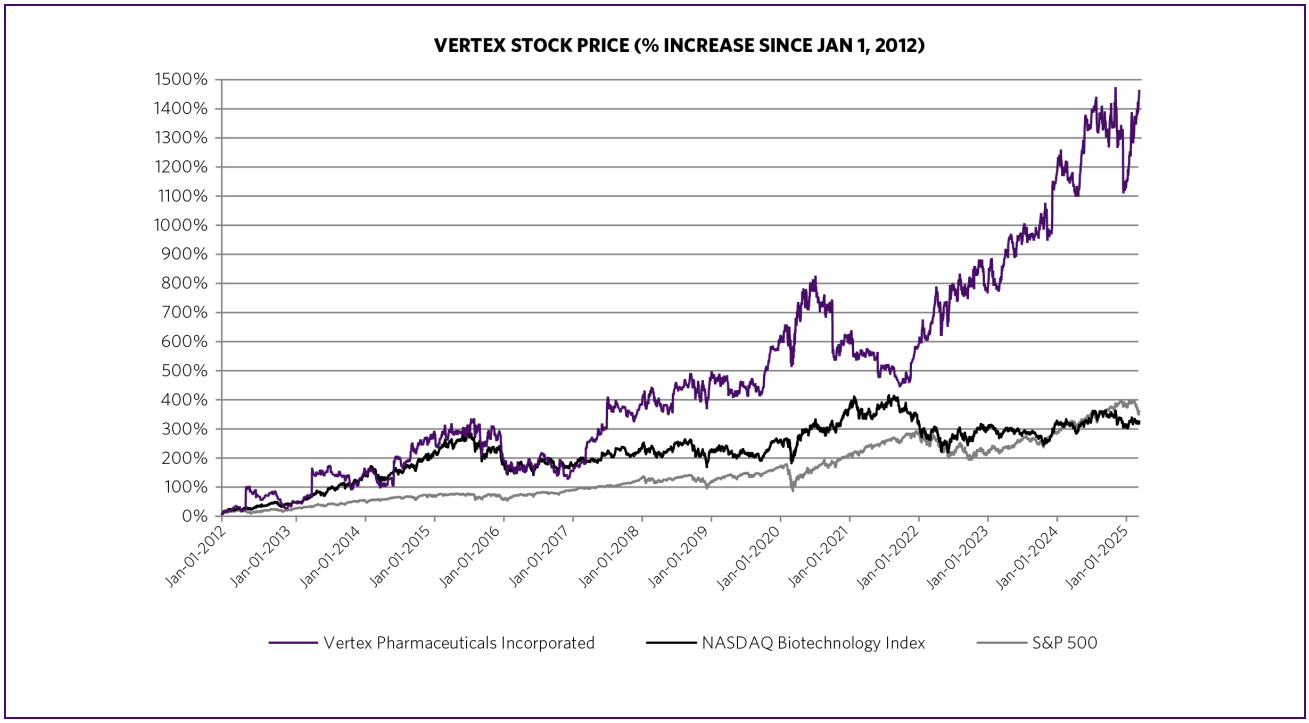
The following chart represents our approved medicines, clinical stage programs and select pre-clinical programs.



SCD: sickle cell disease; TDT: transfusion-dependent beta thalassemia; alt. IS: alternative immunosuppression; CF: cystic fibrosis; AMKD: APOL-1 mediated kidney disease; ADPKD: autosomal dominant polycystic kidney disease; LSR: lumbosacral radiculopathy; PNP: peripheral neuropathic pain; DPN: painful diabetic peripheral neuropathy; CFTR mRNA: cystic fibrosis transmembrane conductance regulator messenger RNA; DM1: myotonic dystrophy type 1; pMN: primary membranous nephropathy; LN: lupus nephritis; AAV: ANCA-associated vasculitides; ITP: idiopathic thrombocytopenia; AIHA: warm autoimmune hemolytic anemia; CAD: cold agglutin disease.

Increasing Shareholder Value

We expect that execution of our differentiated serial innovation strategy will continue to create shareholder value over the long-term. The biotechnology sector is subject to short-term volatility and many biotechnology companies experienced stock price fluctuations in 2024, including Vertex, where our stock price reached an all-time high of $519.88. We believe, however, that biotechnology companies are best measured over the long term as opposed to one-year or other shorter-term increments. The following chart shows our total shareholder return relative to the Nasdaq Biotechnology Index and S&P 500 index since 2012, when our first CF medicine was approved.



2024 Compensation Decisions and Pay-for-Performance

In 2024, our executive compensation program received substantial support from our shareholders, with approval by approximately 91% of the votes cast at the annual meeting of shareholders. We believe this support is consistent with our long-term shareholders' understanding of our business model, our pay-for-performance compensation philosophy and the long-term value we are creating. Our executive compensation program is intended to align executive compensation with the company's short- and long-term performance and to provide the compensation and incentives required to attract, motivate and retain our high-caliber executives who are crucial to Vertex's long-term success. **Our compensation program is highly performance-based, with more than 90% of our NEO compensation tied to performance**. Retention of our talented executives is critical, as their outstanding performance has led to the company's advancement and the creation of significant long-term shareholder value.

In 2024, 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 that we believe has contributed to our short- and long-term successes.
- **Base Salary:** In 2024, based on a comparative analysis of companies in our Peer Group (described below), we increased the base salaries for all of our NEOs.
- **Annual Cash Bonus:** In 2024, we increased the target cash bonus, which is a percentage of base salary, for all of our NEOs based on a comparative analysis of companies in our Peer Group (described below). The company's outstanding performance in 2024, as described above, resulted in the board determining that the company achieved a leading rating for 2024 (a rating of 142 out of a total potential score of 150) and the payment of above-target annual cash bonuses. Please see *Overview of Company Performance Rating & Achievement in 2024*.

- **Long-Term Equity Program:**
  - In 2024, based in part on a comparative analysis of companies in our Peer Group, we maintained the target equity grants for Dr. Kewalramani and our other NEOs.
  - We maintained our mix of equity granted under our compensation program with 50% of the awards 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 consequently are considered by the company to be performance-linked awards. We maintained a performance-specific multiplier range, as outlined under *Annual Equity Awards* on page 72 below.
  - We achieved all three goals established for the 2022-2024 non-financial based PSU awards, and the maximum level of performance for the 2024 financial-based PSU awards, resulting in a 200% payout for each of these awards in February 2025.
  - Based on discussions in late 2024 and early 2025, the MDCC granted new awards of PSUs in early 2025, the value of which were based on named executive officers' individual performance in 2024. The MDCC also established the financial and non-financial metrics, including the addition of a fourth metric focused on manufacturing, 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 net product revenue in 2025, while the remaining 50%, which cliff vest after three years, are tied to specific clinical, research and manufacturing milestones over a three-year period.
- The MDCC extended the term of the employment agreement of our Executive Chairman, Dr. Jeffrey Leiden, until 2027. 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 service as Executive Chairman.

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.

In 2024, we solicited feedback regarding our corporate governance practices from shareholders representing approximately 70% 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, human capital management, corporate governance, political and lobbying disclosures, executive compensation, shareholder proposals, and environmental sustainability 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 metrics	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	Allow payment of dividends on unvested performance shares or units
Independent compensation consultant	280G gross-ups (payments to offset excise taxes) in existing agreements
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 a wide range of 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: one with a leadership position and continued innovation in CF, a landmark gene-edited cell therapy for SCD and TDT, the first in a new class of acute pain medicine approved in more than 20 years, a broad, deep, and advancing pipeline, 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 directly link 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 expect to continue seeking balance in the use of financial metrics and R&D goals to motivate our executive team to achieve financial and strategic 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 a reference point among other factors, such as the performance, competencies, experience and specific role accountabilities of our NEOs, and do not benchmark 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, other executive officers, and senior leaders. 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. The members of the MDCC, each of whom is an independent director, make final compensation decisions for the executive officers 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 or determined.

The MDCC makes a recommendation regarding CEO compensation to the independent directors of the board, who make final compensation decisions for the CEO.

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 our compensation program as a whole, as well as 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 2024, the MDCC continued its engagement with Pearl Meyer as its independent compensation consultant. Pearl Meyer is compensated by the company 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 conduct a thorough assessment about the competitiveness of the elements of executive compensation that we provide to our NEOs, the MDCC and our board of directors consider 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. While revenue and industry are common peer selection criteria, we also use a mix of quantitative and qualitative factors in order to establish our peers for this purpose, 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 $2.2B or 25% of revenue
Number of employees	Greater than 2,000 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

It is unlikely that companies will meet all of the factors listed above; therefore 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 approved the following comparator companies for 2024, which were the same comparator companies used since 2022, except for the removal of Seagen Inc. due to its acquisition by Pfizer in 2023.

2024 Peer Group	
AbbVie Inc.	Eli Lilly and Company
Alnylam Pharmaceuticals	Gilead Sciences, Inc.
Amgen, Inc.	Incyte Corporation
Biogen, Inc.	Jazz Pharmaceuticals plc
BioMarin Pharmaceuticals, Inc.	Moderna, Inc.
Bristol-Myers Squibb Company	Regeneron Pharmaceuticals, Inc.

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[1]		Operational Focus		Innovative and Importance of Medicines				Market Position	
Company	Industry	$ (millions)	% of Revenue	Global	Commercial	Orphan/ Unmet Clinical Need	Approvals: Breakthrough Therapy and Regenerative Medicine Advanced Therapies[2]	Approvals (Last 14 Years): Innovative Drugs and Regenerative Medicine Therapies[3]	Uses Vertex as Peer	Nasdaq 100	S&P 500
AbbVie	Biotech	$ 15,548	28%	✔	✔	✔	7	9			✔
Alnylam	Biotech	$ 1,126	50%	✔	✔	✔	3	2	✔		
Amgen	Biotech	$ 5,964	18%	✔	✔	✔	4	10		✔	✔
Biogen	Biotech	$ 2,489	26%	✔	✔	✔	1	9	✔	✔	✔
BioMarin	Biotech	$ 747	26%	✔	✔	✔	2	5	✔		
Bristol-Myers	Pharma	$ 24,532	51%	✔	✔	✔	16	17			✔
Eli Lilly	Pharma	$ 14,271	32%	✔	✔	✔	6	14			✔
Gilead	Biotech	$ 14,750	51%	✔	✔	✔	6	10	✔	✔	✔
Incyte	Biotech	$ 2,637	62%	✔	✔	✔	2	6			✔
Jazz	Pharma	$ 1,521	37%	✔	✔	✔	1	5	✔		
Moderna	Biotech	$ 4,543	140%	✔	✔	✔	—	1	✔		✔
Regeneron	Biotech	$ 5,424	38%	✔	✔	✔	9	8	✔	✔	✔
Vertex	Biotech	$ 8,259	75%	✔	✔	✔	9	7		✔	✔

(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, 2024 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 and the Center for Biologics Evaluation and Research ("CBER") Regenerative Medicine Advanced Therapy Approvals report, which lists approvals for breakthrough therapy designated regenerative medicines.

