UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM 10-K

☒ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**
For the Fiscal Year Ended December 31, 2024

or

☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**
FOR THE TRANSITION PERIOD FROM _ TO _

Commission file number 000-19319

Vertex Pharmaceuticals Incorporated

(Exact name of registrant as specified in its charter)

Massachusetts	**04-3039129**
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)
50 Northern Avenue, Boston, Massachusetts	**02210**
(Address of principal executive offices)	(Zip Code)

Registrant's telephone number, including area code **(617) 341-6100**

Securities registered pursuant to Section 12(b) of the Exchange Act:

Title of Each Class	**Trading Symbol**	**Name of Each Exchange on Which Registered**
Common Stock, $0.01 Par Value Per Share	VRTX	The Nasdaq Global Select Market

Securities registered pursuant to Section 12(g) of the Exchange Act: None

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes ☒ No ☐

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Exchange Act. Yes ☐ No ☒

Indicate by check mark whether the registrant: (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes ☒ No ☐

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files). Yes ☒ No ☐

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act (Check one):

Large accelerated filer ☒ Accelerated filer ☐ Non-accelerated filer ☐ Smaller reporting company ☐ Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Indicate by check mark whether the registrant has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report. ☒

If securities are registered pursuant to Section 12(b) of the Act, indicate by check mark whether the financial statements of the registrant included in the filing reflect the correction of an error to previously issued financial statements. ☐

Indicate by check mark whether any of those error corrections are restatements that required a recovery analysis of incentive-based compensation received by any of the registrant's executive officers during the relevant recovery period pursuant to § 240.10D-1(b). ☐

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). Yes ☐ No ☒

The aggregate market value of the registrant's common stock held by non-affiliates of the registrant based on the closing price on June 28, 2024 (the last business day of the registrant's most recently completed second fiscal quarter of 2024) was $121.8 billion.

As of February 7, 2025, the registrant had 256,789,869 shares of common stock outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the definitive proxy statement for the 2025 Annual Meeting of Shareholders, which we expect to hold on May 14, 2025, are incorporated by reference into Part III of this Annual Report on Form 10-K.

VERTEX PHARMACEUTICALS INCORPORATED
ANNUAL REPORT ON FORM 10-K
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"Vertex," "we," "us" and "our" as used in this Annual Report on Form 10-K refer to Vertex Pharmaceuticals Incorporated, a Massachusetts corporation, and its subsidiaries.

We use the brand name for our products when we refer to the product that has been approved and with respect to the indications on the approved label. Otherwise, including in discussions of our cystic fibrosis, sickle cell disease, beta thalassemia, and pain development programs, we refer to our product candidates by their scientific (or generic) name or VX developmental designation.

This Annual Report on Form 10-K contains forward-looking statements. Words such as "anticipates," "may," "forecasts," "expects," "intends," "plans," "potentially," "believes," "seeks," "estimates," variations of such words and similar expressions are intended to identify such forward-looking statements, although not all forward-looking statements contain these identifying words. Please refer to "Special Note Regarding Forward-Looking Statements" set forth in Part I, Item 1A, for a discussion of our forward-looking statements and the related risks and uncertainties of such statements.

PART I

ITEM 1. BUSINESS

OVERVIEW

We are a global biotechnology company that invests in scientific innovation to create transformative medicines for people with serious diseases, with a focus on specialty markets. We have seven approved medicines: five that treat the underlying cause of cystic fibrosis ("CF"), a life-threatening genetic disease, one that treats severe sickle cell disease ("SCD") and transfusion dependent beta thalassemia ("TDT"), life shortening inherited blood disorders, and one that treats moderate-to-severe acute pain. Our clinical-stage pipeline includes programs in CF, SCD, beta thalassemia, acute and peripheral neuropathic pain, APOL1-mediated kidney disease, IgA nephropathy and other autoimmune renal diseases and cytopenias, type 1 diabetes, myotonic dystrophy type 1, and autosomal dominant polycystic kidney disease.

Our goal in CF is to continue to extend our leadership by developing treatment regimens that will provide benefits to all people with CF. In December 2024, the U.S. Food and Drug Administration (the "FDA") approved ALYFTREK (vanzacaftor/tezacaftor/deutivacaftor), our fifth medicine for people with CF. In addition to ALYFTREK, our marketed medicines that treat people with CF are TRIKAFTA/KAFTRIO (elexacaftor/tezacaftor/ivacaftor and ivacaftor), SYMDEKO/SYMKEVI (tezacaftor/ivacaftor and ivacaftor), ORKAMBI (lumacaftor/ivacaftor) and KALYDECO (ivacaftor). Collectively, our five marketed CF medicines are being used to treat nearly three quarters of the approximately 94,000 people with CF in the U.S., Europe, Australia, and Canada.

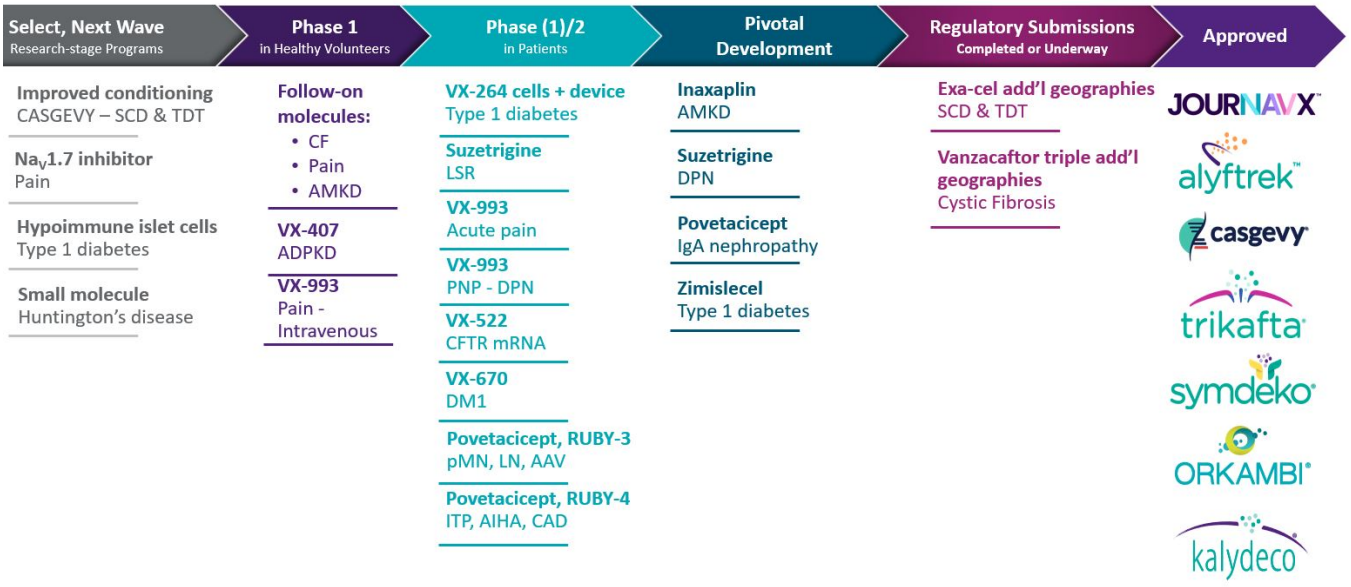
Through approval of new medicines, label expansions, and expanded reimbursement, we are focused on increasing the number of people with CF who are eligible and able to receive our medicines. We are evaluating our current medicines in additional patient populations, including younger children, with the goal of having small molecule treatments for all people who have at least one mutation in their cystic fibrosis transmembrane conductance regulator ("CFTR") gene that is responsive to our CFTR modulators. In December 2024, the FDA approved the expanded use of TRIKAFTA for treatment of people with CF. With this approval, 94 additional non-F508del CFTR mutations have been added to the TRIKAFTA label. We are evaluating VX-522, an investigational messenger ribonucleic acid ("mRNA") therapeutic that we are developing in collaboration with Moderna, Inc. ("Moderna") in a Phase 1/2 clinical trial in people with CF. The multiple ascending dose portion of the clinical trial is ongoing, and we expect to share data in the first half of 2025. VX-522 has the potential to benefit the more than 5,000 people with CF in the U.S., Canada, Europe and Australia who do not make full-length CFTR protein and therefore cannot benefit from CFTR modulators. In addition, we are continuing our research and development of additional CFTR modulators, with the aim of developing best-in-class medicines that can help more patients achieve normal levels of CFTR function, and we are investigating additional potential treatments for people with CF who do not make full-length CFTR protein and cannot benefit from CFTR modulators.

In SCD and TDT, our goal is to eliminate vaso-occlusive crises ("VOCs") (as well as vaso-occlusive organ damage) and transfusion dependence, respectively. Our marketed therapy is CASGEVY (exagamglogene autotemcel), an ex-vivo, non-viral CRISPR/Cas9 gene-edited cell therapy, which has been approved in the United States ("U.S."), the European Union ("E.U."), the United Kingdom ("U.K."), the Kingdom of Saudi Arabia ("Saudi Arabia"), the Kingdom of Bahrain ("Bahrain"), the United Arab Emirates (the "UAE"), Canada and Switzerland for treatment of people 12 years of age and older with SCD or TDT. We estimate approximately 60,000 people with severe SCD or TDT are or could become eligible for CASGEVY in the U.S., Canada, Europe, Saudi Arabia and Bahrain. We are evaluating CASGEVY as a treatment for children 5 to 11 years of age with SCD or TDT in global Phase 3 clinical trials. We are progressing preclinical assets for gentler conditioning for CASGEVY, which could broaden the eligible patient population, and investigating small molecules for the potential treatment of SCD and TDT.

In January 2025, the FDA approved JOURNAVX (suzetrigine), our selective non-opioid NaV1.8 pain signal inhibitor, for the treatment of moderate-to-severe acute pain. We have begun our commercial launch of JOURNAVX in eligible adults in the U.S. In addition, we are enrolling and dosing patients in a Phase 3 clinical trial evaluating suzetrigine for the treatment of diabetic peripheral neuropathy, a common form of peripheral neuropathic pain. We are enrolling and dosing patients in two Phase 2 clinical trials evaluating VX-993, a next-generation selective NaV1.8 pain signal inhibitor, for the treatment of acute pain and for the treatment of diabetic peripheral neuropathy. In December 2024, we announced results from a Phase 2 clinical trial evaluating suzetrigine in people with lumbosacral radiculopathy ("LSR"). Treatment with suzetrigine

demonstrated a statistically significant and clinically meaningful within-group reduction in pain and we plan to advance to pivotal development in LSR, pending discussions with regulators.

The following chart sets forth our approved products, clinical-stage programs, and select pre-clinical programs:



Beyond CF, SCD, TDT and pain, we are advancing programs across multiple disease areas and modalities, including:

- *APOL1-Mediated Kidney Disease.* We are evaluating inaxaplin, our small molecule for the treatment of APOL1-mediated kidney disease ("AMKD"). We continue to enroll and dose people with AMKD in the Phase 3 portion of the global Phase 2/3 clinical trial.

- *IgA Nephropathy*. We are developing povetacicept, a dual inhibitor of the B cell activating factor ("BAFF") and a proliferation-inducing ligand ("APRIL") pathways, as a potentially best-in-class approach to treat IgA nephropathy ("IgAN"), a serious progressive, autoimmune kidney disease that can lead to end-stage renal disease. We are enrolling and dosing patients in the Phase 3 clinical trial evaluating povetacicept in people with IgAN.

- *Type 1 Diabetes. Z*imislecel, 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. Our second clinical program in T1D, VX-264, in which zimislecel is encapsulated in an immunoprotective device, is ongoing. We are also pursuing alternative approaches to immunosuppression that could be used with zimislecel, as well as hypoimmune 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. We completed the single ascending dose portion of the global Phase 1/2 clinical trial evaluating VX-670, an oligonucleotide-based approach that we have in-licensed from Entrada Therapeutics, Inc. ("Entrada"). We are 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 additional research programs aimed at diseases that fit our research and development strategy and follow-on programs in our existing disease areas in accord with our serial innovation approach.

Our core strategy is to discover and develop innovative medicines by combining transformative advances in the understanding of human disease and the science of therapeutics to dramatically advance human health. That strategy focuses on validated targets that address causal human biology, predictive lab assays and clinical biomarkers, rapid paths to registration and approval, and product candidates that hold the potential for transformative patient benefit. Our approach includes advancing multiple compounds or therapies from each program into early clinical trials to obtain patient data that can inform selection of the most promising therapies for later stage development as well as inform our ongoing discovery and development efforts. We aim to rapidly follow our first-in-class therapies that achieve proof-of-concept with potential best-in-class candidates. We plan to continue investing to advance our strategy, fostering scientific innovation by identifying additional product candidates through internal research efforts, and investing in business development transactions to access emerging technologies, products and product candidates.

Our serial innovation approach is intended to increase the likelihood of successfully bringing transformative medicines to patients and to provide durable clinical and commercial success. Our CF medicines are the exemplar of this strategy, as we continue to reach more people with CF than ever before through approvals of new medicines, approvals in new geographies, label expansions, including for younger patients, and expanded reimbursement. In addition, we have diversified our business through the approvals for CASGEVY for the treatment of SCD and TDT and through the approval for JOURNAVX for the treatment of acute pain. We are working to ensure broad access for eligible patients with these conditions in all countries with regulatory approval. Within our clinical pipeline, we have rapidly progressed multiple programs into pivotal development during the last year. As we continue to invest in our serial innovation strategy, launch new products, advance our diverse pipeline, and expand geographically, we continue to maintain a strong financial profile.

MARKETED PRODUCTS

Information regarding our marketed products, including information regarding the disease area, initial approval and age group for which the therapy is approved, are set forth in the table below.

Disease	Initial Approval	Eligible Age Group[(1)]
Cystic Fibrosis		
alyftrek™	2024	6 years of age and older
trikafta®	2019	2 years of age and older
kaftrio®	2020	2 years of age and older
symdeko®	2018	6 years of age and older
symkevi®	2018	6 years of age and older
ORKAMBI®	2015	1 year of age and older
kalydeco®	2012	1 month of age and older
Sickle Cell Disease and Transfusion-Dependent Beta Thalassemia		
casgevy®	2023	12 years of age and older
Acute Pain		
JOURNAVX™	2025	adults

(1) Specifies the youngest eligible age group in any major market.

CF

Our CF medicines are collectively being used by 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.

CF is a life-shortening genetic disease caused by a defective or missing CFTR protein resulting from mutations in the CFTR gene. To develop CF, children must inherit two defective CFTR genes, which are referred to as alleles; one allele is inherited from each parent. The vast majority of patients with CF carry at least one F508del mutation. The F508del mutation results in a defect in the CFTR protein in which the CFTR protein does not reach the surface of the cells in sufficient quantities and does not adequately transport chloride ions.

The absence of working CFTR protein results in poor flow of salt and water into and out of cells in a number of organs, including the lungs. As a result, thick, sticky mucus builds up and blocks the passages in many organs, leading to a variety of symptoms. In particular, mucus builds up and clogs the airways in the lungs, causing chronic lung infections and progressive lung damage. CFTR potentiators, such as ivacaftor and deutivacaftor, increase the probability that the CFTR protein channels open on the cell surface, increasing the flow of salt and water into and out of the cell. CFTR correctors, such as lumacaftor, tezacaftor, elexacaftor and vanzacaftor, increase the proper protein processing and folding of mutant CFTR proteins, such that a larger amount of functional CFTR protein reaches the cell surface. Our CFTR regimens target the underlying cause of disease and have been shown to improve CFTR protein function in people with CF, and as such have been shown to provide transformative benefit for people living with CF.

Our CF medicines are used by patients in over 60 countries, and TRIKAFTA/KAFTRIO is approved and reimbursed or accessible in more than 50 of these countries. We continue to increase the number of patients eligible and able to receive our current medicines through approvals of new medicines, label expansions and expanded reimbursement. In December 2024, the FDA approved the expanded use of TRIKAFTA for the treatment of people with CF 2 years of age and older who have at least one F508del mutation in the CFTR gene or a mutation that is responsive to TRIKAFTA based on clinical and/or in vitro data. With this approval, 94 additional non-F508del CFTR mutations have been added to the TRIKAFTA label.

In December 2024, the FDA approved ALYFTREK for the treatment of people with CF 6 years of age and older who have at least one F508del mutation or another mutation in the CFTR gene that is responsive to ALYFTREK. ALYFTREK is our next-in-class triple combination, which has the benefit of a once-daily dosing regimen and demonstrated non-inferiority to TRIKAFTA in $ppFEV_1$, a measure of lung function, and an improvement in sweat chloride levels as compared to TRIKAFTA. ALYFTREK carries a lower royalty burden than our other approved CF medicines and is also approved for 31 additional mutations not responsive to other CFTR modulator therapies.

Sickle Cell Disease and Transfusion-Dependent Beta Thalassemia

CASGEVY, our therapy for SCD and TDT, is approved in the U.S., the E.U., the U.K., Saudi Arabia, Bahrain, the UAE, Canada and Switzerland. SCD and TDT are hemoglobinopathies, a group of inherited blood disorders that result from gene mutations that alter hemoglobin, a protein in red blood cells that delivers oxygen throughout the body. We estimate approximately 60,000 people with severe SCD or TDT are or could become eligible for CASGEVY in the U.S., Canada, Europe, Saudi Arabia and Bahrain.

SCD is caused by the change of a single amino acid in the β-hemoglobin gene that causes red cells to change shape in settings of low oxygen. These sickled cells block blood flow and can lead to severe pain (known as vaso-occlusive crises), organ damage, and shortened life span. Treatment is typically focused on relieving pain and minimizing organ damage, requiring medication and, for some patients, monthly blood transfusions and frequent hospital visits.

Beta thalassemia is caused by loss-of-function mutations in the same β-hemoglobin gene that lead to severe anemia in patients, which causes fatigue and shortness of breath. In infants, beta thalassemia causes failure to thrive, jaundice, and feeding problems. Complications of beta thalassemia can lead to an enlarged spleen, liver and/or heart, misshapen bones and delayed puberty. Treatment for beta thalassemia varies depending on the disease severity for each patient. Patients with TDT, the most severe form of the disease, require regular blood transfusions, as frequently as every two to four weeks. Repeated blood transfusions eventually cause an unhealthy buildup of iron in the patient, leading to organ damage.

CASGEVY, our ex-vivo, non-viral CRISPR/Cas9-based gene-editing therapy, was developed for the treatment of severe SCD and TDT, with our collaborator, CRISPR Therapeutics AG (“CRISPR”). Patients first undergo a treatment at an authorized treatment center (“ATC”) that mobilizes a population of hematopoietic stem and progenitor cells (“HSPC”) from the bone marrow into the bloodstream. These cells are collected from the patient’s bloodstream and transferred to a manufacturing facility where the HSPCs are purified and CRISPR/Cas9 gene-editing is performed. The gene-editing procedure results in a precise and specific gene-edit in a non-coding intron of the BCL11A gene. Following manufacturing, the edited cells, now called CASGEVY, are transferred back to the ATC. Patients are preconditioned with a myeloablative

conditioning treatment that ablates their bone marrow prior to infusion of CASGEVY. After the edited HSPC cells are returned to the patient and engraft, the gene-edit results in significant increases in the levels of fetal hemoglobin erythrocytes, thereby reducing or eliminating symptoms associated with disease. Efficacy data support the profile of CASGEVY as a potential one-time functional cure for people with severe SCD and TDT.

Our global launch strategy 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, and working with payors to secure broad and equitable access for patients. With more than 50 ATCs activated globally, our strategy is focused on activation of a global ATC network to treat patients and expansion of our globally-enabled manufacturing and supply chain to meet growing patient demand. Our teams are also focused on working to educate patients, physicians and policymakers on the treatment journey and CASGEVY clinical data, where appropriate.

Acute Pain

Acute pain is a disabling condition that may occur suddenly but typically lasts less than 90 days and resolves in days or weeks (for example, following surgery or an injury). It is estimated that over 80 million people are prescribed a medicine for acute pain every year in the U.S. Currently available treatments have limitations around efficacy or side effects, including a risk of addiction. Because of these challenges, over- and under-utilization, as well as misutilization, of current pain medicines may occur.

In January 2025, the FDA approved JOURNAVX for the treatment of moderate-to-severe acute pain in adults. The approval was based on two positive randomized controlled Phase 3 clinical trials and supported by a positive single arm Phase 3 clinical trial evaluating safety and effectiveness. 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 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 a seamless treatment experience for physicians and people with acute pain. We are engaging with payors and formulary decision makers to secure reimbursement and access to JOURNAVX. We are working to secure national retail distribution to facilitate broad availability of JOURNAVX as well as financial and co-pay assistance programs for patients that will support access to JOURNAVX.

RESEARCH AND DEVELOPMENT PROGRAMS

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 strategy is to combine transformative advances in the understanding of human disease and in the science of therapeutics to dramatically advance human health. We focus on:

- disease areas with known causal human biology;
- targets validated by causal human biology;
- predictive lab assays and clinical biomarkers;
- potential for transformative benefit regardless of modality; and
- efficient path to registration and approval.

Our development-stage product candidates are focused on the treatment of serious diseases, including CF, SCD, TDT, acute and peripheral neuropathic pain, AMKD, IgAN and other autoimmune renal diseases and cytopenias, T1D, DM1, and ADPKD. In pursuit of serial innovation, our research and development approach includes advancing multiple candidates into clinical trials and pursuing multiple modalities with the goal of bringing first-in-class and/or best-in-class therapies to patients.

Our research and development strategy has been validated through our success in moving novel product candidates into clinical trials and obtaining marketing approvals for ALYFTREK, TRIKAFTA/KAFTRIO, KALYDECO, ORKAMBI, and

SYMDEKO/SYMKEVI for the treatment of CF, CASGEVY for the treatment of SCD and TDT, and JOURNAVX for the treatment of acute pain. Our approach to drug discovery has been further validated by our successful demonstration of clinical proof-of-concept in four additional disease areas: in diabetic peripheral neuropathy with our NaV1.8 inhibitors, in AMKD with inaxaplin, in T1D with zimislecel, and in IgAN with povetacicept.

Over the last several years, this strategy has led us to expand our capabilities to include additional innovative therapeutic modalities with a focus on cell and genetic therapies, which have the potential to treat, and in some cases, cure diseases by addressing the underlying cause of the disease. CASGEVY, approved in multiple geographies, including the U.S., is one such example. We continue to make significant internal investments in cell and genetic therapies. These investments include the development of a Boston-based campus for research and current Good Manufacturing Practices ("cGMP") clinical manufacturing capabilities dedicated to our portfolio of cell and genetic therapy technologies and teams.

To augment our internal programs, we acquire businesses and technologies and collaborate with biopharmaceutical and technology companies, leading academic research institutions, government laboratories, foundations and other organizations to advance research in our disease areas of interest, as well as to access technologies needed to execute on our strategy. Our internal and external innovation approaches are based on the same strategy, which enables us to effectively integrate and execute on new internal capabilities as we invest in external innovation. Our investments in external innovation include our collaboration with CRISPR, which resulted in the successful development and approval of CASGEVY and the establishment and advancement of other pipeline programs, including our T1D program through our acquisition of Semma Therapeutics, Inc. ("Semma"), our expansion of our renal programs through our acquisition of Alpine Immune Sciences, Inc. ("Alpine"), our mRNA therapeutic, VX-522, for treatment of CF through our collaboration with Moderna, and our intracellular therapeutics for DM1, including VX-670, through our collaboration with Entrada.

CF

We are enrolling and dosing in 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 estimate that approximately 90% of people with CF could benefit from our five approved medicines, including TRIKAFTA/KAFTRIO and the recently approved ALYFTREK. We continue to identify and develop additional CFTR modulators with the goal of developing best-in-class medicines that can help more patients who respond to CFTR modulators achieve normal levels of CFTR function; our next generation of CFTR modulators have completed, or are in the process of completing, Phase 1 clinical trials.

In order to treat people with CF who do not make full-length CFTR protein, and as a result, cannot benefit from our CFTR modulators, we are researching and developing genetic therapies, such as mRNA, and gene-editing approaches to CF. In collaboration with Moderna, we are developing VX-522, a nebulized CF mRNA therapeutic designed to treat the underlying cause of CF lung disease for these people by enabling cells in the lungs to produce functional CFTR protein. The multiple ascending dose portion of the clinical trial is ongoing and we expect data in the first half of 2025. We believe that VX-522 has the potential to benefit more than 5,000 people with CF in the U.S., Canada, Europe and Australia.

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 (the CLIMB SCD-151 clinical trial) and TDT (the CLIMB THAL-141 clinical trial) are ongoing. We have completed enrollment in these two clinical trials, and we expect to complete dosing in 2025.

In connection with our serial innovation approach, we are advancing preclinical assets for myeloablative conditioning agents with improved tolerability profiles, which we refer to as "gentler conditioning agents," which could be used in connection with treatment with CASGEVY, significantly broadening 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.

Pain

Pain can be debilitating and develop from a variety of conditions. Most commonly, patients with pain can be categorized as suffering from one of three types of pain: acute pain, chronic neuropathic pain (caused primarily by damage or dysfunction of peripheral nerves), or chronic musculoskeletal pain (caused primarily by damage to muscle, joints or bone). Acute pain usually resolves in days or weeks (for example, following surgery or an injury), while chronic pain generally lasts greater

than three months due to unresolved or ongoing damage to tissues or nerves. Currently available treatments have limitations around efficacy or side effects, including a risk of addiction. Because of these challenges, over- and under-utilization, as well as mis-utilization, of current pain medicines may occur.

The sodium channels NaV1.8 and NaV1.7 play important roles in the physiology of pain. We have discovered multiple selective small molecule inhibitors of NaV1.8 as potential treatments for pain. We obtained pharmacological validation of NaV1.8 inhibition with a first generation NaV1.8 inhibitor in three clinical pain types: acute pain, chronic neuropathic pain, and chronic musculoskeletal pain.

In acute pain, we are evaluating an oral formulation of VX-993, our next-generation NaV1.8 pain signal inhibitor, for the treatment of moderate-to-severe acute pain following bunionectomy surgery in a Phase 2 clinical trial. We are also enrolling and dosing healthy volunteers in a Phase 1 clinical trial evaluating an intravenous formulation of VX-993. The FDA has granted Fast Track Designation to VX-993 in acute pain in both the oral and intravenous formulations.

In neuropathic pain, we are enrolling and dosing in the Phase 3 pivotal program evaluating suzetrigine in people with diabetic peripheral neuropathy, a common form of peripheral neuropathic pain, with the ultimate goal of securing a broad label for the treatment of peripheral neuropathic pain. In addition, we are enrolling and dosing patients in a Phase 2 clinical trial for the oral formulation of VX-993, for the treatment of diabetic peripheral neuropathy. There are no approved medicines in the U.S. that are labeled for the treatment of peripheral neuropathic pain. The FDA has granted suzetrigine Breakthrough Therapy Designation in diabetic peripheral neuropathy.

In support of this broad peripheral neuropathic pain indication we seek, we completed a Phase 2 clinical trial of suzetrigine for the treatment of people with LSR, which is pain caused by impairment or injury to nerve roots in the area of the lumbar spine, another type of peripheral neuropathic pain. In December 2024, we announced Phase 2 clinical trial results showing that treatment with suzetrigine demonstrated a statistically significant and clinically meaningful within-group reduction in pain on the numeric pain rating scale for people with LSR, and that suzetrigine was safe and generally well-tolerated in the trial. The clinical trial also included a placebo reference arm, which showed a similar within-group reduction. 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. We plan to advance suzetrigine into pivotal development in LSR, pending discussions with regulators on trial design and the regulatory package.

In keeping with our serial innovation approach, we are advancing multiple additional NaV1.8 inhibitors and NaV1.7 inhibitors, which could be used alone or in combination, for the treatment of acute pain and chronic neuropathic pain.

APOL1-Mediated Kidney Disease

Inherited mutations in the APOL1 gene play a causal role in the biology of severe proteinuric kidney diseases referred to as AMKD. In AMKD, the kidney's filtering units known as the glomeruli, and within them the cells known as podocytes, are damaged, leading to leakage of protein into the urine, deterioration in kidney function, scarring, and, ultimately, permanent kidney damage. Patients with proteinuria who inherited two copies of the APOL1 mutations demonstrate rapid progression to end-stage kidney disease. Some patients with AMKD have the histological finding of focal segmental glomerulosclerosis ("FSGS") and co-morbidities such as hypertension. We are evaluating multiple novel small molecules that inhibit the function of the mutant APOL1 protein with the potential to treat APOL1-mediated kidney disease.

In a Phase 2 proof-of-concept clinical trial, patients with APOL1-mediated FSGS treated with inaxaplin on top of standard of care achieved a statistically significant, substantial, and clinically meaningful reduction of proteinuria, and inaxaplin was well tolerated by patients. Based on this positive Phase 2 data, we initiated pivotal development of inaxaplin in a single Phase 2/3 adaptive clinical trial in patients with AMKD in 2022. We completed the Phase 2B portion of the Phase 2/3 clinical trial and initiated the Phase 3 portion of the study in 2024. We continue to enroll and dose people with AMKD in the Phase 3 portion of the global Phase 2/3 pivotal clinical trial ("AMPLITUDE"). We expect to complete enrollment in the interim analysis cohort in 2025 and apply for potential accelerated approval in the U.S., assuming a positive interim analysis.

In addition, we have initiated a Phase 2 proof-of-concept clinical trial ("AMPLIFIED") evaluating inaxaplin as a treatment for people with AMKD and diabetes or other co-morbidities currently not eligible for the AMPLITUDE trial.

IgA Nephropathy and Other B Cell-Mediated Diseases

IgAN is a serious, progressive, life-threatening chronic kidney disease that causes inflammation and damage to the kidneys. It is the most common primary glomerulonephritis worldwide, affecting approximately 300,000 people in the U.S. and Europe, and, in China, there are approximately 750,000 people diagnosed with IgAN. A high percentage of people with IgAN progress to end-stage kidney disease. While there are approved therapies for the treatment of IgAN, there are no approved therapies that specifically target the underlying cause of the disease.

IgAN is thought to occur when the body produces an abnormal form of IgA, a type of antibody that normally helps the body fight infections. The body generates an abnormal immune response, including antibodies (autoantibodies), against this abnormal IgA, and these antibodies can combine to create larger molecules called immune complexes. These immune complexes can deposit in the kidneys, triggering damage and inflammation, especially within the glomeruli, impairing the kidneys' ability to properly filter waste and fluid.

In 2024, we acquired Alpine and its lead asset, povetacicept, which has the potential of being a "pipeline-in-a-product." Povetacicept is a dual antagonist of BAFF and APRIL, which play key roles in pathogenesis of IgAN and multiple other autoimmune diseases via their roles in the activation, differentiation and/or survival of B cells, T cells and innate immune cells. Povetacicept is a protein therapeutic based upon an engineered TACI (transmembrane activator and CAML interactor) domain. It has demonstrated higher binding affinity and greater potency in preclinical studies versus other inhibitors of BAFF and/or APRIL and has demonstrated potential best-in-class efficacy in a clinical trial in people with IgAN. Povetacicept is being studied as a once every four weeks subcutaneous injection, with the aim of at home self-administration upon commercialization.

In 2024, we initiated RAINIER, our global Phase 3 pivotal trial of povetacicept versus placebo in approximately 480 people with IgAN, which is enrolling and dosing people in the U.S., Europe and Asia. The clinical trial design contemplates a pre-planned interim analysis evaluating the change from baseline in urine protein-to-creatine ratio ("UPCR") after a certain number of patients reach 36 weeks of treatment. If positive, the interim analysis may serve as the basis to seek accelerated approval in the U.S. The final analysis will occur when patients reach two years of treatment and will evaluate total eGFR (estimated glomerular filtration rate) slope. We expect to complete enrollment in the interim analysis cohort in 2025 and apply for potential accelerated approval in the U.S., assuming a positive interim analysis.

In January 2025, we entered into a collaboration agreement with Zai Lab Limited ("Zai") for the development and commercialization of povetacicept in mainland China, Hong Kong SAR, Macau SAR, Taiwan region and Singapore. Under this collaboration, Zai will help advance the povetacicept clinical trials and make the regulatory submissions in the licensed territories. Zai will also be responsible for commercialization activities in the licensed territories, if povetacicept becomes an approved product.

We believe povetacicept holds the potential to transform multiple B-cell mediated diseases and deliver on its potential as a pipeline-in-a-product, with significant market opportunity across multiple therapeutic areas. In addition to IgAN, we are evaluating povetacicept as a treatment for other B cell-mediated autoimmune kidney diseases in the RUBY-3 basket trial and as a treatment for autoimmune cytopenias in the RUBY-4 basket trial. Both of these basket trials are ongoing, and we expect data in some of these conditions in 2025.

Type 1 Diabetes

T1D is a chronic metabolic disorder caused by insufficient insulin secretion by the beta cells in the pancreas. In patients with T1D, the insulin-producing islet cells of the pancreas are destroyed by the person's own immune system, resulting in a lack of insulin and impairment of blood glucose control. While insulin therapy allows patients to live for decades with the disease, challenges of insulin therapy include inadequate control of blood sugar (both hyper- and hypo-glycemia), a substantial burden of care on patients and families, and long-term vascular complications. Current standards of care do not address the underlying causes of the disease, and there are limited treatment options beyond insulin for the management of T1D.

We are developing non-autologous (allogeneic) fully differentiated, stem-cell derived islet cell therapies designed to replace insulin-producing islet cells that are destroyed in people with T1D, with the goal of delivering a functional cure. We are pursuing multiple programs for the transplant of functional islets into patients, including: transplantation of islet cells alone followed by standard, chronic immunosuppression to protect the implanted cells, implantation of the islet cells inside a

novel immunoprotective device, alternative approaches to immunosuppression that could be used with the implanted islet cells, and development of hypoimmune islet cells to optimize protection of the implanted islet cells from the immune system.

Zimislecel, our first program, is a stem cell-derived, allogeneic, fully differentiated, insulin-producing islet cell replacement therapy, using standard immunosuppression to protect the implanted cells. The Phase 1/2/3 clinical trial is designed as a sequential, multi-part clinical trial to evaluate the safety and efficacy of zimislecel, and has been expanded to include a total of 50 people. We expect to complete enrollment and dosing in the Phase 3 portion of this clinical trial in 2025 and, assuming positive data, we expect to file for approval after patients have completed one year of insulin-free follow-up. Data presented demonstrate unprecedented efficacy and curative potential. Safety data are consistent with the immunosuppressives, the perioperative period, and past medical history. In addition, we have initiated a clinical trial evaluating zimislecel in people with T1D who have had a kidney transplant.

In our second program, we are evaluating VX-264, in which zimislecel is encapsulated in an immunoprotective device that is implanted in patients, which we believe can obviate the need for immunosuppressive therapy. We are enrolling and dosing patients with VX-264 in a Phase 1/2 clinical trial to evaluate the safety, tolerability and efficacy of VX-264. Part A of the study dosed patients with a partial dose of cells/devices and a stagger between patients, Part B dosed patients with a full target dose and a stagger between patients, and Part C will dose at full target dose without a stagger between patients. We expect to share Part B full-dose data from this clinical trial in 2025.

In our third program, research is directed toward developing hypoimmune cells by gene-editing zimislecel prior to differentiation into fully differentiated islets in order to cloak them from the immune system. This program continues to advance in pre-clinical development. We are also pursuing alternative approaches to immunosuppression that could be used with zimislecel.

Myotonic Dystrophy Type 1

DM1 is an inherited disease that results in the weakening and destruction of skeletal muscles over time. Muscle weakness, muscle wasting and myotonia (sustained muscle contraction and difficulty relaxing muscles) are the hallmark features of DM1. It is a serious life-shortening disease with no approved treatments.

VX-670, our lead approach for DM1, holds the potential to address the underlying cause of DM1. VX-670 is an oligonucleotide connected to a cyclic peptide to promote effective delivery into cells. We completed the single ascending dose portion of the global Phase 1/2 clinical trial evaluating the first candidate, VX-670, in patients with DM1. We are enrolling and dosing the multiple ascending dose portion of the trial, which will evaluate the safety and efficacy of VX-670. We also have a small molecule program for DM1 in preclinical development.

Autosomal Dominant Polycystic Kidney Disease

ADPKD is a life-shortening genetic kidney disease characterized by the growth of numerous kidney-enlarging cysts that impair kidney function and can ultimately lead to kidney failure, requiring dialysis or kidney transplantation, and premature death. Kidney cysts can also lead to severe abdominal pain, cyst infection, blood in the urine and kidney stones, all of which significantly impair quality of life. Around half of patients with ADPKD experience kidney failure by the age of 60.

VX-407 is a first-in-class small molecule corrector that is designed to target the underlying cause of ADPKD in people with a subset of PKD1 variants. We are nearing completion of a Phase 1 clinical trial in healthy volunteers evaluating VX-407 and expect to advance VX-407 into a Phase 2 proof-of-concept clinical trial in people with ADPKD in 2025.

COMMERCIALIZATION OF OUR MEDICINES

Our commercialization efforts focus on supporting the appropriate use of ALYFTREK, TRIKAFTA/KAFTRIO, SYMDEKO/SYMKEVI, ORKAMBI, KALYDECO, CASGEVY and JOURNAVX in the markets where these products have been approved. Our teams are responsible for promoting products to health care providers, ensuring our products are distributed effectively, ensuring the safe use of our products, and obtaining reimbursement for our products from third-party payors, including governmental organizations in the U.S. and ex-U.S. markets. In parallel, our government affairs and public

policy group advocates for policies that promote life sciences innovation and increase awareness of the diseases on which we are focusing with state and federal legislatures, government agencies, public health officials and other policymakers.

Commercialization of CF Medicines

In the U.S., we primarily sell our CF products to a limited number of specialty pharmacy and specialty distributors. In international markets, we sell our CF products primarily through distributor arrangements and to retail pharmacies, as well as to hospitals and clinics, many of which are government-owned or supported. We also have established programs in the U.S. that provide our CF products to qualified uninsured or underinsured patients at no charge or at a reduced charge, based on specific eligibility criteria.

Our U.S. field-based CF commercial team is comprised of a small number of individuals to support commercialization of our medicines for CF. We focus our CF marketing efforts in the U.S. on a relatively small number of physicians and health care professionals who write most of the prescriptions for CF medicines. Many of these physicians and health care professionals are located at a limited number of accredited centers in the U.S. focused on the treatment of CF. In international markets, we or our distributors have small sales forces that support TRIKAFTA/KAFTRIO, SYMDEKO/SYMKEVI, ORKAMBI and KALYDECO in jurisdictions where these products are approved.

In December 2024, the FDA approved ALYFTREK in the U.S. as a treatment for people with CF 6 years of age and older who have at least one F508del mutation or another mutation in the CFTR gene that is responsive to ALYFTREK. This includes people with CF with one of 31 mutations who are now eligible for a CFTR modulator for the first time. ALYFTREK demonstrated non-inferiority to TRIKAFTA in $ppFEV_1$, a measure of lung function, and an improvement in sweat chloride levels as compared to TRIKAFTA, and we believe that this medicine has the potential to improve the care of patients with CF. ALYFTREK has the additional benefit of a once-daily dosing regimen and may lead to a new standard in CF care, reinforcing our established position as the leading company in CF. In addition, this new triple combination regimen has a lower royalty burden than our other CF medicines. We believe ALYFTREK presents an opportunity for three types of patients: (i) those who are currently on a CFTR modulator who may want to switch to ALYFTREK, (ii) those patients who have not yet been initiated on a CFTR modulator or been eligible for a CFTR modulator, and (iii) those who have discontinued from another CFTR modulator. We are supporting the launch of ALYFTREK through our existing commercial infrastructure.

ALYFTREK is under regulatory review in the U.K., the E.U., Canada, Switzerland, Australia and New Zealand.

Additionally, in December 2024, the FDA approved the expanded use of TRIKAFTA for the treatment of people with CF 2 years of age and older who have at least one F508del mutation in the CFTR gene or a mutation that is responsive to TRIKAFTA based on clinical and/or in vitro data. With this approval, 94 additional non-F508del CFTR mutations have been added to the TRIKAFTA label, and approximately 300 additional people with CF in the U.S. are now eligible to receive TRIKAFTA as a treatment.

Commercialization of CASGEVY

We are continuing 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 expect to obtain additional regulatory approvals for CASGEVY in 2025. We estimate approximately 60,000 people with severe SCD and TDT are or could become eligible for CASGEVY in the U.S., Canada, Europe, Saudi Arabia and Bahrain.

As CASGEVY is the first CRISPR-based therapy to be approved, our global launch strategy is focused on educating physicians, patients and caregivers, payors, and policymakers about the significant disease burden of SCD and TDT and the availability of CASGEVY as a treatment option. We have also established a global manufacturing network to ensure adequate production and supply of CASGEVY at commercial scale. Given the geographic concentration of patients, we expect to reach the majority of patients through our specialty commercial model, which is comprised of a small number of field-based individuals. Because the administration of CASGEVY requires specialized experience in stem cell transplantation, we are engaging with experienced hospitals to establish a network of authorized treatment centers across the U.S., Europe and the Middle East. We have activated more than 50 authorized treatment centers across the U.S., Europe, Saudi Arabia, Bahrain and the UAE, and we are working to activate additional centers.

Our teams are actively engaged with key treatment centers, policymakers and third-party payors to ensure that patients who may be eligible for CASGEVY have access to this potentially curative therapy. We are seeking broad access with

government and commercial payors for CASGEVY. In the U.S., there is broad coverage of CASGEVY in the private and public payer space, initially through single case agreements as medical policies are finalized. In addition, we have recently reached an agreement with the Centers for Medicare & Medicaid Services ("CMS") to participate in its cell and gene therapy access model, which may enable additional access mechanisms for states and authorized treatment centers. In England, we have secured access for eligible people with TDT and SCD. In the E.U., we are working with national health authorities to achieve access and reimbursement and have secured reimbursed access for people with SCD or TDT in Luxembourg, we have established a hospital-based reimbursement for CASGEVY in Austria, and the Italian Medicines Agency has approved early access for CASGEVY, on a case-by-case basis, to treat people with TDT or SCD. In the Middle East, we have reached a hospital-based reimbursement for people with SCD or TDT in Saudi Arabia, and for national reimbursement for eligible people in Bahrain. We are actively working to expand access to CASGEVY across Europe and the Middle East.

We are currently treating patients across multiple geographies and more than 50 patients have initiated cell collection. The first commercial patient was infused with CASGEVY in the third quarter of 2024.

Commercialization of JOURNAVX

In January 2025, JOURNAVX was approved by the FDA as a treatment for adults with moderate-to-severe acute pain. We believe JOURNAVX has the potential to establish a new standard of care for the estimated 80 million patients in the U.S. who are prescribed a medicine for their acute pain each year. Approximately half of these patients are prescribed opioids, which, while effective, have significant safety and tolerability concerns, and addictive potential. JOURNAVX provides effective relief of moderate-to-severe acute pain, has a favorable safety and tolerability profile, and based on its mechanism of action, does not have addictive potential.

Our commercial focus at launch for JOURNAVX is securing broad access and investing to ensure a seamless experience for patients and physicians. We are engaging with key health care professionals, formulary decision makers and payers to establish the conditions for rapid patient access and uptake. Our commercial field team is engaging stakeholders to support the launch of JOURNAVX in hospitals and other healthcare settings in the U.S. In addition, we are working to secure broad stocking agreements with national retail pharmacies and regional chains, to ensure access to JOURNAVX for patients across the U.S.

We are also focused on ensuring there is equal access to non-opioid options for pain relief. We continue to see momentum from federal and state policymakers to support the appropriate use of non-opioid pain medications, including addressing financial and other administrative barriers, such as utilization management, to accessing non-opioid options. In addition, as a part of our commitment to patients, we are offering financial and copay support programs for eligible patients who are prescribed JOURNAVX.

Reimbursement of Approved Therapies

Our CF medicines are used by patients in more than 60 countries, and TRIKAFTA/KAFTRIO is reimbursed or accessible in more than 50 of these countries outside the U.S. We expect to continue to focus significant resources to maintain reimbursement and obtain expanded reimbursement for our CF medicines and pipeline therapies in ex-U.S. markets.

In SCD and TDT, CASGEVY is approved in the U.S., the E.U., the U.K., Saudi Arabia, Bahrain, the UAE, Canada and Switzerland, and we are actively engaged with relevant stakeholders to obtain broad access and reimbursement with government and commercial payors for CASGEVY. CASGEVY is broadly reimbursed by third-party payors in the U.S., including the federal government. Currently in the U.S., across commercial and government payors, all eligible CASGEVY patients have case-by-case coverage through single case agreements, and we have signed agreements with national and regional payors, which cover over 250 million lives, to provide access to CASGEVY. Within Medicare, to help address this issue, we applied for and CMS has granted a new technology add-on payment for CASGEVY when used for the treatment of SCD for Medicare patients. Within Medicaid, we have engaged all of the Medicaid administrators in all 50 U.S. states, focused on the 25 states with the highest prevalence of SCD patients, and have confirmed pathways to reimbursement in all 25 of those priority states. In addition, in February 2023, the U.S. Administration established a new demonstration program to help pay for cell and gene therapies in diseases such as SCD through the CMS program known as The Cell and Gene Therapy Access Model ("CGT Access Model"). The CGT Access Model was designed to provide an opportunity to accelerate and enhance broad Medicaid access for eligible patients across all 50 U.S. states by allowing state Medicaid agencies to delegate authority to CMS to coordinate and facilitate outcomes-based payment arrangements ("OBAs") with cell and gene therapy

manufacturers, such as ours. In December 2024, we reached an agreement with CMS to expand access by participating in the CGT Access Model for SCD to benefit Medicaid beneficiaries.

For CASGEVY in ex-U.S. markets, we anticipate some early access programs initially and in parallel we are pursuing long-term reimbursement arrangements. We have successfully achieved national reimbursement in England, Luxembourg, and Bahrain for people with TDT or SCD, and secured hospital-based reimbursement for patients in Saudi Arabia and Austria. We continue to engage with payors in the U.K., the E.U., and the Middle East.

For JOURNAVX in the U.S., we have been working with government and commercial payors pre- and post-approval to support rapid and broad access, including to accelerate targeted contracting and formulary additions at both select payors and targeted hospital systems. In addition, we are finalizing contracts with private and government payors, as well as hospital group purchasing organizations.

STRATEGIC TRANSACTIONS AND COLLABORATIONS

As part of our business strategy, we seek to license or acquire technologies, products, product candidates, and businesses that are aligned with our corporate and research and development strategies and complement and advance our ongoing research and development efforts. In addition, we establish business relationships with collaborators to support our research activities and to lead or support development and/or commercialization of certain product candidates. We expect to continue to identify and evaluate potential acquisitions, licenses and collaborations that may be similar or different from the transactions that we have engaged in previously.

Strategic Transactions

In May 2024, we acquired Alpine for approximately $5.0 billion. Alpine's lead molecule, povetacicept, is a highly potent and effective dual antagonist of BAFF and APRIL. We are evaluating povetacicept for the potential treatment of IgAN in a Phase 3 clinical trial and for the treatment of other serious autoimmune diseases in Phase 2 clinical trials. We believe povetacicept has the potential to treat multiple diseases or conditions and become a pipeline-in-a-product, with significant market opportunity across multiple therapeutic areas.

In addition to Alpine, we have made additional acquisitions which have expanded and advanced our pipeline, including:

- In 2017, we enhanced our CF portfolio through our acquisition of certain CF assets, including deutivacaftor, from Concert Pharmaceuticals Inc. In December 2024, the FDA approved ALYFTREK (vanzacaftor/tezacaftor/deutivacaftor) for people with CF 6 years of age and older.
- In 2019, we established our T1D program through our acquisition of Semma, a privately held company focused on the use of stem cell-derived human islets as a potentially curative treatment for T1D. We are evaluating zimislecel for the potential treatment of T1D in a Phase 1/2/3 clinical trial. We expect to complete enrollment and dosing in the Phase 3 portion of this clinical trial in 2025. In addition, our second clinical program in T1D, VX-264, in which zimislecel is encapsulated in an immunoprotective device, is ongoing.

We expect to continue to identify and make acquisitions to expand and advance our pipeline and business.

Collaboration and Licensing Arrangements

Joint Development and Commercialization Agreement with CRISPR

In December 2017, we entered into a joint development and commercialization agreement ("Original JDCA") with CRISPR, pursuant to which we are co-developing and co-commercializing CASGEVY for SCD and TDT. We entered into the Original JDCA following our exercise of an option to co-develop and co-commercialize the hemoglobinopathies program that was contained in the collaboration agreement that we entered into with CRISPR in 2015.

In April 2021, we and CRISPR amended and restated the Original JDCA (the "A&R JDCA"). Pursuant to the A&R JDCA, the parties agreed to, among other things, (a) adjust the governance structure for the collaboration and adjust the responsibilities of each party thereunder; (b) adjust the allocation of net profits and net losses between the parties; and (c)

exclusively license (subject to CRISPR's reserved rights to conduct certain activities) certain intellectual property rights to us relating to the products that may be researched, developed, manufactured and commercialized under such agreement.

Pursuant to the A&R JDCA, we lead global development, manufacturing and commercialization of CASGEVY, with support from CRISPR. Subject to the terms and conditions of the A&R JDCA, we have the right to conduct all research, development, manufacturing, and commercialization activities relating to the product candidates and products under the A&R JDCA (including CASGEVY) throughout the world, subject to CRISPR's reserved right to conduct certain activities.

In connection with the A&R JDCA, we made a $900.0 million upfront payment to CRISPR in the second quarter of 2021. CRISPR earned an additional one-time $200.0 million milestone payment upon receipt of marketing approval of CASGEVY from the FDA.

We and CRISPR shared equally all expenses incurred under the Original JDCA. On July 1, 2021, with respect to CASGEVY, the net profits and net losses incurred pursuant to the A&R JDCA began to be allocated 60% to us and 40% to CRISPR, subject to certain adjustments, while all other product candidates and products continue to have net profits and net losses shared equally between the parties.

Either party may terminate the A&R JDCA upon the other party's material breach, subject to specified notice and cure provisions, or, in our case, in the event that CRISPR becomes subject to specified bankruptcy, winding up, or similar circumstances. Either party may terminate the A&R JDCA in the event the other party commences or participates in any action or proceeding challenging the validity or enforceability of any patent that is licensed to such challenging party pursuant to the A&R JDCA. We also have the right to terminate the A&R JDCA for convenience at any time after giving prior written notice. If circumstances arise pursuant to which a party would have the right to terminate the A&R JDCA on account of an uncured material breach, such party may elect to keep the A&R JDCA in effect and cause such breaching party to be treated as if it had exercised its opt-out rights with respect to the products associated with such uncured material breach and the royalties payable to the breaching party would be reduced by a specified percentage.

Either party may opt out of the development of a product candidate under the A&R JDCA after predetermined points in the development of the product candidate, on a candidate-by-candidate basis. In the event of such opt-out, the party opting-out will no longer share in the net profits and net losses associated with such product candidate and, instead, the opting out party will be entitled to high single to mid-teen percentage royalties on the net sales of such product, if commercialized.

In-License Agreements

We have entered into various agreements pursuant to which we have obtained access to technologies from third parties and are conducting research and development activities with collaborators. Pursuant to these arrangements, we have obtained development and commercialization rights to resulting product candidates. Depending on the terms of the arrangements, we may be responsible for the costs of research activities, required to make upfront payments and/or milestone payments upon the achievement of certain research, development, and commercial objectives, and/or pay royalties on future sales, if any, of commercial products resulting from the collaboration. Our current in-license agreements include:

- CRISPR Therapeutics AG. In addition to our arrangement with CRISPR described above, we have exercised options to exclusively license treatments for specific targets, including CF, that were subject to the research program under the collaboration agreement we entered into with CRISPR in 2015. In 2019, we obtained exclusive worldwide rights to CRISPR's intellectual property for Duchenne muscular dystrophy ("DMD") and DM1 gene-editing products through a new agreement with CRISPR. In 2023, we obtained non-exclusive rights to CRISPR's intellectual property for the development of hypoimmune gene-edited cell therapies for T1D through a new agreement with CRISPR.

- Moderna, Inc. In 2016, we entered into a collaboration with Moderna for the identification and development of mRNA therapeutics encoding CFTR for the treatment of CF. In December 2022, the FDA cleared our Investigational New Drug Application ("IND") for VX-522, an mRNA therapeutic we are developing with Moderna pursuant to this collaboration. The multiple ascending dose portion of the Phase 1/2 clinical trial of VX-522 in people with CF is ongoing. We expect to share data from this clinical trial in the first half of 2025.

- Entrada Therapeutics, Inc. In 2022, we established a collaboration with Entrada focused on enabling efficient intracellular delivery of an oligonucleotide for DM1. This collaboration includes VX-670, an investigational candidate for the treatment of DM1 that is in clinical development. We completed the single ascending dose portion

of the global Phase 1/2 clinical trial for VX-670 in people with DM1. We are enrolling and dosing the multiple ascending dose portion of the trial, which will evaluate the safety and efficacy of VX-670.

Out-license Agreements

We have entered into various agreements pursuant to which we have out-licensed rights to certain product candidates to third-party collaborators. Pursuant to these out-license arrangements, our collaborators are responsible for all costs related to the continued development of such product candidates and obtain development and commercialization rights to these product candidates. Depending on the terms of the arrangements, our collaborators may be required to make upfront payments, milestone payments upon the achievement of certain research and development objectives and/or pay royalties on future sales, if any, of commercial products licensed under the agreement.

In January 2025, we entered into a collaboration agreement with Zai for the development and commercialization of povetacicept in mainland China, Hong Kong SAR, Macau SAR, Taiwan region and Singapore. Under this collaboration, Zai will help advance the povetacicept clinical trials and make the regulatory submissions in the licensed territories. Zai will also be responsible for commercialization activities in the licensed territories, if povetacicept becomes an approved product.

Cystic Fibrosis Foundation

In 2004, we entered into a collaboration agreement with the Cystic Fibrosis Foundation, as successor in interest to the Cystic Fibrosis Foundation Therapeutics, Inc., to support research and development activities. Pursuant to the collaboration agreement, as amended, we have agreed to pay tiered royalties ranging from single digits to sub-teens on covered compounds first synthesized and/or tested during a research term on or before February 28, 2014, including ivacaftor, lumacaftor and tezacaftor and royalties ranging from low-single digits to mid-single digits on net sales of certain compounds first synthesized and/or tested between March 1, 2014 and August 31, 2016, including elexacaftor. We do not have any royalty obligations on compounds first synthesized and tested on or after September 1, 2016. For combination products, such as ORKAMBI, SYMDEKO/SYMKEVI, TRIKAFTA/KAFTRIO, and ALYFTREK sales are allocated equally to each of the active pharmaceutical ingredients in the combination product, and royalties are then paid for any royalty-bearing components included in the combination.

INTELLECTUAL PROPERTY

Patents and other intellectual property rights such as trademarks, trade secrets, and copyrights are critical to our business. We actively seek protection for our products and proprietary information by means of U.S. and foreign patents, trademarks, and copyrights, as appropriate. In addition, we rely upon trade secret protection and contractual arrangements to protect certain of our proprietary information.

Patents provide a period of exclusivity that can make it more difficult for competitors to market and use our technology. We own and control patents and pending patent applications that relate to compounds, formulations, synthetic routes, intermediates, devices, treatment of diseases, and other inventions.

To protect our intellectual property, we typically apply for patents several years before a product receives marketing approval. Under current law, a patent expires 20 years from its first effective filing date. Since the drug development process may last for many years, there may be a period of time in which we have an issued patent but not marketing approval to sell the drug. To compensate for patent term lost while a product is in clinical trials and undergoing review for marketing approval, we may be able to apply for patent term extensions or supplementary protection certificates (“SPCs”) in some countries. In addition to patent protection, we receive regulatory exclusivity from U.S. and European regulatory agencies for the active pharmaceutical and biological agents and, where applicable, their approved orphan indications for a certain time period. Regulatory exclusivity runs concurrently with patent exclusivity and provides complementary protection for our products.

For our approved commercial products, and those in development, we own or hold exclusive and non-exclusive licenses to several hundred patents around the world. In the U.S., once an NDA, or a supplement thereto, is approved we are required to list with the FDA each U.S. patent with claims that cover our product or a method of using the product. The FDA publishes the patents we list in a book referred to as the Orange Book. We have thirteen issued U.S. patents listed in the Orange Book that cover the active pharmaceutical ingredients in KALYDECO, its marketed formulations, and/or its approved indication.

We have 22 issued U.S. patents listed in the Orange Book that cover the active pharmaceutical ingredients in ORKAMBI, its marketed formulations, and/or its approved indication. We have 25 issued U.S. patents listed in the Orange Book that cover the active pharmaceutical ingredients in SYMDEKO, its marketed formulation, and/or its approved indication. We have 28 issued U.S. patents listed in the Orange Book that cover the active pharmaceutical ingredients in TRIKAFTA, its marketed formulation, and/or its approved indication. We have 35 issued U.S. patents listed in the Orange Book that cover the active pharmaceutical ingredients in ALYFTREK, its marketed formulation, and/or its approved indication. We expect to have an issued patent listed in the Orange Book that covers the active pharmaceutical ingredient in JOURNAVX, its marketed formulation, and/or its approved indication.

Products approved by the FDA under a Biologics Licensing Application ("BLA"), including CASGEVY, receive 12 years of regulatory exclusivity in the U.S. from a product's approval date. Additionally, we have licenses to dozens of issued U.S. patents that cover CASGEVY, its approved indication, and/or its manufacture. Products approved by the FDA under a BLA are not subject to the Orange Book patent listing requirement.

The table below sets forth the year of projected expiration for the basic product patent covering each of our approved products. For products that are combinations of two or more active ingredients, the table lists the projected expiration of the latest expiring patent covering any of the active pharmaceutical ingredients (lumacaftor for ORKAMBI, tezacaftor for SYMDEKO/SYMKEVI, elexacaftor for TRIKAFTA/KAFTRIO and vanzacaftor for ALYFTREK). Unless otherwise noted, patent term extensions, and pediatric exclusivity periods are not reflected in the expiration dates listed in the table below and may extend protection. In some instances, we also own later-expiring patents and applications relating to solid forms, formulations, methods of manufacture, or the use of these drugs in the treatment of particular diseases or conditions. In some cases, however, such patents may not protect our drug from generic competition after the expiration of the basic patent.

Product	Expiration Year of U.S. Basic Product Patent	Expiration Year of European Basic Product Patent
KALYDECO	2027	2027 [1]
ORKAMBI	2031	2030 [1]
SYMDEKO/SYMKEVI	2027	2033 [1]
TRIKAFTA/KAFTRIO	2037	2037
CASGEVY	2035 [2]	2034 [3, 4]
ALYFTREK	2039	2039
JOURNAVX	2040	2040

[1] Expiration date reflects SPCs granted in the five major European markets (France, Germany, Italy, Spain and the U.K.).

[2] Expiration year reflects the expiration of regulatory exclusivity, which expires later than the basic product patent for this product in this market.

[3] Expiration year reflects the expiration of regulatory exclusivity in the E.U., which expires later than the basic product patent for this product in this market.

[4] Product is approved in Great Britain with regulatory exclusivity until November 2033, which is later than the expiration of the basic product patent.

In addition to protecting our marketed products, we actively file patent applications in the U.S. and in foreign countries on inventions relating to our pipeline. For example, we also own and/or control U.S. and foreign patents and/or patent applications relating to the following:

- Other CF potentiators and correctors and many other related compounds, and the use of those compounds for the treatment CF.
- VX-522 and other mRNA-based approaches for treating CF.
- VX-993, VX-973, and other compounds being studied for the potential treatment of pain.
- Inaxaplin and other compounds being studied for the potential treatment of AMKD.
- Povetacicept for the treatment of IgAN.
- Zimislecel, VX-264, and other cell-based approaches for treating T1D.

- VX-670 for the treatment of DM1.
- VX-407 and other compounds being studied for the potential treatment of ADPKD.
- Other pre-clinical and clinical candidates and the use of such candidates to treat specified diseases.
- The manufacture, pharmaceutical compositions, related solid forms, formulations, dosing regimens, and methods of use of many of the above compounds.

We and CRISPR intend to rely upon a combination of rights, including patent rights, trade secret protection, and regulatory exclusivities to protect CASGEVY. CRISPR has licensed certain rights to a worldwide patent portfolio that covers various aspects of the CRISPR/Cas9 editing platform technology including, for example, compositions of matter and methods of use, including their use in targeting or cutting DNA, from Dr. Emmanuelle Charpentier. In addition to Dr. Charpentier, this patent portfolio has named inventors who assigned their rights to the Regents of the University of California or the University of Vienna, to whom we refer, together with Dr. Charpentier, as the CVC Group. CRISPR has non-exclusive or co-exclusive rights to the patent rights that protect the core CRISPR/Cas9 gene-editing technology. For example, certain third parties, including competitors, have reported obtaining a license to rights in this patent portfolio in certain fields. In addition, patents and patent applications in this patent portfolio are the subject of adversarial proceedings in the U.S., Europe, and other jurisdictions, including proceedings in the U.S. Patent and Trademark Office (the "USPTO"), between the CVC Group and, separately, Sigma-Aldrich, Co. LLC ("Sigma-Aldrich"), ToolGen, Inc. ("ToolGen"), and the Broad Institute, Harvard University, and Massachusetts Institute of Technology (collectively, "Broad"). To date, both the CVC Group and Broad have obtained granted patents that purport to cover aspects of CRISPR/Cas9 editing platform technology. The patents and patent applications within the patent portfolios of the CVC Group, Broad, Sigma-Aldrich and/or ToolGen are, or may in the future be, involved in proceedings similar to interferences or priority disputes in Europe or other foreign jurisdictions. In December 2023, we entered into an agreement with Editas Medicine, Inc. ("Editas"), providing us a non-exclusive sublicense to certain patents relating to CRISPR/Cas9 technology, owned by Broad and Harvard, which are licensed to Editas. In addition to the patent portfolios licensed from Dr. Charpentier, Broad, and Harvard, we own patents and/or patent applications relating to the composition, manufacture, and use of CASGEVY.

From time to time, we enter into exclusive and non-exclusive license agreements for proprietary third-party technology used in connection with our research activities. These license agreements typically provide for the payment by us of a license fee but may also include terms providing for milestone payments or royalties for the development and/or commercialization of our drug products arising from the related research.

We cannot be certain that issued patents we own or license will be enforceable or provide adequate protection or that pending patent applications will result in issued patents. The existence of patents does not guarantee our right to practice the patented technology or commercialize the patented product. Litigation, interferences, oppositions, *inter partes* reviews, administrative challenges or other similar types of proceedings may be necessary in some instances to determine the validity and scope of certain patents, regulatory exclusivities or other proprietary rights, and in other instances to determine the validity, scope or non-infringement of intellectual property rights that may be claimed by third parties to be pertinent to the manufacture, use or sale of our products.

MANUFACTURING

As we market and sell our approved products and advance our product candidates through clinical development toward commercialization, we continue to build and maintain our supply chain and quality assurance resources. We rely on internal capabilities and a global network of third parties to manufacture and distribute our product candidates for clinical trials, as well as our products for commercial sale and post-approval clinical trials. In addition to establishing supply chains for each new approved product, we must adapt our supply chain for existing products to include additional formulations that are often required to treat younger patients or to increase scale of production for existing products. We are focused on ensuring the stability of the supply chains for our current products, including KALYDECO, ORKAMBI, SYMDEKO/SYMKEVI, TRIKAFTA/KAFTRIO, ALYFTREK, CASGEVY, JOURNAVX, and for our pipeline programs. In addition, we are focused on identifying and ensuring efficient manufacturing and delivery processes for the biological and cell and genetic therapies we are developing, including our stem cell therapy program for T1D and biologics manufacturing for povetacicept and other product candidates.

We have established our own small molecule manufacturing capabilities in Boston, which we use for clinical trial and commercial supplies, including certain manufacturing steps related to our commercial supply of TRIKAFTA/KAFTRIO. We expect to continue to rely on third parties to meet our commercial supply needs, including for TRIKAFTA/KAFTRIO, CASGEVY, ALYFTREK, JOURNAVX, and pipeline programs, and a significant portion of our clinical supply needs for the foreseeable future. We have established and continue to evaluate additional manufacturing capacity for our current and future products, including recently approved ALYFTREK for CF, and JOURNAVX for pain.

Our supply chain for sourcing raw materials and manufacturing our product and product candidates, including obtaining all necessary supplies, is a multi-step global endeavor. In general, these raw materials and other necessary supplies are available from multiple sources. Third-party contract manufacturers, including some in China, perform different parts of our manufacturing process. Contract manufacturers supply us with raw materials, convert these raw materials into drug substance and/or convert the drug substance or product into final dosage form. In addition, third parties assist us with packaging, warehousing, and global distribution of our products. Establishing and managing this global supply chain for each of our products and product candidates require a significant financial commitment and the creation and maintenance of numerous third-party contractual relationships.

The manufacturing processes for biological and cell and genetic therapies are more complex than those required for small molecule drugs and require different systems, equipment, facilities, and expertise. Additionally, we are unable to utilize a single process for all of our biological and cell and genetic therapies; they must be customized for each program and therapy. We are investing and plan to continue to invest significant resources in expanding and strengthening our manufacturing, infrastructure and capabilities, such as cGMP clinical manufacturing, both independently and through third-party networks, in an effort to develop and commercialize our biological and cell and genetic therapies. We have secured agreements for povetacicept and our T1D cell therapy program to meet our anticipated demands. We continue to evaluate additional suppliers for all of our late-stage clinical programs for additional capacity and redundancy to support commercial supply.

We rely on third-party manufacturers to produce or process cell culture reagents and gene-editing components, such as Cas9 protein and guide RNA molecules for clinical trials and commercial supply of CASGEVY, and to generate gene-edited cells to supply CASGEVY. We continue to rely on third-party manufacturers for commercial supply of CASGEVY. The manufacturing process for CASGEVY involves a number of steps prior to the final infusion of drug product into patients. Following mobilization and collection of blood cells from the patient, cells are transferred to a manufacturing site where HSPCs are purified and CRISPR/Cas9 gene-editing is performed. The edited cellular product, called CASGEVY, is frozen and transported back to the authorized treatment center where it is stored prior to infusion into the patient. Each step must be completed successfully, and in a timely manner, requiring coordination between us, authorized treatment centers, third-party manufacturers and shipping vendors. We are making significant investments to secure additional capacity and to coordinate manufacturing, testing, and logistics activities at a larger scale across multiple facilities to serve the geographies in which we are treating and expect to treat additional patients with CASGEVY.

We have established manufacturing capabilities in the Boston area to support our T1D program. In addition, to further expand our capabilities in cell therapy manufacturing, we have a strategic agreement with Lonza to support the manufacture of our portfolio of investigational allogeneic stem cell-derived, fully differentiated, insulin-producing islet cell therapies. We also rely on third-party manufacturers to produce drug substance and finished drug product for clinical trials for povetacicept.

We have developed systems and processes to track, monitor, and oversee our and our third-party manufacturers' activities, including a quality assurance program intended to ensure that our third-party manufacturers comply with cGMP and the foreign jurisdictional equivalents when applicable. We devote substantial time, resources and effort in the areas of production, quality control, and quality assurance to maintain cGMP compliance. We regularly evaluate the performance of our third-party manufacturers with the objective of confirming their continuing capabilities to meet our needs efficiently and economically. Manufacturing facilities, both foreign and domestic, are subject to inspections by or under the authority of the FDA and other U.S. and foreign government authorities. Although we actively engage with regulatory authorities, the timing of inspections and regulatory approvals for each of these facilities is the remit of the manufacturer and not within our control and may be delayed for a number of reasons.

COMPETITION

The pharmaceutical industry is characterized by extensive research efforts, rapid technological progress, and intense competition. There are many public and private companies, including pharmaceutical companies and biotechnology companies, engaged in developing products for the indications our drugs are approved to treat and the therapeutic areas we are targeting with our research and development activities. Potential competitors also include academic institutions, government agencies, other public and private research organizations and charitable venture philanthropy organizations that conduct research, seek patent protection and/or establish collaborative arrangements for research, development, manufacturing and commercialization. Mergers and acquisitions in the pharmaceutical, biotechnology and gene therapy industries may result in a larger concentration of resources among a smaller number of our competitors. Some of our competitors may have substantially greater financial, technical, marketing and human resources than we do.

We believe that competition in our industry is based on, among other factors, innovative research, the effective and rapid development of product candidates, the ability to market and obtain reimbursement for products and the ability to establish effective patent protection. We face competition based on the safety and efficacy of our product and product candidates, the timing and scope of regulatory approvals, the availability and cost of supply, marketing and sales capabilities, reimbursement coverage, price, patent protection and other factors. Our competitors may develop or commercialize more effective, safer, or more affordable products than we are able to develop or commercialize or obtain more effective patent protection. As a result, our competitors may commercialize products more rapidly or effectively than we do, which would adversely affect our competitive position, the likelihood that our product candidates, if approved, would achieve and maintain market acceptance and our ability to generate meaningful revenues from our products. Future competitive products may render our products, or future products, obsolete or noncompetitive. Another key element of remaining competitive in our industry is recruiting and retaining leading scientific, technical and management personnel to conduct our research activities and advance our development programs, including with the commercial expertise to effectively market our products.

Our success in rapidly developing and commercializing our products may increase the resources that our competitors allocate to the development of potential treatments. In addition, clinical trials conducted by our competitors could take place simultaneously with our own trials and may slow down our pace of development if we are unable to recruit sufficient clinical trial subjects. If one or more competing therapies are successfully developed as a marketable treatment, our revenues from our current products and/or additional products, if then approved, could face significant competitive pressure.

Many other pharmaceutical and biotechnology companies are investing resources for the discovery and development of small molecules and biologic and cell and gene therapies to treat the same disease areas for which we are developing therapies in our pipeline. If any of these competitors develop or successfully commercialize products involving therapies competitive with our pipeline therapies, the potential return on our investment in those pipeline therapies could be impacted.

Cystic Fibrosis

A number of companies are seeking to identify and develop product candidates for the treatment of CF, including CFTR modulators and other therapies intended to address the underlying causes of CF.

Sionna Therapeutics, Inc. has multiple CFTR modulators in Phase 1 or Phase 2 development, including assets in-licensed from AbbVie Inc. in July 2024, and additional CFTR modulators in preclinical development. Proteostasis Therapeutics, Inc. was developing potential CFTR modulator therapies prior to its acquisition by Yumanity Therapeutics, Inc. (“Yumanity”). Following the merger, Yumanity out-licensed the CF program to Fair Therapeutics. In February 2024, HIT-CF Europe, a research project from CF-Europe, a federation of European patient advocacy groups, initiated a Phase 2b trial of a combination of Fair Therapeutics’ CFTR modulators in European CF patients with rare mutations of the CFTR gene.

Other therapeutic approaches include addressing CF utilizing nucleic acid therapies, which are compounds that allow expression of a functional CFTR protein and are relevant for the more than 5,000 people with CF who cannot make full-length CFTR protein and cannot benefit from CFTR modulators. Nucleic acid therapies are under development by companies such as Arcturus Therapeutics Holdings, Inc., ReCode Therapeutics, Inc., Krystal Biotech, Inc., Spirovant Sciences, Inc. Boehringer Ingelheim International, GmbH, 4D Molecular Therapeutics, Inc and SpliSense, Ltd.

Sickle Cell and Beta Thalassemia

There are multiple approved small molecule and biologic treatments for SCD and beta thalassemia, including products from Novartis International AG (“Novartis”), and Bristol Myers Squibb together with Merck & Co. In addition, bluebird bio,

Inc. (“bluebird”) obtained FDA approval of its gene therapy, ZYNTEGLO™ (betibeglogene autotemcel) in August 2022 for the treatment of patients with beta thalassemia who require regular red blood cell transfusions. bluebird withdrew its marketing authorizations for Zynteglo from both the E.U. and U.K. in early 2022. In late 2023, bluebird also obtained FDA approval for its gene therapy for SCD, LYFGENIA™ (lovotibeglogene autotemcel). In September 2024, Pfizer Inc. (“Pfizer”) voluntarily withdrew OXBRYTA® (voxelotor) from all markets. Authorization for Novartis’ ADAKVEO® (crizanlizumab) has been revoked in the U.K. and in Europe, however, this drug remains approved for use in the U.S. by the FDA.

Various companies and private academic/medical institutes are developing therapies for the treatment of SCD or beta thalassemia utilizing CRISPR technology, lentiviral vectors, or transcription activator-like effector nuclease, gene correction, base, or prime editing. For example, Beam Therapeutics has a base-editing asset in clinical development for SCD. In addition, Agios Pharmaceuticals’ Supplemental New Drug Application for PYRUKYND® (mitapivat) is under review in the U.S. for the treatment of adult patients with non-transfusion dependent and transfusion dependent alpha- or beta thalassemia. Mitapivat is also in Phase 3 for SCD.

Pain

The acute pain market largely consists of conventional analgesics, including opioids, non-steroidal anti-inflammatory drugs, acetaminophen and local anesthetics, low-cost generics, and reformulations aiming to provide safer, more tolerable, or more convenient therapies. Peripheral neuropathic pain is a type of chronic pain caused by injury or dysfunction of peripheral nerves. The peripheral neuropathic pain market largely consists of generic anticonvulsants and anti-depressant drugs.

Several companies are pursuing clinical development of novel mechanisms of action for acute and chronic pain indications, including NaV1.8 inhibitors in Phase 1 clinical trials by Latigo Bio, Merck, and SiteOne Therapeutics. Several additional NaV1.8/1.7 inhibitors are in preclinical development for pain, and there are several other compounds with other mechanisms of action in development, including programs by Eli Lilly and Company (“Eli Lilly”) and Lexicon Pharmaceuticals Inc.

T1D

The T1D standard of care of exogenous insulin injections continues to progress as multiple companies are developing novel insulin formulations, advanced pumps and glucose sensors, and fully closed loop systems. Pharmaceutical and biotechnology companies are actively engaged in the research and development of products for T1D, including strategies to prevent the destruction of beta cells, to protect beta cell function, or to replace missing beta cells, as well as other cell therapy approaches such as immune evasive technologies to hide the cell from the immune system, micro- and macro-encapsulation technologies that potentially require no immunosuppression, and islets cell in combination with immunosuppression. In addition to CellTrans, Inc.’s LANTIDRA™ (donislecel), the first FDA-approved cadaveric islet therapy for the treatment of T1D, other companies developing cell therapies for T1D, either directly or through partnerships, include Novo Nordisk A/S, Eli Lilly, Sernova Corp, Sana Biotechnology, Inc., Seraxis, Inc., and Evotec A.G.

AMKD

There are no approved therapies for AMKD. People with chronic kidney disease (“CKD”) take angiotensin-converting enzyme inhibitors and angiotensin receptor blockers to treat hypertension; steroids and immunosuppressants to reduce proteinuria; and SGLT2 inhibitors to reduce the risk of CKD progression. These CKD treatments may reduce proteinuria, but do not stop the rapid disease progression seen in AMKD patients. Several companies have early programs developing APOL1-targeted assets, including AstraZeneca, Maze Therapeutics, and OmniAb. Eli Lilly’s Janus kinase inhibitor (baricitinib) is being investigated in AMKD patients in a Phase 2 study by Duke University.

IgAN

IgAN is a rapidly evolving landscape with multiple potentially disease-modifying therapies in late-stage clinical development. There are three novel therapies for IgAN approved in major markets: Calliditas’ TARPEYO®/KINPEYGO® (delayed release budesonide), Travere Therapeutics’ FILSPARI® (sparsentan), a dual endothelin angiotensin receptor antagonist, and Novartis’ FABHALTA® (iptacopan), a complement factor B inhibitor. Programs in late-stage clinical development include Otsuka Pharmaceutical Co., Ltd’s sibeprenlimab (anti-APRIL mAb), Vera Therapeutics’ atacicept (dual BAFF/APRIL inhibitor), RemeGen’s telitacicept (dual BAFF/APRIL inhibitor), Novartis’ zigakibart (anti-APRIL mAb), and other programs from Novartis, Roche (and partner Ionis Pharmaceuticals), and AstraZeneca. Other mid-stage clinical

programs include anti-CD38 mAbs from Biogen and Takeda. In addition, there is significant global preclinical and earlier stage clinical development activity for IgAN.

GOVERNMENT REGULATION

Our operations and activities are subject to extensive regulation by numerous government authorities in the U.S., Europe and other countries. In the U.S., Europe and other countries, our products are subject to rigorous regulations governing their testing, manufacture, labeling, storage, record keeping, approval, and advertising and promotion. As a result of these regulations, product development and product approval processes are very expensive and time consuming. The regulatory requirements applicable to drug and biologic development, approval, and marketing are subject to change. In addition, regulations and administrative guidance often are revised or reinterpreted by the agencies in ways that may significantly affect our business and our products. It is impossible to predict whether legislative changes will be enacted, or FDA or comparable ex-U.S. regulations, guidance or interpretations will change.

United States Government Regulation

New Drug Application and Biologics License Application Approval Processes

The process required by the FDA before a drug or biologic may be marketed in the U.S. generally involves the following:

- completion of preclinical laboratory tests, animal studies and formulation studies conducted according to Good Laboratory Practices ("GLP"), and other applicable regulations;
- submission to the FDA of an IND, which must become effective before clinical trials in the U.S. may begin;
- performance of adequate and well-controlled clinical trials according to Good Clinical Practices ("GCP"), and other clinical trial-related regulations to establish the safety and efficacy of the proposed drug for its intended use;
- submission to the FDA of a New Drug Application ("NDA") or a BLA;
- satisfactory completion of a pre-approval FDA inspection of the manufacturing facility or facilities at which the product will be produced to assess compliance with cGMP; and
- FDA review and approval of the NDA or BLA.

Once a drug or biologic is identified for development, it enters the preclinical testing stage. Preclinical tests include laboratory evaluations of product chemistry, toxicity and formulation, as well as animal pharmacology and toxicology studies. An IND sponsor must submit the results of the preclinical tests, together with manufacturing information and analytical data, to the FDA as part of the IND, which seeks FDA approval to test the drug or biologic in humans. Preclinical or nonclinical testing typically continues even after the IND is submitted.

If the FDA accepts the IND, the drug or biologic can then be studied in human clinical trials to determine if the product candidate is safe and effective. Clinical trials involve three separate phases that often overlap, can take many years and are expensive. These three phases, which are subject to considerable regulation, are as follows:

- *Phase 1.* The drug or biologic initially is introduced into a limited number of healthy human subjects or patients with the target disease or condition and tested for safety, dosage tolerance, absorption, metabolism, distribution and elimination. In the case of some drugs or biologics for severe or life-threatening diseases, such as cancer, especially when the drug or biologic may be inherently too toxic to ethically administer to healthy volunteers, the initial human testing is often conducted in patients.
- *Phase 2.* Clinical trials are next initiated in a limited patient population with the specified disease or condition the drug or biologic is intended to treat to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the drug or biologic candidate for the disease or condition it is intended to treat and to determine dosage tolerance and optimal dosage.

- *Phase 3.* Clinical trials are undertaken to further evaluate dosage, clinical efficacy and safety in an expanded patient population at geographically dispersed clinical trial sites. These clinical trials are intended to establish the overall risk-benefit ratio of the drug or biologic and provide an adequate basis for regulatory approval and product labeling.

It is possible that Phase 1, Phase 2 and Phase 3 testing may not be completed successfully within any specified period, if at all. The FDA or the sponsor may, at any time during the initial 30-day IND review period or while clinical trials are ongoing under the IND, impose a partial or complete clinical hold or suspend a clinical trial at any time for a variety of reasons, including a finding that the healthy volunteers or patients are being exposed to an unacceptable health risk. Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA and more frequently in other situations, and the occurrence of serious adverse events must also be reported. Information about certain clinical trials must be submitted within specific timeframes to the National Institutes of Health for public dissemination on the *www.clinicaltrials.gov* website.

Post-approval trials, sometimes referred to as Phase 4 clinical trials, may be conducted after initial marketing approval. These trials are used to gain additional experience from the treatment of patients in the intended therapeutic indication and are commonly intended to generate additional safety data regarding use of the product in a clinical setting. In certain instances, the FDA may mandate the performance of Phase 4 clinical trials as a condition of approval of an NDA or BLA.

The results of drug or biologic development, preclinical studies and clinical trials, along with descriptions of the manufacturing process, analytical tests conducted on the chemistry of the drug or biologic, proposed labeling and other relevant information are submitted to the FDA as part of an NDA or BLA requesting approval to market the drug or biologic. The FDA reviews each NDA or BLA submitted to ensure that it is sufficiently complete for substantive review before it accepts it for filing. It may request additional information rather than accept an NDA or BLA for filing.

Once the submission is accepted for filing, the FDA begins an in-depth review. The FDA reviews an NDA or BLA to determine, among other things, whether a drug or biologic is safe and effective for its intended use and whether its manufacturing is cGMP-compliant to assure and preserve the drug or biologic's identity, strength, quality and purity. The FDA may refer the NDA or BLA to an advisory committee for review and recommendation as to whether the NDA or BLA should be approved and under what conditions. The FDA is not bound by the recommendation of an advisory committee, but it generally follows such recommendations. Before approving an NDA or BLA, the FDA will inspect the facility or facilities where the drug or biologic is manufactured and tested. Additionally, before approving an NDA or BLA, the FDA may inspect one or more clinical trial sites to assure compliance with GCP requirements.

The FDA may require, as a condition of approval, restricted distribution and use, enhanced labeling, special packaging or labeling, expedited reporting of certain adverse events, submission of promotional materials, restrictions on direct-to-consumer advertising or commitments to conduct additional research post-approval. The FDA will issue a complete response letter if the agency decides not to approve the NDA or BLA in its present form.

Expedited Review and Approval

The FDA has developed a number of distinct approaches to make new drugs or biologics available as rapidly as possible in cases where there is no available treatment or there are advantages over existing treatments.

The FDA may grant "accelerated approval" to products that have been studied for their safety and effectiveness in treating serious illnesses and that provide meaningful therapeutic benefit to patients over existing treatments. For accelerated approval, the product must have an effect on a surrogate endpoint or an intermediate clinical endpoint that is considered reasonably likely to predict the clinical benefit of a drug, such as an effect on irreversible morbidity and mortality. When approval is based on surrogate endpoints or clinical endpoints other than survival or morbidity, the sponsor will be required to conduct additional post-approval clinical studies to verify and describe the clinical benefit. These studies are known as "confirmatory trials." Approval of a drug may be withdrawn, or the labeled indication of the drug changed if these trials fail to verify clinical benefit or do not demonstrate sufficient clinical benefit to justify the risks associated with the drug or biologic.

The FDA may grant "fast track" status to products that treat serious diseases or conditions and demonstrate the potential to address an unmet medical need. Fast track is a process designed to facilitate the development and expedite the review of such products by providing, among other things, more frequent meetings with the FDA to discuss the product's development plan and rolling review, which allows submission of individually completed sections of an NDA or BLA for FDA review

before the entire submission is completed. Fast track status does not ensure that a product will be developed more quickly or receive FDA approval.

"Breakthrough Therapy" designation is a process designed to expedite the development and review of drugs or biologics that are intended to treat a serious condition and preliminary clinical evidence indicates that the drug or biologic may demonstrate substantial improvement over available therapy on one or more clinically significant endpoints. Breakthrough Therapy designation provides all of the benefits of fast-track designation in addition to robust FDA-sponsor interaction and communication to help to identify the most efficient and expeditious path for clinical development while minimizing the number of patients placed in ineffective control regimens.