(3) Innovative drugs and regenerative therapies in the last fourteen years include: VIEKIRA PAK, IMBRUVICA, VENCLEXTA, ORILISSA, MAVYRET, RINVOQ, SKYRIZI, QULIPTA and EPKINLY (AbbVie), ONPATTRO and GIVLAARI (Alnylam), AIMOVIG, BLINCYTO, XGEVA, PROLIA, KYPROLIS, PARSABIV, EVENITY, TEZSPIRE, LUMAKRAS, and IMDELLTRA (Amgen), TECFIDERA, ALPROLIX, SPINRAZA, ELOCTATE, VUMERITY, ADUHELM, LEQEMBI, SKYCLARYS and QALSODY (Biogen), BRINEURA, PALYNZIQ, VIMIZIM, VOXZOGO and ROCTAVIAN (BioMarin), ABECMA, BREYANZI, SOTYKTU, CAMZYOS, ZESPOSIA, ONUREG, REBLOZYL, INREBIC, IDHIFA, EVOTAZ, OPDIVO, POMALYST, ELIQUIS, YERVOY, OPDUALAG, COBENFY, and KRAZATI (Bristol-Myers), CYRAMZA, EMGALITY, JARDIANCE, OLUMIANT, PORTRAZZA, RETEVMO, REYVOW, TALTZ, VERZENIO, MOUNJARO, JAYPIRCA, OMVOH, EBGLYSS, and KISUNLA (Eli Lilly), YESCARTA, SOVALDI, HARVONI, VEMLIDY, CAYSTON, ZYDELIG, BIKTARVY, VEKLURY, SUNLENCA, and LIVDELZI (Gilead), JAKAFI, OLUMIANT, PEMAZYRE, RUXOLITINIB, ZYNYZ, and NIKTIMVO (Incyte), VYXEOS, DEFITELIO, ZEPZELCA, RYLAZE, and ZIIHERA (Jazz), SPIKEVAX (Moderna), and DUPIXENT, LIBTAYO, PRALUENT, EYLEA, ZALTRAP, INMAZEB, EVKEEZA, and VEOPOZ (Regeneron).

We do not solely benchmark to a particular level of compensation relative to compensation levels at the Peer Group companies, but rather assess compensation levels after considerable deliberation 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 AON/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 with a chief operating officer or similar role and 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
Abbvie Inc.	Charles River Laboratories Int'l, Inc.
Amgen, Inc.	DexCom, Inc.
Jazz Pharmaceuticals plc	Hologic, Inc.
	ResMed, Inc.
	Thermo Fisher Scientific Inc.
	United Therapeutics Corp.

Elements of Annual Compensation

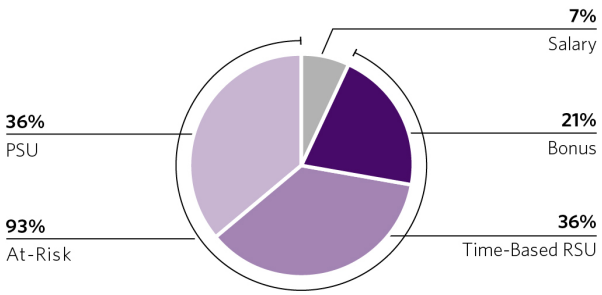
Our practice is to target total direct compensation including base salary, target annual cash incentives, and target long-term incentive awards at market competitive levels depending upon the NEO's responsibilities, expertise, and experience. At superior levels of performance, we aim for the design of 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 our NEOs, this means compensation is primarily in the form of equity and directly tied to changes in shareholder value over time. For our 2024 equity grants, we maintained our mix of equity awards, including PSUs and time-based RSUs.

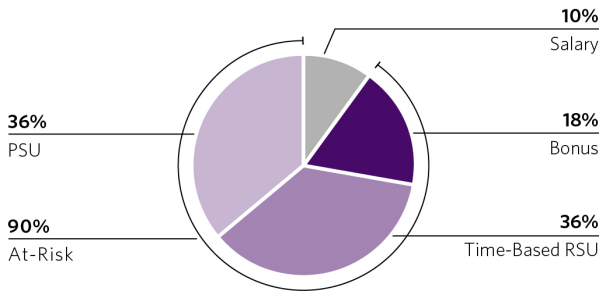
Compensation Program

As shown in the following charts, our compensation program places significant weight on performance-based compensation, **with more than 90% of our NEO compensation linked to performance or "at-risk" if performance is not achieved.**

CEO PAY MIX



OTHER NEOS' PAY MIX



The charts above generally represent the values in the Summary Compensation Table for our NEOs using the target value for PSU grants.

Performance-Based Value-Based Program

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

Compensation Element	Performance Link
Annual Cash Bonus	• Annual bonus dependent on both company and individual performance factors
Equity Awards	• Grant date value of equity awards based on target award values by level with differentiation for individual performance • Value of shares granted based on target set by MDCC and Board, adjusted for individual performance ranging from 0% for below target individual performance, 100% at target performance, and up to 150% for above target individual performance
PSU Awards	• 50% of PSUs with range of shares earned 0% to 200% of target based on one year financial metrics (to the extent earned, vesting in equal installments over a three-year period) • 50% of PSUs with range of shares earned 0% to 200% of target based on three-year non-financial metrics (to the extent earned, cliff-vesting after three years)
Time-Based RSUs	• Value of awards increases or decreases based on stock price over the three-year vesting period • 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 prior to grant as well as the resulting value dependent upon increases or decreases in our stock price over the three-year vesting period

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 measured from the date of grant, 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 goals. The MDCC selected revenue and clinical development milestones as the performance goals applicable to the PSUs 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 financial and strategic objectives through the grant of 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 the interests of the holders of these awards with the interests of our shareholders.

Base Salary

Rather than awarding standard annual merit increases, the MDCC recommends base salaries for our executive officers based on multiple factors, including an annual competitive market analysis on a position-by-position basis. The MDCC reviews a comparison of each executive's prior year base salary to salaries reported for executives with similar responsibilities at Peer Group companies (as supplemented for Mr. Arbuckle, as described above). The MDCC does not solely 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 a review of compensation at Peer Group companies, and taking into consideration the executive's base salary for the previous year or years, the MDCC approves an appropriate base salary for each executive officer other than the CEO and recommends an appropriate base salary for the CEO, subject to final approval by our independent directors. As a result, executive base salaries may be held constant from year to year as was the case last year when we disclosed that all named executive officer base salaries were maintained.

During the 2024 annual review of base salaries, the MDCC recommended salary increases for Dr. Kewalramani, Dr. Altshuler, Mr. Arbuckle, Dr. Tatsis and Mr. Wagner, which reflect each individual executive's past and expected future contributions, performance, experience, specific responsibilities relative to peer benchmarks, and competitive positioning within the Peer Group companies. The resulting increases vary based on the MDCC's review of these factors. For example, the three executive base salary increases of approximately 15% reflects the MDCC's thoughtful approach of reviewing and determining appropriate base salaries on an annual basis, rather than implementing standard annual merit increases. The MDCC's recommended increases recognize the contributions of each executive to the company's success and provide competitive market adjustments.

Name	2024 Base Salary	2023 Base Salary	Increase
Reshma Kewalramani	$ 1,600,000	$ 1,500,000	6.7 %
Charles F. Wagner, Jr.[(1)]	$ 950,000	$ 825,000	15.2 %
David M. Altshuler	$ 950,000	$ 825,000	15.2 %
Stuart A. Arbuckle	$ 1,000,000	$ 950,000	5.3 %
Nia Tatsis	$ 750,000	$ 650,000	15.4 %

(1) As previously announced, Mr. Wagner's base salary will increase to $1,000,000 when he assumes the role of our Chief Operating Officer on July 1, 2025.

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 2024

At the beginning of each year, the MDCC, in consultation with our CEO, establishes company-wide goals for that year under our annual and long-term cash and equity awards. While our performance against these goals is the most important factor considered in assessing our corporate performance, the MDCC considers additional accomplishments and shortcomings and may increase or decrease the performance scores associated with these goals. The aggregate discretionary adjustment may not exceed 10% of the performance score and the total company score may not exceed 150. The MDCC discusses and analyzes the company's performance, including specific performance factors and accomplishment of company goals, and ultimately approves the company's annual performance rating. While the aggregate discretionary adjustment is capped and relatively small, the MDCC believes this element provides an important mechanism to recognize the impact of unplanned events on the business whether positive or negative.

For 2024, 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 marketed and late-stage products goals were designed to incentivize increasing access to our medicines through approvals of new transformative medicines and therapies, label-expansions for our existing medicines, obtaining government reimbursement in ex-U.S. markets, and successfully commercializing new products. Our commercial manufacturing, innovation, quality and operations goals were designed to incentivize supply chain resilience, efficiency in delivery of our CF medicines and commercial manufacturing readiness for medicines and therapies 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. Our organizational development and capability goals were established to incentivize improvements to our organizational structure, processes, and systems. We believe this mix of goals provides an appropriate balance between our near- and long-term objectives and between commercial, pipeline, manufacturing, financial, and organizational development objectives.

Our 2024 weighted goals and the year-end score achieved by the company as approved by the MDCC are set forth in the following table:

Goal(s)	Maximum Score	Actual 2024 Performance Score
Marketed and Late-Stage Products	**50**	**47**
• Achieve CF net product revenue goals through compliant marketing practices, including U.S. and ex-U.S. revenue goals • Launch CASGEVY in the U.S., Europe and Saudi Arabia • Complete cross-functional launch readiness activities for ALYFTREK in the U.S. • Complete cross-functional launch readiness activities for JOURNAVX in the U.S. • Advance disease awareness, diagnosis and genotyping efforts for AMKD in the U.S.		
Pipeline Growth	**57**	**47.5**
• Submit marketing applications and obtain approval for ALYFTREK • Obtain approval for SCD and/or TDT in select countries and expand into pediatric population • Submit marketing application and obtain approval for JOURNAVX • Advance multiple non-CF clinical development programs • Advance multiple research programs, including CF and non-CF programs		
Manufacturing, Innovation, Quality & Operations	**15**	**15**
• Ensure continued and uninterrupted supply of approved therapies and diversify the supply chain • Enhance network capacity and resilience with respect to CASGEVY manufacturing • Complete commercial manufacturing readiness processes for JOURNAVX launch • Advance manufacturing plans and capabilities for pipeline products		
Organizational Development and Capability	**13**	**12**
• Continue to build and appropriately scale the organization to support expanding capabilities • Advance capital projects to support R&D and manufacturing growth • Continue to advance data and technology strategy • Continue outreach and communications to advance business and policy objectives		
Financial Strength	**15**	**15**
• Continue to manage our financial resources and to achieve financial targets		
Additional Accomplishments and Shortcomings, Net (see page 66 of this proxy statement)		**5**
TOTAL (FINAL SCORING ROUNDED TO WHOLE NUMBER)	**150**	**142**

Our 2024 company performance score, as determined by the board, was 142 out of a potential of 150.

Detailed Discussion of Company Performance Rating Factors and Achievements

Achievements - Marketed and Late-Stage Products

In 2024, we made significant progress with respect to our marketed and late-stage products.

- Net product revenues increased to $11.02 billion, up 12% as compared to 2023, primarily due to increased TRIKAFTA/KAFTRIO revenues resulting from strong performance and demand globally, including expansion into younger age groups and label extensions, and higher net realized pricing in the U.S.
- We executed the launch of CASGEVY in the U.S., the E.U., the U.K., Saudi Arabia, Bahrain, the UAE, Canada and Switzerland including with respect to activating ATCs, initiating patients on the CASGEVY treatment journey and securing access, payments and/or reimbursements with payers.
- We completed key cross-functional commercial readiness activities for the launch of ALYFTREK, which was approved by the FDA in December 2024.
- We completed key cross-functional commercial readiness activities for the launch of JOURNAVX in the U.S.
- Increased U.S. AMKD disease awareness, diagnosis and genotyping through testing, awareness and public affairs campaigns.