"Regenerative Medicine Advanced Therapy," ("RMAT") designation is a process created by the 21st Century Cures Act in December 2016. A product is eligible for RMAT designation if it is a regenerative medicine therapy that is intended to treat, modify, reverse or cure a serious disease or condition, and if preliminary clinical evidence indicates that the product has the potential to address unmet medical needs for such disease or condition. The benefits of RMAT designation include the benefits available to breakthrough therapies, including potential eligibility for priority review and accelerated approval based on surrogate or intermediate endpoints.

The FDA may grant "priority review" status to a product that, if approved, would provide significant improvement in the safety or effectiveness of the treatment, diagnosis, or prevention of serious conditions. Priority review is intended to reduce the time it takes for the FDA to review an NDA or BLA, with the goal to take action on the application within six months from when the application is filed, compared to ten months for a standard review.

Manufacturing Quality Control

Among the conditions for NDA or BLA approval is the requirement that the prospective manufacturer's quality control and manufacturing procedures continually conform with cGMP. Manufacturers must devote substantial time, money and effort in the areas of production, quality control, and quality assurance to maintain cGMP compliance. Material changes in manufacturing equipment, location, or process, may result in additional regulatory review and approval. The FDA, and other regulatory agencies, conduct periodic visits to inspect equipment, facilities, and processes following the initial approval of a product. If a manufacturing facility is not in substantial compliance with the applicable regulations and requirements imposed when the product was approved, regulatory or judicial enforcement action may be initiated, which may include a warning letter, suspension of manufacturing, product seizure, or an injunction against shipment of products from the facility and/or recall of products previously shipped. We rely, and expect to continue to rely, on third parties for the production of our products. Future FDA, state, and foreign inspections may identify compliance issues at the facilities of our contract manufacturers that may disrupt manufacture or distribution of our products or require substantial resources to correct.

Post-approval Requirements

Once an approval is granted, the FDA may withdraw the approval if compliance with regulatory requirements is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product may result in restrictions on the product or complete withdrawal of the product from the market. In addition, the sponsor of an approved drug in the U.S. may not promote that drug for unapproved, although a physician may prescribe a drug for an unapproved use in accordance with the practice of medicine. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of unapproved uses, as well as false or misleading promotion. Further, after approval, some types of changes to the approved product, such as adding new indications, manufacturing changes and additional labeling claims, are subject to further FDA review and approval. In addition, the FDA may require testing, including Phase 4 trials, and surveillance programs to monitor the effect of approved products that have been commercialized, and the FDA has the power to prevent or limit further marketing of a product based on the results of these post-marketing programs.

Products we manufacture or distribute pursuant to FDA approvals are subject to continuing regulation by the FDA, including, among other things:

- record-keeping requirements;
- reporting of adverse experiences with the product;
- providing the FDA with updated safety and efficacy information;

- drug sampling and distribution requirements;
- notifying the FDA and gaining its approval of specified manufacturing or labeling changes;
- complying with certain electronic records and signature requirements; and
- complying with FDA promotion and advertising requirements.

Failure to comply with the applicable U.S. requirements at any time during the drug or biologic development process, approval process or after approval, may subject us or our collaborators to administrative or judicial sanctions, any of which could have a material adverse effect on us. These sanctions could include:

- restrictions on marketing or manufacturing of the product;
- safety alerts, Dear Healthcare Provider letters, press releases, or other communications containing warnings or other safety information about the product;
- refusal to approve or delay in review of pending applications;
- withdrawal of an approval or the implementation of limitations on a previously approved indication for use;
- imposition of a clinical hold, a risk evaluation and mitigation strategy ("REMS") or other safety-related limitations;
- warning letters or "untitled letters;"
- product seizures, recalls, or detentions, or refusal to permit the import or export of products;
- total or partial suspension of production or distribution;
- consent decrees, corporate integrity agreements, debarment or exclusion from federal healthcare programs; or
- injunctions, fines, disgorgement, refusals of government contracts, or civil or criminal penalties.

The FDA typically advises that patients treated with gene therapy undergo follow-up observations for potential adverse events for a 15-year period. As part of the FDA approval of CASGEVY for the treatment of SCD and TDT, we are required to conduct two post-marketing requirement ("PMR") safety studies to assess the long-term risk of hematologic malignancies and off-target genome editing effects by CRISPR/Cas9. Both PMR safety studies are consistent with the FDA's guidance for industry on Long Term Follow-up After Administration of Human Gene Therapy Products.

United States Patent Term Restoration and Regulatory Exclusivity

Upon approval, products may be entitled to certain kinds of exclusivity under applicable intellectual property and regulatory regimes. The Drug Price Competition and Patent Term Restoration Act of 1984 (commonly known as the Hatch-Waxman Act) permits a patent restoration term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. The length of the patent extension is roughly based on 50 percent of the period of time from the filing of an IND for a compound to the submission of the NDA for such compound, plus 100 percent of the time period from NDA submission to regulatory approval. The extension, however, cannot exceed five years and the patent term remaining after regulatory approval cannot exceed 14 years.

If the FDA approves a drug product that contains a new chemical entity not previously approved, the product is typically entitled to five years of non-patent regulatory exclusivity. Other products may be entitled to three years of exclusivity if approval was based on the FDA's reliance on new clinical studies essential to approval submitted by the NDA applicant.

Biologics are also entitled to exclusivity under the Biologics Price Competition and Innovation Act (the "BPCIA"), which was passed as Title VII to the ACA. The law provides a pathway for approval of products that are biosimilar to or interchangeable with an FDA-licensed reference biological product. Under the BPCIA, a reference biological product is granted 12 years of data exclusivity, the period of time during which an innovator's clinical data cannot be used by other companies, from the time of first licensure of the product, and an application for a biosimilar product may not be submitted to the FDA until four years following the date that the reference product was first licensed by the FDA. In addition, the approval of a biosimilar product may not be made effective by the FDA until 12 years from the date on which the reference product

was first licensed. The BPCIA also created certain exclusivity periods for biosimilars approved as interchangeable products. At this juncture, it is unclear whether products deemed "interchangeable" by the FDA will, in fact, be readily substituted by pharmacies, which are governed by state pharmacy law. Biologics are also eligible for orphan drug exclusivity, as discussed below. The law also includes an extensive process for the innovator biologic and biosimilar manufacturer to litigate patent infringement, validity, and enforceability prior to the approval of the biosimilar. There have been ongoing federal legislative and administrative efforts as well as judicial challenges seeking to repeal, modify or invalidate some or all of the provisions of the ACA. While none of those efforts have focused on changes to the provisions of the ACA related to the biosimilar regulatory framework, if the ACA is repealed, substantially modified, or invalidated, it is unclear what, if any, impact such action would have on biosimilar regulation.

If the NDA or BLA applicant studies the product for use by children, the FDA may grant pediatric exclusivity, which extends by 180 days each existing exclusivity (patent and regulatory) related to the product.

Orphan Drug Designation and Exclusivity

Under the Orphan Drug Act, the FDA may grant orphan drug designation to drugs or biologics intended to treat a rare disease or condition, which is generally a disease or condition that affects fewer than 200,000 people in the U.S.

If a drug or biologic that has orphan drug designation subsequently receives the first FDA approval for that drug or biologic for the disease for which it has such designation, the product is entitled to orphan drug exclusivity, which means that the FDA may not approve any other applications to market the same drug for the same disease or condition for seven years following marketing approval, except in certain very limited circumstances, such as if the later product is shown to be clinically superior to the orphan product. Orphan drug exclusivity, however, also could block the approval of our products for seven years if a competitor first obtains approval of the same drug, as defined by the FDA, for the same disease or condition for which we were seeking approval. KALYDECO, ORKAMBI, SYMDEKO, TRIKAFTA, ALYFTREK and CASGEVY have been granted orphan drug exclusivity by the FDA.

We may pursue orphan drug designation for certain of our future product candidates. Even if we obtain orphan drug designation for a product candidate, we may not be the first to obtain marketing approval for the product candidate for any particular orphan indication due to the uncertainties associated with developing novel therapies. Further, even if we obtain orphan drug exclusivity for a product candidate, that exclusivity may not effectively protect the product from competition because orphan drug exclusivity does not prevent different drugs from being approved for the same condition. Moreover, orphan drug exclusivity may not prevent the approval of another sponsor's product that is considered to be the same drug for a different disease or condition, even where such product could be prescribed for an unapproved indication that is protected by orphan drug exclusivity. Even after an orphan drug is approved, regulators may subsequently approve the same drug made by another manufacturer for the same condition if the regulator concludes that the later drug is safer, more effective, or makes a major contribution to patient care. Orphan drug designation neither shortens the development time or regulatory review time of a drug or biologic nor gives the drug or biologic any advantage in the regulatory review or approval process.

Foreign Regulation

We conduct clinical trials and market our products in numerous jurisdictions outside the U.S. Most of these jurisdictions have clinical trial, product approval and post-approval regulatory processes that are similar in principle to those in the U.S. Thus, whether or not we obtain FDA approval for a product candidate, we must obtain approval from the comparable regulatory authorities of foreign countries or economic areas, such as the E.U., before we can commence clinical trials or market products in those countries or areas. The approval process and requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary greatly from place to place, and the time may be longer or shorter than that required for FDA approval.

Under the E.U. regulatory system, a company may submit marketing authorization applications either under a centralized or decentralized procedure. The centralized procedure, which is compulsory for orphan medicines, medicines produced by biotechnology, and those medicines intended to treat AIDS, cancer, neurodegenerative disorders, or diabetes, and optional for those medicines that are highly innovative, provides for the grant of a single marketing authorization that is valid for all E.U. member states. In addition to the centralized procedure, the E.U. also has a nationalized procedure, which requires a separate application to and approval determination by each country; a decentralized procedure, whereby applicants submit identical applications to several countries and receive simultaneous approval; and a mutual recognition procedure, where applicants submit an application to one country for review and other countries may accept or reject the initial decision.

Additionally, our European headquarters and European research facility are located in the U.K. Despite the U.K. formally withdrawing from the E.U. on January 31, 2020, a number of E.U. regulations were retained in U.K. law. The U.K. government has communicated an intent to remove or replace some of these E.U. provisions, which may increase some regulatory divergence between the U.K. and the E.U. Given the uncertainty as to what changes may be incorporated into U.K. law, it is unclear if any such changes could adversely affect our business, financial condition, and operating results.

Regulations Concerning Reimbursement

Sales of our products depend, to a large degree, on the extent to which our products will be reimbursed by third-party payors, such as government health programs, commercial insurance, and managed health care organizations. Increasingly, these third-party payors are becoming stricter in the ways they evaluate and reimburse medical products and services. Additionally, the containment of health care costs has become a priority of many governments, and the prices of drugs have been a focus in this effort. The U.S. government, state legislatures and foreign governments have shown significant interest in implementing cost-containment programs, including price controls, restrictions on reimbursement and requirements for substitution of generic products. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could limit our revenues. Decisions by third-party payors to not cover a product could reduce physician usage of the product.

In the U.S., we participate in the Medicaid Drug Rebate program, Medicare, and other governmental pricing programs. Medicaid is a joint federal and state program that is administered by the states for low-income and disabled beneficiaries. Under the Medicaid Drug Rebate program, we are required to pay a rebate to each state Medicaid program for our covered outpatient drugs, which includes select inpatient drugs for which there is "direct reimbursement." Medicaid rebates are based on pricing data reported by us on a monthly and quarterly basis to CMS, the federal agency that administers the Medicaid and Medicare programs.

Any company that participates in the Medicaid Drug Rebate program also must participate in the 340B drug pricing program (the "340B program"), and the Federal Supply Schedule ("FSS") pricing program. The 340B program, which is administered by the Health Resources and Services Administration, requires participating companies to agree to charge statutorily defined "covered entities" no more than the 340B "ceiling price" for covered outpatient drugs. The 340B ceiling price is calculated using a statutory formula, which is based on pricing data calculated under the Medicaid Drug Rebate Program. The FSS pricing program, which is administered by the Department of Veterans Affairs ("VA"), also requires participating companies to extend discounted prices to the VA, Department of Defense, Coast Guard, and Public Health Service. Similar to the 340B program, FSS prices are calculated utilizing pricing data reported by us to the VA on a quarterly and annual basis.

The Medicare program includes "Part A" that generally covers certain hospital services for eligible beneficiaries. In general, Part A covers inpatient hospital services, skilled nursing, and hospice care. Most individuals are enrolled in Medicare Part A upon reaching age 65 (although other individuals qualify for Part A, including those receiving services for end stage renal disease). Prescription drugs that are used as part of an inpatient hospital stay will be covered by Medicare Part A, and these products typically are paid as part of a bundled or composite rate (e.g., diagnosis related group).

The Medicare Part D program provides a voluntary prescription drug benefit to Medicare beneficiaries. Under "Part D," Medicare beneficiaries may enroll in prescription drug plans offered by private entities, which provide coverage of outpatient prescription drugs such as our acute pain and CF medicines. Unlike Medicare Part A and B, Part D coverage is not standardized. Part D prescription drug plan sponsors are not required to pay for all covered Part D drugs, and each drug plan can develop its own drug formulary that identifies which drugs it will cover and at what tier or level. Any formulary used by a Part D prescription drug plan must be developed and reviewed by a pharmacy and therapeutics committee. U.S. government payment for some of the costs of prescription drugs may increase demand for products for which we receive marketing approval.

Private payors often follow Medicare coverage policy and payment limitations in setting their own payment rates. As a result, any reduction in payment that results from Part D reimbursement may result in a similar reduction in payments from non-governmental payors for our products. Additionally, private payors, including health maintenance organizations and pharmacy benefit managers in the U.S., are adopting more aggressive utilization management techniques, and are increasingly applying restrictive plan designs that can impact patients and manufacturers and they continue to push for significant discounts and rebates from manufacturers. As a consequence, these payors may not cover or adequately reimburse for use of our products or may do so at levels that disadvantage them relative to competitive products.

The U.S. government has shown significant interest in implementing cost-containment programs for medicines and has enacted reforms at the state and federal level designed to, among other things, modify prescription drug reimbursement amounts and methodologies, and otherwise control health care costs. The Patient Protection and Affordable Care Act ("ACA") was enacted in March 2010 and was designed to expand coverage for the uninsured while at the same time containing overall health care costs. With regard to pharmaceutical products, among other things, the ACA was designed to expand and increase industry rebates for drugs covered under Medicaid programs, impose an annual fee on branded pharmaceutical manufacturers, subject biological products to potential competition by lower-cost biosimilars, and make changes to the coverage requirements under the Medicare Part D program. Additionally, in August 2022, the Inflation Reduction Act ("IRA") was enacted, establishing a Medicare Drug Price Negotiation Program, a Medicare inflationary rebate, and a redesign of the Part D benefit structure. Certain drugs, including our CF medicines and CASGEVY, are excluded from the IRA negotiation program. Nevertheless, other elements of the IRA may have a material impact on our business, including the redesign of the Part D benefit and the new Manufacturer Discount Program, which will require manufacturers to take on more of the beneficiary cost previously subsidized by the federal government through the application of increased drug discounts. Under the Non-Opioids Prevent Addiction in the Nation ("NOPAIN") Act, CMS reimbursement for novel, oral, non-opioids will include an add-on payment when the drug is used in the hospital outpatient and ambulatory surgery center settings. We expect that JOURNAVX, our recently approved medicine for the treatment of moderate-to-severe acute pain, will qualify for inclusion on the list of applicable drugs under the NOPAIN Act.

We anticipate that the U.S. government will continue to engage in activities seeking to address drug pricing and reimbursement. Furthermore, certain states have enacted laws establishing Prescription Drug Affordability Boards ("PDABs"). Some state PDABs, including those in Colorado, Maryland, Washington, and Minnesota, either have the authority or have defined a pathway pursuant to which they may be granted the authority to establish upper payment limits for prescription drugs. In certain states, there is pending litigation that would establish a PDAB or expand the authority of an existing PDAB.

In Europe and other foreign jurisdictions, the success of our products depends largely on obtaining and maintaining government reimbursement, because patients are generally unable to access prescription pharmaceutical products that are not reimbursed by their governments. In some countries, such as Germany, commercial sales of a new product may begin while pricing and reimbursement terms are under discussion. In other countries, a company must complete reimbursement negotiations prior to the commencement of commercial supply of the pharmaceutical product. The requirements governing drug pricing vary widely country-by-country and region-by-region. For example, the member states of the E.U. can restrict the range of drugs for which their national health insurance systems provide reimbursement and can control the prices of prescription drugs. In addition, many ex-U.S. government payors require companies to provide health economic assessments of products, which are evaluated by government agencies set up for this purpose. A member state may approve a specific price for the drug, or it may instead adopt a system of direct or indirect controls on the total amount of money that a company may receive for supply of a drug. Countries also may consider increasing mandatory discounts over time in an attempt to manage increased demands on healthcare budgets. Reimbursement discussions in foreign countries often result in a reimbursement price that is lower than the net price that companies can obtain for the product in the U.S. In addition, reimbursement discussions may take a significant period of time resulting in commercialization delays. In some countries where reimbursement has not yet been obtained, or where there are a limited number of eligible people and our medicines or therapies are unregistered, the governments of such countries may agree to purchase our medicines and therapies on an unlicensed and/or named patient basis. Reimbursement for our products cannot be assured because a country or region may only provide for reimbursement on terms that we do not deem adequate. Further, many ex-U.S. governments have introduced or are in the process of introducing legislation focusing on cost containment measures in the pharmaceutical industry. The impact of these laws where finalized, the final form of laws under consideration, and their relevant practical application, are unknown at this time, but may lead to lower prices, paybacks, or other forms of discounts or special taxes.

Other Regulations

Pharmaceutical companies are also subject to various laws pertaining to healthcare "fraud and abuse," including the federal Anti-Kickback Statute ("AKS"), the False Claims Act ("FCA"), and other state and federal laws and regulations. In the U.S., the Anti-Kickback Statute generally makes it illegal to knowingly and willfully solicit, offer, receive or pay any remuneration in return for or to induce the referral of business, including the purchase or prescription of a particular drug that is reimbursed by a state or federal health care program. The FCA prohibits knowingly and willingly presenting or causing to be presented for payment to third-party payors (including Medicare and Medicaid), any claims for reimbursed drugs or services that are false or fraudulent, claims for items or services not provided as claimed or claims for medically unnecessary

items or services. Violations of fraud and abuse laws may be punishable by criminal and/or civil sanctions, including fines and civil monetary penalties, as well as by the possibility of exclusion from federal healthcare programs (including Medicare and Medicaid). Liability under the FCA may also arise when a violation of certain laws or regulations related to the underlying products (e.g., violations regarding improper promotional activity, manufacturing regulations, or unlawful payments) contributes to the submission of a false claim. If we were subject to allegations concerning, or convicted of violating, these laws, our business could be harmed.

Laws and regulations also have been enacted by the federal government and various states to regulate the sales and marketing practices of pharmaceutical manufacturers. The laws and regulations generally limit financial interactions between manufacturers and health care providers, require manufacturers to adopt certain compliance standards or require disclosure to the government and public of such interactions. The laws include U.S. federal and state "sunshine" provisions. The federal sunshine provisions apply to pharmaceutical manufacturers with products reimbursed under certain government programs and require those manufacturers to disclose annually to the federal government (for re-disclosure to the public) certain payments and other transfers of value made to physicians, physicians assistants, advanced practice registered nurses, and teaching hospitals. State laws may also require disclosure of pharmaceutical pricing information and marketing expenditures. Many of these laws and regulations contain requirements that are subject to interpretation. Outside the U.S., other countries have implemented requirements for disclosure of financial interactions with healthcare providers and additional countries may consider or implement such laws.

We are subject to various federal and foreign laws that govern our international business practices with respect to payments to government officials. Those laws include the U.S. Foreign Corrupt Practices Act ("FCPA"), which prohibits U.S. companies and their representatives from paying, offering to pay, promising, or authorizing the payment of anything of value to any foreign government official, government staff member, political party, or political candidate for the purpose of obtaining or retaining business or to otherwise obtain favorable treatment or influence a person working in an official capacity. In many countries, the health care professionals we regularly interact with may meet the FCPA's definition of a foreign government official. We are also subject to U.K. Bribery Act 2010 ("the Bribery Act"), which proscribes giving and receiving bribes in the public and private sectors, bribing a foreign public official, and failing to have adequate procedures to prevent employees and other agents from giving bribes. U.S. companies that conduct business in the U.K. generally will be subject to the Bribery Act.

Our collection and use of personal data as part of our business activities is subject to various privacy and data security laws and regulations, including oversight by various regulatory or other governmental bodies, in the U.S., E.U., U.K., Canada, Australia, Brazil, Saudi Arabia and other jurisdictions. Such laws and regulations have the potential to affect our business materially, continue to evolve and increasingly are being enforced.

Our present and future business has been and will continue to be subject to various other laws and regulations. Various laws, regulations, and recommendations relating to safe working conditions, laboratory practices, the experimental use of animals, and the purchase, storage, movement, import, export and use and disposal of hazardous or potentially hazardous substances are or may be applicable to our activities. In addition, as we expand our pipeline and contemplate different approaches that may incorporate the use of medical devices, such approaches may necessitate compliance with regulatory laws applicable to medical devices, including those governing the testing, manufacture, approval, distribution, and marketing of medical devices. Furthermore, the extent of government regulation, which might result from future legislation or administrative action, cannot accurately be predicted.

We have a global corporate compliance program designed to actively identify, prevent, and mitigate healthcare fraud and abuse risk through, among other things, the implementation of compliance policies and systems and through the promotion of a culture of compliance. We will continue to devote substantial resources to enhance and expand our corporate compliance program as necessary to help us manage and mitigate our evolving compliance risk environment as our business grows and expands globally. Even with these measures, however, we cannot guarantee compliance with the various complex laws and regulations to which we are subject now or in the future.

EMPLOYEES AND HUMAN CAPITAL MANAGEMENT

As of December 31, 2024, we had approximately 6,100 employees. Of these employees, approximately 5,100 were based in the U.S. and approximately 1,000 were based outside the U.S. None of our U.S. employees are covered by a collective

bargaining agreement. A small number of employees outside the U.S. are covered by such agreements due to local law or industry requirements. We consider our relations with our employees to be good. We face intense competition for our personnel from our competitors and other companies throughout our industry and from universities and research institutions. At times, when industry conditions are positive, we may face challenges in recruiting and retaining employees across the biotechnology industry due to industry job market dynamics.

We rely on skilled, experienced, and innovative employees to conduct the operations of our company. The biotechnology industry is very competitive, and recruiting and retaining such employees is important to the continued success of our business. We are committed to building an outstanding, committed, and passionate team, and we focus on a culture that values all employees. We focus on recruiting, retaining, and developing qualified and talented employees from a diverse range of backgrounds to conduct our research, development, commercial, and other business activities because we believe that each employee brings unique perspectives and strengths, and by embracing these strengths, we can do our best work for patients.

We view diversity through a broad lens that encompasses culture, backgrounds, experiences, and worldview to foster creativity and innovation. Our initiatives include learning, resources, and forums that promote belonging in our workplaces; five global employee resource networks that promote connectivity and collaboration across levels and functions; and investments to support equal opportunity in our surrounding communities.

To promote our employees' continued well-being, we offer comprehensive benefits and resources, including those focused on health and income protection, such as life insurance and retirement savings programs. We continue to promote and enhance wellness tools supporting our employees' mental, social, physical and financial health. We continually review and augment our programs to include benefits that support the evolving needs of our workforce.

In addition, we 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.

OTHER MATTERS

Financial Information and Significant Customers

We operate in one segment, pharmaceuticals. Financial information about our revenue by product and significant customers is set forth in Note Q, "Segment Information," to our consolidated financial statements included in this Annual Report on Form 10-K.

Information Available on the Internet

Our internet address is *www.vrtx.com.* Our annual reports on Form 10-K, quarterly reports on Form 10-Q and current reports on Form 8-K, and all amendments to those reports, are available to you free of charge through the "Investors/Financial Information/SEC Filings" section of our website as soon as reasonably practicable after those materials have been electronically filed with, or furnished to, the Securities and Exchange Commission.

Corporate Information

Vertex was incorporated in Massachusetts in 1989, and our principal executive offices are located at 50 Northern Avenue Boston, Massachusetts 02210.

INFORMATION ABOUT OUR EXECUTIVE OFFICERS

The names, ages and positions held by our executive officers are as follows:

Name	Age	Position
Reshma Kewalramani, M.D.	52	Chief Executive Officer and President
Jeffrey M. Leiden, M.D., Ph.D.	69	Executive Chairman
David Altshuler, M.D., Ph.D.	60	Executive Vice President, Chief Scientific Officer
Stuart A. Arbuckle	59	Executive Vice President, Chief Operating Officer
E. Morrow "Morrey" Atkinson, III, Ph.D.	59	Executive Vice President, Chief Technical Operations Officer, Head of Biopharmaceutical Science and Manufacturing Operations
Jonathan Biller, J.D.	61	Executive Vice President, Chief Legal Officer
Carmen Bozic, M.D.	62	Executive Vice President, Global Medicines Development and Medical Affairs, and Chief Medical Officer
Amit K. Sachdev, J.D.	57	Executive Vice President, Chief Patient and External Affairs Officer
Ourania "Nia" Tatsis, Ph.D.	55	Executive Vice President, Chief Regulatory and Quality Officer
Charles F. Wagner, Jr.	56	Executive Vice President, Chief Financial Officer
Kristen C. Ambrose, CPA	48	Senior Vice President, Chief Accounting Officer
Duncan J. McKechnie	56	Senior Vice President, Head of North America Commercial

Dr. Kewalramani has been our Chief Executive Officer and President since April 2020 and a member of our Board of Directors since February 2020. Dr. Kewalramani was our Executive Vice President and Chief Medical Officer from April 2018 through April 2020. She was our Senior Vice President, Late Development from February 2017 until April 2018. Dr. Kewalramani also served on the board of Ginkgo Bioworks from September 2021 to June 2024. From August 2004 to January 2017, she served in roles of increasing responsibility at Amgen Inc., most recently as Vice President and Head of U.S. Medical Organization. From 2014 through 2019, Dr. Kewalramani was the industry representative to the FDA's Endocrine and Metabolic Drug Advisory Committee. She completed her internship and residency in Internal Medicine at the Massachusetts General Hospital and her fellowship in Nephrology at the Massachusetts General Hospital and Brigham and Women's Hospital combined program. Dr. Kewalramani holds a B.A. from Boston University and an M.D. from Boston University School of Medicine. She is an alumna of the Harvard Business School, having completed the General Management Program.

Dr. Leiden is our Executive Chairman, a position he has held since in April 2020. He was our Chief Executive Officer and President from 2012 through March 2020. He has been a member of our Board of Directors since July 2009, the Chairman of our Board of Directors since May 2012, and served as our lead independent director from October 2010 through December 2011. Dr. Leiden was a Managing Director at Clarus Ventures, a life sciences venture capital firm, from 2006 through January 2012. Dr. Leiden was President and Chief Operating Officer of Abbott Laboratories, Pharmaceuticals Products Group, and a member of the Board of Directors of Abbott Laboratories from 2001 to 2006. From 1987 to 2000, Dr. Leiden held several academic appointments, including the Rawson Professor of Medicine and Pathology and Chief of Cardiology and Director of the Cardiovascular Research Institute at the University of Chicago, the Elkan R. Blout Professor of Biological Sciences at the Harvard School of Public Health, and Professor of Medicine at Harvard Medical School. He is an elected member of both the American Academy of Arts and Sciences and the Institute of Medicine of the National Academy of Sciences. Dr. Leiden is a member of the Board of Directors of the Massachusetts Mutual Life Insurance Company, a private insurance company, since 2015. Dr. Leiden is the Executive Chairman of the Board of Directors of Odyssey Therapeutics, a private biotechnology company, since 2022, and is the Chairman of the Board of Directors of Casana, a private healthcare technology company, since 2021. Dr. Leiden was a director and the non-executive Vice Chairman of the board of Shire plc, from 2006 to January 2012, a director of Quest Diagnostics, from December 2014 to May 2019, and the Chairman of Revolution Healthcare Acquisition Corp., from April 2021 to December 2022. Dr. Leiden received his M.D., Ph.D. and B.A. degrees from the University of Chicago.

Dr. Altshuler is our Executive Vice President, Chief Scientific Officer, a role he has held since January 2015, and was a member of our Board of Directors from May 2012 through December 2014. Dr. Altshuler was one of four founding members of the Broad Institute, a research collaboration of Harvard University and the Massachusetts Institute of Technology, The Whitehead Institute and the Harvard Hospitals. He served as the Director of the Institute's Program in Medical and

Population Genetics from 2003 through December 2014 and as the Institute's Deputy Director and Chief Academic Officer from 2009 through December 2014. Dr. Altshuler joined the faculty at Harvard Medical School and the Massachusetts General Hospital in 2000 and held the academic rank of Professor of Genetics and Medicine from 2008 through December 2014. He served as Adjunct Professor of Biology at MIT from 2012 through December 2014. Dr. Altshuler earned a B.S. from MIT, a Ph.D. from Harvard University and an M.D. from Harvard Medical School. Dr. Altshuler completed his clinical training in Internal Medicine, and in Endocrinology, Diabetes and Metabolism, at the Massachusetts General Hospital.

Mr. Arbuckle is our Executive Vice President, Chief Operating Officer, a position he has held since July 2021. As previously announced, Mr. Arbuckle will retire from Vertex effective July 1, 2025. Prior to his role at Vertex, Mr. Arbuckle served as Executive Vice President, Chief Commercial and Operations Officer from March 2021 to July 2021, and as our Executive Vice President, Chief Commercial Officer from September 2012 to February 2021. Prior to joining us, Mr. Arbuckle held multiple commercial leadership roles at Amgen, Inc. from July 2004 through August 2012. Mr. Arbuckle has worked in the biopharmaceuticals industry since 1986, including more than 15 years at GlaxoSmithKline plc, where he held sales and marketing roles of increasing responsibility for medicines aimed at treating respiratory, metabolic, musculoskeletal, cardiovascular and other diseases. He has served as a member of the Board of Directors of Rhythm Pharmaceuticals Inc. since July 2019. He served as a member of the Board of Directors of Cerulean Pharma, Inc. from June 2015 through July 2017 and served as a member of the Board of Directors of ImmunoGen, Inc. from January 2018 until it was acquired by AbbVie Inc. in February 2024. Mr. Arbuckle holds a BSc in Pharmacology and Physiology from the University of Leeds.

Dr. Atkinson has been our Executive Vice President, Chief Technical Operations Officer, Head of Biopharmaceutical Sciences and Manufacturing Operations since August 2023. He previously served as our Senior Vice President, Head of Commercial Manufacturing and Supply Chain since July 2020. Prior to joining us, Dr. Atkinson served in various roles at Bristol-Myers Squibb Co., including as Senior Vice President, Global Manufacturing Operations from September 2019 to June 2020; Vice President and Integration Leader, Corporate Cell Therapy and Global Development and Manufacturing from January 2019 to September 2019; Vice President, Internal Manufacturing, Biologics from June 2017 to January 2019; and Vice President, Biologics Development and Clinical Manufacturing from 2012 to June 2017. Before Bristol-Myers Squibb, he held various roles at Cook Pharmica, LLC (now owned by Novo Holdings) and Eli Lilly. Dr. Atkinson has served as a member of the Board of Directors of 89bio, Inc., since February 2022. Dr. Atkinson holds a B.S. in Biology from Indiana University and a Ph.D. in Biological Sciences from Stanford University.

Mr. Biller has been our Executive Vice President, Chief Legal Officer since September 2022. From November 2019 until he joined us, Mr. Biller served in several executive roles at Agios Pharmaceuticals, Inc., including Chief Legal Officer and, most recently, Chief Financial Officer and Head of Corporate Affairs. Prior to Agios, he served as Executive Vice President, General Counsel at Celgene from July 2018 to November 2019, where he was responsible for their global legal function, and served as Senior Vice President, Tax and Treasury from 2011 to June 2018. Prior to Celgene, Mr. Biller was General Counsel, Chief Tax Officer and Secretary at Bunge Limited, a global publicly traded agriculture and food company. Earlier in his career he held various leadership roles at Alcon, Inc. and was a partner at Hopkins & Sutter and Foley & Lardner. Mr. Biller holds a B.A. from Brown University and a J.D. from Yale Law School.

Dr. Bozic is our Executive Vice President, Global Medicines Development and Medical Affairs, a position she has held since October 2019, and she has been our Chief Medical Officer since April 2020. She was our Senior Vice President and Head of Global Clinical Development from May 2019 to October 2019. Prior to joining us, Dr. Bozic spent more than 20 years at Biogen Inc., a biotechnology company focused on neurological diseases, most recently as Senior Vice President of Global Development and Portfolio Transformation from 2015 to May 2019 and as Senior Vice President of Clinical and Safety Sciences from 2013 to 2015. Dr. Bozic has served as the industry representative to the FDA's Risk Communication Advisory Committee, and was a member of PhRMA's Clinical and Preclinical Development Committee and the Board of Managers at BioMotiv. She is a member of the Clinical Advisory Committee at Akili Interactive. She received her M.D., C.M., completed her residency, and was Chief Resident in Internal Medicine at McGill University. She completed her fellowship in Pulmonary and Critical Care Medicine at Brigham and Women's Hospital and was an Associate Physician at Beth Israel Deaconess Medical Center and Harvard Medical School before joining the biopharmaceutical industry.

Mr. Sachdev is our Executive Vice President, Chief Patient and External Affairs Officer, a role he has held since July 2023. From October 2019 to July 2023, he was our Executive Vice President, Chief Patient Officer. In addition, Mr. Sachdev served in the role of Chief of Staff to the CEO from April 2020 to March 2023. He served as our Executive Vice President and Chief Regulatory Officer from January 2017 until September 2019, and as our Executive Vice President, Policy, Access and Value from October 2014 through December 2016. In 2010, he established our first international commercial operations

in Canada. In 2007, he joined us as a Senior Vice President, to establish our government affairs and public policy activities, as well as our patient advocacy programs. Prior to joining us, Mr. Sachdev served as Executive Vice President, Health, of the Biotechnology Industry Organization (BIO) and was the Deputy Commissioner for Policy at the FDA, where he also served in several other senior positions. Prior to the FDA, Mr. Sachdev served as Majority Counsel to the Committee on Energy and Commerce in the U.S. House of Representatives and practiced law at the American Chemistry Council, and subsequently at the law firm of Ropes & Gray LLP. He served as a member of the Board of Directors of Eiger BioPharmaceuticals from April 2019 to September 2024. Mr. Sachdev holds a B.S from Carnegie Mellon University and a J.D. from Emory University School of Law.

Dr. Tatsis is our Executive Vice President, Chief Regulatory and Quality Officer, a position she has held since August 2020. Previously, she was our Senior Vice President and Chief Regulatory Officer from October 2019 to August 2020, and our Senior Vice President, Global Regulatory Affairs from September 2017 to October 2019. Prior to joining us, Dr. Tatsis held positions of increasing responsibility at several pharmaceutical companies, including Sanofi, Stemnion, Pfizer, and Wyeth. Most recently, from 2014 to 2017, she was Vice President, Head of Global Regulatory Affairs, at the Sanofi Genzyme Business Unit focused on Inflammation/Immunology, Rare Disease, Multiple Sclerosis, Ophthalmology, Neurology, and Oncology/Immuno-Oncology. Dr. Tatsis also worked as an associate staff scientist and research fellow in Immunology and Vaccine Development at the Wistar Institute and completed a post-doctoral research fellowship in Immunology at Thomas Jefferson University. Dr. Tatsis has served as a member of the board of directors at Verve Therapeutics since June 2024. She received her Ph.D. in Cell and Molecular Biology from the University of Vermont and holds a B.S. in Biology from Temple University.

Mr. Wagner is our Executive Vice President, Chief Financial Officer, a position he has held since April 2019. As previously announced, Mr. Wagner has been appointed as our Chief Operating Officer effective July 1, 2025. Mr. Wagner will remain an Executive Vice President and our Chief Financial Officer following this appointment. Prior to his role at Vertex, Mr. Wagner was Chief Financial Officer and Executive Vice President, Finance, of Ortho Clinical Diagnostics, a Carlyle Group portfolio company, from June 2015 to March 2019. In that role, he led the finance, accounting, tax, treasury, global financial systems, lender relations, and acquisitions and divestiture groups, and also had shared leadership for several enterprise-wide projects. From July 2012 to June 2015, Mr. Wagner served as Executive Vice President, Chief Financial Officer of Bruker Corporation, a scientific instruments manufacturer. Prior to that, Mr. Wagner served as Chief Financial Officer for Progress Software Corporation, a provider of enterprise software, and Millipore Corporation, a global provider of products and services in the life science tools market. Mr. Wagner served as a director of Good Start Genetics, Inc., from April 2014 to August 2017 and served as a director and member of the Audit Committee of Bruker Corporation from August 2010 to June 2012. He has served as a member of the Board of Directors of The TJX Companies, Inc., since September 2023. Mr. Wagner holds a B.S. in Accounting from Boston College and a M.B.A from Harvard Business School.

Ms. Ambrose is our Senior Vice President, Chief Accounting Officer, a position she has held since May 2021. Ms. Ambrose previously served as our Senior Vice President, Accounting, Tax, Treasury, Strategic Sourcing and Corporate Services since March 2021. From February 2003 until she joined us, Ms. Ambrose held roles of increasing responsibility at Boston Scientific Corporation, a medical device company, most recently as Vice President of Finance and Controller of the Global Endoscopy Division from July 2019 to March 2021 and as Vice President of Global Internal Audit from February 2017 to June 2019. Prior to Boston Scientific Corporation, Ms. Ambrose served as an accountant at Ernst & Young LLP. She received her B.S. in Commerce from the University of Virginia and is a Certified Public Accountant.

Mr. McKechnie is our Senior Vice President, Head of North America Commercial, a position he has held since October 2018. As previously announced, Mr. McKechnie has been appointed as our Executive Vice President, Chief Commercial Officer effective July 1, 2025. Mr. McKechnie previously served as our Vice President of Global Marketing from June 2013 to September 2018. Prior to joining Vertex, Mr. McKechnie held positions of increasing responsibility at Novartis AG, including Vice President, Respiratory Franchise from January 2013 to June 2013; Vice President and Head Brand Maximization and Established Medicines from April 2012 to April 2013; and Vice President, Cardiovascular Marketing from November 2008 to March 2012. Before Novartis, Mr. McKechnie held various roles at GlaxoSmithKline plc. Mr. McKechnie holds a Business & Marketing degree from the University of Plymouth in England.

ITEM 1A. RISK FACTORS

Investing in our common stock involves a high degree of risk, and you should carefully consider the risks and uncertainties described below in addition to the other information included or incorporated by reference in this Annual Report on Form 10-K. If any of the following risks or uncertainties actually occurs, our business, financial condition or results of operations would likely suffer, possibly materially. In that case, the trading price of our common stock could decline.

SUMMARY OF RISK FACTORS

Our business is subject to numerous risks and uncertainties, discussed in more detail in the following section. These risks include, among others, the following key risks:

Risks Related to Our Business

- If we are unable to successfully develop and commercialize additional products, our business could be materially harmed.
- If we are unable to sustain and grow revenues from sales of our CF medicines, our business would be materially harmed and the market price of our common stock would likely decline.
- If we are unable to successfully develop, obtain approval and commercialize treatments for acute and neuropathic pain, our business could be materially harmed.
- If we are not successful in commercializing CASGEVY, our revenue growth could be limited and our business could be materially harmed.
- If our competitors bring products with superior product profiles to market, our products may not be competitive, and our revenues could decline.
- If we discover safety issues with any of our products or if we fail to comply with continuing U.S. and applicable foreign regulations, commercialization efforts for the product could be negatively affected, the approved product could lose its approval, and our business could be materially harmed.
- If physicians and patients do not accept our products, or if patients do not remain on treatment or comply with their prescribed dosing regimen, our product revenues would decline in future periods.
- Cell and genetic therapies face increased scrutiny from the public and medical communities and commercial success will depend, in part, upon the acceptance of those communities.

Risks Related to Pricing of Our Products

- Government and other third-party payors seek to contain costs of health care through legislative and other means. If they fail to provide coverage and adequate reimbursement rates for our products, our revenues will be harmed.
- We may experience pricing pressure on our products, which could reduce our revenues and future profitability.
- Current health care laws and regulations in the U.S. and future legislative or regulatory reforms to the U.S. health care system may affect our ability to commercialize our marketed products profitably.
- We have experienced challenges commercializing products outside of the U.S., and our future revenues will be dependent on our ability to obtain adequate reimbursement for our products in ex-U.S. markets.
- Insurance coverage and reimbursement of our cell or genetic therapies is uncertain.

Risks Related to Development and Clinical Testing of Our Products and Product Candidates

- Our product candidates remain subject to clinical testing and regulatory approval, and our future success is dependent on our ability to successfully develop additional product candidates for both CF and non-CF indications.
- If we are unable to obtain or are delayed in obtaining regulatory approval, we may incur additional costs, experience delays, or be unable to commercialize our product candidates.
- If clinical trials are prolonged or delayed, our development timelines for the affected development program could be extended, our costs to develop the product candidate could increase and the competitive position of the product candidate could be adversely affected.
- Difficulty in enrolling patients could delay or prevent clinical trials of our product candidates, and ultimately delay or prevent regulatory approval.

- Enrollment for clinical trials for our cell and gene therapies may face additional and unique challenges and adverse developments associated with these clinical trials could result in action by regulatory bodies, including revised requirements for approval.

Risks Related to Government Regulation

- If regulatory authorities interpret any of our conduct, including our marketing practices, as being in violation of applicable health care laws, including fraud and abuse laws, laws prohibiting false and misleading promotion, disclosure laws or other similar laws, we may be subject to civil or criminal penalties.
- If we fail to comply with our reporting and payment obligations under the Medicaid Drug Rebate Program or other governmental pricing programs in the U.S., we could be subject to additional reimbursement requirements, penalties, sanctions, and fines that could have a material adverse effect on our business, financial condition, results of operations and growth prospects.
- If our processes and systems are not compliant with regulatory requirements, we could be subject to restrictions on marketing our products or could be delayed in submitting regulatory filings seeking approvals for our product candidates.
- The regulatory approval process for our cell and genetic therapies involves additional consultations with regulatory agencies, costs, and potentially longer timelines as compared to those for small molecules.

Risks Related to Supply, Manufacturing and Reliance on Third Parties

- We may face manufacturing, supply, and distribution difficulties, among other challenges, delays, or interruptions, including at our third-parties.
- We rely on third parties to conduct pre-clinical work, clinical trials and other activities, and those third parties may not perform satisfactorily, including failing to meet established deadlines for the completion of such studies and/or trials or failing to satisfy regulatory requirements.

Risks Related to Business Development Activities

- We face risks in connection with existing and future collaborations with respect to the development, manufacture and commercialization of our products and product candidates.
- Our ability to execute on our long-term strategy depends in part on our ability to engage in transactions and collaborations with other entities that add to our pipeline or provide us with new commercial opportunities.
- We may not realize the anticipated benefits of existing or future acquisitions of businesses or technologies, and the integration following any such acquisition may disrupt our business and management.

Risks Related to Intellectual Property

- If our patents do not protect our products and our products infringe third-party patents, we could be subject to litigation which could result in injunctions preventing us from selling our products, substantial damages, or circumvention of our patents by third parties.
- Uncertainty over intellectual property in the pharmaceutical and biotechnology industry has been the source of litigation and other disputes that are inherently costly and unpredictable.
- We may be subject to claims by third parties asserting that our employees or we have misappropriated their intellectual property, or claiming ownership of what we regard as our own intellectual property.

Risks Related to Our Operations

- If we fail to scale our operations to accommodate growth, our business may suffer.
- A variety of risks associated with operating in foreign countries could materially adversely affect our business.
- A breakdown or breach of our information technology systems could subject us to liability or interrupt the operation of our business.
- If we fail to attract and retain skilled employees, our business could be materially harmed.
- Failure to maintain our third-party relationships or challenges at or with these third parties could materially harm our business.

Risks Related to Financial Results and Holding Our Common Stock

- Our stock price may fluctuate and our quarterly operating results are subject to significant fluctuation.
- Our effective tax rate fluctuates, and changes in tax laws, regulations and treaties, unfavorable resolution to the tax positions we have taken or exposure to additional income tax liabilities could have a material impact on our future taxable income.

Risks Related to Our Business

If we are unable to successfully develop and commercialize additional products, our business could be materially harmed.

We invest significant resources in the research and development of therapies for serious diseases and conditions, including CF, SCD, TDT, acute and peripheral neuropathic pain, IgAN, AMKD, T1D, DM1, and ADPKD. Product development is highly uncertain and expensive. Product candidates that may appear promising in research and development may fail to reach commercial success for many reasons, including:

- the failure to establish safety and efficacy through clinical trials;
- the failure to obtain marketing approval for the product candidate;
- the inability to manufacture the product candidate on economically feasible terms;
- the failure to gain and maintain market acceptance among physicians and patients or other members of the medical community; and
- the failure to obtain market acceptance or adequate reimbursement levels from third-party payors or foreign governments for such product.

If we are not able to successfully develop and commercialize additional products our business could be materially harmed.

If we are unable to sustain and grow revenues from sales of our CF medicines, our business would be materially harmed and the market price of our common stock would likely decline.

Substantially all of our net product revenues have been derived from the sale of our CF medicines over the last several years. As a result, our business is dependent upon our ability to sustain and increase revenues from sales of our CF medicines. We seek to continue to increase our CF product revenue through serial innovation, including development and commercialization of next-generation CF medicines, extending access of CF medicines to younger children with CF, seeking additional approvals for our CF medicines in ex-U.S. markets and securing and maintaining adequate reimbursements for our CF medicines globally, and by developing a nebulized mRNA therapy for the more than 5,000 people with CF who do not make CFTR protein and cannot benefit from CFTR modulators.

Our concentrated source of revenues presents a number of risks to our business, including:

- that one or more competing therapies may be developed successfully by others as a treatment for people with CF;
- that reimbursement policies of payors and other third parties may make it difficult to obtain reimbursement or may reduce the net price we receive for our products;
- that we may experience manufacturing or supply disruptions for our CF medicines; and
- that we may experience adverse developments with respect to development or commercialization of our CF medicines.

Our ability to increase our CF product revenues is dependent in part on our ability to successfully commercialize ALYFTREK, our recently approved once-daily CF medicine. We expect the commercial opportunity for ALYFTREK to depend on three types of patients: (i) those who are currently on a CFTR modulator who may want to switch to ALYFTREK, (ii) those patients who have not yet been initiated on a CFTR modulator or been eligible for a CFTR modulator, and (iii) those who have discontinued from another CFTR modulator. There can be no assurance that people with CF will be willing to switch from their current CFTR modulator or initiate treatment with ALYFTREK if they are not currently being treated by a CFTR modulator.

If any of the above risks were to materialize, if we are otherwise unable to increase revenues from sales of our CF medicines, or if we do not meet the expectations of investors or public equity market analysts, our business would be materially harmed and our ability to fund our operations could be adversely affected.

If we are unable to successfully develop, obtain approval and commercialize treatments for acute and neuropathic pain, our business could be materially harmed.

We believe that a portion of the value attributed to our company by investors is based on our approved and potential treatments for acute and peripheral neuropathic pain. JOURNAVX, which was approved in January 2025 for moderate-to-severe acute pain in adults, may not gain or maintain market acceptance among physicians and patients or other members of the medical community. In addition to the risks normally associated with launching a new branded product, JOURNAVX will need to compete, and obtain reimbursement from third-party payors, in an acute pain market that largely consists of low-cost generic drugs, including opioids, non-steroidal anti-inflammatory drugs, acetaminophen and local anesthetics. Similarly, if we are successful in developing and obtaining approval for suzetrigine in peripheral neuropathic pain, this product will face competition from generic anticonvulsant and antidepressant drugs. If we are not able to successfully develop and commercialize treatments for acute and peripheral neuropathic pain, our future net product revenues and cash flows will be adversely affected and our business could be materially harmed.

If we are not successful in commercializing CASGEVY, our revenue growth could be limited and our business could be materially harmed.

We have invested significant resources in the development and commercialization of CASGEVY. While we have previously successfully commercialized several small molecule drugs, we have limited experience with the commercialization of cell and genetic therapies. Manufacturing and commercialization of CASGEVY is subject to similar risks and uncertainties as small molecules. In addition:

- the manufacturing process for CASGEVY is more complex than the manufacturing processes for our small molecule medicines and we may encounter difficulties in the production of CASGEVY and ensuring that the product meets required specifications;
- there are multiple steps along the CASGEVY patient treatment journey, many of which involve significant clinical complexities performed by third parties, including the collection of blood cells from patients, transfer of those cells to and from a manufacturing facility, and other procedures either before or after delivery of CASGEVY;
- the commercial success of CASGEVY continues to depend in part on the medical community, patients, governments, and third-party or governmental payors accepting it as a medically useful, cost-effective, ethical, and safe, and providing adequate reimbursement; and
- global market acceptance continues to be dependent in part on the prevalence and severity of side effects associated with the procedure by which CASGEVY is administered, including the prevalence and severity of any side effects resulting from the myeloablative preconditioning regime.

In addition, there is actual and potential future competition for CASGEVY, including bluebird's SCD gene therapy, LYFGENIA™, and its TDT gene therapy, ZYNTEGLO™, which are both approved in the U.S. If competing therapies are commercialized, or developed and then commercialized, more successfully by other companies as a treatment for people with SCD or TDT, our future net product revenues and cash flows will be adversely affected and our business could be materially harmed

If we are not successful in commercializing CASGEVY, our business could be materially harmed.

If our competitors bring products with superior product profiles to market, our products may not be competitive, and our revenues could decline.

A number of companies are seeking to identify and develop product candidates for the treatment of CF, SCD, TDT, pain, and other therapeutic areas we are targeting with our research and development activities. Our success in rapidly developing and commercializing our CF medicines may increase the resources that our competitors allocate to the development of potential competitive treatments. If one or more competing therapies are successfully developed as a treatment for people with CF, SCD, TDT, pain or any of the other disease areas we are currently targeting in our pipeline, our products and our net product revenues could face competitive pressures. If one or more competing therapies prove to be superior to our then-existing products and/or product candidates, our business could be materially adversely affected.

In addition, our business faces competition from major pharmaceutical and biotechnology companies possessing substantially greater financial resources than we possess, as well as from numerous smaller public and private companies, academic institutions, government agencies, public and private research organizations, and charitable venture philanthropy organizations that conduct research, seek patent protection, and/or establish collaborative arrangements for research, development, manufacturing, and commercialization. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller and other early-stage companies also may prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These third parties compete with us in recruiting and retaining qualified scientific and management personnel, establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs.

Our products and any products that we develop in the future may not be able to compete effectively with marketed therapies or new therapies that may be developed by competitors. The risk of competition is particularly important to our company because substantially all of our revenues are related to the treatment of people with CF. There are many other companies developing products for the same patient populations that we are pursuing. To compete successfully in these areas, we must demonstrate improved safety, efficacy and/or tolerability, ease of manufacturing, and gain and maintain market acceptance over competing products.

If we discover safety issues with any of our products or if we fail to comply with continuing U.S. and applicable foreign regulations, commercialization efforts for the product could be negatively affected, the approved product could lose its approval, and our business could be materially harmed.

Our products are subject to continuing regulatory oversight, including the review of additional safety information. Products are more widely used by patients once approval has been obtained and therefore side effects and other problems may be observed after approval that were not seen or anticipated, or were not as prevalent or severe, during pre-approval clinical trials or nonclinical studies. The subsequent discovery or appearance of previously unknown or underestimated problems with a product could negatively affect commercial sales of the product, result in restrictions on the product or lead to the withdrawal of the product from the market. Each of our CF products shares at least one active pharmaceutical ingredient with another of our products. As a result, if any of our CF products were to experience safety issues or labeling modifications, our other CF products may be adversely affected. For example, in December 2024, the FDA modified the labeling of TRIKAFTA by revising information regarding liver injury and liver failure and moving it from the "warnings and precautions" section to a "boxed warning" section, and included similar language in the ALYFTREK label. In SCD and TDT, as part of the FDA approval for CASGEVY, we are required to conduct two post-marketing requirement safety studies to assess the long-term risk of hematologic malignancies and off-target genome editing effects by CRISPR/Cas9. Negative or ambiguous results from these studies could have a significant impact on our ability to commercialize our products.

The reporting of adverse safety events involving our products or public speculation about such events could cause our stock price to decline or experience periods of volatility. Our business also may be materially harmed by reduced coverage or reimbursement by payors, impaired sales of our products, denial or withdrawal of regulatory approvals, non-renewal of conditional regulatory approvals, required label changes or additional clinical trials, reputational harm, or government investigations or lawsuits brought against us.

Our products are subject to ongoing regulatory requirements governing the testing, manufacturing, labeling, packaging, storage, advertising, promotion, sale, distribution, import, export, recordkeeping, and submission of safety and other post-market information. We and our third-party manufacturers must comply with cGMP and other applicable regulations governing the manufacturing and distribution of our products. Regulatory authorities periodically inspect our drug manufacturing facilities, and those of our third-party manufacturers, to evaluate compliance with cGMP and other regulatory requirements.

If we or our collaborators, or third-parties acting on our behalf, fail to comply with applicable continuing regulatory requirements, we or our collaborators may be subject to fines, suspension or withdrawal of regulatory approvals for specific products, product recalls and seizures, operating restrictions and/or criminal prosecutions, any of which could have a material adverse effect on our business, reputation, financial condition, and results of operations.

If physicians and patients do not accept our products, or if patients do not remain on treatment or comply with their prescribed dosing regimen, our product revenues would decline in future periods.

Our approved products may not gain or maintain market acceptance among physicians and patients or other members of the medical community. Effectively marketing our products and any of our product candidates or investigational therapies, if approved, requires substantial efforts, both prior to launch and after approval. Physicians may elect not to prescribe or recommend our therapies, and patients may elect not to take them or receive them or they may discontinue use of our products after initiation of treatment, for a variety of reasons including:

- prevalence and severity of adverse side effects;
- lack of reimbursement availability from third-party payors, including governmental entities;
- lower demonstrated efficacy, safety and/or tolerability compared to alternative treatment methods;
- lack of cost-effectiveness;
- a decision to wait for the approval of other therapies in development that have significant perceived advantages over our product;
- inconvenience of, or burdens associated with, administration or treatment;
- limitations or warnings contained in the labeling;
- the timing of market introduction of our product as well as competitive products;
- other potential advantages of alternative treatment methods; and
- inadequate sales, marketing and/or distribution support.

If our medicines fail to achieve or maintain market acceptance, we may not be able to generate significant revenues in future periods.

Cell and genetic therapies face increased scrutiny from the public and medical communities and commercial success will depend, in part, upon the acceptance of those communities.

There is some degree of uncertainty as to whether cell and gene therapy treatments will continue to gain the acceptance of the public or the medical community. The commercial success of cell and gene therapy treatments, including CASGEVY, will depend, in part, on the acceptance of physicians, patients, and third-party payors of gene therapy products in general, and our product candidates in particular, as medically necessary, cost-effective and safe. In particular, our success will depend upon physicians prescribing our therapies in lieu of existing treatments they are already familiar with and for which greater clinical data may be available. Moreover, physicians and patients may delay acceptance of cell and gene therapies until the therapies have been on the market for a certain amount of time. In addition, medical centers, including authorized treatment centers, that administer procedures accompanying treatment could experience capacity constraints, and these centers are subject to competing priorities that could delay patient access to procedures associated with cell and gene therapy products. Negative public opinion or more restrictive government regulations may delay or impair the successful commercialization of, and demand for, cell and gene therapies.

Risks Related to Pricing of Our Products

Government and other third-party payors seek to contain costs of health care through legislative and other means. If they fail to provide coverage and adequate reimbursement rates for our products, our revenues will be harmed.

Sales of our products depend in part upon the availability of reimbursement from third-party payors. Third-party payors include government health programs such as Medicare and Medicaid in the U.S. and the national health care systems in ex-U.S. markets, managed care providers, private health insurers and other organizations. The trend in the health care industry is cost containment, and efforts of third-party payors to contain or reduce health care costs may adversely affect our ability to establish or maintain appropriate prices for our products or any drugs that we may develop and commercialize.

In the U.S., there have been, and we expect that there will continue to be, a number of federal and state proposals to implement governmental controls that are similar to those that currently exist in Europe. For example, the Affordable Care Act ("ACA") required manufacturers of Medicare Part D brand name drugs to provide discounts on those drugs to Medicare Part D beneficiaries during the coverage gap; increased the rebates paid by pharmaceutical companies to state Medicaid programs on drugs covered by Medicaid; and imposed an annual fee, which increases annually, on sales by branded pharmaceutical manufacturers. Additionally, private payors, including health maintenance organizations and pharmacy benefit managers in the U.S., are adopting more aggressive utilization management techniques and are increasingly applying restrictive plan designs that can impact patients and manufacturers, and they continue to push for significant discounts and rebates from manufacturers.

On August 16, 2022, the IRA was enacted. Among other things, the IRA establishes a Drug Price Negotiation Program, under which the government may negotiate maximum fair prices for certain drugs covered by Medicare that do not have generic or biosimilar competition. The first set of maximum fair prices will be effective in 2026. Certain products are excluded from the negotiation program including drugs that have a single orphan drug designation and that are not approved for any other orphan or non-orphan diseases or conditions. We cannot predict with certainty whether there will be future legislative changes to the scope of these exclusions or how they will affect future drugs that we may develop and commercialize. The law also requires manufacturers to pay a rebate to Medicare if the price of a Medicare drug (under both Part B and Part D) increases faster than the rate of inflation and redesigns the Part D benefit. Starting in 2025, manufacturers of brand drugs and biologics will be required to provide a 10% discount during the initial phase and a 20% discount during the catastrophic phase of the Part D benefit. The IRA continues a trend in the U.S. toward reducing drug prices and limiting spending by the federal health care programs on drugs. We expect that this law will affect our business once fully implemented, and it is possible that other legislative updates will have an adverse impact on our revenue. The IRA also requires the Secretary of the Department of Health and Human Services (the "Secretary") to issue program guidance on numerous areas associated with implementation of the law's requirements, including for drug price negotiation and inflation rebates. While CMS has issued guidance covering the first two years of the program (2026 and 2027), we do not know with certainty what guidance will apply in future years or how such guidance will affect our business.

It is possible the U.S. Congress or administration may take further actions to address health care costs and access to medicine, and specifically address coverage and reimbursement of cell and gene therapies. For example, the Center for Medicare and Medicaid Innovation ("CMMI") was directed to consider new healthcare payment and delivery models that would lower drug costs and promote access to innovative drug therapies for Medicare and Medicaid beneficiaries. In February 2023, the U.S. Administration addressed access for cell and gene therapies in diseases such as SCD through the CMS program known as The Cell and Gene Therapy Access Model ("CGT Access Model"). The CGT Access Model was designed to provide an opportunity to accelerate and enhance broad Medicaid access for eligible patients across all 50 U.S. states by allowing state Medicaid agencies to delegate authority to CMS to coordinate and facilitate outcomes-based payment arrangements ("OBAs") with cell and gene therapy manufacturers, such as ours. In 2024, we reached an agreement with CMS to expand access by participating in the CGT Access Model for SCD to benefit Medicaid beneficiaries. States may begin participating in the Cell & Gene Therapy Access Model on a rolling-basis, between January 2025 and January 2026. In January 2025, President Trump repealed Executive Order 14087, which had directed CMS to consider innovative pricing models, ultimately leading to the CGT Access Model. The rescission currently does not appear to impact our agreement with CMS or CMS' authority to proceed with the CGT Access Model; however, any discontinuation of the CGT Access Model, or CMS' termination of our agreement to participate in the model in the future, could impact access to CASGEVY.

Third-party payors throughout the world also have been attempting to control drug spending in light of global economic pressures. In reimbursement negotiations, many payors are requesting price discounts and caps on total expenditures and limiting both the types and variety of drugs that they will cover if they are not able to secure them. Some payors restrict reimbursement of drugs through implementing utilization management controls. As part of these negotiations, many ex-U.S. government payors also are requiring companies to establish product cost-effectiveness as a condition of reimbursement. These cost-effectiveness reviews may overlook many of the benefits provided by innovative medicines, and for the most part, have not taken into account the specific circumstances of products that treat rare diseases. This has led to conclusions that certain medicines, including our products in certain jurisdictions, are not cost-effective. As a result, certain countries have declined to reimburse, or delayed their reimbursement of, some of our products. Although not mandated in the U.S., various organizations have started advocating for cost-effectiveness analyses in the U.S. as well as value-based contracting in which the amount of reimbursement for a product is based on patient outcomes and other clinical or economic metrics related to the performance of such product. If U.S. payors were to adopt such assessments and make negative coverage determinations or utilize value-based contracts that result in penalties to, or lower rates of, reimbursement, it could adversely affect our product

revenues. Our business would be materially adversely affected if we are not able to obtain or maintain coverage and reimbursement of our products from third-party payors on a broad, timely, or satisfactory basis, or if such coverage is subject to overly broad or restrictive utilization management controls.

The increasing availability and use of innovative specialty pharmaceuticals for rare or other diseases or conditions, combined with their higher cost as compared to other types of pharmaceutical products, is generating significant third-party payor interest in developing cost-containment strategies targeted to this sector. Government regulations in both U.S. and ex-U.S. markets could further limit the prices that can be charged for our products, including for those with broader patient populations, and may limit our commercial opportunity. The increasing use of cost-effectiveness assessments in markets around the world and the financial challenges faced by many governments may lead to significant adverse effects on our business.

We may experience pricing pressure on our products, which could reduce our revenues and future profitability.

There also has been an increase in state legislation and regulations related to drug pricing and drug pricing transparency. In the U.S., various states, including Nevada, Maryland, Louisiana, New York, California, Washington, Massachusetts, New Jersey, Connecticut, Vermont, New Hampshire, Utah, Minnesota, Oregon, Colorado, New Mexico, Virginia, Maine, Texas, North Dakota, West Virginia, Florida, and New Jersey have passed legislation requiring companies to disclose extensive information relating to drug prices, drug price increases, and spending on research, development, and marketing, among other things. Although it is not always clear what states will do with the collected information, some laws were designed to obtain additional product discounts. Additionally, certain states have enacted laws establishing Prescription Drug Affordability Boards ("PDABs"). Some state PDABs either have the authority or have defined a pathway where they may be granted the authority to establish upper payment limits for prescription drugs, including Colorado, Maryland, Washington, and Minnesota. Under the Washington law, the PDAB cannot select for an affordability review drugs that are solely for the treatment of an orphan-designated disease or condition. In August 2023, the Colorado PDAB selected five drugs for an affordability review, including TRIKAFTA; later that year, it found TRIKAFTA to be not unaffordable, and thus not eligible for an upper payment limit. We cannot, however, predict whether future reviews by the Colorado PDAB, or any other PDAB, will come to the same conclusion about TRIKAFTA or any of our other therapies, or the amount of any potential upper payment limit. We may continue to see more state action requiring additional disclosures or other actions. In addition, we could see increased federal activity related to drug pricing and transparency requiring disclosures or other actions instead of, or in addition to, state requirements. Similar initiatives also are occurring in, or being considered by, some of our ex-U.S. markets, including Italy and Brazil.

Additional state actions, including the importation of drugs from other countries, also may affect the availability and accessibility of our medicines. For example, on January 5, 2024, the FDA authorized Florida's Agency for Health Care Administration's drug importation program under section 804 of the Federal Food, Drug, and Cosmetic Act, which eventually would allow Florida to import certain prescription drugs from Canada. The importation of drugs from Canada or other countries that potentially could compete with our medicines could create increased pressure on our revenue and profitability.

Complying with these laws can be expensive and requires significant personnel and operational resources. Furthermore, any additional required discounts would adversely affect the pricing of, and revenues from, our products. Finally, while we seek to comply with all statutory and regulatory requirements, we face increased enforcement activity by the U.S. federal government, state governments, and private payors against pharmaceutical and biotechnology companies for pricing and reimbursement-related issues as well as inquiries from the U.S. Congress.

Other federal activities seeking to specifically address drug pricing and reimbursement include:

- rulemaking related to importation of prescription drugs from Canada, as well as guidance related to importation of prescription drugs from other foreign countries;
- attempts to establish reference pricing for certain physician-administered drugs;
- executive orders relating to drug pricing that are intended to broadly impact the pharmaceutical industry;
- changes to the federal anti-kickback statute safe harbors that eliminate anti-kickback statute discount safe harbor protection for certain manufacturer rebate arrangements; and

- legislation relating to drug pricing, including enhanced transparency measures into drug pricing.

We expect government scrutiny over drug pricing, reimbursement, and distribution to continue. Potential future government regulation of drug prices or reimbursement creates uncertainties about our portfolio and could have a material adverse effect on our operations. Moreover, antitrust and/or competition laws are increasingly being used to scrutinize pricing on high-value medicines and entities involved in drug distribution or reimbursement, including some with whom we do business. Defending against an antitrust or competition claim can be expensive and requires significant personnel and operational resources, may ultimately lead to a reduction in the prices of our products, and can ultimately result a material adverse effect on profitability and our business overall. Additionally, governmental efforts to pursue compulsory licensing, including the pursuit of so-called "march in" rights, could affect our pricing strategy and result in an adverse impact on our revenue.

Current health care laws and regulations in the U.S. and future legislative or regulatory reforms to the U.S. health care system may affect our ability to commercialize our marketed products profitably.

The U.S. government, individual states and some foreign jurisdictions also have been aggressively pursuing legislative and regulatory reforms that could affect our ability to sell products. For example, in the U.S., there have been federal legislative and administrative efforts to repeal, substantially modify, or invalidate some or all of the provisions of the ACA, which could affect coverage and payment for medicines. The federal government additionally has proposed and enacted legislation leading to aggregate reductions of Medicare payments to providers, which ultimately could affect utilization of medicines.

Other reforms include the Bipartisan Budget Act of 2018, which contained various provisions that affect coverage and reimbursement of drugs, including an increase in the discount that manufacturers of Medicare Part D brand name drugs must provide to Medicare Part D beneficiaries during the coverage gap from 50% to 70%. Under the IRA, the coverage gap phase and the associated coverage gap discount program will be eliminated after the 2024 plan year. Starting in 2025, there will be a new Part D manufacturer discount program, which requires a 10% discount in the initial phase and a 20% discount in the catastrophic phase of the benefit. The IRA also authorizes the government to negotiate maximum fair prices for certain Medicare drugs. It also establishes mandatory rebates for Part B and Part D drugs with prices that increase faster than inflation. These new laws or any other similar laws introduced in the future may result in additional reductions in Medicare and other health care funding, which could negatively affect our customers and accordingly, our financial operations. Moreover, payment methodologies may be subject to changes in health care legislation and regulatory initiatives. For example, CMS may develop new payment and delivery models, such as bundled payment models.

Adoption of new health care reform legislation at the federal or state level could affect demand for, or pricing of, our products or product candidates if approved for sale. We cannot, however, predict the ultimate content, timing, or effect of any health care reform legislation or action, or its impact on us, including increased compliance requirements and costs, all of which may adversely affect our future business, operations, and financial results.

We have experienced challenges commercializing products outside of the U.S., and our future revenues will be dependent on our ability to obtain adequate reimbursement for our products in ex-U.S. markets.

In most ex-U.S. markets, the pricing and reimbursement of therapeutic and other pharmaceutical products is subject to governmental control and government authorities are making greater efforts to limit or regulate the price of drug products. The reimbursement process in ex-U.S. markets can take a significant time to conclude and reimbursement decisions are made on a country by country or region by region basis. Further, many ex-U.S. governments are introducing new legislation focusing on cost containment measures in the pharmaceutical industry. The final form of these laws and the relevant practical application is unknown at this time, but may lead to lower prices, paybacks or other forms of discounts or special taxes.

Our CF medicines and CASGEVY treat life-threatening conditions and address relatively small patient populations, and our research and development programs are primarily focused on developing medicines to treat similar diseases. Both government and private payors are targeting these types of therapies, in some cases refusing to pay for them. We have experienced challenges in obtaining timely reimbursement for our products in various countries outside the U.S. Our future product revenues, including from TRIKAFTA/KAFTRIO, ALYFTREK, and CASGEVY, depend on, among other things, our ability to maintain reimbursement in ex-U.S. markets for our products. There is no assurance that coverage and reimbursement will be available outside of the U.S. for our approved or future therapies and, even if it is available, whether

the timing or the level of reimbursement will be sufficient to allow us to market them. Adverse pricing limitations or a delay in obtaining coverage and reimbursement would decrease our future net product revenues and harm our business.

Insurance coverage and reimbursement of cell and genetic therapies is uncertain.

There is uncertainty related to the insurance coverage and reimbursement of cell or genetic therapies, including those gene therapies that are potential one-time treatments. While coverage has not been a significant obstacle in the launch of CASGEVY, it is difficult to predict what third party payors, including U.S. or ex-U.S. governments or private insurance companies, will decide with respect to reimbursement for the other novel cell and genetic therapies in our pipeline. Additionally, reimbursement rates for cell and genetic therapies approved before ours could create an adverse environment for reimbursement of any therapies we ultimately commercialize. The administration of our products may require procedures for the collection of cells from patients, followed by other procedures either before or after delivery of the cell or genetic therapy. The manner and level at which reimbursement is provided for these services also is important. Inadequate reimbursement for such services may discourage physicians and hospitals from recommending our cell and genetic therapies and impair our ability to market or sell such therapies. Moreover, the treatment center network for our products and growth of such network could also impact uptake and necessitate out-of-state access for some beneficiaries if an authorized treatment center is not available within their home state, which could result in further underpayment from out-of-state Medicaid programs.

Risks Related to Development and Clinical Testing of Our Products and Product Candidates

Our product candidates remain subject to clinical testing and regulatory approval, and our future success is dependent on our ability to successfully develop additional product candidates for both CF and non-CF indications.

Our business depends upon the successful development and commercialization of product candidates. These product candidates are in various stages of development and must satisfy rigorous standards of safety and efficacy before they can be approved for sale by the FDA or comparable foreign regulatory authorities. To satisfy these standards, we must allocate resources among our various development programs and must engage in expensive and lengthy testing of our product candidates. Discovery and development efforts for new pharmaceutical and biological products, including new combination therapies, are resource-intensive and may take 10 to 15 years or longer for each product candidate. It is impossible to predict when or if any of our product candidates will prove effective and safe in humans or will receive regulatory approval. Despite our efforts, our product candidates may not:

- offer therapeutic or other improvement over existing competitive therapies;
- show the level of safety and efficacy, including the level of statistical significance, required by the FDA or other regulatory authorities for approval of a drug or biologic;
- meet applicable regulatory standards;
- be capable of being produced in commercial quantities at acceptable costs; or
- if approved for commercial sale, be successfully marketed as pharmaceutical or biological products.

We have recently completed and/or have ongoing or planned clinical trials for several of our product candidates. The strength of our product portfolio and pipeline will depend in large part upon the outcomes of these clinical trials, including those evaluating TRIKAFTA/KAFTRIO and ALYFTREK in younger children with CF, VX-522 in CF, suzetrigine in peripheral neuropathic pain, VX-993 in acute and diabetic peripheral neuropathy, and zimislecel and VX-264 in T1D. Failure to advance product candidates through clinical development could impair our ability to ultimately commercialize products, which could materially harm our business and long-term prospects.

Results of our clinical trials and findings from our nonclinical studies, including toxicology findings in nonclinical studies conducted concurrently with clinical trials, could lead to abrupt changes in our development activities, including the possible cessation of development activities associated with a particular product candidate or program.

Moreover, clinical data are often susceptible to varying interpretations, and many companies that have believed their product candidates performed satisfactorily in clinical trials have nonetheless failed to obtain marketing approval of their product candidate. Furthermore, results from our clinical trials may not meet the level of statistical significance or otherwise

provide the level of evidence or safety and efficacy required by the FDA or other regulatory authorities for approval of a product candidate. Finally, clinical trials are expensive and require significant operational resources to implement and maintain.

Many companies in the pharmaceutical and biotechnology industries, including our company, have suffered significant setbacks in later-stage clinical trials even after achieving promising results in earlier-stage clinical trials. For example, the results from completed preclinical studies and clinical trials may not be replicated in later clinical trials, and ongoing clinical trials for our product candidates may not be predictive of the results we may obtain in later-stage clinical trials or of the likelihood of approval of a product candidate for commercial sale.

In addition, from time to time, we report interim, topline, and preliminary data from our clinical trials, which is based on a preliminary analysis of then-available data, and the results and related findings and conclusions are subject to change. Interim or preliminary data from a clinical trial may not be predictive of final results from the clinical trial and are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment and treatment continues and more patient data become available or as patients from our clinical trials continue other treatments for their disease. Topline data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, topline data should be viewed with caution until the final data are available. If the interim, topline, or preliminary data that we report differ from actual results, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for, and commercialize, our product candidates may be harmed, which could harm our business, operating results, prospects or financial condition.

The ability of third parties to review and/or analyze data from our clinical trials, including as a result of government disclosure, also may increase the risk of commercial confidentiality breaches and result in enhanced scrutiny of our clinical trial results. For example, Clinical Trial Regulation (EU) No. 536/2014, and the EMA policy on publication of clinical data for medicinal products for human use, both permit the EMA to publish clinical information submitted in marketing authorization applications. Third party review and scrutiny could result in public misconceptions regarding our drugs and product candidates. These publications could also result in the disclosure of information to our competitors that we might otherwise deem confidential, which could harm our business.

If we are unable to obtain or are delayed in obtaining regulatory approval, we may incur additional costs, experience delays, or be unable to commercialize our product candidates.

The time required to complete clinical trials and to satisfy the FDA and other countries' regulatory review processes is uncertain and typically takes many years. Our analysis of data obtained from nonclinical and clinical activities is subject to confirmation and interpretation by regulatory authorities, which could delay, limit or prevent regulatory approval. We may encounter unanticipated delays or increased costs due to government regulation from future legislation or administrative action or changes in governmental policy during the period of drug development, clinical trials and governmental regulatory review. We also may be unable to obtain or be delayed in obtaining regulatory approval due to competition developments that impact our regulatory pathways.

We may seek a Fast Track, Priority Review, Breakthrough Therapy, and/or RMAT designation for some of our product candidates. Product candidates that receive one or more of these designations may be eligible for, among other things, a priority regulatory review. Each of these designations is within the discretion of the FDA. Accordingly, even if we believe one of our product candidates meets the criteria for Fast Track, Priority Review, Breakthrough Therapy and/or RMAT designation, the FDA may disagree and instead determine not to make such designation. The receipt of one or more of these designations for a product candidate does not guarantee a faster development process, review or approval compared to products developed or considered for approval under conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, even if one or more of our products or product candidates qualifies for Fast Track, Priority Review, Breakthrough Therapy and/or RMAT designation, the FDA may later decide to withdraw such designation if it determines that the product or product candidate no longer meets the conditions for qualification.

Any failure to obtain regulatory approvals for a product candidate would prevent us from commercializing that product candidate. Any delay in obtaining required regulatory approvals could materially adversely affect our ability to successfully commercialize a product candidate. Furthermore, any regulatory approval to market a product may be subject to limitations that we do not expect including with respect to the indicated uses for which we may market the product or required conditions of use. Any such limitations could reduce the size or demand of the market for the drug.

We also are subject to numerous foreign regulatory requirements governing the conduct of clinical trials, manufacturing and marketing authorization, pricing and third-party reimbursement. Non-U.S. jurisdictions have different approval procedures than those required by the FDA, and these jurisdictions may impose additional testing requirements for our product candidates. The foreign regulatory approval process includes all of the risks associated with the FDA approval process described above, as well as risks attributable to the satisfaction of foreign requirements. Approval by the FDA does not ensure approval by regulatory authorities outside the U.S. and approval by a foreign regulatory authority does not ensure approval by the FDA. In addition, although the FDA may accept data from clinical trials conducted outside the U.S., acceptance of this data is subject to conditions imposed by the FDA. For example, the clinical trial must be well designed and conducted and performed by qualified investigators in accordance with ethical principles. The trial population also must adequately represent the U.S. population, and the data must be applicable to the U.S. population and U.S. medical practice in ways that the FDA deems clinically meaningful. In addition, while these clinical trials are subject to applicable local laws, FDA acceptance of the data will depend on its determination that the trials also complied with all applicable U.S. laws and regulations. If the FDA does not accept the data from any trial that we conduct outside the U.S., it would likely result in the need for additional trials, which would be costly and time-consuming and delay or permanently halt our development of the applicable product candidate.

If clinical trials are prolonged or delayed, our development timelines for the affected development program could be extended, our costs to develop the product candidate could increase and the competitive position of the product candidate could be adversely affected.

We cannot predict whether or not we will encounter problems with any of our completed, ongoing or planned clinical trials that will cause us or regulatory authorities to delay or suspend clinical trials, or delay the analysis of data from our completed or ongoing clinical trials. Among the factors that could delay our development programs are:

- ongoing discussions with the FDA or comparable foreign authorities regarding the scope or design of our clinical trials and the number of clinical trials we must conduct;
- failure or delay in reaching agreement on acceptable terms with prospective contract research organizations ("CROs") and clinical trial sites;
- failure to add or delay in adding a sufficient number of clinical trial sites and obtaining institutional review board or independent ethics committee approval at each clinical trial site;
- suspension or termination of clinical trials of product candidates for various reasons, including non-compliance with regulatory requirements;
- clinical trial sites deviating from clinical trial protocol or dropping out of a clinical trial;
- delays in enrolling volunteers or patients into clinical trials, including as a result of low numbers of patients that meet the eligibility criteria for the trial;
- a lower than anticipated retention rate of volunteers or patients in clinical trials;
- the need to repeat clinical trials as a result of unfavorable or inconclusive results, unforeseen complications in testing or clinical investigator error;
- inadequate supply or deficient quality of product candidate materials or other materials necessary for the conduct of our clinical trials;
- unfavorable FDA or foreign regulatory authority inspection and review of a manufacturing facility that supplied clinical trial materials or its relevant manufacturing records or a clinical trial site or records of any clinical or preclinical investigation;
- unfavorable or inconclusive scientific results from clinical trials;
- serious and unexpected treatment-related side-effects experienced by participants in our clinical trials or by participants in clinical trials being conducted by our competitors to evaluate product candidates with similar mechanisms of action or structures to therapies that we are developing;

- favorable results in testing of our competitors' product candidates, or FDA or foreign regulatory authority approval of our competitors' product candidates; or
- action by the FDA or a foreign regulatory authority to place a clinical hold or partial clinical hold on a trial or compound or deeming the clinical trial conduct as problematic.

For planning purposes, we estimate the timing of the accomplishment of various scientific, clinical, regulatory, and other product development goals, which we sometimes refer to as milestones. These milestones may include the commencement or completion of scientific studies and clinical trials and the submission of regulatory filings. From time to time, we publicly announce the expected timing of some of these milestones. All of these milestones are based on a variety of assumptions. The actual timing of these milestones can vary dramatically compared to our estimates, in many cases for reasons beyond our control. If we do not meet these milestones as publicly announced, the commercialization of our products may be delayed and the credibility of our estimates may be adversely affected and, as a result, our stock price may decline.

Difficulty in enrolling patients could delay or prevent clinical trials of our product candidates, and ultimately delay or prevent regulatory approval.

Our ability to enroll patients in our clinical trials in sufficient numbers and on a timely basis is subject to a number of factors. Clinical trials are expensive and require significant operational resources. Delays in patient enrollment or unforeseen drop-out rates may result in increased costs and longer development times. The enrollment of patients further depends on many factors, including:

- the proximity of patients to clinical trial sites;
- the size of the patient population, the nature of the protocol, and the design of the clinical trial;
- our ability to recruit clinical trial investigators with the appropriate competencies and experience;
- the number of other clinical trials ongoing and competing for patients in the same indication;
- our ability to obtain and maintain patient consents;
- reporting of the preliminary results of any of our clinical trials;
- the availability of effective treatments for the relevant disease and eligibility criteria for the clinical trial;
- the risk that patients enrolled in clinical trials will drop out of the clinical trials before clinical trial completion; and
- factors we may not be able to control, such as pandemics that may limit patients, principal investigators or staff or clinical site availability.

We, our collaborators, the FDA, or other applicable regulatory authorities may suspend clinical trials of a product candidate at any time if we or they believe the healthy volunteers or patients participating in such clinical trials are being exposed to unacceptable health risks or for other reasons. Any such suspension could materially adversely affect the development of a particular product candidate and our business.

Enrollment for clinical trials for our cell and gene therapies may face additional and unique challenges and adverse developments associated with these clinical trials could result in action by regulatory bodies, including revised requirements for approval.

For cell and genetic therapy programs addressing rare genetic diseases with small patient populations, we may not be able to identify, recruit and enroll a sufficient number of patients, or those with required or desired characteristics, to complete our clinical studies in an adequate and timely manner. Additionally, patients may be unwilling to participate in our clinical trials because of concerns that cell and genetic therapies are unsafe or unethical, negative publicity from adverse safety events in the biotechnology or gene therapy industries, or for other reasons, including competitive clinical studies for similar patient populations. Moreover, adverse developments in clinical trials conducted by others of cell and genetic therapy products or products created using similar technology, or adverse public perception of the field of cell and genetic therapies, may cause the FDA and other regulatory bodies to revise the requirements for approval of any cell or genetic therapy product

candidates we may develop or limit the use of products utilizing technologies such as ours, either of which could materially harm our business.

Risks Related to Government Regulation

If regulatory authorities interpret any of our conduct, including our marketing practices, as being in violation of applicable health care laws, including fraud and abuse laws, laws prohibiting false and misleading promotion, disclosure laws or other similar laws, we may be subject to civil or criminal penalties.

We are subject to health care fraud and abuse laws, such as the FCA and the AKS, and other similar laws and regulations both in the U.S. and in non-U.S. markets.

In the U.S., the Federal Anti-Kickback Statute prohibits knowingly and willfully offering, paying, soliciting, receiving or providing remuneration, directly or indirectly, in exchange for or to induce either the referral of an individual, or the ordering, furnishing, arranging for or recommending of an item or service that is reimbursable, in whole or in part, by a federal health care program, such as Medicare or Medicaid. Because of the broad scope of the prohibition, most financial interactions between pharmaceutical manufacturers and prescribers, purchasers, third party payors and patients would be subject to the statute. Although there are a number of statutory exceptions and regulatory safe harbors protecting certain common activities from prosecution, financial interactions must be structured carefully to qualify for protection or otherwise withstand scrutiny.

Federal false claims laws, including the FCA, prohibit any person from knowingly presenting, or causing to be presented, a false claim for payment to the federal government, or knowingly making, or causing to be made, a false statement to get a false claim paid. Pharmaceutical companies have been prosecuted under these laws for a variety of alleged promotional and marketing activities, such as providing free product to customers with the expectation that the customers would bill federal programs for the product; reporting to pricing services inflated average wholesale prices that were then used by federal programs to set reimbursement rates; engaging in promotion for uses that the FDA has not approved, that caused claims to be submitted to Medicaid for those unapproved uses; submitting inflated “best price” information to the Medicaid Rebate Program; and certain manufacturing-related violations. The scope of this and other laws may expand in ways that make compliance more difficult and expensive.