For our marketed and late-stage products goal, our board assigned the company a score of 47 out of 50, due to exceeding goals with respect to total CF net product revenues, successfully executing the initial CASGEVY launch, and successfully achieving launch readiness for both ALYFTREK and JOURNAVX.

Achievements - Pipeline Growth

In 2024, we made significant progress advancing our pipeline of CF and non-CF medicines.

- We obtained FDA approval for ALYFTREK and completed regulatory submissions in multiple additional geographies.
- We advanced the CFTRm portfolio in clinical trials in younger age groups.
- We advanced our CF mRNA program, VX-522.
- We obtained approval of CASGEVY in the E.U., Saudi Arabia, and other jurisdictions.
- We completed enrollment for Phase 3 clinical trials evaluating CASGEVY in children 5 to 11 years of age with severe SCD and TDT.
- We submitted applications for FDA approval for JOURNAVX for the treatment of moderate-to-severe acute pain in adults, receiving approval in January 2025.
- We completed the suzetrigine LSR Phase 2 trial; initiated the Phase 2 clinical trial in the oral formulation of VX-993, our next generation $Na_V1.8$ pain signal inhibitor, and initiated the Phase 1 clinical trial in the intravenous formulation of VX-993.
- We successfully completed End-Of-Phase 2 regulatory interactions and advanced the pivotal program in zimislecel for the treatment of T1D to Phase 3. We also advanced the clinical trial of VX-264.
- We advanced the global Phase 1/2 clinical trial evaluating VX-670 for the treatment of DM1.
- We advanced the Phase 1 clinical trial evaluating VX-407 for the treatment of ADPKD.
- We advanced a broad research-stage pipeline of potentially transformative small molecule, biologics, cell and genetic therapies aimed at treating serious diseases.

On the basis of the accomplishments in advancing our R&D programs including approvals for CASGEVY, ALYFTREK and JOURNAVX, and the advancement of multiple clinical and pre-clinical candidates across multiple modalities, our board assigned the company a score of 47.5 out of 57 for our pipeline growth goal.

Achievements - Manufacturing, Innovation, Quality and Operations

- We ensured the continued uninterrupted supply of our CF medicines by meeting stock targets, building redundancy and resilience of the commercial supply chain, and achieving successful inspection results.
- We advanced lifecycle management plans and enhanced network capacity for CASGEVY.
- We advanced various commercial manufacturing readiness processes for the launches of ALYFTREK and JOURNAVX.
- We continued development of our commercial manufacturing network strategy and made advancements in our manufacturing processes for pipeline products.

In recognition of achieving manufacturing milestones, including ensuring commercial manufacturing launch readiness for ALYFTREK and JOURNAVX, advancing the lifecycle management of CASGEVY, the continued development of the commercial manufacturing strategy for pipeline programs and strengthening of our CF supply chain, the board assigned the company a score of 15 out of 15 for our manufacturing, innovation quality and operations goal.

Achievements - Organizational Development and Capability

- Throughout 2024, we maintained above-industry benchmark employee satisfaction and sense of belonging scores as measured through our bi-annual pulse surveys.
- We evolved organizational design changes, advanced our hiring plans, and maintained low voluntary attrition.
- We invested in capital projects to support headcount, R&D and manufacturing growth with completion of the design of a new laboratory, office and amenity space and initiation of construction of the same.
- We continued to ensure information security, enhanced operational infrastructure, and innovative data and technology solutions.
- We continued to enhance our corporate reputation.
- We continued to engage with policymakers to ensure rapid and sustained access to innovative therapies.

To reflect the advancements to our organizational design, as well as the continued achievements in employee satisfaction and enhancements in corporate risk and reputation achieved in 2024, our board assigned the company a score of 12 out of 13 for our organizational development and capability goals.

Achievements - Financial Strength

We exceeded our financial goals in 2024. We surpassed our targets for both adjusted non-GAAP EBITDA, and adjusted non-GAAP net income.

As a result of our strong financial performance, including surpassing both our target adjusted non-GAAP EBITDA and our target adjusted non-GAAP net income, 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 2024 company rating, the MDCC made positive and negative adjustments based on factors not anticipated when the company's original goals for 2024 were established. By design, potential adjustments are capped at ±10% (or ±15 points), not to exceed total achievement of 150%, and used by the board to address and highlight important achievements and shortcomings. While the aggregate discretionary adjustment is capped and relatively small, the MDCC believes this element provides an important mechanism to recognize the impact of unplanned events on the business whether positive or negative. Positive adjustments were related to the successful identification, acquisition and integration of Alpine, advancing additional, novel molecules and therapies, beyond what was planned, and exemplary execution of JOURNAVX regulatory submissions and launch planning. Overall, the board of directors increased our company rating by seven points for these positive additional accomplishments, which was offset by a two point reduction related to slower than planned progression in one program and a reimbursement challenge in another program. As a result, our final company rating was increased by five points to a total of 142 points (rounded).

2024 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'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 2024 results-based rating recommendation for each NEO, other than our CEO, 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 regarding the executive, 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. Kewalramani and Dr. Leiden discussed each recommendation at length, on both an individual and comparative basis. Upon completion of these discussions, the MDCC determined and approved the results-based rating for each executive. The final results-based ratings reflect 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 below that, along with the annual corporate performance factor, determined each NEO's annual bonus. 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 are 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.

2024 Actual Individual Ratings for Named Executive Officers

Reshma Kewalramani CEO and President	2024 Rating:	Leading Exemplary
	2024 Salary:	$1,600,000
	2024 Bonus:	$4,941,600
	LTI Equity Grants (Feb 2025):	$17,145,000

On the basis of the MDCC's recommendation, our independent directors rated Dr. Kewalramani's overall performance for 2024 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 2024, including:

- Exemplary leadership over all aspects of the company, including research, development, manufacturing, commercial, and financial, as well as in executing our corporate strategy to develop transformative medicines for serious diseases and achieving our business goals
- Notable achievements include over-achievement of our financial goals, including significantly increasing CF net product revenues, strengthening our balance sheet, and continued delivery of strong operating margins, exemplary leadership of the successful acquisition and integration of Alpine, approval for the expanded use of TRIKAFTA for ultra-rare mutations, approval for ALYFTREK, and approval for JOURNAVX, the first-in-class, oral pain signal inhibitor for the treatment of moderate-to-severe acute pain in adults
- Oversight of the rapid advancement of the R&D pipeline advancing multiple programs to pivotal development, while also advancing the earlier stage programs as well as our preclinical pipeline
- Continued execution in growing, transforming, and diversifying our pipeline and commercial medicines into multiple new disease areas, utilizing multiple therapeutic modalities with increasing complexity, while ensuring that quality and compliance remain paramount
- Exhibiting outstanding leadership qualities in scaling the organization, advancing Vertex's culture and values, and recruiting, retaining and developing top-tier talent across the organization
- Continued strong engagement with the external community including analysts, investors, and policy makers
- Building an excellent relationship with the board based on trust, transparency, clear communication and responsiveness

Charles F. Wagner, Jr. EVP, Chief Financial Officer	2024 Rating:	Leading Exemplary
	2024 Salary:	$950,000
	2024 Bonus:	$1,821,150
	LTI Equity Grants (Feb 2025):	$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 150%. Mr. Wagner's rating derived from his leadership of the finance, accounting, investor relations, and facilities and real estate functions, including the following:

- Overseeing another excellent year of financial performance for Vertex, including managing operating expenses in accordance with our budget and guidance and continued success managing our capital allocation strategy
- Successfully managing our investment in pivotal studies for T1D, IgAN, AMKD, and DPN, as well as a build-out of capabilities for both our expanding pipeline and ongoing commercial launches while hitting profitability and cash flow targets
- Continued maintenance of a high level of shareholder engagement
- Outstanding leadership and oversight of the successful acquisition and integration of Alpine
- Exemplary leadership of the finance, accounting, investor relations, business development, and facilities organizations, including global reorganization of the finance and accounting organizations in support of continued growth and scalability
- Driving significant progress with respect to the construction of new facilities, lease negotiations with current facilities, and successfully recruiting, developing, and mentoring key talent
- Continuing to improve financial systems and processes while focusing on areas that increase operational efficiencies, agility, and mitigate risk

David M. Altshuler EVP, Chief Scientific Officer	2024 Rating:	Strong
	2024 Salary:	$950,000
	2024 Bonus:	$1,456,920
	LTI Equity Grants (Feb 2025):	$4,800,000

The MDCC recommended and the board adopted an overall rating of "Strong" for Dr. Altshuler based on a results-based rating of "strong" and a behaviors-based rating of "living the values" with an individual performance factor of 120%. 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:

- Continued advancement of the research pipeline with potentially transformative therapies across multiple modalities
- Excellent oversight of the continued advancement of next-generation CF therapies beyond next-generation 2.0 (ALYFTREK) with next-generation 3.0 triple combo regimen
- Leadership and oversight of the advancement of multiple novel preclinical candidates in disease areas outside CF
- Strong leadership of business development efforts including the acquisition of Alpine and strategic collaborations with Orna Therapeutics, Orum Therapeutics and TreeFrog Therapeutics.
- Transforming the data science and the data, technology and engineering organizations and driving operational excellence, with a focus on information security, advanced analytics and innovative data solutions

Stuart A. Arbuckle	2024 Rating:	Leading Exemplary
EVP, Chief Operating Officer	2024 Salary:	$1,000,000
	2024 Bonus:	$2,130,000
	LTI Equity Grants (Feb 2025):	$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, corporate communications, and human resources organizations, including the following:

- Superior continued commercial execution - delivering net product revenues of $11.02 billion in 2024, an increase of 12% compared to 2023, and exceeding our revenue forecast
- Strong performance with the initial global launch of CASGEVY, including activation of ATCs securing access and reimbursement in multiple geographies, and the initiation of cell collection in more than 50 patients
- Outstanding leadership of cross-functional launch readiness activities to support commercialization of ALYFTREK following U.S. approval
- Outstanding leadership of cross-functional launch readiness activities to support commercialization of JOURNAVX following U.S. approval, including build-out and training of sales team, engagement with payors to secure reimbursement and access, and securing national retail distribution to facilitate broad availability
- Exemplary leadership of the human resources, corporate communications, and program management functions

Ourania "Nia" Tatsis	2024 Rating:	Leading Exemplary
EVP, Chief Regulatory and Quality Officer	2024 Salary:	$750,000
	2024 Bonus:	$1,341,900
	LTI Equity Grants (Feb 2025):	$5,600,000

The MDCC recommended and the board adopted an overall rating of "Leading Exemplary" for Dr. Tatsis based on a results-based rating of "leading" and a behaviors-based rating of "exemplary demonstration" with an individual performance factor of 140%. Dr. Tatsis' rating derived from her leadership of the global regulatory and quality organizations, including the following:

- Superior execution of the submission for the FDA approval for expanded use of TRIKAFTA and multiple regulatory applications to the European Medicines Agency for TRIKAFTA/KAFTRIO
- Exemplary oversight and leadership of submissions for regulatory approval of ALYFTREK in the U.S. and multiple additional geographies, as well as interactions with global regulatory agencies regarding the same
- Excellent leadership and oversight of the 2024 submission for the 2025 FDA approval of JOURNAVX
- Outstanding performance of the Regulatory Affairs and Quality organizations through numerous regulatory interactions across the pipeline, including multiple approval processes and GxP audits and inspections
- Stand-out progress building and scaling the Regulatory Affairs and Quality functions to ensure excellent support of the organization, particularly with respect to the growing biologics, cell therapy, and gene therapy portfolio and geographic expansion

Annual Cash Bonus

The 2024 cash bonus for each NEO (referred to in the *Summary Compensation Table* on page 78 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			x	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
		90%-150% based on role		0%-150%		0-150%		

The individual incentive targets are established and reviewed by the MDCC based on available data about Peer Group company compensation (as supplemented for Mr. Arbuckle, as described above). The MDCC reviewed the competitive data for peer counterparts and sought to align incentive targets closer to the median. For 2024, Dr. Kewalramani's individual incentive target increased from 120% to 150% of her base salary and Mr. Arbuckle's individual incentive target increased from 90% to 100% of his base salary. The individual incentive target for Mr. Wagner, Dr. Altshuler and Dr. Tatsis increased from 70% to 90% of their respective base salary during 2024. As previously announced, Mr. Wagner's individual incentive target will be 100% of his base salary upon his transition to the role of our Chief Operating Officer on July 1, 2025. 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 2024 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, the MDCC approved individual performance factors and annual bonus awards for each of the NEOs other than our CEO for which the MDCC recommended, and our independent directors approved, on account of 2024 performance, as set forth in the table below.