The FDA and other regulatory agencies closely regulate the post-approval marketing and promotion of products to ensure that they are marketed only for the approved indications and in accordance or consistent with the provisions of the approved labeling. Although physicians are generally permitted, based on their medical judgment, to prescribe products for indications other than those approved by the applicable regulatory agency, manufacturers are prohibited from promoting such unapproved uses. We market our products to eligible people with CF, SCD, TDT, and acute pain for whom the applicable product has been approved and provide promotional materials and informational programs to physicians regarding the use of each product in these patient populations. These eligible people do not represent all people with CF, SCD, TDT, and acute pain. If a regulatory agency determines that our promotional materials, or other activities constitute promotion of unapproved uses or otherwise false and misleading promotion, it could request that we modify our promotional materials or other activities, conduct corrective advertising, or subject us to regulatory enforcement actions, such as the issuance of a warning or untitled letter, injunction, seizure, civil fines and criminal penalties. It also is possible that other federal, state, or foreign enforcement authorities might take action if they believe that the alleged improper promotion led to the submission and payment of claims for an unapproved use, which could result in significant fines or penalties under other statutory authorities, such as laws prohibiting false claims for reimbursement. Even if it is later determined we were not in violation of these laws, we may be faced with negative publicity, incur significant expenses defending our actions, and have to divert significant management resources from other matters.

In the U.S., federal and state laws regulate financial interactions between pharmaceutical manufacturers and healthcare providers, require disclosure to government authorities and the public of such interactions, and mandate the adoption of compliance standards or programs. For example, the so-called federal “sunshine law” requires pharmaceutical manufacturers to report annually to CMS payments or other transfers of value made by that entity to physicians, physicians assistants, advanced practice registered nurses, and teaching hospitals. We also have similar reporting obligations with respect to financial interactions throughout the E.U. We expended significant efforts to establish, and are continuing to devote significant resources to maintain and enhance, systems and processes to comply with these regulations. Requirements to track and disclose financial interactions with health care providers and organizations increase government and public scrutiny of these financial interactions. As we commercialize products in areas with broader patient populations, we will have more

interactions with a broader set of healthcare practitioners. Failure to comply with the reporting requirements could result in significant civil monetary penalties.

The sales and marketing practices of our industry have been the subject of increased scrutiny from government authorities in the U.S. and other countries in which we market our products, and we believe that this trend will continue. Many of these laws have not been fully interpreted by the government authorities or the courts, and their provisions are subject to a variety of interpretations. While we have a corporate compliance program which, together with our policies and procedures, is designed to actively identify, prevent and mitigate risk through the implementation of compliance policies and systems and the promotion of a culture of compliance, if we are found not to be in full compliance with these laws and regulations, our business could be materially harmed. We may be subject to penalties, including civil and criminal penalties, damages, fines, exclusion from federal health care programs and/or the curtailment or restructuring of our operations. Even if we successfully defend against government challenge, responding to the challenge may cause us to incur significant legal expenses and divert our management's attention from the operation of our business.

If we fail to comply with our reporting and payment obligations under the Medicaid Drug Rebate Program or other governmental pricing programs in the U.S., we could be subject to additional reimbursement requirements, penalties, sanctions, and fines that could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

We participate in the Medicaid Drug Rebate Program, the 340B program, and a number of other federal and state government pricing programs in the U.S. to obtain coverage for our products by certain government health care programs. These programs require us to pay rebates or provide discounts to certain government payors or private purchasers in connection with our products when dispensed to beneficiaries of these programs. In some cases, such as with the Medicaid Drug Rebate Program, the rebates are based on pricing and rebate calculations that we report on a monthly and quarterly basis to the government agencies that administer the programs. The terms, scope and complexity of these government pricing programs may change. For example, regulations finalized in December 2020 created an alternative Medicaid rebate formula for "line extensions" of oral solid dosage forms. Moreover, in December 2020, CMS finalized changes to Medicaid Drug Rebate Program pricing calculations regarding the provision of co-payment assistance to patients that may be impacted by so-called accumulator programs operated by private insurers or pharmacy benefit managers. The portion of this rule dealing with manufacturer co-payment assistance was struck down by the U.S. District Court for the District of Columbia in May 2022 (and the deadline for an appeal has lapsed). In September 2024, CMS issued a final rule withdrawing the challenged accumulator adjustment regulations. The rule made significant changes to, among other things, penalties for misclassification and the definitions of a covered outpatient drug, internal investigation and market date, which may have an impact on our Medicaid rebate liability.

Additionally, the expansion of the 340B Drug Discount Program through the ACA has increased the number of purchasers, known as covered entities, who are eligible for significant discounts on branded drugs. In general, covered entities distribute 340B drugs through their own in-house pharmacies. A growing number of covered entities have been contracting with retail and/or specialty pharmacies, known as contract pharmacies, to distribute 340B drugs. Manufacturers have begun to implement restrictions on covered entities that use contract pharmacies. Similarly, we limit hospital covered entities to contract with one contract pharmacy if the covered entity does not have an in-house outpatient pharmacy. Otherwise, hospital covered entities that have an in-house outpatient pharmacy are not permitted to use contract pharmacies. Our policy applies to our CF and pain products, and it does not apply to Federal grantees and hospitals and any covered entities in states that prohibit manufacturers from restricting covered entities from accessing 340B drugs through contract pharmacies. Certain states, including Arkansas, Kansas, Louisiana, Maryland, Minnesota, Mississippi, Missouri, and West Virginia, have passed laws to regulate the relationship between manufacturers and contract pharmacies. A number of manufacturers have filed lawsuits against these states. These and future changes to government pricing programs, laws, and regulations may have a material adverse impact on our revenue and operations.

We also may have reimbursement obligations or be subject to penalties if we fail to provide timely and accurate information to the government, pay the correct rebates, or offer the correct discounted pricing. Changes to the price reporting or rebate requirements of these programs would affect our obligations to pay rebates or offer discounts. For example, the removal of the current statutory 100% of Average Manufacturer Price per-unit cap on Medicaid rebate liability for single source and innovator multiple source drugs, effective as of January 1, 2024, under the American Rescue Plan Act of 2021, may affect the prices that are required to be charged to covered entities under the 340B Drug Discount Program. Additionally, the IRA requires manufacturers to pay rebates for Medicare Part B and Part D drugs with prices that increase

faster than the rate of inflation. Responding to current and future changes to these and other Medicaid Drug Rebate Program requirements may reduce our net revenues and the complexity of compliance, will be time-consuming, and could have a material adverse effect on our results of operations.

If our processes and systems are not compliant with regulatory requirements, we could be subject to restrictions on marketing our products or could be delayed in submitting regulatory filings seeking approvals for our product candidates.

We have a number of regulated processes and systems that are required both prior to and following approval of our drugs and product candidates. These processes and systems are subject to continual review and periodic inspection by the FDA and other regulatory bodies. In addition, the clinical research organizations and other third parties that we work with in our non-clinical studies and clinical trials and our oversight of such parties are subject to similar reviews and periodic inspection by the FDA and other regulatory bodies. If compliance issues are identified at any point in the development and approval process, we may experience delays in filing for regulatory approval for our product candidates, or delays in obtaining regulatory approval after filing, if at all. Any later discovery of previously unknown problems or safety issues with approved products or manufacturing processes, or failure to comply with regulatory requirements, may result in restrictions on such products or manufacturing processes, withdrawal of products from the market, the imposition of civil or criminal penalties or a refusal by the FDA and/or other regulatory bodies to approve pending applications for marketing approval of new products or supplements to approved applications, any of which could have a material adverse effect on our business. In addition, we are party to agreements that transfer responsibility for complying with specified regulatory requirements, such as filing and maintenance of marketing authorizations and safety reporting or compliance with manufacturing requirements, to our collaborators and third-party manufacturers. If our collaborators or third-party manufacturers do not fulfill these regulatory obligations, any products for which we or they obtain approval may be subject to later restrictions on manufacturing or sale, which could have a material adverse effect on our business.

The regulatory approval process for our cell or genetic therapies involves additional consultations with regulatory agencies, costs, and potentially longer timelines as compared to those for small molecules.

As we advance our cell and genetic therapy product candidates, we will be required to consult with various regulatory authorities, and we must comply with all applicable laws, rules, and regulations, which may change from time to time, including during the course of development of our cell and genetic therapy product candidates. If we fail to do so, we may be required to delay or discontinue the clinical development of certain of our cell and genetic therapy product candidates. These additional processes may result in a review and approval process that is longer than we otherwise would have expected. Even if we comply with applicable laws, rules, and regulations, and even if we maintain close coordination with the applicable regulatory authorities with oversight over our cell and genetic therapy product candidates, our development programs may experience delays or fail to succeed. Delay or failure to obtain, or unexpected costs in obtaining, the regulatory approval necessary to bring a potential cell or genetic therapy product to market would materially adversely affect our business, financial condition, results of operations and prospects.

The regulatory approval process and clinical trial requirements for cell and genetic therapies can be more expensive and take longer than for other, better known or more extensively studied product candidates, and regulatory requirements governing cell and genetic therapy products have changed frequently and may continue to change in the future. For example, the FDA established the Office of Tissues and Advanced Therapies within its Center for Biologics Evaluation and Research ("CBER") to consolidate the review of cell therapies and related products, and the Cellular, Tissue and Gene Therapies Advisory Committee to advise CBER on its review. These and other regulatory review agencies, committees and advisory groups, and the requirements and guidelines they promulgate, may lengthen the regulatory review process, require us to perform additional preclinical studies or clinical trials, increase our development costs, lead to changes in regulatory positions and interpretations, delay or prevent approval and commercialization of these treatment candidates or lead to significant post-approval limitations or restrictions.

We are subject to various and evolving laws and regulations governing the privacy and security of personal data, and our failure to comply could adversely affect our business, result in fines and/or criminal penalties, and damage our reputation.

We are subject to data privacy and security laws and regulations in various jurisdictions that apply to the collection, storage, use, sharing, and security of personal data, including health information, and impose significant compliance obligations. In addition, numerous other federal and state laws, including state security breach notification laws, state health information privacy laws and federal and state consumer protection laws, govern the collection, use, disclosure and security

of personal information. The legislative and regulatory landscape for privacy and data protection continues to evolve, and there has been an increasing focus on privacy and data protection issues with the potential to affect our business. As we enter into new disease areas and jurisdictions both commercially and for clinical trials, we must continue to evaluate new and evolving privacy laws.

For example, the E.U. General Data Protection Regulation ("GDPR") went into effect in 2018 and has imposed new obligations on us with respect to our processing of personal data and the cross-border transfer of such data, including higher standards of obtaining consent, more robust transparency requirements, data breach notification requirements, requirements for contractual language with our data processors, and stronger individual data rights. Different E.U. member states have interpreted the GDPR differently and many have imposed additional requirements, which add to the complexity of processing personal data in the E.U. The GDPR also imposes strict rules on the transfer of personal data to countries outside the E.U., including the U.S. and the U.K., and permits data protection authorities to impose large penalties for violations of the GDPR. Similarly, other jurisdictions have either introduced or enacted legislation or executive orders restricting cross-border data transfers. These regulations restrict the transfer of certain types of data (e.g., sensitive personal data) or restrict the transfer of data to certain jurisdictions. The rules related to cross border data transfers continue to evolve based on court decisions and regulator guidance, which presents certain practical challenges to compliance. Regulators also continue to focus enforcement efforts on behavioral advertising and other online tracking technologies commonly used by companies. Compliance with these evolving rules is challenging, as country specific guidance and rules are continually changing and limited alternatives currently exist in the market. Compliance with the these laws and regulations is a rigorous and time-intensive process that may increase our cost of doing business or require us to change our business practices, and despite those efforts, there is a risk that we may be subject to fines and penalties, litigation, and reputational harm in connection with any activities falling within the scope of the GDPR or other privacy laws or regulations.

In the U.S., numerous states have introduced or enacted comprehensive privacy legislation. Similar to the California Consumer Rights Act, which came into effect in January 2023), these comprehensive privacy laws place numerous obligations on businesses with respect to the collection and processing of personal data. Some states have passed privacy legislation focusing specifically on the collection and processing of consumer health data. Enforcement at the federal level in the U.S. from the FTC has been focused on the use of health information for targeted advertising. While we continue to address the implications of the new data privacy regulations, data privacy remains an evolving landscape at both the domestic and international level, with new regulations coming into effect and continued legal challenges. Each law is also subject to various interpretations by courts and regulatory agencies, creating even more uncertainty. While we have a global privacy program that addresses such laws and regulations, our efforts to comply with the evolving data protection rules may be unsuccessful.

We must devote significant resources to understanding and complying with the changing landscape in this area. Failure to comply with data protection laws may expose us to risk of enforcement actions taken by data protection authorities, private rights of action in some jurisdictions, and potential significant penalties if we are found to be non-compliant. Failure to comply with the GDPR and applicable national data protection laws of European Economic Area member states could lead to fines of up to €20,000,000 or up to 4% of the total worldwide annual revenue of the preceding financial year, whichever is higher. Some of these laws and regulations also carry the possibility of criminal sanctions. For example, while we are not directly subject to the Health Insurance Portability and Accountability Act of 1996, as amended by the Health Information Technology for Economic and Clinical Health Act ("HIPAA"), we could be subject to penalties, including criminal penalties if we knowingly obtain or disclose individually identifiable health information from a HIPAA-covered health care provider or research institution that has not complied with HIPAA's requirements for disclosing such information. In addition, the commercialization of cell and gene therapies requires the collection and processing of a greater amount of personal data than traditional therapies, potentially increasing risk. Furthermore, the number of government investigations and enforcement actions related to data security incidents and privacy violations, with a specific focus on online data sharing, continue to increase and government investigations typically require significant resources and generate negative publicity, which could harm our business and our reputation.

If we do not comply with laws regulating the protection of the environment and health and human safety, our business could be adversely affected.

Our research and development efforts involve the regulated use of hazardous materials, chemicals, and various controlled and radioactive compounds. Although we believe that our safety procedures for handling and disposing of these materials comply with the standards prescribed by state, federal and foreign regulations, the risk of loss of, or accidental contamination

or injury from, these materials cannot be eliminated. If an accident occurs, we could be held liable for resulting damages, which could be substantial. We also are subject to numerous environmental, health, and workplace safety laws and regulations, including those governing laboratory procedures, exposure to blood-borne pathogens, and the handling of biohazardous materials. Although we maintain workers' compensation insurance to cover us for costs we may incur due to injuries to our employees resulting from the use of these materials, this insurance may not be sufficient to cover all potential liabilities. We maintain insurance to cover pollution conditions or other extraordinary or unanticipated events relating to our use and disposal of hazardous materials that we believe is appropriate based on the small amount of hazardous materials we generate. Additional federal, state and local laws and regulations affecting our operations may be adopted in the future. We may incur substantial costs to comply with, and substantial fines or penalties if we violate, any of these laws or regulations.

Risks Related to Supply, Manufacturing and Reliance on Third Parties

We may face manufacturing, supply, and distribution difficulties, among other challenges, delays, or interruptions, including at our third-party providers.

We rely on a worldwide network of third-party manufacturers and our internal capabilities, including our own manufacturing facilities in Boston, to manufacture product candidates for clinical trials as well as our medicines for commercial use. We also depend on third-party logistics providers to manage our shipments globally, and on approved distributors for supply, sales and marketing in certain markets. While we have developed internal capabilities to supply product candidates for use in our clinical trials as well as some of our products for commercial sale, a majority of the manufacturing steps needed to produce our medicines, therapies, product candidates, and drug products are performed through a third-party manufacturing network. The manufacture of our products and product candidates can be complex, which may require lengthy technology transfers between us and the third parties on which we rely. We expect that we will continue to rely on third parties to meet our commercial supply needs and a significant portion of our clinical supply needs for the foreseeable future.

We could be subject to significant supply interruptions as a result of disruptions to third party or our internal manufacturing capabilities. Our supply chain for sourcing raw materials and manufacturing drug product ready for distribution, including obtaining necessary supplies, is a multi-step international endeavor. Third-party contract manufacturers, including some in China, perform different parts of our manufacturing process. Contract manufacturers may supply us with raw materials, convert these raw materials into drug substance and/or convert the drug substance into final dosage form. We also use third parties are used for packaging, warehousing, and distribution of products. We maintain property insurance to cover potential losses that may result from supply interruptions or destruction at these third parties, however, this insurance may not be sufficient to cover all potential losses that may result.

The manufacturing and logistics for cell and genetic therapies are highly complex, often short lead time operations that require partnership with an extensive network of third parties to deliver product. These manufacturing and logistics operations require significant investment by us to secure capacity at third parties with expertise to meet our requirements. Even with the relevant experience and expertise, manufacturers of cell and genetic therapy products often encounter difficulties in production, including difficulties with production costs and yields, quality control, and compliance with federal, state and foreign regulations. There are many risks that could result in delays and additional costs, including the need to hire and train qualified employees and obtain access to necessary equipment and third-party technology. This capacity may be limited by the number of other clinical trials and commercial manufacturing ongoing for other companies seeking similar support.

If third parties are unwilling or unable to meet our requirements, we could experience supply disruptions outside of our control. Additionally, manufacturing facilities, both foreign and domestic, are subject to inspections by the FDA and other U.S. and foreign government authorities. Although we actively engage with regulatory authorities, the timing of regulatory approvals for each of these facilities may be delayed for a variety of reasons. We may experience supply disruptions if regulatory agencies are unable to inspect the manufacturing facilities on which we rely. In addition, we and the third parties with whom we engage are required to maintain compliance with quality regulations globally. An inability to maintain compliance with such regulations, including cGMP requirements, could cause significant disruptions to our business and operations.

Additionally, establishing, managing and expanding our global manufacturing and supply chain requires a significant financial commitment and the creation and maintenance of our numerous third-party contractual relationships. We may not

be able to agree on contractual terms with third parties as needed for manufacturing of our products. Although we attempt to manage the business relationships with our partners, we could be subject to supply disruptions outside of our control.

Supply disruptions may result from a number of factors, including shortages in product raw materials, labor or technical difficulties, regulatory inspections or restrictions, shipping or customs delays, general global supply chain disruptions, events beyond our control, or any other performance failure by us or any third-party manufacturer on which we rely. Additionally, unfavorable geopolitical events or situations could affect our ability to interact with or conduct business with specific vendors within our global supply network, or could prevent or delay the transportation of supplies or products to their planned destination. Any such disruptions could disrupt sales of our products and/or the timing or advancement of our clinical trials.

If we or our third-party manufacturers become unable (including potentially through governmental actions or legislation targeted toward them) or unwilling to continue manufacturing product and we are not able to promptly identify another manufacturer, we could experience a disruption in the commercial supply of our then-marketed medicines, which would have a significant effect on patients, our business, and our product revenues. Similarly, a disruption in the clinical supply of product candidates could delay the completion of clinical trials and affect timelines for regulatory filings. We have a limited number of critical steps and key materials for our manufacturing process that are single sourced, including for commercialized products. To ensure the stability of our supply chains, we continue to develop alternative suppliers for our manufacturing processes and key materials. However, there can be no assurance that we will be able to establish and maintain additional manufacturers or capacity for all of our product candidates and products on a timely basis or at all.

In the course of providing its services, a contract manufacturer may develop process technology related to the manufacture of our products or product candidates that the manufacturer owns, either independently or jointly with us. This would increase our reliance on that manufacturer or require us to obtain a license from that manufacturer to have our products or product candidates manufactured by other suppliers utilizing the same process.

We rely on third parties to conduct pre-clinical work, clinical trials and other activities, and those third parties may not perform satisfactorily, including failing to meet established deadlines for the completion of such studies and/or trials or failing to satisfy regulatory requirements.

We rely on third parties such as CROs to help manage certain pre-clinical work and our clinical trials and on medical institutions, clinical investigators, and clinical research organizations such as the Therapeutic Development Network, which is primarily funded by the Cystic Fibrosis Foundation, to assist in the design and review of, and to conduct our clinical trials, including enrolling qualified patients. In addition, we engage third party contractors to support numerous other research, commercial and administrative activities. Our reliance on these third parties for clinical development activities reduces our control over these activities but does not relieve us of our responsibilities. For example, we remain responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocols for the clinical trial. Moreover, the FDA and other relevant regulatory authorities around the world require us to comply with standards, commonly referred to as good laboratory practices and good clinical practices, for conducting, recording and reporting the results of pre-clinical and clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity and confidentiality of trial participants are protected. Such standards, particularly with respect to newer cell and genetic therapies, will continue to evolve and subject us and third parties to new or changing requirements.

If these third parties do not successfully carry out their contractual duties or meet expected deadlines, we may be required to replace them. Although we believe that there are a number of other third-party contractors we could engage to continue the activities, it may result in a delay of the affected clinical trial, product development program or applicable activity. If clinical trials are not conducted in accordance with our contractual expectations or regulatory requirements, action by regulatory authorities might significantly and adversely affect the conduct or progress of these clinical trials or in specific circumstances might result in a requirement that a clinical trial be redone. Accordingly, our efforts to obtain regulatory approvals for and commercialize our product candidates could be delayed. In addition, failure of any third-party contractor to conduct activities in accordance with our expectations, could adversely affect the relevant research, development, commercial or administrative activity.

Risks Related to Business Development Activities

We face risks in connection with existing and future collaborations with respect to the development, manufacture and commercialization of our products and product candidates.

The risks that we face in connection with our current collaborations, including with CRISPR, Moderna, Entrada, and Zai, and any future collaborations, include the following:

- Collaborators may develop and commercialize, either alone or with others, drugs or therapies that are similar to or competitive with the products or product candidates that are the subject of their collaborations with us.
- Disagreements with collaborators, including disagreements over proprietary rights, contract interpretation or the preferred course of development, might cause delays or termination of the research, development or commercialization of product candidates, might lead to additional responsibilities or costs for us with respect to product candidates, or might result in litigation or arbitration. Any such disagreements would divert management attention and resources and would be time-consuming and expensive.
- Collaborators may not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential litigation.
- Collaborators may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability.
- Investigations and/or compliance or enforcement actions against a collaborator, which may expose us to indirect liability as a result of our partnership with such collaborator.

If a collaborator were to be involved in a business combination with a third party, it might de-emphasize or terminate the development or commercialization of any product candidate licensed to it by us. If one of our collaborators terminates its agreement with us, we may find it more difficult to attract new collaborators and our perception in the business and financial communities could be harmed.

Moreover, as part of our ongoing strategy, we may seek additional collaborative arrangements for certain of our development programs and/or seek to expand existing collaborations to cover additional commercialization and/or development activities. Whether we reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator's evaluation of a number of factors. Those factors may include the design or results of clinical trials, the likelihood of approval by the FDA, EMA or other regulatory authorities, the potential market for the subject product candidate, the costs and complexities of manufacturing and delivering such product candidate to patients, the potential of competing products, the existence of uncertainty with respect to our ownership of the applicable intellectual property, which can exist if there is a challenge to such ownership without regard to the merits of the challenge, and industry and market conditions generally. No assurance can be given that any efforts we make to seek additional collaborative arrangements will be successfully completed on a timely basis or at all.

Our ability to execute on our long-term strategy depends in part on our ability to engage in transactions and collaborations with other entities that add to our pipeline or provide us with new commercial opportunities.

To achieve our long-term business objectives, we seek to license or acquire products, product candidates and other technologies that have the potential to complement our ongoing research and development efforts, access emerging technologies and license or acquire pipeline assets. These transactions may be similar to prior transactions, may be structured differently than prior transactions, or may involve larger transactions or later-stage assets. We have faced and will continue to face significant competition for the acquisition of rights to these types of products, product candidates and other technologies from a variety of other companies, some of which have significantly more financial resources and experience in business development activities than we have. In addition, investors and non-profit organizations may be willing to provide capital to the companies that control additional products, product candidates or technologies, which may provide incentives for companies to advance these products, product candidates or technologies independently. Also, the cost of acquiring, in-licensing or otherwise obtaining rights to such products, product candidates or other technologies has grown dramatically in recent years and may be at levels that we cannot afford or that we believe are not justified by market potential. As a result, we

may not be able to acquire, in-license or otherwise obtain rights to additional products, product candidates or other technologies on acceptable terms or at all.

We may not realize the anticipated benefits of existing or future acquisitions of businesses or technologies, and the integration following any such acquisition may disrupt our business and management.

Effectively integrating acquired businesses, technologies and exclusive licenses is challenging. We may not realize the benefits anticipated from our external innovation transactions, including the value of Alpine's pipeline and candidates, which could adversely affect our business and financial condition. Achieving the anticipated benefits of any transaction and successfully integrating acquired businesses or technologies, including Alpine, involves a number of risks, including:

- failure to successfully develop and commercialize the acquired products, product candidates or technologies or to achieve other strategic objectives;
- delays or inability to progress preclinical programs into clinical development or unfavorable data from clinical trials evaluating the acquired or licensed product or product candidates;
- difficulty in integrating the products, product candidates, technologies, business operations and personnel of an acquired asset or company;
- disruption of our ongoing business and distraction of our management and employees from daily operations or other opportunities and challenges;
- the potential loss of key employees of an acquired company;
- entry into markets in which we have no or limited direct prior experience or where competitors in such markets have stronger market positions;
- potential failure of the due diligence processes to identify significant problems, liabilities or challenges of an acquired company, or acquired or licensed products, product candidate or technology, including problems, liabilities or challenges with respect to intellectual property, clinical or non-clinical data, safety, accounting practices, employee, or third-party relations and other known and unknown liabilities;
- liability for activities of the acquired company or licensor before the acquisition or license, including intellectual property infringement claims, violations of laws, commercial disputes, tax liabilities, and other known and unknown liabilities;
- exposure to litigation or other claims in connection with, or inheritance of claims or litigation risk as a result of an acquisition or license, including claims from terminated employees, customers, former equity holders or other third parties; and
- difficulties in the integration of the acquired company's departments, systems, including accounting, human resource and other administrative systems, technologies, books and records, and procedures, as well as in maintaining uniform standards, controls, including internal control over financial reporting required by the Sarbanes-Oxley Act of 2002 and related procedures and policies.

Acquisitions, licensing arrangements and other strategic transactions are inherently risky, and ultimately, if we do not complete an announced acquisition, collaboration or strategic transaction or integrate an acquired or licensed asset, business or technology successfully and in a timely manner, we may not realize the anticipated benefits of the strategic transaction. We may later incur impairment charges related to assets acquired in any such transaction. Moreover, relatively small changes in key assumptions and judgements may result in the recognition of significant intangible asset impairment charges, which could have a material adverse impact on our results of operations.

Even if we achieve the long-term benefits associated with our strategic transactions, our expenses and short-term costs may increase materially and adversely affect our liquidity and short-term net income. Future strategic transactions could result in increased operating expenses, potentially dilutive issuances of equity securities, the incurrence of debt, the creation of contingent liabilities, impairment expenses related to goodwill, or impairment or amortization expenses related to other intangible assets, all of which could harm our financial condition.

Risks Related to Intellectual Property

If our patents do not protect our products or our products infringe third-party patents, we could be subject to litigation which could result in injunctions preventing us from selling our products, substantial damages, or circumvention of our patents by third parties.

We own and/or control numerous issued patents and pending patent applications in the U.S., as well as counterparts in other countries. Our success will depend, in significant part, on our ability to obtain and defend U.S. and foreign patents covering our products, their uses and our processes, to preserve our trade secrets and to operate without infringing the proprietary rights of third parties. We cannot be certain that any patents will issue from our pending patent applications or, even if patents issue or have issued, that the issued claims will provide us with adequate protection against competitive products or otherwise be commercially valuable. U.S. and foreign patent applications typically are maintained in confidence for a period of time after they initially are filed with the applicable patent office. Consequently, we cannot be certain that we were the first to file patent applications on our products or product candidates or their use. If a third-party has an earlier filed patent application relating to our product or product candidates, their uses, or a similar invention, we may be unable to obtain an issued patent from our application.

Due to evolving legal standards relating to the patentability, validity, and enforceability of patents covering pharmaceutical and biotechnological inventions and the scope of claims made under these patents, our ability to obtain, maintain and enforce patents is uncertain and involves complex legal and factual questions.

We have many pending patent applications covering our products. These pending patent applications may not issue, and we may not receive any additional patents. The issuance of a patent is not conclusive as to its inventorship, scope, validity, or enforceability. Our patents may be challenged by third parties and certain of our patents have been challenged. This could result in the patent being deemed invalid, unenforceable or narrowed in scope, or the third party may circumvent any such issued patents, including through compulsory licensing mechanisms. When market exclusivity ends or if our patents are circumvented, generic versions of our medicines may be approved and marketed, which could cause substantial and rapid declines in the sales of our products.

Our patents or patents we license might not contain claims that are sufficiently broad to prevent others from developing competing products. For instance, issued patents, or patents that may issue in the future, (i) relating to our small molecules may be limited to a particular molecule or molecules and may not cover similar molecules that have similar clinical properties, and (ii) relating to cell or genetic therapies may not cover similar technologies that would allow competitors to achieve similar results. Consequently, our competitors may independently develop competing products that do not infringe our patents or other intellectual property.

The laws of many foreign jurisdictions do not protect intellectual property rights to the same extent as in the U.S. We, like many companies in our segment of the pharmaceutical industry, have encountered challenges in protecting and defending such rights in foreign jurisdictions. Difficulties or preclusion from protecting our intellectual property rights in foreign jurisdictions, including through compulsory licensing, could substantially harm our business.

Because of the extensive time required for the discovery, development, testing and regulatory review of product candidates, it is possible that a patent may expire before a product candidate can be commercialized, or a patent may expire or remain in effect for only a short period following commercialization of such product candidate. This would result in a minimal or non-existent period of patent exclusivity. If our product candidates are not commercialized significantly ahead of the expiration date of any applicable patent, or if we have no patent protection on such product candidates, then, to the extent available we would rely on other forms of exclusivity, such as data exclusivity or orphan drug exclusivity.

Uncertainty over intellectual property in the pharmaceutical and biotechnology industry has been the source of litigation and other disputes that are inherently costly and unpredictable.

There is considerable uncertainty within our industry about the validity, scope, and enforceability of many issued patents in the U.S. and elsewhere in the world, and, to date, the law and practice remains in flux both in the agencies that grant patents and in the courts. We cannot currently determine the ultimate scope and validity of patents which may be granted to third parties in the future or which patents might be asserted as being infringed by the manufacture, use and sale of our products.

There has been, and we expect that there may continue to be, significant litigation and other disputes in the pharmaceutical industry regarding patents and other intellectual property rights. Litigation, arbitrations, administrative proceedings, and other legal actions with private parties and governmental authorities concerning patents and other intellectual property rights may be protracted, expensive, and distracting to management. Competitors may sue us as a way of delaying the introduction of our products or to remove our products from the market. Any litigation, including litigation related to Abbreviated New Drug Applications ("ANDA"), litigation related to 505(b)(2) applications, interference proceedings to determine priority of inventions, derivations proceedings, *inter partes* review, oppositions to patents in foreign countries, litigation against our collaborators or similar actions, may be costly and time consuming and could harm our business. We expect that litigation may be necessary in some instances to determine the validity and scope of certain of our proprietary rights. Litigation may be necessary in other instances to determine the validity, scope or non-infringement of certain patent rights claimed by third parties to be pertinent to the manufacture, use or sale of our products. Ultimately, the outcome of such litigation could adversely affect the validity and scope of our patent or other proprietary rights, hinder our ability to manufacture and market our products, or result in the assessment of significant monetary damages against us that may exceed amounts, if any, accrued in our consolidated financial statements.

On July 22, 2022, we filed a lawsuit against Lupin in the U.S. District Court for the District of Delaware alleging infringement of U.S. Patent Nos. 10,646,481 ("the '481 patent"), 8,883,206 ("the '206 patent"), 10,272,046 ("the '046 patent"), and 11,147,770 ("the '770 patent"). The lawsuit follows our receipt of a Notice Letter on June 9, 2022, advising that Lupin had submitted an ANDA to the FDA seeking approval to manufacture and market a generic version of KALYDECO granules in the U.S. The Notice Letter indicated that Lupin submitted a "Paragraph IV" certification to the FDA in which Lupin asserts that the '481 patent, the '206 patent, and the '046 patent are invalid or would not be infringed by Lupin's generic product. On February 28, 2023, U.S. Patent No. 11,564,916 ("the '916 patent") was listed in the Orange Book as covering KALYDECO granules. By letter dated April 25, 2023, Lupin notified us that it had amended its ANDA to include a Paragraph IV certification with respect to the '916 patent. On May 26, 2023, we filed a lawsuit against Lupin in the U.S. District Court for the District of Delaware alleging infringement of the '916 patent. On October 11, 2023, U.S. Patent No. 11,752,106 (the "'106 patent") was listed in the Orange Book as covering KALYDECO granules. By letter dated February 27, 2024, Lupin notified Vertex that it had amended its ANDA to include a Paragraph IV certification with respect to the '106 patent. On April 11, 2024, Vertex filed a lawsuit against Lupin in the U.S. District Court for the District of Delaware alleging infringement of the '106 patent. The Court subsequently entered a scheduling order, which consolidated the lawsuit asserting infringement of the '106 patent with the earlier filed lawsuits asserting infringement of the '481, '206, '046, '770, and '916 patents. A three-day trial is scheduled for September 15, 2025. Other than the '770 patent, which was listed in the Orange Book on April 14, 2022, Lupin does not appear to challenge our other U.S. patents covering KALYDECO granules, the last of which expires on August 5, 2027. Therefore, regardless of the outcome of the litigation, Lupin cannot receive final approval of its ANDA before that date. We intend to vigorously enforce our intellectual property rights relating to KALYDECO granules and the '481, '206, '046, '770, '916, and '106 patents.

CRISPR has licensed certain rights to a worldwide patent portfolio that covers various aspects of the CRISPR/Cas9 editing platform technology including, for example, compositions of matter and methods of use in targeting or cutting DNA from Dr. Emmanuelle Charpentier, one of the named inventors of this patent portfolio. The patent portfolio also has named inventors who assigned their rights to the CVC Group. For example, in connection with their collaboration, Novartis and Intellia Therapeutics, Inc. have reportedly obtained a license to this patent portfolio in certain fields. Both the CVC Group and Broad have obtained granted patents that purport to cover aspects of CRISPR/Cas9 editing platform technology. Patents and patent applications in this patent portfolio have been the subject of numerous contentious proceedings in the U.S., Europe, and other jurisdictions, including interference proceedings in the USPTO between the CVC Group and (separately) Broad, Sigma-Aldrich and ToolGen. On February 28, 2021, the USPTO issued a decision in Interference No. 106, 115, concluding that Broad invented certain applications of CRISPR/Cas9 technology in eukaryotic cells before the CVC Group. The CVC Group has appealed the decision to the U.S. Court of Appeals for the Federal Circuit. If the decision is upheld on appeal (including a potential subsequent appeal to the Supreme Court), Broad would maintain its granted patents directed to those applications CRISPR/Cas9 technology in eukaryotic cells, and the CVC Group's pending patent applications directed to that subject matter would not proceed to grant. We can give no assurances to the ultimate outcome of these proceedings or the disputes between the CVC Group and Broad, Sigma-Aldrich and ToolGen. In December 2023, we entered into an agreement with Editas, providing us a non-exclusive sublicense to certain patents relating to CRISPR/Cas9 technology owned by Broad and Harvard, which are licensed to Editas.

In addition to Broad, other third parties have filed patent applications claiming CRISPR/Cas9-related inventions and may allege that they invented one or more of the inventions claimed by the CVC Group. Thus, the USPTO may, in the future,

declare an interference between certain CVC Group patent applications and one or more patent applications. Third parties could seek to assert their patents, if issued, against us based on our CRISPR/Cas9-based activities, including commercialization. Defense of these claims, regardless of their merit, could involve substantial litigation expense and could result in a substantial diversion of management and other employee resources from our business. In the event of a successful claim of infringement against us, we may have to pay substantial damages, obtain one or more licenses from third parties, pay royalties or redesign our infringing products, which may be impossible or require substantial time and monetary expenditure. In that event, we could be unable to further develop and commercialize CASGEVY or other products that we may develop using the CRISPR/Cas9 technology we license from CRISPR.

To the extent that valid present or future third-party patents or other intellectual property rights cover our products, product candidates or technologies, we or our strategic collaborators may seek licenses or other agreements from the holders of such rights to avoid or settle legal claims. Such licenses may not be available on acceptable terms, which may hinder our ability to, or prevent us from being able to, manufacture and market our products. Payments under any licenses that we are able to obtain would reduce our profits derived from the covered products.

We may be subject to claims by third parties asserting that our employees or we have misappropriated their intellectual property, or claiming ownership of what we regard as our own intellectual property.

Many of our employees were previously employed at universities or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although we try to ensure that our employees do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that these employees or we have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such employee's former employer. Litigation may be necessary to defend against these claims.

In addition, while it is our policy to require our employees and contractors who may be involved in the development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who in fact develops intellectual property that we regard as our own. Our and their assignment agreements may not be self-executing or may be breached, and we may be forced to bring claims against third parties, or defend claims they may bring against us, to determine the ownership of what we regard as our intellectual property.

If we fail in prosecuting or defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. Even if we are successful in prosecuting or defending against such claims, litigation could result in substantial costs and be a distraction to management.

Risks Related To Our Operations

If we fail to scale our operations to accommodate growth, our business may suffer.

We have expanded and are continuing to expand our global operations and capabilities, which has placed, and will continue to place, significant demands on our management and our operational, research and development and financial infrastructure. To effectively manage our business, we need to continue to adapt as our business grows in scale and complexity across multiple disease states, modalities, and geographies, including by:

- implement and clearly communicating our corporate-wide strategies;
- enhancing our operational and financial infrastructure, including expansion of our controls over data, records and information;
- enhancing our operational, administrative, financial and management processes, including our cross-functional decision-making processes and our budget prioritization systems;
- effectively growing, training and managing our global employee base; and
- expanding our compliance and legal resources.

A variety of risks associated with operating in foreign countries could materially adversely affect our business.

We have expanded our international operations over the past several years to market our medicines and expand our research and development capabilities. New laws and industry codes in the E.U. and elsewhere have expanded transparency requirements regarding payments and transfers of value to healthcare professionals, requirements surrounding patient-level clinical trial data, the protection of personal data and increased sanctions for violations. Collectively, our expansion and these new requirements are adding to our compliance costs and potentially exposes us to sanctions in the event of an infringement or failure to report in these jurisdictions. In addition, a significant portion of our commercial supply chain, including sourcing of raw materials and manufacturing, is located in China and the E.U. Consequently, we are, and will continue to be, subject to risks related to operating in foreign countries, including risks relating to intellectual property protections and business interruptions. Risks associated with operating a global biotechnology company include:

- differing regulatory requirements for drug approvals and regulation of approved drugs in foreign countries;
- varying reimbursement regimes and difficulties or the inability to obtain reimbursement for our products in foreign countries in a timely manner;
- differing patient treatment infrastructures, particularly since our business is focused on the treatment of serious diseases that affect relatively smaller numbers of patients and are typically prescribed by specialist physicians;
- collectability of accounts receivable;
- changes in tariffs, trade barriers, and regulatory requirements, the risks of which appear to have increased in the current political environment;
- economic weakness, including recession and inflation, or political instability in particular foreign economies and markets;
- differing levels of enforcement and/or recognition of contractual and intellectual property rights;
- circulation of unauthorized copy versions of our medicines that infringe our intellectual property rights;
- governments seeking to override our intellectual property rights through the introduction of compulsory license or similar mechanisms;
- complying with local laws and regulations, which can change significantly over time;
- foreign taxes, including withholding of payroll taxes;
- foreign currency fluctuations, which could result in reduced revenues or increased operating expenses, and other obligations incident to doing business or operating in another country;
- workforce uncertainty in countries where labor unrest is more common than in the U.S.;
- reliance on third-party vendors, distributors and suppliers;
- import and export licensing requirements, tariffs, and other trade and travel restrictions;
- global or regional public health emergencies that could affect our operations or business;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad; and
- business interruptions resulting from geo-political actions, including war and terrorism.

These risks are increased with respect to countries such as China that have substantially different local laws and business practices and weaker protections for intellectual property. In particular, there is currently significant uncertainty about the future relationship between the U.S. and various other countries, including China, with respect to trade policies, treaties, tariffs, taxes, and other limitations on cross-border operations. The U.S. government has made and continues to make significant additional changes in U.S. trade policy and may continue to take future actions that could negatively impact U.S.

trade. For example, legislation has been introduced in Congress to limit certain U.S. biotechnology companies from using equipment or services produced or provided by select Chinese biotechnology companies, and others in Congress have advocated for the use of existing executive branch authorities to limit those Chinese service providers' ability to engage in business in the U.S. We cannot predict what actions may ultimately be taken with respect to trade relations between the United States and China or other countries, what products and services may be subject to such actions or what actions may be taken by the other countries in retaliation. If we are unable to obtain or use services from existing service providers or become unable to export or sell our products to any of our customers or service providers, our business could be materially and adversely affected.

Our revenues are subject to foreign exchange rate fluctuations due to the global nature of our operations. Although we have a foreign currency risk management program, our efforts to reduce currency exchange volatility may not be successful. As a result, currency fluctuations among our reporting currency, the U.S. dollar, and the currencies in which we do business will affect our operating results, often in unpredictable ways.

In addition, our international operations are subject to regulation under U.S. law. For example, the FCPA prohibits U.S. companies and their representatives from offering, promising, authorizing or making payments to foreign officials for the purpose of obtaining or retaining business abroad. In many countries, the health care professionals we regularly interact with may meet the definition of a foreign government official for purposes of the FCPA. We also are subject to import/export control laws. Failure to comply with domestic or foreign laws could result in various adverse consequences, including the possible delay in approval or refusal to approve a product, recalls, seizures, withdrawal of an approved product from the market, the imposition of civil or criminal sanctions, the prosecution of executives overseeing our international operations and corresponding bad publicity and negative perception of our company in foreign countries.

Our business has a substantial risk of product liability claims and other litigation liability.

We are or may be involved in various legal proceedings, including securities/shareholder matters and claims related to product liability, intellectual property, employment law, competition law, data privacy, and breach of contract. Such proceedings may involve claims for, or the possibility of, damages or fines and penalties involving substantial amounts of money or other relief, including civil or criminal fines and penalties. If any of these legal proceedings were to result in an adverse outcome, it could have a material adverse effect on our business.