Name	2024 Base Salary		Individual Incentive Target		2024 Target Bonus		Company Performance Factor		Individual Performance Factor		2024 Performance Cash Bonus
Reshma Kewalramani	$ 1,600,000	x	150 %	=	$ 2,400,000	x	142 %	x	145 %	=	$ 4,941,600
Charles F. Wagner, Jr.	$ 950,000	x	90 %	=	$ 855,000	x	142 %	x	150 %	=	$ 1,821,150
David M. Altshuler	$ 950,000	x	90 %	=	$ 855,000	x	142 %	x	120 %	=	$ 1,456,920
Stuart A. Arbuckle	$ 1,000,000	x	100 %	=	$ 1,000,000	x	142 %	x	150 %	=	$ 2,130,000
Nia Tatsis	$ 750,000	x	90 %	=	$ 675,000	x	142 %	x	140 %	=	$ 1,341,900

Annual Equity Awards

Value-Based Guidelines for Annual NEO Equity Grants

Under our compensation program, equity awards for our CEO and EVPs are calculated by multiplying the individual's target equity award by his or her performance rating-based equity modifier based on a performance-specific multiplier range, as outlined below. This performance-specific multiplier range increases the performance sensitivity of the program by adding the flexibility to adjust the equity modifier to reflect individual performance and expected contributions, further aligning the interests of our CEO and EVPs with the interests of our shareholders.

The target value, available individual ratings and corresponding performance rating-based equity modifier ranges for our executive officers are set forth in the table below.

			Performance Rating-Based Equity Modifiers				
		Target value	Not Building	Building	Strong	Leading	Leading Exemplary
CEO	$	13,500,000	— %	50% - 86.5%	86.5% - 113.5%	100% - 127%	113.5% - 127%
COO	$	4,750,000	— %	50% - 80%	80% - 120%	100% - 150%	120% - 150%
EVP (excluding the COO)	$	4,000,000	— %	50% - 80%	80% - 120%	100% - 150%	120% - 150%

The CEO equity modifier range is narrower relative to the COO and EVP ranges in order to reflect the tighter distribution of equity award values among the peer CEO comparators.

Based on a comparative analysis of our Peer Group companies, as supplemented to address Mr. Arbuckle's COO role, the MDCC maintained the target equity value for Dr. Kewalramani, Mr. Arbuckle and our other EVPs of $13.5 million, $4.75 million and $4.0 million, respectively. The mid-point of the performance factor range for Leading and highest performance factor for Leading Exemplary performance were selected based on award values approximating the 75th and mid upper quartile percentiles, respectively, of executives at our Peer Group companies. 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).

As previously announced, Mr. Wagner's target equity value will increase to $4,750,000 when he assumes the role of our Chief Operating Officer on July 1, 2025.

February 2025 Grants Based on 2024 Performance

In February 2025, the MDCC approved individual performance factors and equity awards for each of the NEOs other than our CEO, as set forth in the table below. For our CEO, upon the MDCC's recommendation, our independent directors approved the individual performance factor and equity award for our CEO as set forth in the table below.

Name	Individual Performance Rating	Performance Rating-Based Equity Modifier	Performance-Based RSU (50%)	Time-based RSU (50%)	Total Equity Value
Reshma Kewalramani	Leading Exemplary	127 %	$ 8,572,500	$ 8,572,500	$ 17,145,000
Charles F. Wagner, Jr.	Leading Exemplary	150 %	$ 3,000,000	$ 3,000,000	$ 6,000,000
David M. Altshuler	Strong	120 %	$ 2,400,000	$ 2,400,000	$ 4,800,000
Stuart A. Arbuckle	Leading Exemplary	150 %	$ 3,562,500	$ 3,562,500	$ 7,125,000
Nia Tatsis	Leading Exemplary	140 %	$ 2,800,000	$ 2,800,000	$ 5,600,000

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 revenues complements our long-term strategic objectives to progress our clinical portfolio and obtain approvals for additional transformative medicines for serious diseases.

The performance goal for the 2024 financial-based PSU was established in February 2024 based on 2024 net product revenues using budgeted foreign currency rates. The final performance multipliers for our 2024 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 2025. The following chart shows the pre-established financial goals and the actual results for the financial-based PSU awards granted in 2024:

		Below Threshold	Threshold	Target	Max	Results	
Award Year	Company Goal	0% Payout	50% Payout	100% Payout	200% Payout	Product Revenue	Payout
2024	2024 Net Product Revenues[1]	<$10.315 billion	$10.315 billion	$10.465 to $10.565 billion	>$10.715 billion	$10.75 billion	200%

(1) Reflects certain pre-established foreign exchange-related adjustments, and excludes product revenue from certain markets.

Consistent with our philosophy of aligning compensation with performance, for 2024, a year in which we substantially exceeded our net product revenue expectations, the payout on our one-year financial PSU awards achieved the maximum level.

The performance goals for the 2022 non-financial PSUs were established in February 2022 and our performance against these goals was determined in the first quarter of 2025. 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 would have resulted in a payout of 200%.

			Payout
2022	CF Portfolio Milestone - Complete regulatory submissions in US and EU for vanzacaftor triple	Achieved	200%
	Deliver at least two completed proof of concepts in non-CF programs, at least one of which is in cell and gene therapies to the extent not already counted for other proof-of-concept performance milestones; programs may be in-licensed or acquired	Achieved	
	Submit a non-cystic fibrosis product candidate or a non-small-molecule cystic fibrosis candidate for regulatory approval	Achieved	

The final performance multipliers for our 2022 non-financial PSUs 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 2025. Performance achievement for the 2023, 2024 and 2025 non-financial based PSU awards will be determined in the first quarter of 2026, 2027 and 2028, respectively, based on performance over the relevant three-year performance period. The non-financial goals contained in our three-year PSU awards for 2023, 2024 and 2025 are based on multiple clinical milestones, and are not disclosed for competitive reasons and because the relevant performance periods are ongoing. In 2025, we added a fourth non-financial milestone to the PSU award related to manufacturing excellence.

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 eligibility for 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.

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 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 who retire (our "Career Employment Provision"). 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. In 2024, the MDCC assessed our Career Employment Provision to review peer practices, ensure alignment with our philosophy of rewarding and incentivizing long-term service with the Company as well as to provide a competitive advantage to attract talent with significant industry experience and expertise. As a result of the review, the MDCC amended the Career Employment Provision effective for any newly hired employees on or after January 1, 2025.

Under the legacy Career Employment Provision, equity awards granted, including those granted to our NEOs, contain a retirement vesting provision, under which a "legacy 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 "legacy qualified" participant is a participant (1) who is at least age 55 and who was most recently hired before January 1, 2025, (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.

Under the amended Career Employment Provision, equity awards granted contain a retirement vesting provision under which a "qualified" participant who retires under the terms of the provision will receive full accelerated vesting of all shares underlying the award. A "qualified" participant is a participant (1) who is at least age 55 and who was most recently hired on or after January 1, 2025, (2) has completed at least ten full years of service, and (3) who has completed a mandatory transitional period of employment with the company following notice of their planned termination of service.

The Career Employment provision amendments are effective as of January 1, 2025, and apply to future grants of equity awards. The applicable provisions will be based on the employee's most recent hire date. Currently all NEOs were hired prior to January 1, 2025, therefore they meet the definition of a "legacy qualified" participant with eligibility for the partial vesting acceleration benefit once meeting the age, service and transitional period requirements of the provision. Mr. Arbuckle has met the age and service requirements under the definition of a "legacy qualified" participant. In connection with his retirement on July 1, 2025, the MDCC considered Mr. Arbuckle as eligible for the retirement vesting provisions of his equity awards.

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 an important element of our compensation program that align corporate shareholder and company interests, even though these awards may not result in full tax deductibility.

Compensation Practices

Equity Grant Practices

Our MDCC and board of directors generally determines annual equity grants at its meeting each February when it evaluates individual performance for the year. This meeting may occur prior to the company's release of earnings and filing of its Annual Report on Form 10-K. In such cases, the annual equity awards will be granted on the second full trading day following the company's release of earnings. This is generally the same date that the company's trading window opens. 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. The MDCC and board thus ensure that the market has had time to adjust to earnings news before the value used to convert to shares has been set.

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. As a matter of practice, the MDCC and board do not take material non-public information into account when determining the timing and terms of equity awards, and the company has not timed the disclosure of material non-public information for the purpose of affecting the value of executive compensation. We do not currently grant options to our employees, including our executive officers.

Compensation Recoupment ("Clawback") Policies

We have adopted a recoupment or clawback policy that is intended to comply with the requirements of the Dodd-Frank Act. Under this policy, in the event we are required to prepare an accounting restatement due to material noncompliance with financial reporting requirements, we are required to recover incentive-based compensation erroneously received by current and former executive officers during the three completed fiscal years immediately preceding the year of the restatement. Erroneous payments will be recovered under the policy even if there was no misconduct or failure of oversight on the part of an individual executive officer.

We also have a clawback policy relating to fraud and intentional misconduct. Under that policy, 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.

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

Employee	Minimum Shareholding Requirement
CEO	6X base salary
EVPs	4X base salary

Individual holdings, and holdings of immediate family members, of (a) common stock, (b) unvested RSUs, (c) shares held in a family trust; and (d) shares held through our 401(k) plan count toward meeting these guidelines; unearned PSUs and unexercised stock options do not count toward meeting these guidelines. As of March 17, 2025, 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 acquisition and development 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 2025 annual meeting of shareholders and incorporated by reference into Vertex's Annual Report on Form 10-K for the year ended December 31, 2024. This report is provided by the following directors who comprise the Management Development and Compensation Committee:

Bruce I. Sachs (Chair)
Diana McKenzie
Jennifer Schneider
Suketu Upadhyay

COMPENSATION AND EQUITY TABLES

Summary Compensation Table

The following table provides summary information concerning the compensation for each of our NEOs for 2024, 2023, and 2022.