For example, we pay royalties on certain sales of TRIKAFTA/KAFTRIO, SYMDEKO/SYMKEVI, KALYDECO, ORKAMBI and ALYFTREK pursuant to our agreement with the Cystic Fibrosis Foundation. The third-party to whom the Cystic Fibrosis Foundation has assigned rights to receive these royalty payments has made public statements related to the calculation of royalties associated with ALYFTREK. Based on the agreement between Vertex and the Cystic Fibrosis Foundation, we believe the third party is wrong. If any potential future adversarial proceedings were not resolved in our favor, however, we could be required to pay a higher royalty percentage on ALYFTREK sales than we currently expect, and our future cost of goods with respect to ALYFTREK could increase above our current expectations.

The use of our approved products and our product candidates exposes us to the risk of product liability claims. Product liability claims may be brought against us by people participating in clinical trials, patients, healthcare providers, or others selling or coming in contact with our products or our product candidates. There is a risk that our products or our product candidates may induce adverse events. For instance, the product labels for TRIKAFTA and ALYFTREK include a boxed warning regarding liver injury and liver failure. If we cannot successfully defend ourselves against product liability claims, we could incur substantial liability and costs, which could have a material adverse effect on our business or financial condition. In addition, regardless of merit or eventual outcome, product liability claims may result in:

- Decreased demand for our approved products, such as TRIKAFTA and ALYFTREK, or any product candidate for which we obtain marketing approval;
- Inability to successfully commercialize approved products;
- Impairment of our business reputation and exposure to adverse publicity;
- New or increased warnings on our product labels;
- Withdrawal of clinical trial participants;

- Costs as a result of related litigation;
- Distraction of management's attention from our primary business;
- Substantial monetary awards to patients or other claimants; and
- Loss of revenue.

We have product liability insurance and clinical trial insurance in amounts that we believe are adequate to cover this risk. However, our insurance may not provide adequate coverage against all potential liabilities. If a claim is brought against us, we might be required to pay legal and other expenses to defend the claim, as well as pay uncovered damage awards and these damages could be significant and have a material adverse effect on our financial condition. Furthermore, whether or not we are ultimately successful in defending any such claims, we might be required to direct significant financial and managerial resources to such defense and adverse publicity is likely to result.

A breakdown or breach of our information technology systems could subject us to liability or interrupt the operation of our business.

We maintain and rely extensively on information technology systems and network infrastructures for the effective operation of our business. In the course of our business, we collect, store, and transmit confidential information (including personal information and intellectual property), and it is critical that we do so in a secure manner to maintain the confidentiality, integrity, and availability of such confidential information. A disruption, infiltration, or failure of our information technology systems or any of our data centers as a result of software or hardware malfunctions, computer viruses, cyber-attacks, employee theft or misuse, power disruptions, natural disasters, floods or accidents could cause breaches of data security and loss of critical data, which in turn could materially adversely affect our business and subject us to both private and governmental causes of action. While we have implemented security measures to minimize these risks to our data and information technology systems and have adopted a business continuity plan to deal with a disruption to our information technology systems, there can be no assurance that our efforts to protect our data and information systems will prevent breakdowns or breaches in our systems that could adversely affect our business. In addition, we maintain cyber liability insurance, however, this insurance may not be sufficient to cover the financial, legal, business or reputational losses that may result from an interruption or breach of our systems and those of critical third parties.

Cyber-attacks are increasing in their frequency, sophistication, and intensity, and are becoming increasingly difficult to detect. They are often carried out by well-resourced and skilled parties, including nation states, organized crime groups, "hacktivists" and employees or contractors acting carelessly or with malicious intent. Cyber-attacks include deployment of harmful malware and key loggers, ransomware, denial-of-service attacks, malicious websites, the use of social engineering, and other means to affect the confidentiality, integrity and availability of our technology systems and data. Cyber-attacks also include manufacturing, hardware or software supply chain attacks, which could cause a delay in the manufacturing of products or products produced for contract manufacturing or lead to a data privacy or security breach. Our business partners face similar risks and when they experience a security breach of their systems, our security can be adversely affected. Similar to other companies, we have experienced immaterial cybersecurity incidents, including temporary service interruptions of third-party suppliers. In addition, our increased use of cloud technologies heightens these third party and other operational risks, and any failure by cloud or other technology service providers to adequately safeguard their systems and prevent cyber-attacks could disrupt our operations and result in misappropriation, corruption, or loss of confidential or propriety information. A significant portion of our workforce continues to leverage hybrid work. Risk of cyber-attack is increased with employees working remotely. Remote work increases the risk we may be vulnerable to cybersecurity-related events such as phishing attacks and other security threats.

We rely on third parties to carry out our operations. Failure to maintain our third-party relationships or challenges at or with these third parties could materially harm our business.

Our business depends on relationships with third parties for a variety of functions, including activities critical to supply and manufacturing, commercialization, research and development, and technology. Failure by these parties to meet their contractual, regulatory, or other obligations, or any disruption in the relationship between Vertex and these third parties, could have an adverse effect on our business. Furthermore, these third parties are subject to their own unique operational and financial risks that are out of our control. When one of our third parties encounters financial, operational, or other difficulties, our business and results of operations could be negatively affected.

If we fail to attract and retain skilled employees, our business could be materially harmed.

Due to the highly technical nature of our drug discovery and development activities, we require the services of highly qualified and trained scientists who have the skills necessary to conduct these activities. In addition, we need to attract and retain employees with experience in development, marketing and commercialization of medicines and therapies, including cell and genetic therapies. We provide stock-related compensation benefits to all of our key employees that vest over time and therefore induce them to remain with us and have entered into employment agreements with some executives. However, the employment agreements can be terminated by the executive on relatively short notice. The value to employees of stock-related benefits that vest over time can be significantly affected by movements in our stock price and business performance, and may, at any point in time, be insufficient to counteract more lucrative offers from other companies. We face intense competition for our personnel from our competitors and other companies throughout our industry, especially with respect to employees with expertise in cell or genetic therapies. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. Moreover, the growth of local biotechnology companies and the expansion of major pharmaceutical companies into the Boston area has increased competition for the available pool of skilled employees, especially in technical fields. The high cost of living can make it difficult to attract employees to our global headquarters in Boston and our international headquarters in London. Challenges could adversely affect our operations and financial results if we do not have sufficient staff to perform necessary functions. In addition, the available pool of skilled employees would be further reduced if immigration laws change in a manner that increases restrictions on immigration. Our ability to continue to commercialize our products and achieve our research and development objectives depends on our ability to respond effectively to these demands. If we are unable to hire and retain qualified personnel, there could be a material adverse effect on our business.

If our facilities were to experience a catastrophic loss, our operations would be seriously harmed.

Most of our operations, including our research and development activities, are conducted in a limited number of facilities. If any of our major facilities were to experience a catastrophic loss, due to an earthquake, flood, severe storms, fire or similar event, our operations could be seriously harmed. For example, our corporate headquarters, as well as additional leased space that we use for certain logistical and laboratory operations and manufacturing, are located in a flood zone along the Massachusetts coast. We have adopted business continuity plans to address most crises. However, if we are unable to fully implement our business continuity plans, we may experience delays in recovery of data and/or an inability to perform vital corporate functions, which could result in a significant disruption in our research, development, manufacturing and/or commercial activities, large expenses to repair or replace the facility and/or the loss of critical data, which could have a material adverse effect on our business. In addition, we maintain property insurance, however, this insurance may not be sufficient to cover all potential losses that may result from an interruption to our operations.

The use of social media platforms and artificial intelligence tools presents risks and challenges.

Social media is being used by third parties to communicate about our products and product candidates and the diseases our therapies are designed to treat. We believe that members of the communities supporting serious diseases may be more active on social media as compared to other patient populations due to the demographics of those patient populations. Social media practices in the pharmaceutical and biotechnology industries are evolving, which creates uncertainty and risk of noncompliance with regulations applicable to our business. For example, patients may use social media platforms to comment on the effectiveness of, or adverse experiences with, a product or a product candidate, which could result in reporting obligations. In addition, our employees may engage on social media in ways that may not comply with legal or regulatory requirements, which may give rise to liability, lead to the loss of trade secrets and other intellectual property, or result in public disclosure of protected personal information. There is a risk of inappropriate disclosure of sensitive information or negative or inaccurate posts or comments about us on any social networking website. Negative sentiment about us or our business shared over social media, or misinformation disseminated from fraudulent accounts impersonating our employees or our business, or otherwise, could harm our business and reputation, whether or not it is based in fact. Certain data protection regulations, such as the GDPR, apply to personal data contained on social media. If any of these events were to occur or we otherwise fail to comply with applicable regulations, we could incur liability, face regulatory actions or incur harm to our business, including damage to our reputation. Similar risks relating to inappropriate disclosure of sensitive information or inaccurate information appearing in the public domain may also apply from our employees engaging with and use of new artificial intelligence tools, such as ChatGPT.

Risks Related to Financial Results and Holding Our Common Stock

Our stock price may fluctuate.

Market prices for securities of companies such as ours are highly volatile. From January 1, 2024 to December 31, 2024, our common stock traded between $377.85 and $519.88 per share. The market for our stock, like that of other companies in the biotechnology industry, has experienced significant price and volume fluctuations. The future market price of our securities could be significantly and adversely affected by factors such as:

- the information contained in our quarterly earnings releases, including updates regarding our commercialized products or our product candidates, our net product revenues and operating expenses for completed periods and financial guidance regarding future periods;
- announcements of FDA actions with respect to our therapies or those of our competitors, or regulatory filings for our therapies or those of our competitors, or announcements of interim or final results of clinical trials or nonclinical studies relating to our therapies or those of our competitors;
- announcements we make or commentary by public equity analysts with respect to clinical development of the product candidates in our pain program;
- developments in domestic and international governmental policy or regulation, for example, relating to drug pricing and tax law changes;
- technological innovations or the introduction of new drugs by our competitors;
- government regulatory action;
- public concern as to the safety of drugs developed by us or our competitors;
- developments in patent or other intellectual property rights or announcements relating to these matters;
- information disclosed by third parties regarding our business or products;
- developments relating specifically to other companies and market conditions for pharmaceutical and biotechnology stocks or stocks in general;
- business development, capital structuring or financing activities; and
- general worldwide or national economic, political and capital market conditions, including as a result of inflation and rapid fluctuations in interest rates.

Following periods of volatility in the market price of a company's securities, stockholder derivative lawsuits and securities class action litigation are common. Such litigation, if instituted against us or our officers and directors, could result in substantial costs and a diversion of management's attention and resources.

Our effective tax rate fluctuates, and changes in tax laws, regulations and treaties, unfavorable resolution to the tax positions we have taken or exposure to additional income tax liabilities could have a material impact on our future taxable income.

Our effective tax rate is derived from a combination of applicable tax rates in the various places that we operate globally. Our effective tax rate may be different than experienced in the past due to numerous factors, including changes in the mix of our profitability from country to country, tax authority examinations/audits of our tax filings, adjustments to the value of our uncertain tax positions, changes in accounting for income taxes, and changes in tax laws or modifications of treaties in various jurisdictions. Any of these factors could cause us to experience an effective tax rate that is significantly different from previous periods or our current expectations.

Various jurisdictions in which the group operates, including the U.K. and the E.U. member states have agreed to implement the minimum tax component ("Pillar Two") of the Organization for Economic Co-operation and Development's (the "OECD's"), global international tax reform initiative that aims to reform international taxation policies and ensure that multinational companies pay taxes wherever they operate and generate profits. Although aspects of Pillar Two have been

implemented that affect accounting periods withing our group starting on or after December 31, 2023, the full impact of this initiative on our effective tax rate will depend on the timing of implementation within each country in which we operate, the exact nature of each country's implementation legislation, guidance and regulations thereon, and their application by tax authorities either prospectively or retrospectively. We are continuing to evaluate the potential impact on future periods of the Pillar Two guidance, pending legislative adoption by individual countries, including those in which we do business.

We are subject to ongoing tax audits in various jurisdictions, and local tax authorities may disagree with certain positions we have taken and assess additional taxes. We regularly assess the probable outcomes of these audits to determine the appropriateness of our tax provision, and we have established contingency reserves for material tax exposures. However, there can be no assurance that we will accurately predict the outcomes of these disputes or other tax audits or that issues raised by tax authorities will be resolved at a financial cost that does not exceed our related reserves and the actual outcomes of these disputes and other tax audits could have a material impact on our results of operations or financial condition.

Our quarterly operating results are subject to significant fluctuation.

Our operating results have fluctuated from quarter to quarter in the past, and we expect that they will continue to do so in the future. Our revenues are primarily dependent on the amount of net product revenues from sales of our CF medicines. Our total net product revenues could vary on a quarterly basis based on, among other factors, the timing of orders from our significant customers. Additional factors that have caused quarterly fluctuations to our operating results in recent years include variable amounts of revenues; expenses resulting from our significant investments in research and development, acquired in-process research and development, and commercialization activities; changes in the fair values of our strategic investments, and contingent consideration liabilities; charges for excess and obsolete inventories; and our provision for income taxes. Our revenues also are subject to foreign exchange rate fluctuations due to the global nature of our operations. Although we have a foreign currency risk management program, our efforts to reduce currency exchange volatility may not be successful. As a result, currency fluctuations among our reporting currency, the U.S. dollar, and the currencies in which we do business may affect our operating results, often in unpredictable ways. Our quarterly results also could be materially affected by significant charges, which may or may not be similar to charges we have experienced in the past. Most of our operating expenses relate to our research and development activities, do not vary directly with the amount of revenues and are difficult to adjust in the short term. As a result, if revenues in a particular quarter are below expectations, we are unlikely to reduce operating expenses proportionately for that quarter. These examples are only illustrative and other risks, including those discussed in these "Risk Factors," could also cause fluctuations in our reported financial results. Our operating results during any one period do not necessarily suggest the results of future periods.

We expect that results from our clinical development activities and the clinical development activities of our competitors will continue to be released periodically, and may result in significant volatility in the price of our common stock.

Any new information regarding our products and product candidates, or competitive products or potentially competitive product candidates, can substantially affect investors' perceptions regarding our future prospects. We, our collaborators, and our competitors periodically provide updates regarding drug and therapy development programs, typically through press releases, conference calls and presentations at medical conferences. These periodic updates often include interim or final results from clinical trials conducted by us or our competitors and/or information about our or our competitors' expectations regarding regulatory filings and submissions as well as future clinical development of our products or product candidates, competitive products or potentially competitive product candidates. The timing of the release of information by us regarding our drug and therapy development programs is often beyond our control and is influenced by the timing of receipt of data from our clinical trials and by the general preference among pharmaceutical companies to disclose clinical data during medical conferences. In addition, the information disclosed about our clinical trials, or our competitors' clinical trials, may be based on interim rather than final data that may involve interpretation difficulties and may in any event not accurately predict final results. The release of such information may result in volatility in the price of our common stock.

General Risk Factors

Future indebtedness could materially and adversely affect our financial condition, and the terms of our credit agreements impose restrictions on our business, reducing our operational flexibility and creating default risks.

In July 2022, we entered into a credit agreement providing for a $500.0 million revolving credit facility. If we borrow under our current credit agreement or any future credit agreements, such indebtedness could have important consequences to our business, including increasing our vulnerability to general adverse financial, business, economic and industry conditions,

as well as other factors that are beyond our control. The credit agreement requires that we comply with certain financial covenants, including a consolidated leverage ratio covenant. Further, the credit agreement includes negative covenants, subject to exceptions, restricting or limiting our ability and the ability of our subsidiaries to, among other things, incur additional indebtedness, grant liens, engage in certain investment, acquisition and disposition transactions, and enter into transactions with affiliates. As a result, we may be restricted from engaging in business activities that may otherwise improve our business. Failure to comply with the covenants could result in an event of default that could trigger acceleration of our indebtedness, which would require us to repay all amounts owed under the credit agreements and/or our finance leases and could have a material adverse effect on our business. Additionally, our obligations under the credit agreement are unconditionally guaranteed by certain of our domestic subsidiaries. If we incur additional indebtedness, the risks related to our business and our ability to service or repay our indebtedness would increase.

Issuances of additional shares of our common stock could cause the price of our common stock to decline.

As of December 31, 2024, we had 256.9 million shares of common stock issued and outstanding. As of December 31, 2024, we also had 2.7 million unvested restricted stock units ("RSUs"), 0.9 million unvested performance stock units ("PSUs") at target, and outstanding options to purchase 1.6 million shares of common stock with a weighted-average exercise price of $156.36 per share.

The majority of our unvested RSUs are likely to vest based on our employees' continued employment. The number of PSUs that vest is dependent on a potential range of shares issuable pursuant to certain financial and non-financial milestones, and our employees' continued employment. Outstanding vested options are likely to be exercised if the market price of our common stock exceeds the applicable exercise price.

In addition, we may issue additional common stock or restricted securities in the future as part of financing activities or business development activities and any such issuances may have a dilutive effect on our then-existing shareholders. Sales of substantial amounts of our common stock in the open market, or the availability of such shares for sale, could adversely affect the price of our common stock. The issuance of restricted common stock or common stock upon exercise of any outstanding options would be dilutive, and may cause the market price for a share of our common stock to decline.

There can be no assurance that we will repurchase shares of common stock or that we will repurchase shares at favorable prices.

In February 2023, our Board of Directors approved a share repurchase program pursuant to which we are authorized to repurchase up to $3.0 billion of our common stock from time to time through open market or privately negotiated transactions, of which $1.6 billion has been repurchased as of December 31, 2024. Our stock repurchases will depend upon, among other factors, market conditions, our cash balances and potential future capital requirements, results of operations, financial condition, and other factors that we may deem relevant. We can provide no assurance that we will repurchase stock at favorable prices, if at all.

We have adopted provisions in our articles of organization and by-laws and are subject to Massachusetts corporate laws that may frustrate any attempt to remove or replace members of our board or to effectuate certain types of business combinations involving us.

Provisions of our articles of organization, by-laws and Massachusetts state laws may frustrate any attempt to remove or replace members of our current Board of Directors and may discourage certain types of business combinations involving us. Our by-laws allow the Board of Directors to adjourn any meetings of shareholders prior to the time the meeting has been convened. We may issue shares of any class or series of preferred stock in the future without shareholder approval and upon such terms as our Board of Directors may determine. The rights of the holders of common stock will be subject to, and may be adversely affected by, the rights of the holders of any class or series of preferred stock that may be issued in the future. Massachusetts state law also prohibits us from engaging in specified business combinations with an interested stockholder, subject to certain exceptions, unless the combination is approved or consummated in a prescribed manner, and places restrictions on voting by any shareholder who acquires 20% or more of the aggregate shareholder voting power without approval by non-interested shareholders. As a result, shareholders or other parties may find it difficult to remove or replace our directors or to effectuate certain types of business combinations involving us.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K, including the descriptions of our Business set forth in Part I, Item 1, our Risk Factors set forth in Part I, Item 1A, and our Management's Discussion and Analysis of Financial Condition and Results of Operations set forth in Part II, Item 7, contains forward-looking statements. Forward-looking statements are not purely historical and may be 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 relate to:

- our expectations regarding the amount of, timing of, and trends with respect to our financial performance, including revenues, costs and expenses, and other gains and losses;
- our expectations regarding clinical trials, including expectations for patient enrollment, development timelines, the expected timing of data from our ongoing and planned clinical trials, and regulatory authority filings and other submissions for our therapies;
- our beliefs, expectations, and plans with respect to the commercial 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;
- our ability to maintain and obtain adequate reimbursement for our products and product candidates, our ability to launch, commercialize and market our products or any of our other therapies for which we obtain regulatory approval, and our ability to obtain label expansions for existing therapies;
- our expectations regarding our ability to continue to grow our CF business by increasing the number of people with CF eligible and able to receive our medicines and providing improved treatment options for people who are already eligible for one of our medicines;
- the data that will be generated by ongoing and planned clinical trials and the ability to use that data to advance compounds, continue development, 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 and from Part B of the ongoing clinical trial evaluating VX-264 in patients with T1D, and our plans to file for accelerated regulatory approvals based on interim analyses from the AMPLITUDE study in AMKD and the RAINIER study in IgAN;
- our beliefs that ALYFTREK will provide additional clinical benefits to eligible people with CF, regarding the durable efficacy and effectiveness of CASGEVY as one-time functional cure for people with SCD and TDT, and regarding the clinical benefits of JOURNAVX without the evidence of the limitations of other available therapies;
- our beliefs regarding the support provided by clinical trials and preclinical and nonclinical studies of our therapies for further investigation, clinical trials or potential use as a treatment;
- our plans to continue investing in our research and development programs, including anticipated timelines for our programs, and our strategy to develop our pipeline programs, alone or with third party-collaborators;
- our beliefs regarding the approximate patient populations for the disease areas on which we focus;
- the potential benefits and therapeutic scope of our acquisitions and collaborations, including our acquisition of Alpine and its lead asset, povetacicept, its potential to become a pipeline-in-a-product, and our expectations regarding the Zai collaboration;
- our expectations regarding the lower royalty burden for ALYFTREK;
- our plans to expand, strengthen, and invest in our global supply chains and manufacturing infrastructure and capabilities, including for biologic and cell and gene therapies;
- potential business development activities, including the identification of potential collaborative partners or acquisition targets;
- our ability to expand and protect our intellectual property portfolio and otherwise maintain exclusive rights to products;
- the establishment, development and maintenance of collaborative relationships, including potential milestone payments or other obligations;
- potential fluctuations in foreign currency exchange rates and the effectiveness of our foreign currency management program;
- our expectations regarding the amount of cash to generated by operations, our cash balance and expected generation and interest income;

- our expectations regarding our provision for or benefit from income taxes and the utilization of our deferred tax assets;
- our ability to use our research programs to identify and develop new product candidates to address serious diseases and significant unmet medical needs;
- the effectiveness of our governance, plans and strategy with respect to managing cybersecurity risks and other threats to our information technology systems;
- our ability to attract and retain skilled personnel;
- our expectations involving governmental cost containment and other regulatory efforts;
- our expectations surrounding the competitive landscape facing our products and product candidates; and
- our liquidity and our expectations regarding the possibility of raising additional capital.

Forward-looking statements are subject to certain risks, uncertainties, or other factors that are difficult to predict and could cause actual events or results to differ materially from those indicated in any such statements. These risks, uncertainties, and other factors include, but are not limited to, those described in our Risk Factors, set forth in Part I, Item 1A, and elsewhere in this report and those described from time to time in our future reports filed with the Securities and Exchange Commission.

Any such forward-looking statements are made on the basis of our views and assumptions as of the date of the filing and are not estimates of future performance. Except as required by law, we undertake no obligation to publicly update any forward-looking statements. The reader is cautioned not to place undue reliance on any such statements.

ITEM 1B. UNRESOLVED STAFF COMMENTS

We did not receive any written comments from the Securities and Exchange Commission prior to the date 180 days before the end of the fiscal year ended December 31, 2024 regarding our filings under the Securities Exchange Act of 1934, as amended, that have not been resolved.

ITEM 1C. CYBERSECURITY

Risk Management and Strategy

We recognize the critical importance of developing, implementing, and maintaining robust cybersecurity measures to maintain the security, confidentiality, integrity, and availability of our business systems and confidential information, including personal information and intellectual property. Our cybersecurity program includes systems and processes for assessing, identifying and managing material risks from cybersecurity threats and include maintenance and monitoring of information security policies aligned with global regulatory controls and aligned with National Institute of Standards and Technology Cybersecurity Framework; user and employee awareness of cyber policies and practices; information systems configuration management; third-party risk management systems; identity and information asset protection; infrastructure security systems; and cyber threat operations with continuous monitoring and threat hunting. This program includes processes to oversee and identify material risks from cybersecurity threats associated with our use of third-party service providers. We also engage a range of third-party experts in connection with various development, implementation, and maintenance activities related to our cybersecurity program, including audit and compliance, threat hunting, monitoring, and end-user support.

Our cybersecurity program is integrated into our overall risk management systems, including our annual enterprise risk management program, internal audit program, business continuity and crisis management programs, third-party risk management program, insurance risk management program, and employee compliance programs. As part of our overall risk management program, we maintain a global insurance portfolio with comprehensive cyber coverage. Our Chief Information Security Officer (“CISO”) and the Information Security function advises, consults with, or provides input to each of these programs to ensure that material risks from cybersecurity threats are appropriately assessed, identified, and managed.

As of the date of this report, there have been no cybersecurity threats that have materially affected or are reasonably likely to materially affect our business, operations, or financial condition. Similar to other companies, we have experienced cybersecurity incidents, including temporary service interruptions of third-party suppliers. As of the date of this report, however, known cybersecurity incidents, individually or in aggregate, have not had a material impact on our company. Over the last three years, net expenses incurred from any information security breaches, including any penalties and settlements, are not material relative to our total revenue. For additional discussion on cybersecurity risks we face, see Item 1.A Risk Factors — *A breakdown or breach of our information technology systems could subject us to liability or interrupt the operation of our business*.

Governance

While our board of directors has oversight responsibility for risk management generally, the Audit and Finance Committee ("Audit Committee") is specifically responsible for overseeing our cybersecurity risk management program to ensure that cybersecurity risks are identified, assessed, managed, and monitored. Our CISO provides quarterly updates to the Audit Committee in this regard, and covers the state of our cybersecurity program, supported by key performance indicators across the range of cybersecurity functions related to risk management and governance, identity and information asset protection, core security and endpoint security, and cyber threat operations. These updates include descriptions of cybersecurity incidents of interest, including those associated with our third-party service providers; the board will be informed promptly of material risks from cybersecurity threats.

We strive to create a culture of cybersecurity resilience and awareness and believe that cybersecurity is the responsibility of every employee and contractor. At the same time, primary responsibility for assessing, monitoring, and managing our cybersecurity risks lies with our CISO, Michael Daly, who has more than 35 years of experience in security and information systems and spent 25 years with Raytheon Technologies, most recently as Chief Technology Officer of Cybersecurity, Special Missions, Training & Services. Our CISO supported the U.S. President's National Security Telecommunications Advisory Committee for more than 20 years, is a member of the Massachusetts Cybersecurity Strategy Council, and previously served as Chair of the Kogod Cybersecurity Governance Center at American University. He also served on the Rhode Island Homeland Security Advisory Board and was a member of various commercial cyber product councils.

Our CISO oversees a team of skilled cybersecurity professionals who have Certified Information Systems Security Professional ("CISSP") credentials, Global Information Assurance Certification from the SANS Institute, and other security and network certifications. The cybersecurity team monitors and evaluates our cybersecurity posture and performance on an ongoing basis, including through regular vulnerability scans, penetration tests, and threat intelligence feeds. The cybersecurity team uses various tools and methodologies to manage cybersecurity risk that are tested on a regular cadence, and assesses and evaluates cybersecurity incidents, escalating certain cybersecurity incidents to the CISO according to protocol. The CISO is continually informed regarding the performance of the cybersecurity program, as well as the latest developments in cybersecurity, including potential threats and innovative risk management techniques aligned with industry standards. The CISO reports to our Chief Scientific Officer ("CSO"). Our CSO is an executive officer and leads internal research and external innovation, corporate data strategy, technology and data sciences, and reports directly to our CEO.

ITEM 2. PROPERTIES

Corporate Headquarters

We lease approximately 1.1 million square feet of office and laboratory space at our corporate headquarters in Boston, Massachusetts in two buildings pursuant to two leases that we entered into in May 2011 and amended in August 2024 to, among other terms, extend the lease termination dates from December 2028 to June 2044. We have the option to extend the term of the leases for up to two additional ten-year periods.

Additional United States and Worldwide Locations

In addition to our corporate headquarters, we lease an aggregate of approximately 850,000 square feet of space globally. This space includes logistical, laboratory, commercial and manufacturing operations, as well as laboratory and office space to support our research and development organizations. We also own approximately 213,000 square feet at our continuous manufacturing facility in Massachusetts.

ITEM 3. LEGAL PROCEEDINGS

We are not currently subject to any material legal proceedings.

ITEM 4. MINE SAFETY DISCLOSURES

Not applicable.

PART II

ITEM 5. MARKET FOR REGISTRANT'S COMMON EQUITY, RELATED STOCKHOLDER MATTERS AND ISSUER PURCHASES OF EQUITY SECURITIES

Market Information

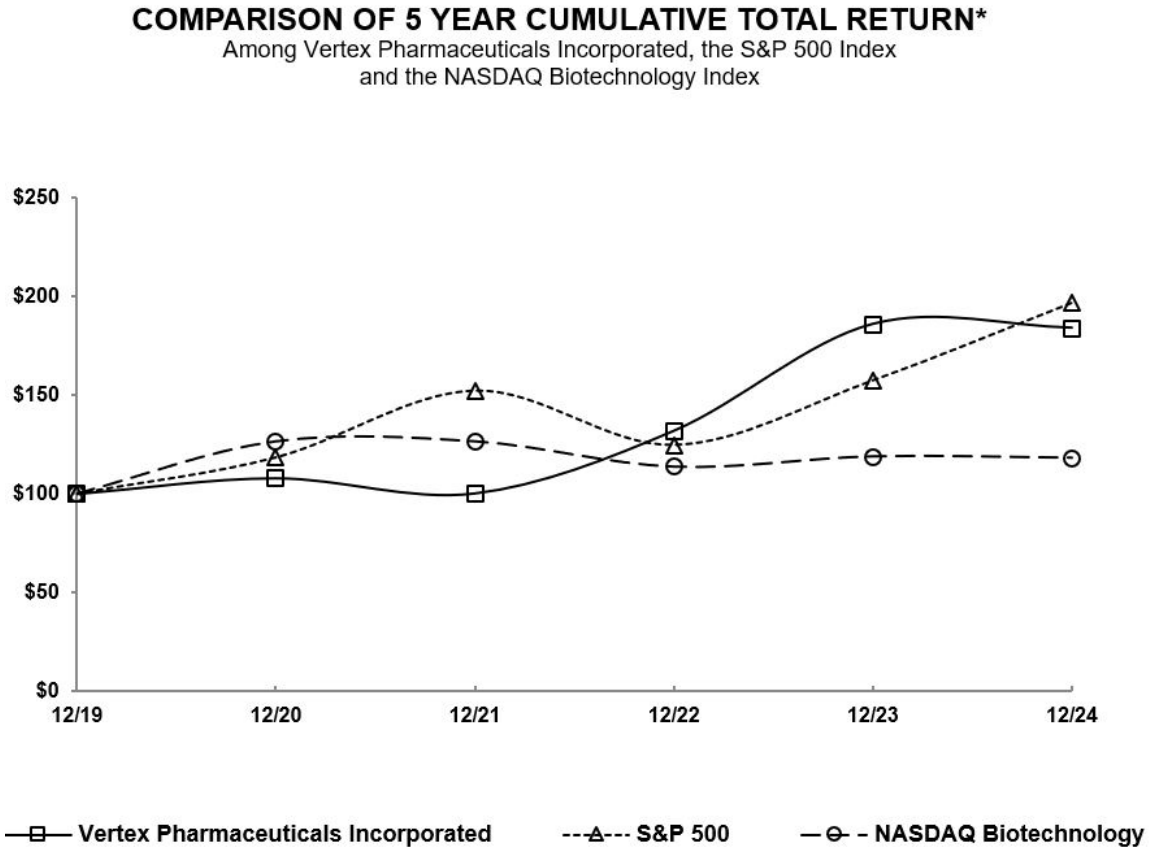
Our common stock is traded on The Nasdaq Global Select Market under the symbol "VRTX."

Shareholders

As of February 7, 2025, there were 101 holders of record of our common stock.

Performance Graph

Our performance graph includes the NASDAQ Biotechnology Index, which we believe is a comparable index consisting of companies with similar industry classifications, and which we plan to use in our future performance graphs.



Dividends

We have never paid any cash dividends on our common stock, and we do not anticipate paying any in the foreseeable future.

Issuer Repurchases of Equity Securities

In February 2023, our Board of Directors approved a share repurchase program (the "Share Repurchase Program") pursuant to which we are authorized to repurchase up to $3.0 billion of our common stock. Our Share Repurchase Program does not have an expiration date and can be discontinued at any time. The table set forth below shows repurchases of securities by us during the three months ended December 31, 2024 under our Share Repurchase Program.

Period	Total Number of Shares Purchased	Average Price Paid per Share	Total Number of Shares Purchased as Part of Publicly Announced Programs (1)	Approximate Dollar Value of Shares that May Yet Be Purchased Under the Programs (1)
Oct. 1, 2024 to Oct. 31, 2024	230,000	$ 472.77	230,000	$ 1,699,865,374
Nov. 1, 2024 to Nov. 30, 2024	221,000	$ 471.15	221,000	$ 1,595,740,301
Dec. 1, 2024 to Dec. 31, 2024	510,129	$ 420.46	510,129	$ 1,381,251,940
Total	961,129	$ 444.63	961,129	$ 1,381,251,940

(1) Under our Share Repurchase Program, we are authorized to purchase shares from time to time through open market or privately negotiated transactions. Such purchases may be made pursuant to Rule 10b5-1 plans or other means as determined by our management and in accordance with the requirements of the Securities and Exchange Commission.

ITEM 6. [RESERVED]

ITEM 7. MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

Our discussion and analysis of our financial condition and results of operations for 2024 as compared to 2023 are discussed below. For a discussion of our financial condition and results of operations for 2023 as compared to 2022, please refer to Item 7, "Management's Discussion and Analysis of Financial Condition and Results of Operations" in our 2023 Annual Report on Form 10-K, except as set forth below.

OVERVIEW

We are a global biotechnology company that invests in scientific innovation to create transformative medicines for people with serious diseases, with a focus on specialty markets. We have seven approved medicines: five that treat the underlying cause of cystic fibrosis ("CF"), a life-threatening genetic disease, one that treats severe sickle cell disease ("SCD") and transfusion dependent beta thalassemia ("TDT"), life shortening inherited blood disorders, and one that treats moderate-to-severe acute pain. Our clinical-stage pipeline includes programs in CF, SCD, beta thalassemia, acute and peripheral neuropathic pain, APOL1-mediated kidney disease, IgA nephropathy and other autoimmune renal diseases and cytopenias, type 1 diabetes, myotonic dystrophy type 1, and autosomal dominant polycystic kidney disease.

In December 2024, the U.S. Food and Drug Administration (the "FDA") approved ALYFTREK (vanzacaftor/tezacaftor/deutivacaftor), our once-daily next-in-class triple combination for the treatment of people with CF 6 years of age and older, and our fifth CF medicine. Collectively, our five medicines, led by TRIKAFTA/KAFTRIO (elexacaftor/tezacaftor/ivacaftor and ivacaftor), are being used to treat nearly three quarters of the approximately 94,000 people with CF in the U.S., Europe, Australia, and Canada. Through approvals of new medicines, label expansions, and expanded reimbursement, we are focused on increasing the number of people with CF who are eligible and able to receive our medicines. In December 2024, the FDA approved the expanded use of TRIKAFTA for the treatment of people with CF 2 years of age and older who have at least one F508del mutation in the cystic fibrosis transmembrane conductance regulator ("CFTR") gene or a mutation that is responsive to TRIKAFTA. With this approval, 94 additional non-F508del CFTR mutations have been added to the TRIKAFTA label, and approximately 300 additional people with CF in the U.S. are now eligible for TRIKAFTA. In addition, we are evaluating our CF medicines in additional patient populations, including younger children, with the goal of having small molecule treatments for all people who have at least one mutation in their CFTR gene that is responsive to our CFTR modulators. We also are pursuing messenger ribonucleic acid ("mRNA") and 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.

CASGEVY (exagamglogene autotemcel), our ex-vivo, non-viral CRISPR/Cas9 gene-edited cell therapy, is approved in the U.S., the European Union ("E.U."), the United Kingdom ("U.K."), the Kingdom of Saudi Arabia ("Saudi Arabia"), the Kingdom of Bahrain ("Bahrain"), the United Arab Emirates (the "UAE"), Switzerland and Canada for the treatment of people 12 years of age and older with SCD or TDT. We estimate approximately 60,000 people with severe SCD or TDT are or could become eligible for CASGEVY in the U.S., Canada, Europe, Saudi Arabia, and Bahrain.

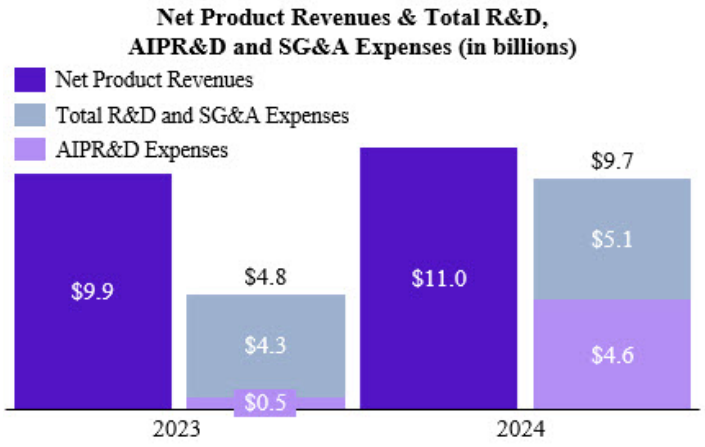
In January 2025, the FDA approved JOURNAVX, our selective non-opioid NaV1.8 pain signal inhibitor, for the treatment of people with moderate-to-severe acute pain. We have begun our commercial launch of JOURNAVX in the U.S. for eligible adults. In addition, we are enrolling and dosing patients in a Phase 3 clinical trial evaluating suzetrigine for the treatment of diabetic peripheral neuropathy, a common form of peripheral neuropathic pain. In December 2024, we announced Phase 2 clinical trial results showing that treatment with suzetrigine demonstrated a statistically significant and clinically meaningful within-group reduction in pain on the numeric pain rating scale for people with lumbosacral radiculopathy ("LSR"), a form of peripheral neuropathic pain. The clinical trial also included a placebo reference arm, which showed a similar within-group reduction. Suzetrigine was safe and generally well-tolerated in the Phase 2 clinical trial. 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. We plan to advance suzetrigine into pivotal development in LSR, pending discussions with regulators on trial design and the regulatory package.

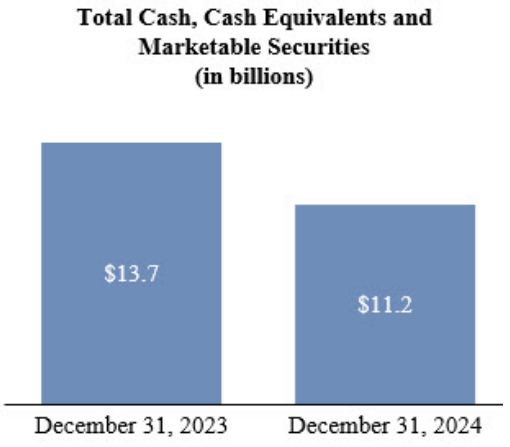
Financial Highlights

Revenues In 2024, our net product revenues increased to $11.0 billion as compared to $9.9 billion in 2023, primarily due to increased TRIKAFTA/KAFTRIO product revenues resulting from strong performance and demand globally, including expansions into younger age groups and label extensions, and higher net realized pricing in the U.S.

Expenses Our total research and development ("R&D"), and selling, general and administrative ("SG&A") expenses increased to $5.1 billion in 2024 as compared to $4.3 billion in 2023, primarily due to continued investment to support additional therapies in mid-to-late stage development and increased commercial investments to support launches of our therapies globally. In 2024, total acquired in-process research and development expenses ("AIPR&D") of $4.6 billion included $4.4 billion related to our acquisition of Alpine Immune Sciences, Inc. ("Alpine"). Cost of sales were 14% of our net product revenues in 2024 as compared to 13% in 2023, with the increase primarily due to costs associated with CASGEVY.

Cash Our total cash, cash equivalents and marketable securities decreased to $11.2 billion as of December 31, 2024 as compared to $13.7 billion as of December 31, 2023 primarily due to cash paid to acquire Alpine and repurchases of our common stock, partially offset by cash flows provided by other operating activities.





Note: Charts above may not add due to rounding.

Business Updates

Marketed Products

Cystic Fibrosis

We expect to grow our CF business by increasing the number of people with CF who are eligible and able to receive our medicines. We have revised estimates for the number of people with CF in the U.S., Europe, Australia, and Canada from approximately 92,000 to approximately 94,000 people. 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.

Recent progress in activities expanding our CF business is included below:

- In December 2024, the FDA approved ALYFTREK (vanzacaftor/tezacaftor/deutivacaftor), the once-daily next-in-class 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 mutation in the CFTR gene that is responsive to ALYFTREK, which includes a total of 303 CFTR mutations. Regulatory submissions for ALYFTREK, including in the U.K., the E.U., Canada, Switzerland, Australia, and New Zealand, are currently under review.

- 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. We have also submitted regulatory applications to the European Medicines Agency ("EMA") for TRIKAFTA/KAFTRIO for the treatment of people with CF and rare responsive 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 reimbursed in all 27 countries of the E.U.

Sickle Cell Disease and Beta Thalassemia

- 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. We expect significant growth in the number of new patients initiating cell collection throughout 2025.
- 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 with NHS England for eligible people with TDT to access CASGEVY.
- 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. We are working to secure broad stocking agreements for JOURNAVX with national retail pharmacies and regional pharmacy chains. We expect to begin shipping JOURNAVX to pharmacies nationwide by the end of February, with retail availability beginning shortly thereafter.
- We expect that JOURNAVX will be qualified for the add-on payment under the Non-Opioids Prevent Addiction in the Nation ("NOPAIN") Act, which provides for a separate payment in the hospital outpatient or surgical center setting for FDA-approved non-opioid treatments for pain.

Pipeline

We continue to advance a diversified pipeline of potentially transformative medicines for serious diseases utilizing a range of modalities. Recent and anticipated progress in activities supporting these efforts is included below:

Cystic Fibrosis

- We are enrolling and dosing in 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.
- In collaboration with Moderna, Inc. ("Moderna"), we are developing VX-522, a CFTR mRNA therapeutic for the treatment of people with CF who do not produce full-length CFTR protein. The multiple ascending dose portion of the Phase 1/2 clinical trial for VX-522 is underway, with data expected in the first half of 2025. In the U.S., the FDA has granted Fast Track designation for VX-522.
- We continue to advance new oral small molecule combination therapies through preclinical and clinical development with the aim of achieving normal levels of CFTR function. The most advanced of the next generation of CFTR modulators have completed, or are in the process of completing, Phase 1 clinical trials. We also are investigating additional potential treatments for people with CF who do not make full-length CFTR protein and cannot benefit from CFTR modulators.

Sickle Cell Disease and Beta Thalassemia

- We have completed enrollment of children 5 to 11 years of age with SCD or TDT in two global Phase 3 clinical trials evaluating CASGEVY, and we expect to complete dosing of this age group in 2025.
- We continue to advance preclinical assets for myeloablative conditioning agents that would have milder side-effects and could be used in connection with CASGEVY, which could broaden the eligible patient population.

Acute Pain

- We are enrolling and dosing patients in a Phase 2 clinical trial evaluating an oral formulation of VX-993, a next-generation selective NaV1.8 pain signal inhibitor, for the treatment of moderate-to-severe acute pain following bunionectomy surgery.
- We are enrolling and dosing healthy volunteers in a Phase 1 clinical trial evaluating an intravenous formulation of VX-993.
- The FDA has granted Fast Track Designation to VX-993 in moderate-to-severe acute pain in both the oral and intravenous formulations.
- We are advancing multiple NaV1.7 inhibitors, including in combination with NaV1.8 inhibitors, through research and earlier stages of development for both acute and peripheral neuropathic pain.

Peripheral Neuropathic Pain

- A Phase 3 clinical trial evaluating suzetrigine is enrolling and dosing patients with diabetic peripheral neuropathy, a common form of peripheral neuropathic pain. The FDA has granted suzetrigine Breakthrough Therapy designation in diabetic peripheral neuropathy.
- In December 2024, we announced Phase 2 clinical trial results for suzetrigine as a treatment for LSR, a form of peripheral neuropathic pain. The clinical trial met its primary endpoint, but the suzetrigine arm did not separate from the placebo reference arm. We plan to initiate a Phase 3 clinical trial evaluating suzetrigine in LSR, pending discussions with regulators on the regulatory package and optimized trial design.
- We are enrolling and dosing patients in a Phase 2 clinical trial evaluating the oral formulation of VX-993, a next generation NaV1.8 pain signal inhibitor, for the treatment of diabetic peripheral neuropathy.

APOL1-Mediated Kidney Disease

- Inaxaplin is our small molecule for the treatment of APOL1-mediated kidney disease (“AMKD”). We continue to enroll and dose people with AMKD in the Phase 3 portion of the global Phase 2/3 pivotal clinical trial (“AMPLITUDE”). We expect to complete enrollment in the interim analysis cohort in 2025 and apply for potential accelerated approval in the U.S., assuming a positive interim analysis.
- We initiated a Phase 2 proof-of-concept clinical trial (“AMPLIFIED”) evaluating inaxaplin as a treatment for people with AMKD and diabetes or other co-morbidities who are not currently eligible for the AMPLITUDE Phase 2/3 pivotal trial.
- The FDA granted Breakthrough Therapy designation to inaxaplin for APOL1-mediated focal segmental glomerulosclerosis (“FSGS”) and the EMA granted Orphan Drug and PRIME designations to inaxaplin for AMKD.

IgA Nephropathy and Other B Cell-Mediated Diseases

- In May 2024, we acquired Alpine, whose lead compound was povetacicept, a dual inhibitor of B cell activating factor (“BAFF”) and a proliferation-inducing ligand (“APRIL”) pathways. We are developing povetacicept as a potentially best-in-class approach to treat immunoglobulin A (“IgA”) nephropathy (“IgAN”), a serious progressive, autoimmune kidney disease that can lead to end-stage renal disease.
- We are enrolling and dosing patients in the U.S., Europe and Asia in our global pivotal Phase 3 trial evaluating povetacicept in people with IgAN (“RAINIER”). The trial is designed to have a pre-planned interim analysis

evaluating the change from baseline in urine protein creatinine ratio ("UPCR") after a certain number of patients reach 36 weeks of treatment. If positive, the interim analysis may serve as the basis for seeking accelerated approval in the U.S. Final analysis will occur at two years of treatment, with a primary endpoint of total eGFR slope through Week 104. We expect to complete enrollment in the interim analysis cohort in 2025 and apply for potential accelerated approval in the U.S., assuming a positive interim analysis.

- We are evaluating povetacicept as a potential treatment for additional B cell-mediated renal diseases in the RUBY-3 basket trial and hematologic conditions in the RUBY-4 basket trial. Both of these trials are ongoing, and we expect data in some of these conditions in 2025.

Type 1 Diabetes

- Zimislecel is an allogeneic stem cell-derived, fully differentiated, insulin-producing islet cell replacement therapy, using standard immunosuppression to protect the implanted cells. We are evaluating zimislecel as a potential treatment for type 1 diabetes ("T1D") in a sequential, three-part Phase 1/2 clinical trial. 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 potential approval after patients have completed one year of insulin-free follow-up. In addition, we have initiated a clinical trial evaluating zimislecel in people with T1D who have had a kidney transplant.

- Our second program in T1D evaluates VX-264, which encapsulates zimislecel in a novel device designed to eliminate the need for immunosuppression. The Phase 1/2 clinical trial is evaluating the safety, tolerability and efficacy of VX-264. We have completed Part A of this clinical trial and we are enrolling and dosing people with TID in Part B of the clinical trial, where patients receive the full-target dose with a stagger period between patients. Part C will dose at a full target dose without a stagger between patients. We expect to share Part B full-dose data from this clinical trial in 2025.

- Our hypoimmune islet cell program uses CRISPR/Cas9 technology to gene-edit the same allogeneic stem cell-derived, fully differentiated islets used in the zimislecel and VX-264 programs. The goal is to cloak the cells from the immune system to explore another possible path to eliminate the need for immunosuppressive therapy. This program continues to progress through the research stage. We are also pursuing alternative approaches to immunosuppression that could be used with zimislecel.

Myotonic Dystrophy Type 1

- Our lead approach for myotonic dystrophy type 1 ("DM1"), VX-670, was in-licensed from Entrada Therapeutics, Inc. ("Entrada"). VX-670 is an oligonucleotide connected to a cyclic peptide to promote effective delivery into cells, which holds the potential to address the underlying cause of DM1.

- We completed the single ascending dose portion of the global Phase 1/2 clinical trial for VX-670 in people with DM1. We are 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 evaluating VX-407 in healthy volunteers, 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 PKD1 variants. In 2025, we expect to advance VX-407 into a Phase 2 proof-of-concept clinical trial in people with ADPKD.

External Innovation

Recent investments in external innovation are included below.

- In January 2025, we entered into a collaboration agreement with Zai Lab Limited ("Zai") for the development and commercialization of povetacicept in mainland China, Hong Kong SAR, Macau SAR, Taiwan region and Singapore. Under this collaboration, Zai will help advance the povetacicept clinical trials, make the regulatory submissions in these territories, and will be responsible for commercialization activities in these territories, if povetacicept becomes an approved product.

- In December 2024, we entered into a strategic collaboration and license agreement with Orna Therapeutics ("Orna") to utilize Orna's novel and proprietary lipid nanoparticle delivery solutions to enhance our efforts in developing next generation gene-editing therapies for patients with SCD and TDT.

Our Business Environment

In 2024, our net product revenues came primarily from the sale of our medicines for the treatment of CF. Our CF strategy involves continuing to develop and obtain approval and reimbursement for treatment regimens that will provide benefits to all people with CF and increasing the number of people with CF eligible and able to receive our medicines. We are continuing to progress commercialization of CASGEVY, which has received marketing approvals in the U.S., the E.U., the U.K., Saudi Arabia, Bahrain, the UAE, Switzerland and Canada for the treatment of SCD and TDT. In addition, we have begun our commercial launch of JOURNAVX for the treatment of acute pain, which received marketing approval in the U.S. in January 2025. We also continue to advance our pipeline of product candidates for the treatment of serious diseases outside of CF, SCD, TDT, and acute pain.

Our strategy is to combine transformative advances in the understanding of causal human biology and the science of therapeutics to discover and develop innovative medicines. This approach includes advancing multiple compounds or therapies from each program, spanning multiple modalities, into early clinical trials to obtain patient data that can inform selection of the most promising therapies for later-stage development, as well as to inform discovery and development efforts. We aim to rapidly follow our first-in-class therapies that achieve proof-of-concept with potential best-in-class candidates to provide durable clinical and commercial success.

In pursuit of new product candidates and therapies in specialty markets, we invest in research and development. We believe that pursuing research in diverse areas allows us to balance the risks inherent in product development and may provide product candidates that will form our pipeline in future years. To supplement our internal research programs, we acquire technologies and programs and collaborate with biopharmaceutical and technology companies, leading academic research institutions, government laboratories, foundations and other organizations, as needed, to advance research in our areas of therapeutic interest and to access technologies needed to execute on our strategy.

Discovery and development of a new pharmaceutical or biological product is a difficult and lengthy process that requires significant financial resources along with extensive technical and regulatory expertise. Across the industry, most potential drug or biological products never progress into development, and most products that do advance into development never receive marketing approval. Our investments in product candidates are subject to considerable risks. We closely monitor our research and development activities, and frequently evaluate our pipeline programs in light of new data and scientific, business and commercial insights, with the objective of balancing risk and potential. This process can result in rapid changes in focus and priorities as new information becomes available and as we gain additional understanding of our ongoing programs and potential new programs, as well as those of our competitors.

Our business also requires ensuring appropriate manufacturing and supply of our products. As we advance our product candidates through clinical development toward commercialization and market and sell our approved products, we build and maintain our supply chain and quality assurance resources. We rely on a global network of third parties, including some in China, and our internal capabilities to manufacture and distribute our products for commercial sale and post-approval clinical trials and to manufacture and distribute our product candidates for clinical trials. In addition to establishing supply chains for each new approved product, we adapt our supply chain for existing products to include additional formulations or to increase scale of production for existing products as needed. Our foreign third-party manufacturers and suppliers may be subject to U.S. legislation, including the BIOSECURE Act, sanctions, trade restrictions and other foreign regulatory requirements which could increase costs or reduce the supply of material available to us, or delay the procurement or supply of such material. The processes for biological and cell and genetic therapies can be more complex than those required for small molecule drugs and require additional investments in different systems, equipment, facilities and expertise. We are focused on ensuring the stability of the supply chains for our current products, as well as for our pipeline programs.

Sales of our products depend, to a large degree, on the extent to which our products are reimbursed by third-party payors, such as government health programs, commercial insurance and managed health care organizations. Reimbursement for our products, including our potential pipeline therapies, cannot be assured and may take significant periods of time to obtain. We dedicate substantial management and other resources to obtain and maintain appropriate levels of reimbursement for our products from third-party payors, including governmental organizations in the U.S. and ex-U.S. markets.

In the U.S., we have worked successfully with third-party payors to promptly obtain appropriate levels of reimbursement for our CF medicines. In addition, we are working with U.S. government and commercial payors with respect to CASGEVY and JOURNAVX. We anticipate broad access with government and commercial payors for CASGEVY in the U.S., and we have recently entered into multiple agreements with government and commercial health insurance providers to provide such access. For JOURNAVX in the U.S., we have been working with government and commercial payors pre- and post-approval to support rapid and broad access. We plan to continue to engage in discussions with numerous commercial insurers and managed health care organizations, along with government health programs that are typically managed by authorities in the individual states, to ensure that payors recognize the significant benefits that all our therapies provide and provide patients with appropriate levels of access to our medicines and therapies now and in the future. We cannot, however, predict how changes in the law, including through the Inflation Reduction Act of 2022 and passage of state laws (e.g., transparency laws and prescription drug affordability boards), will affect our ability to negotiate successfully with third-party payors and distribute our products. Similarly, in ex-U.S. markets, we seek government reimbursement for our medicines on a country-by-country or region-by-region basis, as required. This is necessary for each new medicine, as well as for label expansions for our current medicines. We are working with ex-U.S. payors with respect to CASGEVY, and we are pursuing long-term reimbursement agreements. We have secured reimbursed access for people with SCD or TDT in Saudi Arabia, Bahrain, Luxembourg, and England. In addition, the Italian Medicines Agency has approved early access for CASGEVY, on a case-by-case basis, to treat people with SCD and TDT. We expect to continue to focus significant resources to expand and maintain reimbursement for our CF medicines, CASGEVY, JOURNAVX, and, ultimately, our pipeline therapies, in U.S. and ex-U.S. markets.

Strategic Transactions

Acquisitions

As part of our business strategy, we seek to acquire technologies, products, product candidates and other businesses that are aligned with our corporate and research and development strategies and complement and advance our ongoing research and development efforts. We have acquired multiple biotechnology companies over the last several years and expect to continue to identify and evaluate such opportunities. The accounting for these acquisitions can vary significantly based on whether we conclude the transactions represent business combinations or asset acquisitions. In 2024, we acquired Alpine for approximately $5.0 billion in cash. Alpine's lead molecule, povetacicept, has shown potential to treat multiple diseases or conditions and become a pipeline-in-a-product. We accounted for the Alpine transaction as an asset acquisition because povetacicept represented substantially all of the fair value of the gross assets that we acquired. As a result, $4.4 billion of the fair value attributed to povetacicept was expensed as AIPR&D in 2024. In 2019 and 2022, we acquired Semma Therapeutics, Inc. ("Semma") and ViaCyte, Inc. ("ViaCyte"), respectively, pursuant to which we established and accelerated the development of our T1D program. We accounted for each of these acquisitions as a business combination.

Please refer to our critical accounting policies, "Acquisitions," for further information regarding the significant judgments and estimates related to our acquisitions.

Collaboration and In-Licensing Arrangements

We enter into arrangements with third parties, including collaboration and licensing arrangements, for the development, manufacture and commercialization of products, product candidates, and other technologies that have the potential to complement our ongoing research and development efforts.

Over the last several years, we entered into collaboration agreements with a number of companies, including CRISPR Therapeutics AG ("CRISPR"), Entrada, and Moderna. Generally, when we in-license a technology or product candidate, we make upfront payments to the collaborator, assume the costs of the program and/or agree to make contingent payments, which could consist of milestone, royalty and option payments. Most of these collaboration payments are expensed as AIPR&D, including, a $75.0 million milestone paid to Entrada in 2024, and, in 2023, total payments of $242.6 million to Entrada and total upfront and milestone payments of $170.0 million to CRISPR related to T1D. These payments were expensed to AIPR&D because they were primarily attributable to acquired in-process research and development for which there was no alternative future use. However, depending on many factors, including the structure of the collaboration, the stage of development of the acquired technology, the significance of the in-licensed product candidate to the collaborator's operations and the other activities in which our collaborators are engaged, the accounting for these transactions can vary significantly. We expect to continue to identify and evaluate collaboration and licensing opportunities that may be similar to or different from the collaborations and licenses that we have engaged in previously.

Joint Development and Commercialization Agreement with CRISPR

In 2017, we entered into a joint development and commercialization agreement with CRISPR (the "CRISPR JDCA"), which we amended and restated in 2021.

Pursuant to the CRISPR JDCA, we lead global development, manufacturing and commercialization of CASGEVY, with support from CRISPR. We also conduct all research, development, manufacturing and commercialization activities relating to other product candidates and products under the CRISPR JDCA throughout the world subject to CRISPR's reserved right to conduct certain activities.

CASGEVY was approved by the FDA in December 2023 for the treatment of SCD. In connection with this approval, we made a $200.0 million milestone payment to CRISPR in January 2024, which we accrued to "Other current liabilities" and recorded within "Other intangible assets, net" on our consolidated balance sheet as of December 31, 2023. We are recording intangible asset amortization expense to "Cost of sales" related to this intangible asset. Subsequent to receiving marketing approval for CASGEVY, we continue to lead the research and development activities under the CRISPR JDCA, subject to CRISPR's reserved right to conduct certain activities. We are reimbursed by CRISPR for its 40% share of these research and development activities, subject to certain adjustments, and we record this reimbursement from CRISPR as a credit within "Research and development expenses." We also share with CRISPR 40% of the net commercial profits or losses incurred with respect to CASGEVY, subject to certain adjustments, which is recorded to "Cost of sales." The net commercial profits or losses equal the sum of the product revenues, cost of sales and selling, general and administrative expenses that we have recognized related to the CRISPR JDCA.

Prior to receiving marketing approval from the FDA for CASGEVY in December 2023, we accounted for the CRISPR JDCA as a cost-sharing arrangement, with costs incurred related to CASGEVY allocated 60% to us and 40% to CRISPR, subject to certain adjustments. In 2023 and 2022, we recognized net reimbursements from CRISPR as credits to "Research and development expenses" and to "Selling, general and administrative expenses," related to CRISPR's share of the CRISPR JDCA's operating expenses.

Acquired In-Process Research and Development Expenses

In 2024 and 2023, our AIPR&D included $4.6 billion and $527.1 million, respectively, related to upfront, contingent milestone, or other payments pursuant to our business development transactions, including the asset acquisitions, collaborations, and licenses of third-party technologies described above. Please refer to Note B, "Collaboration, License and Other Arrangements," for further information regarding our asset acquisitions, collaboration, in-license agreements.

Out-licensing Arrangements

We also have out-licensed certain development programs to collaborators who are leading the development or commercialization of these programs, either globally or within certain geographic regions. Pursuant to these out-licensing arrangements, our collaborators are responsible for the research, development, and commercialization costs associated with these programs, and we are entitled to receive contingent milestone and/or royalty payments. As a result, we do not expect to incur significant expenses in connection with these programs and have the potential for future collaborative and royalty revenues resulting from these programs. None of our out-license agreements had a significant impact on our consolidated statements of operations during the three years ended December 31, 2024.

As noted above, in January 2025, we entered into a collaboration agreement with Zai for the development and commercialization of povetacicept in mainland China, Hong Kong SAR, Macau SAR, Taiwan region and Singapore.

RESULTS OF OPERATIONS

	2024	% Change	2023	% Change	2022
	(in millions, except percentages and per share amounts)				
Product revenues, net	$ 11,020.1	12%	$ 9,869.2	11%	$ 8,930.7
Acquired in-process research and development expenses	4,628.4	**	527.1	356%	115.5
Other operating costs and expenses	6,624.6	20%	5,510.1	22%	4,507.8
(Loss) income from operations	(232.9)	(106)%	3,832.0	(11)%	4,307.4
Other non-operating income (expense), net	481.4	(12)%	547.8	**	(75.0)
Provision for income taxes	784.1	3%	760.2	(16)%	910.4
Net (loss) income	$ (535.6)	(115)%	$ 3,619.6	9%	$ 3,322.0
Net (loss) income per diluted common share	$ (2.08)		$ 13.89		$ 12.82
Diluted shares used in per share calculations	257.9		260.5		259.1

** Not meaningful

Revenues

	2024	% Change	2023	% Change	2022
	(in millions, except percentages)				
TRIKAFTA/KAFTRIO	$ 10,238.6	14%	$ 8,944.7	16%	$ 7,686.8
Other product revenues	781.5	(15)%	924.5	(26)%	1,243.9
Total revenues	$ 11,020.1	12%	$ 9,869.2	11%	$ 8,930.7

Product Revenues, Net

In 2024, our net product revenues increased by $1.2 billion, or 12%, as compared to 2023. Increases in our TRIKAFTA/KAFTRIO product revenues were due to strong performance and demand globally, including expansions into younger age groups and label extensions, and higher net realized pricing in the U.S. The decrease in our "Other product revenues" was primarily the result of CF patients switching to TRIKAFTA/KAFTRIO from our other CF products. In 2024, "Other product revenues" included $10.0 million related to CASGEVY. There were no ALYFTREK sales in 2024.

Our net product revenues from the U.S. and from ex-U.S. markets were as follows:

	2024	% Change	2023	% Change	2022
	(in millions, except percentages)				
United States	$ 6,684.9	11%	$ 6,040.4	6%	$ 5,699.3
ex-U.S.	4,335.2	13%	3,828.8	18%	3,231.4
Product revenues, net	$ 11,020.1	12%	$ 9,869.2	11%	$ 8,930.7

In 2025, we expect our net product revenues to increase due to the approval of ALYFTREK for CF in the U.S., continued demand globally for TRIKAFTA/KAFTRIO, including in younger age groups and from label expansions, increased CASGEVY patient infusions, and contribution from the launch of JOURNAVX.

Operating Costs and Expenses

	2024	% Change	2023	% Change	2022
	(in millions, except percentages)				
Cost of sales	$ 1,530.5	21%	$ 1,262.2	17%	$ 1,080.3
Research and development expenses	3,630.3	15%	3,162.9	25%	2,540.3
Acquired in-process research and development expenses	4,628.4	**	527.1	356%	115.5
Selling, general and administrative expenses	1,464.3	29%	1,136.6	20%	944.7
Change in fair value of contingent consideration	(0.5)	**	(51.6)	**	(57.5)
Total costs and expenses	$ 11,253.0	86%	$ 6,037.2	31%	$ 4,623.3

** Not meaningful

Cost of Sales

Our cost of sales primarily consists of third-party royalties payable on net sales of our CF products as well as the cost of producing inventories. Pursuant to our agreement with the Cystic Fibrosis Foundation, our tiered third-party royalties on sales of ALYFTREK, TRIKAFTA/KAFTRIO, SYMDEKO/SYMKEVI, KALYDECO, and ORKAMBI, calculated as a percentage of net sales, range from the single digits to the sub-teens, with lower royalties on sales of ALYFTREK and TRIKAFTA/KAFTRIO than for our other products. Over the last several years, our cost of sales has been increasing due to increased net product revenues. Our cost of sales as a percentage of our net product revenues was 14% and 13% in 2024 and 2023, respectively. The increase in costs of sales as a percentage of our net product revenues was primarily due to costs associated with CASGEVY following its regulatory approval in the fourth quarter of 2023. In 2025, we expect our total cost of sales to increase due to expected increased net product revenues, CASGEVY contract manufacturing costs, and costs associated with JOURNAVX, partially offset by lower royalties due to sales of ALYFTREK.

Research and Development Expenses

	2024	% Change	2023	% Change	2022
	(in millions, except percentages)				
Research expenses	$ 804.5	14%	$ 705.6	13%	$ 626.7
Development expenses	2,825.8	15%	2,457.3	28%	1,913.6
Total research and development expenses	$ 3,630.3	15%	$ 3,162.9	25%	$ 2,540.3

Our research and development expenses include internal and external costs incurred for research and development of our products and product candidates. We do not assign our internal costs, such as salary and benefits, stock-based compensation expense, laboratory supplies and other direct expenses and infrastructure costs, to individual products or product candidates, because the employees within our research and development groups typically are deployed across multiple research and development programs. We assign external costs of services provided to us by clinical research organizations and other outsourced research by individual program. Our internal costs are greater than our external costs. All research and development costs for our products and product candidates are expensed as incurred.

Over the past three years, we have incurred $9.3 billion in research and development expenses associated with product discovery and development. The successful development of our product candidates is highly uncertain and subject to a number of risks. In addition, the duration of clinical trials may vary substantially according to the type, complexity and novelty of the product candidate and the disease indication being targeted. The FDA and comparable agencies in foreign countries impose substantial requirements on the introduction of therapeutic pharmaceutical products, typically requiring lengthy and detailed laboratory and clinical testing procedures, sampling activities and other costly and time-consuming procedures. Data obtained from nonclinical and clinical activities at any step in the testing process may be adverse and lead to discontinuation or redirection of development activities. Data obtained from these activities also are susceptible to varying interpretations, which could delay, limit or prevent regulatory approval. The duration and cost of discovery, nonclinical studies and clinical trials may vary significantly over the life of a project and are difficult to predict. Therefore, accurate and meaningful estimates of the ultimate costs to bring our product candidates to market are not available.

Any estimates regarding development and regulatory timelines for our product candidates are highly subjective and subject to change. Until we have data from Phase 3 clinical trials, we cannot make a meaningful estimate regarding when, or if, a clinical development program will generate revenues and cash flows.

Research Expenses

	2024	Change %	2023	Change %	2022
	(in millions, except percentages)				
Research Expenses:					
Salary and benefits	$ 210.7	14%	$ 184.1	15%	$ 159.5
Stock-based compensation expense	112.1	21%	92.4	10%	84.0
Outsourced services and other direct expenses	271.4	15%	237.0	25%	189.6
Intangible asset impairment charge	—	**	—	**	13.0
Infrastructure costs	210.3	9%	192.1	6%	180.6
Total research expenses	$ 804.5	14%	$ 705.6	13%	$ 626.7

** Not meaningful

Our research expenses have been increasing over the last several years as we invested in our pipeline and expanded our cell and genetic therapy capabilities, resulting in increased headcount and stock-based compensation expense, and outsourced services, other direct expenses, and infrastructure costs. We expect to continue to invest in our research programs with a focus on creating transformative medicines for serious diseases.

Development Expenses

	2024	Change %	2023	Change %	2022
	(in millions, except percentages)				
Development Expenses:					
Salary and benefits	$ 686.7	16%	$ 590.9	24%	$ 475.1
Stock-based compensation expense	313.7	20%	262.5	23%	213.9
Compensation expense for cash-settled unvested Alpine equity awards	151.9	**	—	**	—
Outsourced services and other direct expenses	1,239.1	0%	1,238.7	36%	912.9
Infrastructure costs	434.4	19%	365.2	17%	311.7
Total development expenses	$ 2,825.8	15%	$ 2,457.3	28%	$ 1,913.6

** Not meaningful

Our development expenses increased by $368.5 million, or 15%, in 2024 as compared to 2023, due to continued investments in internal headcount and related expenses and infrastructure to support advancement of additional therapies into mid-to-late-stage development, including our T1D program. Growth in internal headcount over the last several years has increased our stock-based compensation expense, which has historically fluctuated and is expected to continue to fluctuate from one period to another based on the probability of achieving milestones associated with our performance-based awards. In 2024, development expenses also included compensation expense associated with cash-settled unvested equity awards related to our acquisition of Alpine. Outsourced services and other direct expenses in 2024 were similar to 2023 as increased expenses to support our T1D program were offset by the completion of our Phase 3 trials for ALYFTREK and JOURNAVX and the commercialization of CASGEVY. In 2025, we expect our development expenses to continue to increase due to our advancing pipeline programs, including our IgAN, pain and T1D programs.

Acquired In-process Research and Development Expenses

	2024	% Change	2023	% Change	2022
	(in millions, except percentages)				
Acquired in-process research and development expenses	$ 4,628.4	**	$ 527.1	356%	$ 115.5

** Not meaningful

In 2024, AIPR&D included $4.4 billion resulting from our acquisition of Alpine, which was accounted for as an asset acquisition, the $75.0 million milestone to Entrada, and a $40.0 million upfront payment to Orna. In 2023, AIPR&D consisted of our $225.1 million upfront payment to Entrada, $100.0 million upfront payment and $70.0 million T1D research milestone to CRISPR, $47.5 million acquisition of a novel GPCR program from Septerna, and various other payments. Our AIPR&D has historically fluctuated, and is expected to continue to fluctuate, from one period to another due to upfront, contingent milestone, and other payments pursuant to our existing and future business development transactions, including collaborations, licenses of third-party technologies, and asset acquisitions.

Selling, General and Administrative Expenses

	2024	% Change	2023	% Change	2022
	(in millions, except percentages)				
Selling, general and administrative expenses	$ 1,464.3	29%	$ 1,136.6	20%	$ 944.7

Selling, general and administrative expenses increased by 29% in 2024 as compared to 2023, primarily due to increased commercial investments to prepare for the launch of JOURNAVX and support the launch of CASGEVY, and stock-based compensation expense. We expect our selling, general and administrative expenses to continue to increase in 2025 to support these new product launches and additional investments in infrastructure to scale our organization.

Contingent Consideration

In 2024, the fair value of our contingent consideration decreased by $0.5 million. In 2023, the fair value of our contingent consideration decreased by $51.6 million primarily due to our determination that additional pre-clinical studies of the delivery system for our gene-editing components for Duchenne muscular dystrophy (“DMD”) would be required. In future periods, we expect the fair value of contingent consideration to increase or decrease based on, among other things, our estimates of the probability of achieving and the timing of these contingent development and regulatory milestone payments, as well as the time value of money and changes in market interest rates.

Other Non-Operating Income (Expense), Net

Interest Income

Interest income decreased from $614.7 million in 2023 to $598.1 million in 2024, primarily due to decreased cash equivalents and available-for-sale debt securities following our acquisition of Alpine in the second quarter of 2024. Our future interest income is dependent on the amount of, and prevailing market interest rates on, our outstanding cash equivalents and available-for-sale debt securities.

Interest Expense

Interest expense was $30.6 million in 2024, as compared to $44.1 million in 2023. The majority of our interest expense in these years was related to imputed interest expense associated with finance leases for our corporate headquarters in Boston. As discussed in Note L, “Leases,” our corporate headquarters leases were amended in August 2024, which resulted in an accounting classification change from finance to operating leases. As a result, we expect our interest expense to decrease in future periods because operating lease expenses are recorded within operating expenses in our consolidated statements of operations.

Other Income (Expense), Net

Other income (expense), net was expenses of $86.1 million and $22.8 million in 2024 and 2023, respectively. These amounts primarily related to net unrealized losses resulting from changes in the fair value of certain of our strategic equity investments, which consist of investments in our collaborators that may be public or privately-held companies. To the extent that we continue to hold strategic equity investments in publicly traded biotechnology companies, we expect that our other income (expense), net will continue to fluctuate in future periods due to the volatility in the stock prices of these companies that impacts the fair value of our investments. As of December 31, 2024, the fair value of our investments in publicly traded companies was $36.6 million. We discuss these potential future fluctuations further in Item 7a. Quantitative and Qualitative Disclosures About Market Risk.

Income Taxes

Our effective tax rate fluctuates from year to year due to the global nature of our operations. The factors that most significantly impact our effective tax rate include changes in tax laws, variability in the amount and allocation of our taxable earnings among multiple jurisdictions, the amount and characterization of our research and development expenses, the levels of certain deductions and credits, adjustments to the value of our uncertain tax positions, acquisitions and third-party collaboration and licensing transactions.

Our provision for income taxes was $784.1 million for 2024 and $760.2 million for 2023. In 2024, our 315.5% effective tax rate was materially different than the U.S. statutory rate primarily due to the $4.4 billion of non-deductible AIPR&D resulting from our acquisition of Alpine, which significantly lowered our pre-tax income. The non-deductible AIPR&D was partially offset by a benefit from a research and development tax credit study that was completed in 2024 and excess tax benefits related to stock-based compensation.

In 2023, our 17.4% effective tax rate was lower than the U.S. statutory rate primarily due to a benefit from a research and development tax credit study that was completed in 2023 and excess tax benefits related to stock-based compensation, partially offset by changes in uncertain tax positions.

LIQUIDITY AND CAPITAL RESOURCES

The following table summarizes the components of our financial condition as of December 31, 2024 and 2023:

	2024	2023	% Change
	(in millions, except percentages)		
Cash, cash equivalents and marketable securities:			
Cash and cash equivalents	$ 4,569.6	$ 10,369.1	
Marketable securities	1,546.3	849.2	
Long-term marketable securities	5,107.9	2,497.8	
Total cash, cash equivalents and marketable securities	$ 11,223.8	$ 13,716.1	(18)%
Working Capital:			
Total current assets	$ 9,596.4	$ 14,144.2	(32)%
Total current liabilities	(3,564.6)	(3,547.4)	—%
Total working capital	$ 6,031.8	$ 10,596.8	(43)%

Working Capital

As of December 31, 2024, total working capital was $6.0 billion, which represented a decrease of $4.6 billion from $10.6 billion as of December 31, 2023 primarily due to cash paid to acquire Alpine.

Cash Flows

	2024	2023	2022
		(in millions)	
Net cash (used in) provided by:			
Operating activities	$ (492.6)	$ 3,537.3	$ 4,129.9
Investing activities	$ (3,770.0)	$ (3,141.7)	$ (321.1)
Financing activities	$ (1,494.9)	$ (562.2)	$ (67.7)

Operating Activities

Cash used in operating activities was $492.6 million in 2024 as compared to cash provided by operating activities of $3.5 billion in 2023. The largest driver of the decrease in cash provided by operating activities was cash paid to acquire Alpine.

Investing Activities

Cash used in investing activities were $3.8 billion and $3.1 billion in 2024 and 2023, respectively. The largest portion of our investing activities in each year were net purchases of available-for-sale debt securities.

Financing Activities

Cash used in financing activities were $1.5 billion and $562.2 million in 2024 and 2023, respectively. Our financing activities in each year were primarily related to repurchases of our common stock pursuant to our share repurchase program and payments related to our employee stock benefit plans.

Sources and Uses of Liquidity

We intend to rely on our existing cash, cash equivalents and current marketable securities together with our operating profitability as our primary source of liquidity. We expect that cash flows from our product sales together with our cash, cash equivalents and current marketable securities will be sufficient to fund our operations for at least the next twelve months. The adequacy of our available funds to meet our future operating and capital requirements will depend on many factors, including our future sales of currently marketed products, and the potential introduction of one or more new product candidates to the market, our business development activities and the number, breadth and cost of our research and development programs.

Credit Facilities & Financing Strategy

We may borrow up to a total of $500.0 million pursuant to a revolving credit facility that we entered into in July 2022 and could repay and reborrow amounts under this revolving credit agreement without penalty. Subject to certain conditions, we could request that the borrowing capacity be increased by an additional $500.0 million, for a total of $1.0 billion. Negative covenants in our credit agreement could prohibit or limit our ability to access this source of liquidity. As of December 31, 2024, the facility was undrawn, and we were in compliance with these covenants.

We may also raise additional capital by borrowing under credit agreements, through public offerings or private placements of our securities, or securing new collaborative agreements or other methods of financing. We will continue to manage our capital structure and will consider all financing opportunities, whenever they may occur, that could strengthen our long-term liquidity profile. There can be no assurance that any such financing opportunities will be available on acceptable terms, if at all.

Future Capital Requirements

We have significant future capital requirements, including:

- Expected operating expenses to conduct research and development activities, manufacture and commercialize our existing and future products, and to operate our organization.
- Cash that we pay for income taxes.
- Royalties we pay related to sales of our CF products.

- Facility, operating and finance lease obligations as described below.
- Firm purchase obligations related to our supply and manufacturing processes.

In addition, other potential significant future capital requirements may include:

- We have entered into certain agreements with third parties that include the funding of certain research, development, manufacturing and commercialization efforts. Certain of our transactions, including collaborations, licensing arrangements, and asset acquisitions, include the potential for future milestone and royalty payments by us upon the achievement of pre-established developmental and regulatory targets and/or commercial targets. Other transactions include the potential for future lease-related expenses and other costs. Our obligation to fund these research and development and commercialization efforts and to pay these potential milestones, expenses and royalties is contingent upon continued involvement in the programs and/or the lack of any adverse events that could cause their discontinuance. We may enter into additional agreements, including acquisitions, collaborations, licensing arrangements and equity investments, which require additional capital.
- To the extent we borrow amounts under our existing credit agreement, we would be required to repay any outstanding principal amounts in 2027.
- As of December 31, 2024, we had $1.4 billion remaining authorization available under our $3.0 billion Share Repurchase Program that our Board of Directors approved in February 2023. This program does not have an expiration date and can be discontinued at any time. We expect to fund these programs through a combination of cash on hand and cash generated by operations.

Additional information on several of our future capital requirements is provided below.

Research and Development Costs

We have ongoing clinical trials of product candidates at various stages of clinical development. Our clinical trial costs are dependent on, among other things, the size, number, and length of our clinical trials. These costs can increase as product candidates move from earlier-stage clinical trials into later-stage clinical development.

Leases

We account for the majority of our real estate leases and each of our embedded leases with contract manufacturing organizations as operating leases. These include leases for our corporate headquarters at Fan Pier in Boston, Massachusetts and office and laboratory space at the Jeffrey Leiden Center for Cell and Genetic Therapies (the "Jeffrey Leiden Center") near our corporate headquarters. We amended our corporate headquarters leases in 2024 to, among other terms, extend the lease termination dates from December 2028 to June 2044. Our lease for the Jeffrey Leiden Center commenced in 2021 pursuant to an initial 15-year lease term for this building. We also have several embedded leases with contract manufacturing organizations related to the manufacturing and commercialization of our products with remaining lease terms up to 8 years as of December 31, 2024.

As of December 31, 2024, our largest finance lease relates to the lease for our research site in San Diego, California, which commenced in 2019 pursuant to an initial 16-year lease term.

Our total future minimum lease payments for our leases for each of the next five years and in total are included in Note L, "Leases." The total future undiscounted minimum lease payments were $2.7 billion and $189.0 million related to our operating and finance leases, respectively, as of December 31, 2024. To support future product development and commercialization efforts, we may enter into additional lease agreements, which require additional capital.

CRITICAL ACCOUNTING POLICIES AND ESTIMATES

Our discussion and analysis of our financial condition and results of operations are based upon our consolidated financial statements prepared in accordance with generally accepted accounting principles in the U.S. The preparation of these financial statements requires us to make certain estimates and assumptions that affect the reported amounts of assets and liabilities, the disclosure of contingent assets and liabilities at the date of the consolidated financial statements and the reported amounts of revenues and expenses during the reported periods. These items are monitored and analyzed by management for changes in facts and circumstances, and material changes in these estimates could occur in the future.

Changes in estimates are reflected in reported results for the period in which the change occurs. We base our estimates on historical experience and various other assumptions that we believe to be reasonable under the circumstances. Actual results may differ from our estimates if past experience or other assumptions do not turn out to be substantially accurate.

We believe that our application of the following accounting policies, each of which requires significant judgments and estimates on the part of management, are the most critical to aid in fully understanding and evaluating our reported financial results:

- revenue recognition;
- acquisitions, including intangible assets, goodwill and contingent consideration;
- inventories; and
- income taxes.

Our accounting policies, including the ones discussed below, are more fully described in Note A, "Nature of Business and Accounting Policies."

Revenue Recognition

Product Revenues, Net

We generate product revenues from sales in the U.S. and in international markets. We sell our products principally to a limited number of specialty pharmacy and specialty distributors in the U.S., which account for the largest portion of our total revenues. Our customers in the U.S. subsequently resell our products to patients, health care providers, or authorized treatment centers ("ATCs") for CASGEVY. We contract with government agencies so that our products will be eligible for purchase by, or partial or full reimbursement from, such third-party payors. We make international sales primarily through distributor arrangements and to retail pharmacies, as well as to hospitals and clinics, many of which are government-owned or supported customers. In certain markets, we may not utilize a specialty distributor or specialty pharmacy to distribute CASGEVY. In these markets, we sell CASGEVY directly to ATCs. We recognize net product revenues from sales of our products when our customers obtain control of our products, which typically occurs upon delivery to customers for our small molecule products, including CF, and upon infusion of our gene-therapy products, including CASGEVY. Revenues from our product sales are recorded at the net sales price, or transaction price, which requires us to make several significant estimates regarding the net sales price.

The most significant estimate we are required to make for our product revenues is related to government, commercial, and private payor rebates, chargebacks, discounts and fees, collectively rebates. The values of the rebates provided to third-party payors per course of treatment vary significantly and are based on government-mandated discounts and our arrangements with other third-party payors. To estimate our total rebates, we estimate the percentage of prescriptions that will be covered by each third-party payor, which is referred to as the payor mix. We track available information regarding changes, if any, to the payor mix for our products, to our contractual terms with third-party payors and to applicable governmental programs and regulations and levels of our products in the distribution channel. We adjust our estimated rebates based upon new information as it becomes available, including information regarding actual rebates for our products. Claims by third-party payors for rebates are submitted to us significantly after the related sales, potentially resulting in adjustments in the period in which the new information becomes known.

The following table summarizes activity related to our product revenue accruals for rebates for 2024, 2023 and 2022:

	(in millions)
Balance at December 31, 2021	$ 838.6
Provision related to 2022 sales	2,977.2
Adjustments related to prior year(s) sales	(10.4)
Credits/payments made	(2,514.0)
Balance at December 31, 2022	$ 1,291.4
Provision related to 2023 sales	3,481.4
Adjustments related to prior year(s) sales	(6.5)
Credits/payments made	(3,064.7)
Balance at December 31, 2023	$ 1,701.6
Provision related to 2024 sales	3,673.0
Adjustments related to prior year(s) sales	(42.1)
Credits/payments made	(3,725.4)
Balance at December 31, 2024	$ 1,607.1

We have also entered into annual contracts with government-owned and supported customers in international markets that limit the amount of annual reimbursement we can receive for our products. Upon exceeding the annual reimbursement amount provided by the customer's contract with us, products are provided free of charge, which is a material right. If we estimate that the annual reimbursement amount under a contract will be exceeded for an annual period, we defer a portion of the consideration received, which includes upfront payments and fees, for shipments made up to the annual reimbursement limit as "Other current liabilities." Once the annual reimbursement limit has been reached, we recognize the deferred amount as revenue when we deliver the free products. To estimate the portion of the consideration received to be recognized as revenue and the portion of the amount to be deferred, we rely on our forecast of the number of units we will distribute during the applicable annual period in each international market in which our contracts with government-owned and supported customers limit the amount of annual reimbursement we can receive. Our forecasts are based on, among other things, our historical experience.

The preceding estimates and judgments materially affect our recognition of net product revenues. Changes in our estimates of net product revenues could have a material effect on net product revenues recorded in the period in which we determine that change occurs.

Acquisitions

As part of our business strategy, we seek to acquire products, product candidates and other technologies and businesses that are aligned with our corporate and research and development strategies and complement and advance our ongoing research and development efforts.