Name and Principal Position	Year	Salary	Bonus	Stock Awards [1]	Non-Equity Incentive Plan Compensation	All Other Compensation	Total
Reshma Kewalramani	2024	$ 1,541,154	$ —	$ 15,002,202	$ 4,941,600	$ 53,712	$ 21,538,668
CEO and President	2023	$ 1,500,000	$ —	$ 15,001,894	$ 4,050,000	$ 42,547	$ 20,594,441
	2022	$ 1,396,154	$ —	$ 10,640,784	$ 3,784,500	$ 43,059	$ 15,864,497
Charles F. Wagner, Jr.	2024	$ 876,443	$ —	$ 5,250,328	$ 1,821,150	$ 51,519	$ 7,999,440
EVP & Chief Financial Officer	2023	$ 825,000	$ —	$ 5,250,552	$ 1,256,063	$ 40,136	$ 7,371,751
	2022	$ 793,269	$ —	$ 3,750,197	$ 1,239,315	$ 28,830	$ 5,811,611
David M. Altshuler	2024	$ 876,443	$ —	$ 5,250,328	$ 1,456,920	$ 53,787	$ 7,637,478
EVP & Chief Scientific Officer	2023	$ 825,000	$ —	$ 4,375,089	$ 1,299,375	$ 41,636	$ 6,541,100
	2022	$ 810,577	$ —	$ 4,500,090	$ 1,172,325	$ 42,137	$ 6,525,129
Stuart A. Arbuckle	2024	$ 941,154	$ —	$ 6,234,857	$ 2,130,000	$ 77,452	$ 9,383,463
EVP & Chief Operating Officer	2023	$ 900,000	$ —	$ 6,234,712	$ 1,822,500	$ 41,737	$ 8,998,949
	2022	$ 900,000	$ —	$ 12,294,259	$ 1,761,750	$ 43,097	$ 14,999,106
Nia Tatsis	2024	$ 691,154	$ —	$ 5,250,328	$ 1,341,900	$ 50,934	$ 7,334,316
EVP & Chief Regulatory and Quality Officer							

(1) Pursuant to applicable SEC rules, the grant-date fair values of the equity awards granted in February 2024 for 2023 performance are included in 2024 compensation. Also included in 2022 compensation is the grant-date fair value of a one-time equity awards granted in December 2022 to Mr. Arbuckle. The equity awards granted in February 2025 to Dr. Kewalramani, Mr. Wagner, Dr. Altshuler, Mr. Arbuckle and Dr. Tatsis for 2024 performance are discussed in the *Compensation Discussion and Analysis* section and are not reflected in the Summary Compensation Table above.

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 for each NEO for 2024 as reflected in the table above is significantly affected by such executive’s performance during 2023.

The "Stock Awards" for 2024, 2023, and 2022 consist of PSU awards and time-vested RSU awards granted in February of each year. In each of 2024, 2023, and 2022, 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 (with fair values determined based on the value of our common stock on the date of grant of the applicable award). In 2024, 2023, and 2022, the non-financial PSU awards had grant-date values of 50%, 50% and 0%, 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	2024	2023	2022
Reshma Kewalramani	$ 25,718,361	$ 25,717,533	$ 21,281,812
Charles F. Wagner, Jr.	$ 9,000,561	$ 9,000,945	$ 7,500,393
David M. Altshuler	$ 9,000,561	$ 7,500,153	$ 9,000,180
Stuart A. Arbuckle	$ 10,688,325	$ 10,688,305	$ 26,488,914
Nia Tatsis	$ 9,000,561	N/A	N/A

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 2024, 2023 and 2022 performance, each of which was paid in the first quarter of the subsequent year. The cash bonus awards to the NEOs for 2024 performance were determined as follows:

Name	Base Salary		Individual Incentive Target		2024 Target Bonus		Company Performance Factor		Individual Performance Factor		2024 Performance Cash Bonus
Reshma Kewalramani	$ 1,600,000	x	150 %	=	$ 2,400,000	x	142 %	x	145 %	=	$ 4,941,600
Charles F. Wagner, Jr.	$ 950,000	x	90 %	=	$ 855,000	x	142 %	x	150 %	=	$ 1,821,150
David M. Altshuler	$ 950,000	x	90 %	=	$ 855,000	x	142 %	x	120 %	=	$ 1,456,920
Stuart A. Arbuckle	$ 1,000,000	x	100 %	=	$ 1,000,000	x	142 %	x	150 %	=	$ 2,130,000
Nia Tatsis	$ 750,000	x	90 %	=	$ 675,000	x	142 %	x	140 %	=	$ 1,341,900

All Other Compensation

The amounts set forth under the caption "All Other Compensation" in the table for 2024 consist of:

Name	401(k) Match	Life Insurance Premiums	Matching Gift Program	Other	Total
Reshma Kewalramani	$ 15,525	$ 2,697	$ 25,000	$ 10,490 (1)	$ 53,712
Charles F. Wagner, Jr.	$ 15,525	$ 1,776	$ 25,000	$ 9,218 (2)	$ 51,519
David M. Altshuler	$ 15,525	$ 1,786	$ 25,000	$ 11,476 (3)	$ 53,787
Stuart A. Arbuckle	$ 15,525	$ 1,887	$ 25,000	$ 35,040 (4)	$ 77,452
Nia Tatsis	$ 15,525	$ 1,549	$ 25,000	$ 8,860 (5)	$ 50,934

(1) Amount includes $7,361 of tax reimbursements, and company activities and gifts.
(2) Amount includes $6,129 of tax reimbursements, and company activities and gifts.
(3) Amount includes $7,686 of tax reimbursements, and company activities and gifts.
(4) Amount reflects $12,525 of tax reimbursements, company activities and gifts, and travel and entertainment expenses for Mr. Arbuckle's spouse in connection with certain business trips.
(5) Amount includes $6,218 of tax reimbursements, and company activities and gifts.

Grants of Plan-Based Awards During 2024

The following table provides information with respect to grants of awards to each of our NEOs during 2024. Pursuant to SEC rules, (i) the threshold, target and maximum amounts payable pursuant to our 2024 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 2024 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 2024 is set forth under "All Other Stock Awards: Number of Shares of Stock or Units."

			Estimated Possible Payouts Under Non-Equity Incentive Plan Awards			Estimated Future Payouts Under Equity Incentive Plan Awards (shares)			All Other Stock Awards: Number of Shares of Stock or Units	Grant-Date Fair Value of Stock and Option Awards
Name		Grant Date	Threshold ($)	Target ($)	Maximum ($)	Threshold (#)	Target (#)	Maximum (#)	(#)	($)
Reshma Kewalramani	(1)		$ —	$ 2,400,000	$ 5,400,000					
	(2a)	2/7/2024				—	10,164	20,328		$ 4,286,464
	(2b)	2/7/2024				—	10,164	20,328		$ 2,143,232
	(3)	2/7/2024							20,327	$ 8,572,506
Charles F. Wagner, Jr.	(1)		$ —	$ 855,000	$ 1,923,750					
	(2a)	2/7/2024				—	3,557	7,114		$ 1,500,094
	(2b)	2/7/2024				—	3,557	7,114		$ 750,047
	(3)	2/7/2024							7,114	$ 3,000,187
David M. Altshuler	(1)		$ —	$ 855,000	$ 1,923,750					
	(2a)	2/7/2024				—	3,557	7,114		$ 1,500,094
	(2b)	2/7/2024				—	3,557	7,114		$ 750,047
	(3)	2/7/2024							7,114	$ 3,000,187
Stuart A. Arbuckle	(1)		$ —	$ 1,000,000	$ 2,250,000					
	(2a)	2/7/2024				—	4,224	8,448		$ 1,781,388
	(2b)	2/7/2024				—	4,224	8,448		$ 890,694
	(3)	2/7/2024							8,448	$ 3,562,775
Nia Tatsis	(1)		$ —	$ 675,000	$ 1,518,750					
	(2a)	2/7/2024				—	3,557	7,114		$ 1,500,094
	(2b)	2/7/2024				—	3,557	7,114		$ 750,047
	(3)	2/7/2024							7,114	$ 3,000,187

(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 2024 annual cash bonus program. Actual amounts paid to each of the NEOs under this program for 2024 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 2024. 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 50% of the target shares in 2024. 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 2024* 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 2024, which generally vest annually over three years.

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

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

Outstanding Equity Awards at Fiscal Year-End for 2024

The following table provides information with respect to outstanding equity awards held by each of our NEOs on December 31, 2024, based on the closing price of $402.70 per share of our common stock on December 31, 2024:

	Option Awards				Stock Awards			
Name	Number of Securities Underlying Unexercised Options Exercisable (shares)	Number of Securities Underlying Unexercised Options Unexercisable (shares)	Option Exercise Price (per share)	Option Expiration Date [1]	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**							
					9,706 [2]	$ 3,908,606		
					17,982 [3]	$ 7,241,351		
					20,327 [4]	$ 8,185,683		
	Performance-based RSU							
					9,706 [5]	$ 3,908,606		
					17,982 [6]	$ 7,241,351		
					29,118 [7]	$ 11,725,819		
					20,328 [8]	$ 8,186,086		
							26,972 [9]	$ 10,861,624
							20,328 [10]	$ 8,186,086
Charles F. Wagner, Jr.	**Time-based RSU**							
					3,421 [2]	$ 1,377,637		
					6,294 [3]	$ 2,534,594		
					7,114 [4]	$ 2,864,808		
	Performance-based RSU							
					3,422 [5]	$ 1,378,039		
					6,294 [6]	$ 2,534,594		
					10,262 [7]	$ 4,132,507		
					7,114 [8]	$ 2,864,808		
							9,440 [9]	$ 3,801,488
							7,114 [10]	$ 2,864,808
	Stock Options							
	9,532	0	$189.38	4/9/2029				
David M. Altshuler	**Time-based RSU**							
					4,105 [2]	$ 1,653,084		
					5,244 [3]	$ 2,111,759		
					7,114 [4]	$ 2,864,808		
	Performance-based RSU							
					4,106 [5]	$ 1,653,486		
					5,244 [6]	$ 2,111,759		
					12,314 [7]	$ 4,958,848		
					7,114 [8]	$ 2,864,808		
							7,866 [9]	$ 3,167,638
							7,114 [10]	$ 2,864,808

Outstanding Equity Awards at Fiscal Year-End for 2024

	Option Awards				Stock Awards			
Name	Number of Securities Underlying Unexercised Options Exercisable (shares)	Number of Securities Underlying Unexercised Options Unexercisable (shares)	Option Exercise Price (per share)	Option Expiration Date (1)	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**							
					4,875 (2)	$ 1,963,163		
					7,473 (3)	$ 3,009,377		
					8,448 (4)	$ 3,402,010		
					12,753 (11)	$ 5,135,633		
	Performance-based RSU							
					4,876 (5)	$ 1,963,565		
					7,474 (6)	$ 3,009,780		
					14,624 (7)	$ 5,889,085		
					8,448 (8)	$ 3,402,010		
							11,210 (9)	$ 4,514,267
							8,448 (10)	$ 3,402,010
							37,622 (12)	$ 15,150,379
Nia Tatsis								
	Time-based RSU				3,421 (2)	$ 1,377,637		
					5,244 (3)	$ 2,111,759		
					7,114 (4)	$ 2,864,808		
	Performance-based RSU							
					3,422 (5)	$ 1,378,039		
					5,244 (6)	$ 2,111,759		
					10,262 (7)	$ 4,132,507		
					7,114 (8)	$ 2,864,808		
							7,866 (9)	$ 3,167,638
							7,114 (10)	$ 2,864,808
	Stock Options							
	2,854	0	$155.57	2/5/2028				
	6,145	0	$187.53	2/5/2029				

(1) 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, which were granted on February 1, 2022, vest in three annual installments. The shares listed on the table above represent the third annual installment, which vested on February 24, 2025.

(3) These time-based RSU awards, which were granted on February 1, 2023, vest in three annual installments. The shares listed on the table above represent the second and third annual installments, which vested on February 10, 2025 and are scheduled to vest February 10, 2026, respectively.

(4) These time-based RSU awards, which were granted on February 7, 2024, vest in three annual installments. The shares listed on the table above represent the three annual installments, the first of which vested on February 17, 2025, and are scheduled to vest in two remaining annual installments on February 17, 2026 and 2027.

(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 2022, with vesting of the earned shares in three equal installments on 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. The shares listed on the table above represent the final installment of the earned shares, which vested on February 24, 2025.

(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 2023, with vesting of the earned shares in three equal installments on each of February 10, 2024, 2025 and 2026. In February 2024, our MDCC certified as to the level of performance at 200% of the number of target shares. The shares listed on the table above represent the second and third installments of earned shares, which vested on February 10, 2025 and are scheduled to vest on February 10, 2026, respectively.

(7) This PSU award is based on the achievement of three-year non-financial performance metrics, which were established by the MDCC on January 24, 2022. The performance conditions associated with the awards consist of multiple clinical and research milestones, with a payout range of zero to 200%. In February 2025, 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 26, 2025.

(8) This PSU award was based on the achievement of one-year financial performance metrics, which were established by the MDCC on February 6, 2024, and are tied to our net product revenue during 2024, with vesting of the earned shares generally occurring in three equal installments scheduled for each of February 17, 2025, 2026 and 2027. In February 2025, 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, which were established by the MDCC on February 1, 2023, with the number and value of shares reported assuming maximum performance (200%). 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 2026.

(10) This PSU award is based on the achievement of three-year non-financial performance metrics, which were established by the MDCC on February 6, 2024, with the number of shares reported assuming maximum performance (200%). 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 2027.

(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. The number of shares reported assumes maximum performance (200%). 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 on or before July 2025.

Option Exercises and Stock Vested for 2024

The following table sets forth the value realized by our NEOs from options to purchase common stock exercised by the NEOs during 2024 and shares of stock that vested during 2024. 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. Options to purchase common stock are no longer provided as an element of our executive compensation program.

	Option Awards		Stock Awards	
Name	Number of Shares Acquired on Exercise	Value Realized on Exercise	Number of Shares Acquired on Vesting	Value Realized on Vesting
Reshma Kewalramani	1,565	$ 421,721	71,263	$ 30,294,626
Charles F. Wagner, Jr.	—	$ —	26,699	$ 11,345,933
David M. Altshuler	—	$ —	27,019	$ 11,493,590
Stuart A. Arbuckle	—	$ —	33,499	$ 14,246,333
Nia Tatsis	—	$ —	28,364	$ 12,049,255

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 NEO experienced an employment termination on December 31, 2024 and/or a change of control of the company had occurred on such date.

	Voluntary Termination or Retirement/ Termination for Cause	Separate From a Change of Control, Involuntary Termination Other Than for Cause/ Termination by Executive for Good Reason	In Connection With a Change of Control, Involuntary Termination Other Than for Cause/ Termination by Executive for Good Reason	Disability	Death
Reshma Kewalramani					
Cash Severance Benefits	$ —	$ 10,400,000	$ 14,360,000	$ 2,400,000	$ 2,400,000
Continuation of Employee Benefits	—	47,697	47,697	—	—
Accelerated Vesting of Restricted Stock Units	—	25,013,306	49,965,405	49,965,405	49,965,405
TOTAL	**$ —**	**$ 35,461,003**	**$ 64,373,102**	**$ 52,365,405**	**$ 52,365,405**
Charles F. Wagner, Jr.					
Cash Severance Benefits	$ —	$ 1,805,000	$ 2,660,000	$ —	$ —
Continuation of Employee Benefits	—	28,513	28,513	—	—
Accelerated Vesting of Restricted Stock Units	—	—	17,521,477	17,521,477	17,521,477
TOTAL	**$ —**	**$ 1,833,513**	**$ 20,209,990**	**$ 17,521,477**	**$ 17,521,477**
David M. Altshuler					
Cash Severance Benefits	$ —	$ 1,805,000	$ 2,660,000	$ —	$ —
Continuation of Employee Benefits	—	31,798	31,798	—	—
Accelerated Vesting of Restricted Stock Units	—	—	17,322,947	17,322,947	17,322,947
TOTAL	**$ —**	**$ 1,836,798**	**$ 20,014,745**	**$ 17,322,947**	**$ 17,322,947**
Stuart A. Arbuckle					
Cash Severance Benefits	$ —	$ 2,000,000	$ 3,000,000	$ —	$ —
Continuation of Employee Benefits	—	31,798	31,798	—	—
Accelerated Vesting of Restricted Stock Units	—	—	34,662,403	34,662,403	34,662,403
TOTAL	**$ —**	**$ 2,031,798**	**$ 37,694,201**	**$ 34,662,403**	**$ 34,662,403**
Nia Tatsis					
Cash Severance Benefits	$ —	$ 1,425,000	$ 2,100,000	$ —	$ —
Continuation of Employee Benefits	—	19,095	19,095	—	—
Accelerated Vesting of Restricted Stock Units	—	—	16,358,882	16,358,882	16,358,882
TOTAL	**$ —**	**$ 1,444,095**	**$ 18,477,977**	**$ 16,358,882**	**$ 16,358,882**

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:

- No amounts have been included with respect to stock options held by NEOs as all of their outstanding stock options are fully vested.
- 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 $402.70 per share (the closing price on the last trading day of 2024). The value of any PSUs that have not been certified as to the level of performance by the MDCC as of December 31, 2024 are reported above assuming target performance (100%).
- 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 2024 individual and company performance ratings on December 31, 2024 as they assigned in the first quarter of 2025.
- 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, 2024.

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 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. All options held by our NEOs are fully vested and, as a result, would not have their vesting accelerated as a result of change in control or otherwise. 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. 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 and restricted stock unit awards then unvested at the time of termination.

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

Employment Agreements

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

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

Severance Payment:	A)	The sum of his or her (i) base salary at the time of termination and (ii) target bonus for the year in which his or her employment is terminated
	B)	Any annual bonus for the year prior to the year in which the termination occurs, if not yet paid
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, Dr. Tatsis and Mr. Wagner that was entered into at the time the respective officer joined our company or, in the case of Dr. Tatsis, at the time she became Chief Regulatory and Quality Officer. Under this agreement and the executive's equity agreements, if we terminate the employment of the officer without cause on a date within the 90 days prior to or the 12 months after a change of control or any of these individuals terminates his or her employment within 30 days of an event giving rise to a right to terminate for good reason, subject to notice and cure provisions, and the event occurs on a date within the 90 days prior to or the 12 months after a change of control, he would be entitled to receive:

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

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

PAY RATIO

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 2024, Dr. Kewalramani's annual total compensation, as reported in the Summary Compensation Table, was $21,538,668 and the median of the annual total compensation of all employees of the company (other than our Chief Executive Officer) was $245,708. The ratio of annual total compensation for Dr. Kewalramani to that of our median employee's annual total compensation was approximately 88:1.

Due to growth in our employee population, we identified a new median employee as of October 1, 2024 using target total annual compensation in 2024. 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, 2024) and includes:

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

The methodology included all 6,062 company employees across 24 countries as of October 1, 2024.

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 51.

Year	Summary Compensation Table Total for CEO[1]	Summary Compensation Table Total for CEO[2]	Compensation Actually Paid to CEO[1][3]	Compensation Actually Paid to CEO[2][4]	Average Summary Compensation Table Total for Non-CEO NEOs[5]	Average Compensation Actually Paid to Non-CEO NEOs[6]	Total Shareholder Return (Value of Initial Fixed $100 Investment)		Net Income (Loss)[9]	Net Product Revenue[10]
							VRTX TSR[7]	NBI TSR[8]		
2024	$ 21,538,668	N/A	$ 43,611,733	N/A	$ 8,088,674	$ 18,370,307	$ 183.92	$ 118.20	$ (0.5)Billion	$ 11.0 Billion
2023	$ 20,594,441	N/A	$ 44,202,174	N/A	$ 7,376,771	$ 18,104,165	$ 185.84	$ 118.87	$ 3.6 Billion	$ 9.9 Billion
2022	$ 15,864,497	N/A	$ 29,529,089	N/A	$ 8,982,257	$ 18,263,330	$ 131.89	$ 113.65	$ 3.3 Billion	$ 8.9 Billion
2021	$ 15,198,856	N/A	$ 18,341,489	N/A	$ 7,193,835	$ 8,969,051	$ 100.30	$ 126.45	$ 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	$ 107.94	$ 126.42	$ 2.7 Billion	$ 6.2 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, 2022, 2023 and 2024.

(2) This column reflects the amounts reported in the "Total" column of the Summary Compensation Table for Jeffrey Leiden, our CEO for 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, 2022, 2023 and 2024. 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 Pension/Non-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 Added/ Deducted for Awards that Vested During Fiscal Year	Amounts Added/ Deducted for the Change in Fair Value of Awards Outstanding at Fiscal Year End[a]	Compensation Actually Paid
2024	$ 21,538,668	$ (15,002,202)	$ 24,557,854	$ —	$ 1,298,423	$ 11,218,990	$ 43,611,733
2023	$ 20,594,441	$ (15,001,894)	$ 24,692,933	$ —	$ 272,767	$ 13,643,927	$ 44,202,174
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, 2024, 2023, 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 100%, 50% and 50% as of December 31, 2023, 2022 and 2021, respectively; the non-financial PSU award for 2022 was valued at 200%, 50% and 0% as of December 31, 2024, 2023 and 2022, respectively; the non-financial PSU award for 2023 was valued at 100% and 50% as of December 31, 2024 and 2023, respectively; the non-financial PSU award for 2024 was valued at 200% as of December 31, 2024.

(4) The amounts in this column reflect the Compensation Actually Paid for Jeffrey Leiden, our CEO for a portion of 2020 (until April 1, 2020). 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 Pension/Non-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 Added/ Deducted for Awards that Vested During Fiscal Year	Amounts Added/ Deducted for the Change in Fair Value of Awards Outstanding at Fiscal Year End[a]	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

(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 and 2019; and, the non-financial PSU award for 2017 was valued at 200% as of December 31, 2019; the non-financial PSU award for 2018 was valued at 200% and 100% as of December 31, 2020 and 2019, 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 2024, Mr. Wagner, Dr. Altshuler, Mr. Arbuckle, and Dr. Tatsis; for 2023 and 2022, Mr. Wagner, Dr. Altshuler, Mr. Arbuckle, and Dr. Leiden; for 2021, Mr. Wagner, Mr. Arbuckle, Dr. Leiden, and Dr. Tatsis; and for 2020, Mr. Wagner, Dr. Altshuler, Mr. Arbuckle, and Michael Parini.

(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. Adjustments (additions/deductions) are not listed for Pension/Non-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 Added/ Deducted for Awards that Vested During Fiscal Year	Amounts Added/ Deducted for the Change in Fair Value of Awards Outstanding at Fiscal Year End[(a)]	Compensation Actually Paid
2024	$ 8,088,674	$ (5,496,460)	$ 8,997,325	$ —	$ 526,590	$ 6,254,178	$ 18,370,307
2023	$ 7,376,771	$ (5,590,153)	$ 8,606,944	$ 812,533	$ 236,286	$ 6,661,784	$ 18,104,165
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

(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, 2024, 2023, 2022, 2021, 2020 and 2019; and, the non-financial PSU award for 2017 was valued at 200% as of December 31, 2019; the non-financial PSU award for 2018 was valued at 200% and 100% as of December 31, 2020 and 2019, 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 100%, 50% and 50% as of December 31, 2023, 2022 and 2021, respectively; the non-financial PSU award for 2022 was valued at 200%, 50% and 0% as of December 31, 2024, 2023 and 2022, respectively; the non-financial PSU award for 2023 was valued at 100% and 50% as of December 31, 2024 and 2023, respectively; the non-financial PSU award for 2024 was valued at 200% as of December 31, 2024.

(7) This column represents our cumulative total shareholder return ("TSR") under SEC rules from December 31, 2019, the last trading day before the start of 2020, 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, which is the same peer group used for purposes of Item 201(e) of Regulation S-K from December 31, 2019, the last trading day before the start of 2020, 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.

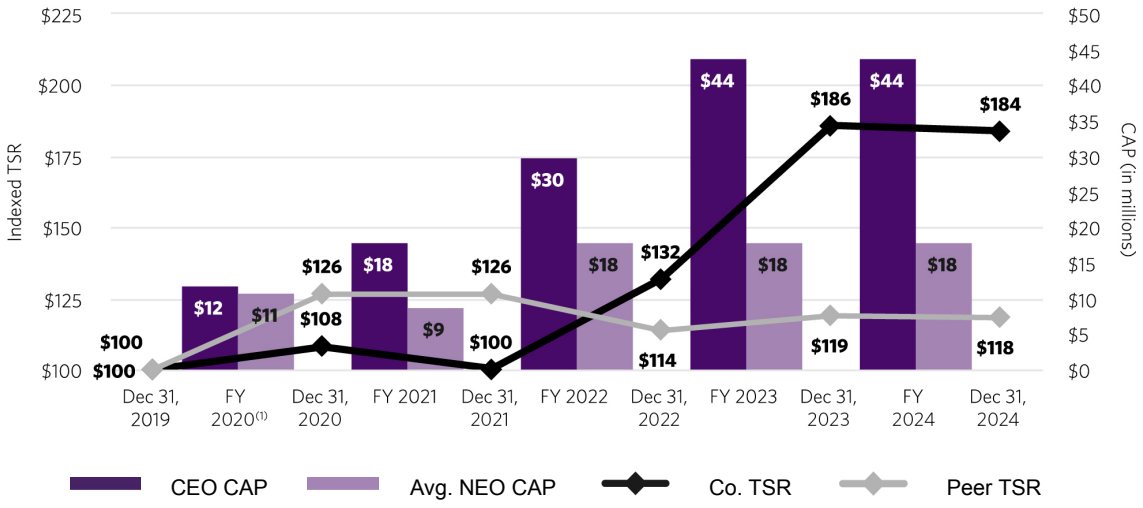
(9) This column reflects net income (loss) as reported for each year in our Annual Report on Form 10-K. In 2024, we had a net loss of $536 million, which reflected our strong operating results offset by $4.4 billion of AIPR&D expense related to the Alpine acquisition.

(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 51 of this proxy statement for additional information.

Relationship Between Pay and Performance

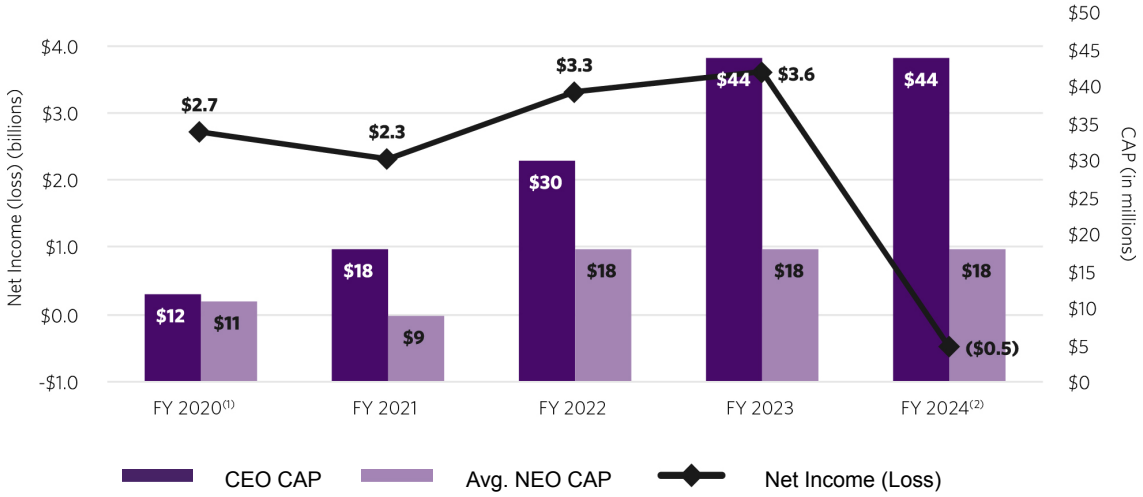
The relationships between certain specified measures in the pay-versus-performance table over the five most recently completed fiscal years are provided below.

Compensation Actually Paid vs TSR (and TSR vs Peer Group 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.

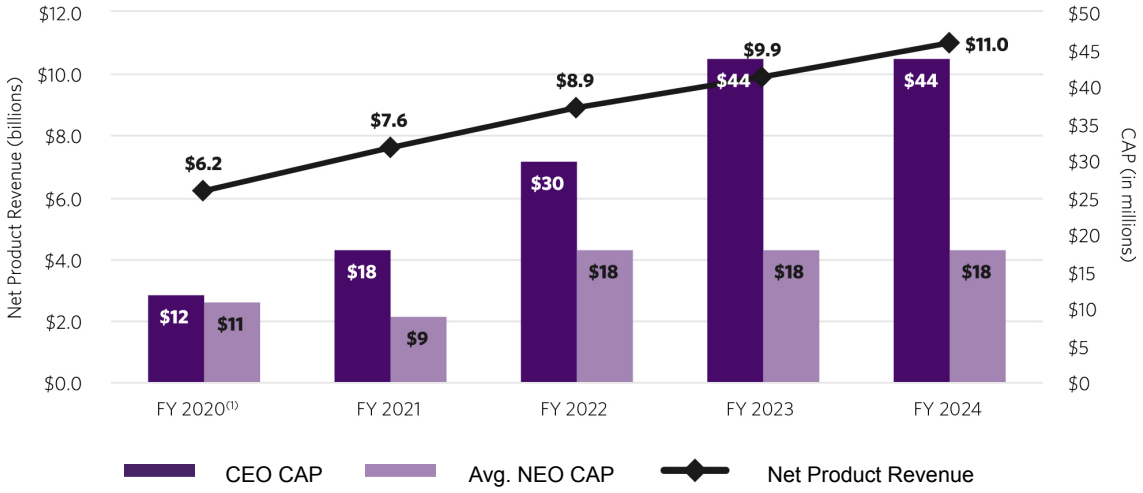
Compensation Actually Paid vs Net Income (Loss)



(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.

(2) As discussed in (9) above, our net loss in 2024 was primarily related to our acquisition of Alpine.

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 2024. 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(1)
Adjusted Non-GAAP EBITDA(2)

(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 and certain other adjustments primarily related to our acquisition of Alpine, from net income (loss), 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 13, 2025 for the twelve months ended December 31, 2024.

SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT

The following table sets forth information regarding beneficial ownership of our common stock as of March 17, 2025, by:

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

Name and Address	Shares Beneficially Owned[1]	Percentage of Total[2]
Capital World Investors[3] 333 South Hope Street, 55th Floor Los Angeles, California 90071	28,739,975	11.2 %
The Vanguard Group[4] 100 Vanguard Blvd. Malvern, Pennsylvania 19355	22,281,729	8.7 %
BlackRock, Inc.[5] 50 Hudson Yards New York, New York 10001	21,881,203	8.5 %
Sangeeta N. Bhatia[6]	4,435	*
Lloyd Carney[6]	6,319	*
Alan Garber[6]	36,029	*
Reshma Kewalramani[6]	41,813	*
Michel Lagarde[6]	4,274	*
Jeffrey M. Leiden[6]	161,540	*
Diana McKenzie[6]	8,633	*
Bruce I. Sachs[6]	86,712	*
Jennifer Schneider[6]	922	*
Nancy Thornberry[6]	3,208	*
Suketu Upadhyay[6]	5,130	*
David M. Altshuler[6]	3,226	*
Stuart A. Arbuckle[6]	23,680	*
Nia Tatsis[6]	39,296	*
Charles F. Wagner, Jr.[6]	38,766	*
All directors and executive officers as a group (19 persons)[6]	584,514	0.2 %

* 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 2025.

(2) Percentage ownership is based on 257,080,844 shares of our common stock outstanding on March 17, 2025.

(3) This information is based on the Schedule 13G/A filed by Capital World Investors with the SEC on February 13, 2025 reporting beneficial ownership as of December 31, 2024. Capital World Investors has sole voting power with respect to 28,619,648 shares and sole dispositive power with respect to 28,739,975 shares.

(4) This information is based on the Schedule 13G/A filed by The Vanguard Group with the SEC on February 13, 2024 reporting beneficial ownership as of December 29, 2023. The Vanguard Group has sole voting power with respect to 0 shares, shared voting power with respect to 342,185 shares, sole dispositive power with respect to 21,173,929 shares, and shared dispositive power with respect to 1,107,800 shares.

(5) This information is based on the Schedule 13G filed by BlackRock, Inc with the SEC on January 25, 2024 reporting beneficial ownership as of December 31, 2023. BlackRock, Inc. has sole voting power with respect to 19,950,678 shares and sole dispositive power with respect to 21,881,203 shares.

(6) Includes shares that may be acquired upon the exercise of options exercisable within 60 days after March 17, 2025, unvested RSUs vesting within 60 days of March 17, 2025 and deferred stock units as of March 17, 2025 issued pursuant to our Non-Employee Director Deferred Compensation Plan, as follows:

	Stock Options Exercisable Within 60 Days of March 17, 2025	Unvested Restricted Stock Units Vesting Within 60 Days of March 17, 2025	Deferred Stock Units as of March 17, 2025
Sangeeta N. Bhatia	—	1,001	—
Lloyd Carney	—	1,001	—
Alan Garber	29,555	—	—
Reshma Kewalramani	—	—	—
Michel Lagarde	3,142	—	—
Jeffrey M. Leiden	137,074	—	—
Diana McKenzie	—	—	6,991
Bruce I. Sachs	31,567	—	15,145
Jennifer Schneider	—	922	—
Nancy Thornberry	1,571	501	—
Suketu Upadhyay	—	—	2,404
David Altshuler	—	—	—
Stuart A. Arbuckle	—	—	—
Nia Tatsis	8,999	—	—
Charles F. Wagner, Jr.	9,532	—	—
All directors and executive officers as a group (19 persons)	275,374	3,425	24,540

OTHER INFORMATION

Other Matters

The 2025 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 2025 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 2026 Annual Meeting

Shareholder Proposals. In order to submit a shareholder proposal to be considered for inclusion in our proxy statement for our 2026 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 4, 2025. To introduce a proposal for presentation at the 2026 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 14, 2026 and no later than February 13, 2026. 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 2026 Annual Meeting. If a shareholder wishes to nominate a candidate for election to our board of directors at the 2026 annual meeting of shareholders, but is not eligible or does not elect to have such candidate included in the proxy statement for our 2026 annual meeting of shareholders, such nomination may be submitted to our corporate secretary no earlier than January 14, 2026 and no later than February 13, 2026, 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 2026 annual meeting of shareholders, and is eligible and elects to have such candidate included in the proxy statement for our 2026 annual meeting of shareholders pursuant to our proxy access by-law, such nomination must be submitted to our corporate secretary no earlier than January 14, 2026 and no later than February 13, 2026, 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 2026 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 15, 2026. 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 2026 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 17, 2026), 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 Sodali & Co to assist in the solicitation of proxies at an estimated cost of approximately $25,000. 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. Forward-looking statements are not purely historical and maybe accompanied by words such as “anticipates,” “may,” “forecasts,” “expects,” “intends,” “plans,” “potentially,” “believes,” “seeks,” “estimates,” and other words and terms of similar meaning. Such statements may include, 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, our beliefs, expectations, and plans with respect to the launches of CASGEVY for the treatment of SCD and TDT, ALYFTREK for the treatment of CF, and JOURNAVX for the treatment of moderate-to-severe acute pain, expectations for the data that will be generated by ongoing and planned clinical trials and the ability to use that data to advance compounds, continue development or support regulatory filings, or accelerate regulatory approval, including our plans to share data in 2025 from the ongoing clinical trial of VX-522 in patients with CF, our plans to submit zimislecel for regulatory approval in 2026, our plans to file for accelerated regulatory approvals based on interim analyses from the ongoing clinical trials evaluating inaxaplin in AMKD and povetacicept in IgAN, expectations that ALYFTREK will provide additional clinical benefits to eligible people with CF, expectations for a broadened patient population eligible for CASGEVY by advancing myeloablative conditioning agents with improved tolerability profiles, expectations for the clinical benefits of JOURNAVX, particularly as a treatment for pain without the evidence of the limitations of other available therapies, including the addictive potential of opioids, beliefs regarding trial design innovation for the LSR clinical trial to better control the placebo effect and succeed in pivotal development, expectations for the potential benefits and therapeutic scope of our acquisitions and collaborations, including our acquisition of Alpine and its lead asset, povetacicept, and its potential to become a pipeline-in-a-product and a best-in-class approach to treat multiple B cell-mediated autoimmune diseases, as well as statements with respect to Vertex’s potential future financial performance and our beliefs regarding the patient populations for CF, SCD, TDT and pain, 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. There are a number of risks and uncertainties that are difficult to predict and 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 clinical trials or preclinical testing, especially if based on a limited number of patients, may not be indicative of final results, that data from the company’s developmental 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, that regulatory authorities may not approve regulatory filings for our pipeline products on a timely basis, or at all, and other risks listed under the heading “Risk Factors” in our Annual Report on Form 10-K for the fiscal year ended December 31, 2024, filed with the SEC on February 13, 2025, and available through the company’s website at www.vrtx.com. You should not place undue reliance on these statements, or any data presented. We disclaim any obligation to update the information contained in this proxy statement as new information becomes available, except as required by law.

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, 2025, there were 11,621,839 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, 2025, under our equity plans:

- Stock options covering 1,522,772 shares of our common stock, with a weighted average exercise price of $157.44 and a weighted average remaining term of 3.12 years, were outstanding; and
- Unvested PSUs and RSUs covering 3,446,406 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, 2024. 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, 2024. Accordingly, the figures in the table below do not reflect the equity grants made to our employees under the 2013 Plan, since December 31, 2024.

Plan Category	Number of Securities to be Issued Upon Exercise of Outstanding Options, Restricted Stock Units and Rights	Weighted-Average Exercise Price of Outstanding Options and Rights	Number of Securities Remaining Available for Future Issuance Under Equity Compensation Plans (excluding securities reflected in first column)
Equity Compensation Plans Approved by Shareholders (1)	5,144,160 (2)	$156.36 (3)	14,866,672 (4)
Equity Compensation Plans Not Approved by Shareholders	—	—	—
TOTAL	5,144,160		14,866,672

(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, 2024, and includes 1,579,538 options granted under the 2013 Plan, 2,665,963 RSUs granted under the 2013 Plan, 862,194 PSUs granted under the 2013 Plan, 22,426 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 14,039 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 13,758,061 shares available for future issuance under the 2013 Plan and 1,108,611 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, 2025.

FREQUENTLY ASKED QUESTIONS REGARDING THE ANNUAL MEETING

What is the Purpose of the Annual Meeting?

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

- The election of directors;
- The ratification of the appointment of Ernst & Young LLP as our independent registered public accounting firm;
- To hold an advisory vote on our 2024 named executive officer compensation; and
- A shareholder proposal regarding excessive golden parachutes, if properly presented at the meeting.

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

What is a Proxy?

It is your legal designation of another person to vote the stock you own in the manner you direct. That other person is called a proxy. If you designate someone as your proxy in a written document, that document also is called a proxy or a proxy card. The board of directors has designated Jeffrey Leiden, Reshma Kewalramani, Jonathan Biller, and Joy Liu to serve as proxies at the annual meeting.

What is a Proxy Statement?

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

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

We are distributing our proxy materials to shareholders via the Internet under the “Notice and Access” approach permitted by rules of the SEC. This approach provides a timely and convenient method of accessing the materials and voting. On or about April 3, 2025, 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, 2024 and how to vote your shares. The Notice of Internet Availability of Proxy Materials also contains instructions on how to receive a paper copy of the proxy materials and our Annual Report, if you prefer.

What is the Difference between a Shareholder of Record and a Shareholder Who Holds Stock in Street Name?

Shareholders of Record. If your shares are registered in your name with our transfer agent, Computershare, you are a shareholder of record with respect to those shares, and the Notice of Internet Availability of Proxy Materials was sent directly to you by Computershare.

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

How May I Attend the Annual Meeting?

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/MXD5MZM 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?

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, 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 9, 2025. 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?

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 wireless network connection wherever you intend to participate in the meeting. We encourage you to access the meeting prior to the start time. For further assistance should you need it you may call 1-888-724-2416.

How Many Shares Must be Represented in Order to Hold the Annual Meeting?

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

How Can I Vote My Shares?

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

1. **Vote by Internet** by going to the web address www.envisionreports.com/VRTX before the annual meeting and following the instructions for Internet voting on the Notice of Internet Availability or proxy card. Have the Notice of Internet Availability of Proxy Materials, which contains your control number, available when voting by Internet.
2. **Vote by proxy card,** if you have received written proxy materials, by completing, signing, dating, and mailing your proxy card in the envelope provided. **If you vote by Internet, please do not mail your proxy card.**
3. **Vote by telephone** by following the instructions on the Notice of Internet Availability of Proxy Materials or proxy card.
4. **By attending the annual meeting online.** During the annual meeting, you may vote online by following the instructions at https://meetnow.global/MXD5MZM. Have the Notice of Internet Availability of Proxy Materials, which contains your control number, available when you access the virtual meeting webpage.

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

What is the Record Date and What Does it Mean?

The record date for the annual meeting is March 17, 2025 and was established by our board of directors. On the record date, there were 257,080,844 shares of our common stock outstanding, each of which is entitled to one vote on each matter properly brought before the annual meeting. Owners of record of common stock at the close of business on the record date are entitled to:

- receive notice of the annual meeting; and
- vote at the annual meeting and any adjournment or postponement of the annual meeting.

If I Submit a Proxy, May I Later Revoke it and/or Change my Vote?

Shareholders may revoke a proxy and/or change their vote prior to the completion of voting at the annual meeting by:

- subsequently submitting a vote by Internet at www.envisionreports.com/VRTX or by telephone by following the directions on the Notice of Internet Availability of Proxy Materials voting instruction form or your proxy card;
- signing another proxy card with a later date and delivering it to our corporate secretary at 50 Northern Avenue, Boston, Massachusetts 02210, before the annual meeting; or
- voting at the annual meeting online, if you are a shareholder of record or hold your shares in street name and have obtained a legal proxy from your bank or broker.

What if I do not Specify a Choice for a Matter when Returning a Proxy?

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

- FOR the election of each director nominee;
- FOR ratification of the appointment of Ernst & Young LLP as our independent registered public accounting firm for the year ending December 31, 2025;
- FOR our 2024 named executive officer compensation; and
- AGAINST the shareholder proposal regarding excessive golden parachutes.

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

If you are a shareholder of record and do not provide a proxy, you must attend the annual meeting in order to vote. If you hold shares through an account with a bank or broker, your shares may be voted by the bank or broker on certain matters if you do not provide voting instructions. Banks and brokers have the authority under applicable rules to vote shares on routine matters for which their customers do not provide voting instructions. The ratification of Ernst & Young LLP as our independent registered public accounting firm is considered a routine matter. Each of the other proposals, including the election of directors, the advisory vote with respect to our executive compensation program, and the two shareholder proposals are considered not routine, and banks and brokers cannot vote shares without instruction on those matters. Shares that banks and brokers are not authorized to vote on those matters are counted as “broker non-votes” and will have no effect on the results of those votes.

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

Proposal No. 1: Election of Directors

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

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?

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.

Designed and published by www.labrador-company.com

www.vrtx.com

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VERTEX

VOTE

Your vote matters – here's how to vote!

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

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

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

AT THE VIRTUAL MEETING
To access the virtual Annual Meeting, please visit https://meetnow.global/MXD5MZM

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

X

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	☐	☐	☐	02 - Lloyd Carney	☐	☐	☐	03 - Alan Garber	☐	☐	☐
04 - Reshma Kewalramani	☐	☐	☐	05 - Michel Lagarde	☐	☐	☐	06 - Jeffrey Leiden	☐	☐	☐
07 - Diana McKenzie	☐	☐	☐	08 - Bruce Sachs	☐	☐	☐	09 - Jennifer Schneider	☐	☐	☐
10 - Nancy Thornberry	☐	☐	☐	11 - Suketu Upadhyay	☐	☐	☐				

The Board of Directors recommends a vote FOR Proposals 2 and 3.

	For	Against	Abstain
2. Ratification of Ernst & Young LLP as independent Registered Public Accounting firm for the year ending December 31, 2025.	☐	☐	☐
3. Advisory vote to approve named executive officer compensation.	☐	☐	☐

The Board of Directors recommends a vote AGAINST Proposal 4.

	For	Against	Abstain
4. Shareholder proposal, if properly presented at the meeting, regarding excessive golden parachutes.	☐	☐	☐

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

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

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

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The 2025 Annual Meeting of Shareholders of Vertex Pharmaceuticals Incorporated will be held on May 14, 2025 at 9:00 a.m. Eastern Time, via the Internet at https://meetnow.global/MXD5MZM.

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 14, 2025: The Notice of Annual Meeting of Shareholders, Proxy Statement, and Annual Report are available at www.envisionreports.com/vrtx

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

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

VERTEX®

Proxy — Vertex Pharmaceuticals Incorporated

ANNUAL MEETING OF SHAREHOLDERS — May 14, 2025

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 14, 2025, at 9:00 A.M. Eastern Time, via live audio webcast available at https://meetnow.global/MXD5MZM 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 AGAINST 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. ☐