We are required to make several significant judgments and estimates to determine the accounting treatment for each acquisition transaction. If we determine that substantially all the fair value associated with an acquisition is concentrated in a single asset, or the acquisition does not constitute a business, we account for it as an asset acquisition. For example, we accounted for our $5.0 billion acquisition of Alpine in 2024 as an asset acquisition because povetacicept, Alpine's lead molecule, represented substantially all of the fair value of the gross assets that we acquired. As a result, $4.4 billion of the fair value attributed to povetacicept was expensed to AIPR&D in 2024. If the fair value that we acquired in an acquisition is distributed among more than one asset, and the acquisition constitutes a business, we account for it as a business combination.

For an asset acquisition involving rights to intellectual property related to in-process research and development that is not yet associated with a product that has achieved regulatory approval, we generally expense our upfront payment to AIPR&D, because there is no alternative future use for the asset that was acquired.

For business combinations, we are required to make several significant judgments and estimates to calculate and allocate the purchase price to the assets that we have acquired and the liabilities that we have assumed on our consolidated balance sheet. The most significant judgments and estimates relate to the fair value of the in-process research and development assets and contingent consideration liabilities related to these business combinations. Based on these judgments and estimates, the fair value of the goodwill that we record as a result of these business combinations may be material.

In-process Research and Development Intangible Assets

As of both December 31, 2024 and 2023, we had $603.6 million of in-process research and development assets on our consolidated balance sheet within "Other intangible assets, net," which primarily relate to our T1D clinical program established through our acquisitions of Semma and ViaCyte.

We characterize in-process research and development assets on our consolidated balance sheets as indefinite-lived intangible assets until the completion or abandonment of the associated research and development efforts. We test our in-process research and development intangible assets for impairment on an annual basis, and more frequently if indicators are present or changes in circumstances suggest that impairment may exist. When we determine that an indefinite-lived intangible asset has become impaired or we abandon the associated research and development project, we write down the carrying value to its fair value and record an impairment charge in the period in which the impairment occurs. For example, we recorded a $13.0 million impairment of an in-process research and development intangible asset to "Research and development expenses" in 2022 due to a decision to revise the scope of certain acquired gene-editing programs. If one of our product candidates achieves regulatory approval, the in-process research and development intangible assets associated with the product candidate become finite-lived intangible assets as described below.

We use significant judgment to determine the fair value of our in-process research and development assets and have utilized either the multi-period excess earnings or the relief from royalty methods of the income approach. Each method requires us to estimate the probability of technical and regulatory success, revenue projections and growth rates, and appropriate discount and tax rates. The multi-period excess earnings method also requires us to estimate development and commercial costs. The relief from royalty method also requires us to estimate the after-tax royalty savings expected from ownership of the asset that we acquired.

Contingent Consideration

We may owe Exonics former equity holders up to $678.3 million upon the achievement of certain events associated with research programs focused on DMD and other severe neuromuscular diseases, including DM1. As of December 31, 2024 and 2023, we had $76.9 million and $77.4 million, respectively, of liabilities on our consolidated balance sheets attributable to the fair value of these contingent development and regulatory payments.

We record an increase or a decrease in the fair value of the contingent consideration liabilities on our consolidated balance sheet and in our consolidated statement of income on a quarterly basis. We determine the fair value of our contingent consideration liabilities using a probability weighted discounted cash flow method of the income approach, which requires us to make estimates of the timing of regulatory and commercial milestone achievement and the corresponding estimated probability of technical and regulatory success rates. We use significant judgment in determining the appropriateness of these assumptions during each reporting period. Reasonable changes in these assumptions can cause material changes to the fair value of our contingent consideration liabilities. Due to the early stage of Exonics' programs, these significant assumptions could be affected by future economic and market conditions.

In November 2023, we determined that additional pre-clinical studies of the delivery system for our gene-editing components for DMD will be required. As a result, we revised our estimates regarding the timing of the development and regulatory milestones and the probability of achieving those milestones, which reduced the estimated fair value of our contingent consideration as of December 31, 2023.

Goodwill

As of December 31, 2024 and 2023, we had goodwill of $1.1 billion on our consolidated balance sheets. During 2024, we did not have any business development transactions accounted for as a business combination. Goodwill reflects the difference between the fair value of the consideration transferred and the fair value of the net assets acquired. Thus, the goodwill that we record is dependent on the significant judgments and estimates inherent in these fair values. We have one reporting unit for goodwill reporting purposes. We evaluate our goodwill for impairment on an annual basis, and more

frequently if indicators are present or changes in circumstances suggest that impairment may exist. We have not identified any goodwill impairment to date.

Finite-lived Intangible Assets

As of December 31, 2024 and 2023, we had $222.3 million and $236.3 million, respectively, of finite-lived intangible assets on our consolidated balance sheet within "Other intangible assets, net." These finite-lived intangible assets primarily relate to $208.0 million of CASGEVY regulatory approval milestones recorded in 2023.

We amortize our finite-lived intangible assets related to our marketed products, which represent the majority of our finite-lived intangible assets, using the straight-line method within "Cost of sales" over the remaining estimated life of the assets beginning in the period in which regulatory approval is achieved or the assets are acquired and continuing through the period that we no longer have either exclusive rights to market the products associated with the assets or in-license rights to the intellectual property underlying the assets. We test finite-lived intangible assets for impairment if indicators are present or changes in circumstances suggest that the carrying value of an asset may not be recoverable. If we determine that the carrying value of a finite-lived intangible asset may not be recoverable, we compare the carrying value of the asset to the undiscounted cash flows that we expect the asset to generate. When we determine that a finite-lived intangible asset has become impaired, we write down the carrying value of the asset to its fair value and record an impairment charge in the period in which the impairment occurs.

Inventories

We capitalize inventories prior to regulatory approval when we consider the related product candidate to have a high likelihood of regulatory approval and expect to recover the related costs. In making this determination, we evaluate, among other factors, the status of regulatory submissions and communications with regulatory authorities, information regarding the product candidate's safety and efficacy, and the outlook for commercial sales, including the existence of any competition. During the first quarter of 2024, following positive results related to our Phase 3 trials for JOURNAVX, we began capitalizing inventories produced in preparation for our planned product launch. In January 2025, we received approval from the FDA to market JOURNAVX in the U.S. Prior to making this determination, we expensed inventoriable and related costs associated with JOURNAVX, as well as ALYFTREK, as "Research and development expenses."

Income Taxes

We utilize the asset and liability method of accounting for income taxes. Under this method, deferred tax assets and liabilities are determined based on the difference between the financial statement carrying amounts and tax basis of assets and liabilities using enacted tax rates in effect for years in which the temporary differences are expected to reverse. If our estimate of the tax effect of reversing temporary differences is (i) not reflective of actual outcomes, (ii) modified to reflect new developments or interpretations of the tax law, or (iii) revised to incorporate new accounting principles, or changes in the expected timing or manner of the reversal, our results of operations could be materially impacted.

We provide a valuation allowance when it is more likely than not that deferred tax assets will not be realized. On a periodic basis, we reassess our valuation allowances on our deferred tax assets, weighing positive and negative evidence to assess the recoverability of the deferred tax assets. Significant judgment is required in making these assessments to maintain or adjust our valuation allowances and, to the extent our future expectations change we would have to assess the recoverability of these deferred tax assets at that time. As of December 31, 2024, we maintained a valuation allowance of $272.9 million related primarily to U.S. state tax attributes.

We record liabilities related to uncertain tax positions by prescribing a minimum recognition threshold and measurement attribute for the financial statement recognition and measurement of a tax position taken or expected to be taken in a tax return. We adjust our liability to reflect any subsequent changes in the relevant facts and circumstances surrounding the uncertain positions. We are subject to tax laws and audits in multiple jurisdictions and significant judgment is required in making this assessment. Consequently, we regularly re-evaluate uncertain tax positions and consider various factors, including changes in tax law, the measurement of tax positions taken or expected to be taken in tax returns, and changes in facts or circumstances related to a tax position. As of December 31, 2024, our liability for uncertain tax positions was $706.2 million.

RECENT ACCOUNTING PRONOUNCEMENTS

Refer to Note A, "Nature of Business and Accounting Policies," in the accompanying notes to the consolidated financial statements for a discussion of recent accounting pronouncements and new accounting pronouncements adopted during 2024.

ITEM 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

Interest Rate Risk

Financial Instruments

As part of our investment portfolio, we own financial instruments that are sensitive to market risks. The investment portfolio is used to preserve our capital, provide adequate liquidity and earn returns commensurate with our risk appetite. We invest in instruments that meet the credit quality standards outlined in our investment policy, which also limits the amount of credit exposure to any one issue or type of instrument. These instruments primarily include securities issued by the U.S. government and its agencies, investment-grade corporate bonds and commercial paper, and money market funds. These investments are primarily denominated in U.S. Dollars and none are held for trading purposes.

All of our interest-bearing securities are subject to interest rate risk and could change in value if interest rates fluctuate. Substantially all of our investment portfolio consists of marketable securities with active secondary or resale markets to help ensure portfolio liquidity, and we have implemented guidelines limiting the term-to-maturity of our investment instruments. Since we account for these securities as available-for-sale, no gains or losses are realized due to changes in the fair value of our investments unless we sell our investments prior to maturity or incur a credit loss. Due to the conservative nature of these instruments, we do not believe that the fair value of our investments has a material exposure to interest rate risk.

While we are exposed to global interest rate fluctuations, our investment portfolio is most affected by fluctuations in U.S. interest rates, which affect the interest earned on our cash, cash equivalents and marketable securities.

Credit Agreement

In 2022, we entered into a $500.0 million unsecured revolving credit facility ("credit agreement"). Loans under this credit agreement bear interest, at our option, at a base rate or a Secured Overnight Financing Rate ("SOFR"), plus an applicable margin based on our consolidated leverage ratio (the ratio of our total consolidated funded indebtedness to our consolidated EBITDA for the most recently completed four fiscal quarter period). Pursuant to our credit agreement, the applicable margin on base rate loans ranges from 0.000% to 0.500% and the applicable margin on SOFR loans ranges from 1.000% to 1.500%. We do not believe that changes in interest rates related to our credit agreement would have a material effect on our consolidated financial statements. As of December 31, 2024, we had no principal or interest outstanding under our credit facility. A portion of our "Interest expense" in 2025 will be dependent on whether, and to what extent, we borrow amounts under this facility.

Foreign Exchange Market Risk

As a result of our foreign operations, we face significant exposure to movements in foreign currency exchange rates, primarily the Euro and British Pound against the U.S. dollar. Fluctuations in the amounts of our foreign revenues and fluctuations in foreign currency exchange rates, may have a positive or negative effect on our foreign exchange rate exposure. The current exposures arise primarily from cash, accounts receivable, intercompany receivables and payables, payables, and accruals, and inventories.

We have a foreign currency management program, which is separate from our investment policy and portfolio, with the objective of reducing the effect of exchange rate fluctuations on our operating results and forecasted revenues denominated in foreign currencies. We currently have cash flow hedges for the Euro, British Pound, Canadian Dollar, Swiss Franc and Australian Dollar related to a portion of our forecasted product revenues that qualify for hedge accounting treatment under U.S. GAAP. We do not seek hedge accounting treatment for our foreign currency forward contracts related to monetary assets and liabilities that impact our operating results. As of December 31, 2024, we held foreign exchange forward contracts that were designated as cash flow hedges with notional amounts totaling $2.9 billion representing a net asset of $142.5 million on our consolidated balance sheet.

Although not predictive in nature, we believe a hypothetical 10% threshold reflects a reasonably possible near-term change in exchange rates. If the December 31, 2024 exchange rates were to change by a hypothetical 10%, the fair value recorded on our consolidated balance sheet related to our foreign exchange forward contracts that were designated as cash flow hedges as of December 31, 2024 would change by approximately $286.0 million. However, since these contracts hedge a specific portion of our forecasted product revenues denominated in certain foreign currencies, any change in the fair value of these contracts is recorded in "Accumulated other comprehensive income (loss)" on our consolidated balance sheets and is reclassified to earnings in the same periods during which the underlying product revenues affect earnings. Therefore, any change in the fair value of these contracts that would result from a hypothetical 10% change in exchange rates would be entirely offset by the change in value associated with the underlying hedged product revenues resulting in no impact on our future anticipated earnings and cash flows with respect to the hedged portion of our forecasted product revenues.

Equity Price Risk

We hold strategic equity investments in certain public and private companies, and we expect to make additional strategic equity investments in the future. In 2024 and 2023, we recorded net losses of $9.5 million and $0.6 million, respectively, to "Other income (expense), net" in our consolidated statements of income to reflect changes in the fair value of equity investments with readily determinable fair values (including publicly traded securities). The fair value of our equity investments in publicly traded companies was less than $50.0 million as of December 31, 2024.

To the extent that we continue to hold strategic equity investments in publicly traded companies, we expect that due to the volatility of the stock price of biotechnology companies, our "other income (expense), net" will fluctuate in future periods based on increases or decreases in the fair value of our strategic equity investments.

ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA

The information required by this Item 8 is contained on pages F-1 through F-49 of this Annual Report on Form 10-K.

ITEM 9. CHANGES IN AND DISAGREEMENTS WITH ACCOUNTANTS ON ACCOUNTING AND FINANCIAL DISCLOSURE

Not applicable.

ITEM 9A. CONTROLS AND PROCEDURES

(1) Evaluation of Disclosure Controls and Procedures. Our chief executive officer and chief financial officer, after evaluating the effectiveness of our disclosure controls and procedures (as defined in Rule 13a-15(e) and Rule 15d-15(e) promulgated under the Securities Exchange Act of 1934, as amended (the "Exchange Act")) as of the end of the period covered by this Annual Report on Form 10-K, have concluded that, based on such evaluation, our disclosure controls and procedures were effective. In designing and evaluating the disclosure controls and procedures, management recognized that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving the desired control objectives, and management necessarily was required to apply our judgment in evaluating the cost-benefit relationship of possible controls and procedures.

(2) Management's Annual Report on Internal Control Over Financial Reporting. Management is responsible for establishing and maintaining adequate internal control over financial reporting. Internal control over financial reporting is defined in Rule 13a-15(f) and Rule 15d-15(f) promulgated under the Exchange Act, as a process designed by, or under the supervision of, our principal executive and principal financial officers and effected by our board of directors, management and other personnel, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. Our internal control over financial reporting include those policies and procedures that:

- pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of our assets;

- provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that our receipts and expenditures are being made only in accordance with authorizations of management and our directors; and

- provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use or disposition of our assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

Management assessed the effectiveness of our internal control over financial reporting as of December 31, 2024. In making this assessment, we used the criteria set forth in the *Internal Control—Integrated Framework (2013)* issued by the Committee of Sponsoring Organizations of the Treadway Commission ("COSO"). Based on our assessment, management has concluded that, as of December 31, 2024, our internal control over financial reporting is effective based on those criteria.

Our independent registered public accounting firm, Ernst & Young LLP, issued an attestation report on our internal control over financial reporting. See Section 4 below.

(3) Changes in Internal Controls. During the quarter ended December 31, 2024, there were no changes in our internal control over financial reporting that materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

(4) Report of Independent Registered Public Accounting Firm

To the Shareholders and the Board of Directors of Vertex Pharmaceuticals Incorporated

Opinion on Internal Control Over Financial Reporting

We have audited Vertex Pharmaceuticals Incorporated's internal control over financial reporting as of December 31, 2024, based on criteria established in Internal Control–Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework) (the COSO criteria). In our opinion, Vertex Pharmaceuticals Incorporated (the Company) maintained, in all material respects, effective internal control over financial reporting as of December 31, 2024, based on the COSO criteria.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the 2024 consolidated financial statements of the Company and our report dated February 13, 2025, expressed an unqualified opinion thereon.

Basis for Opinion

The Company's management is responsible for maintaining effective internal control over financial reporting and for its assessment of the effectiveness of internal control over financial reporting included in the accompanying Management's Annual Report on Internal Control Over Financial Reporting. Our responsibility is to express an opinion on the Company's internal control over financial reporting based on our audit. We are a public accounting firm registered with the PCAOB and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audit in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether effective internal control over financial reporting was maintained in all material respects.

Our audit included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, testing and evaluating the design and operating effectiveness of internal control based on the assessed risk, and performing such other procedures as we considered necessary in the circumstances. We believe that our audit provides a reasonable basis for our opinion.

Definition and Limitations of Internal Control Over Financial Reporting

A company's internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company's internal control over financial reporting includes those policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

/s/ Ernst & Young LLP

Boston, Massachusetts
February 13, 2025

ITEM 9B. OTHER INFORMATION

Rule 10b5-1 Trading Plans

Our policy governing transactions in our securities by our directors, officers, and employees permits our officers, directors and employees to enter into trading plans complying with Rule 10b5-1 under the Exchange Act. The following table describes the written plans for the sale of our securities adopted by our directors and officers (as defined in Rule 16a-1(f) under the Exchange Act) during the fourth quarter of 2024, each of which is intended to satisfy the affirmative defense conditions of Rule 10b5-1 (each, a "Trading Plan"). Other than as described in the table below, none of our directors or officers adopted, modified or terminated a Trading Plan in the fourth quarter of 2024.

Name and Title	Date of Adoption of Trading Plan	Scheduled Expiration Date of Trading Plan (1)	Maximum Shares Subject to Trading Plan
Ourania "Nia" Tatsis *EVP, Chief Regulatory and Quality Officer*	11/22/2024	10/31/2025	11,270

(1) A Trading Plan may expire on an earlier date if all contemplated transactions are completed before such Trading Plan's expiration date, upon termination by broker or the holder of the Trading Plan, or as otherwise provided in the Trading Plan.

2025 Restated Bylaws

On February 11, 2025, our Board of Directors approved our Amended and Restated By-Laws (the "2025 Restated Bylaws") to reduce the percentage of our capital stock required to call a special meeting of shareholders from 40% to 25%.

A copy of the 2025 Restated By-Laws is attached as Exhibit 3.2 to this Annual Report on Form 10-K and is incorporated by reference herein.

ITEM 9C. DISCLOSURE REGARDING FOREIGN JURISDICTIONS THAT PREVENT INSPECTIONS.

None.

PART III

Portions of our definitive Proxy Statement for the 2025 Annual Meeting of Shareholders ("2025 Proxy Statement") are incorporated by reference into this Part III of our Annual Report on Form 10-K.

ITEM 10. DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE

The information regarding directors required by this Item 10 will be included in our 2025 Proxy Statement and is incorporated herein by reference. We expect this information to be provided under "Election of Directors," "Corporate Governance and Risk Management," "Shareholder Proposals for the 2026 Annual Meeting and Nominations for Director," "Delinquent Section 16(a) Reports" and "Code of Conduct." The information regarding executive officers required by this Item 10 is included in Part I of this Annual Report on Form 10-K.

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 Vertex 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 has been filed as Exhibit 19.1 to this Annual Report on Form 10-K.

ITEM 11. EXECUTIVE COMPENSATION

The information required by this Item 11 will be included in the 2025 Proxy Statement and is incorporated herein by reference. We expect this information to be provided under "Compensation Committee Interlocks and Insider Participation," "Compensation Discussion and Analysis," "Compensation and Equity Tables," "Director Compensation," "Management Development and Compensation Committee Report" and/or "Corporate Governance and Risk Management."

ITEM 12. SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT AND RELATED STOCKHOLDER MATTERS

The information required by this Item 12 will be included in the 2025 Proxy Statement and is incorporated herein by reference. We expect this information to be provided under "Security Ownership of Certain Beneficial Owners and Management" and "Equity Compensation Plan Information."

ITEM 13. CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS, AND DIRECTOR INDEPENDENCE

The information required by this Item 13 will be included in the 2025 Proxy Statement and is incorporated herein by reference. We expect this information to be provided under "Election of Directors," "Corporate Governance and Risk Management," and "Audit and Finance Committee."

ITEM 14. PRINCIPAL ACCOUNTANT FEES AND SERVICES

The information required by this Item 14 will be included in the 2025 Proxy Statement and is incorporated herein by reference. We expect this information to be provided under "Ratification of the Appointment of Independent Registered Public Accounting Firm."

PART IV

ITEM 15. EXHIBITS AND FINANCIAL STATEMENT SCHEDULES

(a)(1) The Financial Statements required to be filed by Items 8 and 15(c) of Form 10-K, and filed herewith, are as follows:

(a)(2) Financial Statement Schedules have been omitted because they are either not applicable or the required information is included in the consolidated financial statements or notes thereto listed in (a)(1) above.

(a)(3) Exhibits.

The following is a list of exhibits filed as part of this Annual Report on Form 10-K.

Exhibit Number	Exhibit Description	Filed with this report	Incorporated by Reference herein from—Form or Schedule	Filing Date/ Period Covered	SEC File/Reg. Number
Governance Documents					
3.1	Restated Articles of Organization of Vertex Pharmaceuticals Incorporated, as amended.		10-Q (Exhibit 3.1)	July 26, 2018	000-19319
3.2	Amended and Restated By-Laws of Vertex Pharmaceuticals Incorporated.	X			
Stock Certificate					
4.1	Specimen Stock Certificate.		10-K (Exhibit 4.1)	February 15, 2018	000-19319
4.2	Description of Securities.	X			
Collaboration Agreement					
10.1	Research, Development and Commercialization Agreement, dated as of May 24, 2004, between Vertex Pharmaceuticals Incorporated and Cystic Fibrosis Foundation Therapeutics Incorporated.†		10-Q (Exhibit 10.1)	November 3, 2021	000-19319
10.2	Amendment No. 1 to Research, Development and Commercialization Agreement, dated as of January 6, 2006, between Vertex Pharmaceuticals Incorporated and Cystic Fibrosis Foundation Therapeutics Incorporated.†		10-Q (Exhibit 10.2)	November 3, 2021	000-19319
10.3	Amendment No. 2 to Research, Development and Commercialization Agreement, dated as of March 17, 2006, between Vertex Pharmaceuticals Incorporated and Cystic Fibrosis Foundation Therapeutics Incorporated.		10-Q/A (Exhibit 10.6)	August 19, 2011	000-19319
10.4	Amendment No. 5 to Research, Development and Commercialization Agreement, effective as of April 1, 2011, between Vertex Pharmaceuticals Incorporated and Cystic Fibrosis Foundation Therapeutics Incorporated.†		10-Q (Exhibit 10.3)	November 3, 2021	000-19319
10.5	Amendment No. 7 to Research, Development and Commercialization Agreement, dated October 13, 2016, between Vertex Pharmaceuticals Incorporated and Cystic Fibrosis Foundation Therapeutics Incorporated.†		10-Q (Exhibit 10.4)	November 3, 2021	000-19319
10.6	Amended and Restated Joint Development and Commercialization Agreement, dated April 16, 2021, between Vertex Pharmaceuticals Incorporated, Vertex Pharmaceuticals (Europe) Limited and CRISPR Therapeutics AG, CRISPR Therapeutics Limited, CRISPR Therapeutics, Inc., TRACR Hematology Ltd.†		10-Q (Exhibit 10.1)	July 30, 2021	000-19319

Exhibit Number	Exhibit Description	Filed with this report	Incorporated by Reference herein from—Form or Schedule	Filing Date/ Period Covered	SEC File/Reg. Number
10.7	Amendment No. 1 to Amended and Restated Joint Development and Commercialization Agreement, dated December 12, 2023, between Vertex Pharmaceuticals Incorporated, Vertex Pharmaceuticals (Europe) Limited and CRISPR Therapeutics AG, CRISPR Therapeutics Limited, CRISPR Therapeutics, Inc., TRACR Hematology Ltd.†		10-K (Exhibit 10.7)	February 15, 2024	000-19319
Leases					
10.8	Lease, dated May 5, 2011, between Fifty Northern Avenue LLC and Vertex Pharmaceuticals Incorporated.†		10-Q (Exhibit 10.2)	July 30, 2021	000-19319
10.9	2024 Amendment to the Lease (50 Northern Avenue), dated August 15, 2024, between Vertex Pharmaceuticals Incorporated and SNH Seaport LLC. †		10-Q (Exhibit 10.1)	November 5, 2024	000-19319
10.10	Lease, dated May 5, 2011, between Eleven Fan Pier Boulevard LLC and Vertex Pharmaceuticals Incorporated.†		10-Q (Exhibit 10.3)	July 30, 2021	000-19319
10.11	2024 Amendment to Lease (11 Fan Pier Boulevard), dated August 15, 2024, between Vertex Pharmaceuticals Incorporated and SNH Seaport LLC.†		10-Q (Exhibit 10.2)	November 5, 2024	000-19319
Financing Agreements					
10.12	Credit Agreement, dated as of July 1, 2022, by and among Vertex Pharmaceuticals Incorporated, Bank of America, N.A. and the other lenders party thereto.		10-Q (Exhibit 10.1)	August 5, 2022	000-19319
10.13	First Amendment to Credit Agreement, dated June 20, 2024 by and between Vertex Pharmaceuticals Incorporated and Bank of America N.A.		10-Q (Exhibit 10.1)	August 2, 2024	000-19319
Equity Plans					
10.14	Amended and Restated 2006 Stock and Option Plan.*		10-Q (Exhibit 10.1)	October 25, 2018	000-19319
10.15	Form of Stock Option Agreement under Amended and Restated 2006 Stock and Option Plan (granted on or after July 30, 2013).*		10-K (Exhibit 10.20)	February 13, 2015	000-19319
10.16	Amended and Restated 2013 Stock and Option Plan.*		DEF 14A (Appendix A)	April 7, 2022	000-19319
10.17	Form of Non-Qualified Stock Option Agreement under 2013 Stock and Option Plan.*		10-K (Exhibit 10.17)	February 13, 2015	000-19319
10.18	Form of Restricted Stock Unit Agreement under 2013 Stock and Option Plan (U.S.).*		10-K (Exhibit 10.25)	February 16, 2016	000-19319
10.19	Form of Restricted Stock Unit Agreement under 2013 Stock and Option Plan (International).*		10-K (Exhibit 10.19)	February 13, 2015	000-19319
10.20	Form of Restricted Stock Unit Agreement Under 2013 Stock and Option Plan.*		10-K (Exhibit 10.17)	February 13, 2020	000-19319
10.21	Form of Restricted Stock Unit Agreement under 2013 Stock and Option Plan (granted on or after January 1, 2025).*	X			
10.22	Form of Restricted Stock Unit Agreement (with performance conditions) under 2013 Stock and Option Plan.*	X			
10.23	Non-Employee Director Deferred Compensation Plan.*		10-K (Exhibit 10.27)	February 16, 2016	000-19319
10.24	Vertex Pharmaceuticals Incorporated Employee Stock Purchase Plan.*		DEF 14A (Appendix B)	April 26, 2019	000-19319
Agreements with Executive Officers and Directors					
10.25	Employment Agreement, dated as of April 1, 2020, by and between Vertex Pharmaceuticals Incorporated and Jeffrey M. Leiden, M.D., Ph.D.*		8-K (Exhibit 10.1)	April 1, 2020	000-19319
10.26	Amendment No. 1 to Employment Agreement, between Jeffrey M. Leiden and Vertex Pharmaceuticals Incorporated, dated as of February 7, 2022.*		10-K (Exhibit 10.24)	February 9, 2022	000-19319
10.27	Amendment No. 2 to Employment Agreement, between Jeffrey M. Leiden and Vertex Pharmaceuticals Incorporated, dated as of February 8, 2023*		10-K (Exhibit 10.23)	February 10, 2023	000-19319
10.28	Amendment No.3 to Employment Agreement, between Jeffrey M. Leiden and Vertex Pharmaceuticals Incorporated, dated as of November 1, 2024.*		10-Q (Exhibit 10.3)	November 5, 2024	000-19319
10.29	Employee Non-disclosure, Non-competition and Inventions Agreement between Jeffrey M. Leiden and Vertex Pharmaceuticals Incorporated, dated December 14, 2011.*		10-K (Exhibit 10.35)	February 22, 2012	000-19319
10.30	Employment Agreement, dated as of July 24, 2019, between Vertex Pharmaceuticals Incorporated and Reshma Kewalramani.*		8-K (Exhibit 10.1)	July 25, 2019	000-19319
10.31	Change of Control Agreement, dated as of July 24, 2019, between Vertex Pharmaceuticals Incorporated and Reshma Kewalramani.*		8-K (Exhibit 10.2)	July 25, 2019	000-19319

Exhibit Number	Exhibit Description	Filed with this report	Incorporated by Reference herein from—Form or Schedule	Filing Date/ Period Covered	SEC File/Reg. Number
10.32	Employment Agreement, dated as of August 27, 2012, between Vertex Pharmaceuticals Incorporated and Stuart Arbuckle.*		10-Q (Exhibit 10.1)	November 6, 2012	000-19319
10.33	Change of Control Agreement, dated as of August 27, 2012, between Vertex Pharmaceuticals Incorporated and Stuart Arbuckle.*		10-Q (Exhibit 10.2)	November 6, 2012	000-19319
10.34	Employment Agreement, dated as of December 12, 2014, between Vertex Pharmaceuticals Incorporated and David Altshuler.*		10-K (Exhibit 10.34)	February 16, 2016	000-19319
10.35	Change of Control Agreement, dated as of December 10, 2014, between Vertex Pharmaceuticals Incorporated and David Altshuler.*		10-K (Exhibit 10.35)	February 16, 2016	000-19319
10.36	Third Amended and Restated Employment Agreement, dated as of February 26, 2013, between Vertex Pharmaceuticals Incorporated and Amit Sachdev.*		10-K (Exhibit 10.42)	February 23, 2017	000-19319
10.37	Third Amended and Restated Change of Control Agreement, dated as of February 26, 2013, between Vertex Pharmaceuticals Incorporated and Amit Sachdev.*		10-K (Exhibit 10.43)	February 23, 2017	000-19319
10.38	Employment Agreement, dated February 7, 2025, by and between Vertex Pharmaceuticals Incorporated and Charles F. Wagner, Jr.*	X			
10.39	Change of Control Agreement, dated as of February 7, 2025, by and between Vertex Pharmaceuticals Incorporated and Charles F. Wagner, Jr.*	X			
10.40	Employment Agreement, dated August 1, 2020, by and between Vertex Pharmaceuticals Incorporated and Nia Tatsis.*		10-K (Exhibit 10.36)	February 9, 2022	000-19319
10.41	Change of Control Agreement, dated August 1, 2020, by and between Vertex Pharmaceuticals Incorporated and Nia Tatsis.*		10-K (Exhibit 10.37)	February 9, 2022	000-19319
10.42	Vertex Pharmaceuticals Employee Compensation Plan.*		10-K (Exhibit 10.36)	February 15, 2024	000-19319
10.43	Vertex Pharmaceuticals Non-Employee Board Compensation.*	X			
Insider Trading Policy					
19.1	Vertex Pharmaceuticals Incorporated Insider Trading Policy. *	X			
Subsidiaries					
21.1	Subsidiaries of Vertex Pharmaceuticals Incorporated.	X			
Consent					
23.1	Consent of Independent Registered Public Accounting Firm, Ernst & Young LLP.	X			
Certifications					
31.1	Certification of the Chief Executive Officer under Section 302 of the Sarbanes-Oxley Act of 2002.	X			
31.2	Certification of the Chief Financial Officer under Section 302 of the Sarbanes-Oxley Act of 2002.	X			
32	Certification of the Chief Executive Officer and the Chief Financial Officer under Section 906 of the Sarbanes-Oxley Act of 2002.	X			
Clawback Policy					
97.1	Policy Relating to Recovery of Erroneously Awarded Compensation		10-K (Exhibit 97.1)	February 15, 2024	000-19319
101.INS	XBRL Instance	X			
101.SCH	XBRL Taxonomy Extension Schema	X			
101.CAL	XBRL Taxonomy Extension Calculation	X			
101.LAB	XBRL Taxonomy Extension Labels	X			
101.PRE	XBRL Taxonomy Extension Presentation	X			
101.DEF	XBRL Taxonomy Extension Definition	X			
104	Cover Page Interactive Data File—the cover page interactive data file does not appear in the Interactive Data File because its XBRL tags are embedded within the Inline XBRL document.	X			

* Management contract, compensatory plan or agreement.

† Confidential portions of this document have been redacted according to the applicable rules.

ITEM 16. FORM 10-K SUMMARY

Not applicable.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

Vertex Pharmaceuticals Incorporated

February 13, 2025 By: /s/ Reshma Kewalramani

Reshma Kewalramani
Chief Executive Officer

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed below by the following persons on behalf of the registrant and in the capacities and on the dates indicated.

Name	Title	Date
/s/ Reshma Kewalramani Reshma Kewalramani	President, Chief Executive Officer and Director (Principal Executive Officer)	February 13, 2025
/s/ Charles F. Wagner, Jr. Charles F. Wagner, Jr.	Executive Vice President and Chief Financial Officer (Principal Financial Officer)	February 13, 2025
/s/ Kristen C. Ambrose Kristen C. Ambrose	Senior Vice President and Chief Accounting Officer (Principal Accounting Officer)	February 13, 2025
/s/Jeffrey M. Leiden Jeffrey M. Leiden	Executive Chairman	February 13, 2025
/s/ Sangeeta N. Bhatia Sangeeta N. Bhatia	Director	February 13, 2025
/s/ Lloyd Carney Lloyd Carney	Director	February 13, 2025
/s/ Alan Garber Alan Garber	Director	February 13, 2025
/s/ Michel Lagarde Michel Lagarde	Director	February 13, 2025
/s/ Diana McKenzie Diana McKenzie	Director	February 13, 2025
/s/ Nancy A. Thornberry Nancy A. Thornberry	Director	February 13, 2025
/s/ Bruce I. Sachs Bruce I. Sachs	Director	February 13, 2025
/s/ Jennifer Schneider Jennifer Schneider	Director	February 13, 2025
/s/ Suketu Upadhyay Suketu Upadhyay	Director	February 13, 2025

Report of Independent Registered Public Accounting Firm

To the Shareholders and the Board of Directors of Vertex Pharmaceuticals Incorporated

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Vertex Pharmaceuticals Incorporated (the Company) as of December 31, 2024 and 2023, the related consolidated statements of income, comprehensive income, shareholders' equity and cash flows for each of the three years in the period ended December 31, 2024, and the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2024 and 2023, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2024, in conformity with U.S. generally accepted accounting principles.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the Company's internal control over financial reporting as of December 31, 2024, based on criteria established in Internal Control-Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework), and our report dated February 13, 2025, expressed an unqualified opinion thereon.

Basis for Opinion

These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's financial statements based on our audits. We are a public accounting firm registered with the PCAOB and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

Critical Audit Matters

The critical audit matters communicated below are matters arising from the current period audit of the financial statements that were communicated or required to be communicated to the audit committee and that: (1) relate to accounts or disclosures that are material to the financial statements and (2) involved our especially challenging, subjective or complex judgments. The communication of the critical audit matters does not alter in any way our opinion on the consolidated financial statements, taken as a whole, and we are not, by communicating the critical audit matters below, providing separate opinions on the critical audit matters or on the accounts or disclosures to which they relate.

Medicaid Drug Rebate Program in the U.S.

Description of the Matter

As discussed in Note A to the Company's consolidated financial statements, the Company recognizes revenue from product sales based on amounts due from customers net of allowances for variable consideration, which include, among others, rebates mandated by law under Medicaid and other government pricing programs. The most significant estimates relate to government and private payor rebates, chargebacks, discounts and fees, collectively rebates. The Company includes an estimate of variable consideration in its transaction price at the time of sale, when control of the product transfers to the customer. The Company estimates its Medicaid and other government pricing accruals based on monthly sales, historical experience of claims submitted by the various states and jurisdictions, historical rebate rates and estimated lag time of the rebate invoices. Rebate accruals inclusive of estimated amounts due for claims not yet received or processed as part of the Company's Medicaid program are recorded within accrued expenses on the Company's consolidated balance sheet.

Auditing the allowances for rebates owed pursuant to the Medicaid Drug Rebate Program in the U.S. was complex and judgmental due to the significant estimation required in determining certain assumptions including the levels of expected utilization of these rebates based on the amount of product sold to eligible patients, as well as the complexity of the government mandated rebate calculations. The allowances for rebates owed pursuant to the Medicaid Drug Rebate Program in the U.S. are sensitive to these significant assumptions and calculations.

How We Addressed the Matter in Our Audit

We obtained an understanding, evaluated the design and tested the operating effectiveness of controls over the Company's revenue recognition process, including controls over management's computation and review of the allowances for Medicaid rebates. We tested the Company's controls to assess the completeness and accuracy of the current and historical data that supports the Medicaid estimate, significant assumptions related to the inputs utilized as well as management's review of the application of the government pricing regulations.

Our audit procedures to test the allowances for rebates owed pursuant to the Medicaid Drug Rebate Program in the U.S., included the following: we assessed the methodology used to determine the estimate and tested the significant assumptions as well as the underlying data used by the Company in its analysis. We also assessed the historical accuracy of the Company's estimates of Medicaid rebates by comparing assumptions to historical trends and evaluating the change from prior periods. We further tested the completeness and accuracy of the underlying data used in the Company's calculations through reconciliation to third-party invoices, claims data and actual cash payments. In addition, we involved our government pricing specialists to assist in evaluating management's methodology and calculations used in the measurement of certain estimated rebates.

Evaluating the fair value of the in-process research and development assets acquired in the Alpine Immune Sciences, Inc. acquisition

Description of the Matter

As described in Note B to the consolidated financial statements, on May 20, 2024, the Company acquired Alpine Immune Sciences, Inc. ("Alpine"), a publicly traded biotechnology company focused on discovering and developing innovative, protein-based immunotherapies for approximately $5.0 billion in cash.

The Company determined substantially all the fair value of the gross assets acquired were concentrated in Alpine's lead molecule, povetacicept. Therefore, the Company accounted for the Alpine transaction as an asset acquisition under U.S. GAAP. The acquired in-process research and development asset was valued at $4.4 billion, which was expensed on the date of acquisition as it did not have alternative future use at the acquisition date.

Auditing the fair value of the in-process research and development assets acquired in the Alpine transaction was judgmental due to the significant estimation uncertainty and subjectivity of the significant assumptions used by management in determining the present value of future discounted cash flows. The significant assumptions used in determining the fair value of the in-process research and development assets acquired included the amount and timing of future product revenues, the discount rate and probability of technical and regulatory success. The valuation of the in-process research and development assets is sensitive to these significant assumptions.

How We Addressed the Matter in Our Audit

We obtained an understanding, evaluated the design and tested the operating effectiveness of controls over management's review of the valuation of the in-process research and development assets of Alpine. For example, we tested controls over management's review of the significant assumptions and the completeness and accuracy of the data used in the valuation.

To test the fair value of the povetacicept in-process research and development assets, we performed audit procedures that included, among others, evaluating the Company's methodologies used and testing the significant assumptions discussed above. For example, we compared the significant assumptions used by management to current published scientific studies, industry, market and economic trends, and to other relevant factors. In addition, to evaluate the probability of technical and regulatory success, we considered the phase of development of the in-process research and development assets and compared the Company's assumptions to third-party data regarding clinical trial success rates. We also performed various sensitivity analyses of the significant assumptions to evaluate the change in the fair value of the in-process research and development assets resulting from changes in the assumptions. In addition, we involved our valuation specialists to assist in our evaluation of the methodologies and the discount rate used in the fair value estimates.

/s/ Ernst & Young LLP

We have served as the Company's auditor since 2005.

Boston, Massachusetts
February 13, 2025

VERTEX PHARMACEUTICALS INCORPORATED
Consolidated Statements of Income
(in millions, except per share amounts)

	Year Ended December 31,		
	2024	**2023**	**2022**
Product revenues, net	$ 11,020.1	$ 9,869.2	$ 8,930.7
Costs and expenses:			
Cost of sales	1,530.5	1,262.2	1,080.3
Research and development expenses	3,630.3	3,162.9	2,540.3
Acquired in-process research and development expenses	4,628.4	527.1	115.5
Selling, general and administrative expenses	1,464.3	1,136.6	944.7
Change in fair value of contingent consideration	(0.5)	(51.6)	(57.5)
Total costs and expenses	11,253.0	6,037.2	4,623.3
(Loss) income from operations	(232.9)	3,832.0	4,307.4
Interest income	598.1	614.7	144.6
Interest expense	(30.6)	(44.1)	(54.8)
Other expense, net	(86.1)	(22.8)	(164.8)
Income before provision for income taxes	248.5	4,379.8	4,232.4
Provision for income taxes	784.1	760.2	910.4
Net (loss) income	$ (535.6)	$ 3,619.6	$ 3,322.0
Net (loss) income per common share:			
Basic	$ (2.08)	$ 14.05	$ 12.97
Diluted	$ (2.08)	$ 13.89	$ 12.82
Shares used in per share calculations:			
Basic	257.9	257.7	256.1
Diluted	257.9	260.5	259.1

The accompanying notes are an integral part of these consolidated financial statements.

VERTEX PHARMACEUTICALS INCORPORATED
Consolidated Statements of Comprehensive Income
(in millions)

	Year ended December 31,		
	2024	**2023**	**2022**
Net (loss) income	$ (535.6)	$ 3,619.6	$ 3,322.0
Other comprehensive income (loss):			
Unrealized holding (losses) gains on marketable securities, net of tax of $0.6, $(2.7) and zero, respectively	(2.5)	9.7	0.4
Unrealized gains (losses) on foreign currency forward contracts, net of tax of $(38.2), $14.0 and $1.0, respectively	136.0	(50.9)	(4.1)
Foreign currency translation adjustment	8.6	26.1	(11.4)
Total other comprehensive income (loss)	142.1	(15.1)	(15.1)
Comprehensive (loss) income	$ (393.5)	$ 3,604.5	$ 3,306.9

The accompanying notes are an integral part of these consolidated financial statements.

VERTEX PHARMACEUTICALS INCORPORATED
Consolidated Balance Sheets
(in millions, except share data)

	December 31, 2024	December 31, 2023
Assets		
Current assets:		
Cash and cash equivalents	$ 4,569.6	$ 10,369.1
Marketable securities	1,546.3	849.2
Accounts receivable, net	1,609.4	1,563.4
Inventories	1,205.4	738.8
Prepaid expenses and other current assets	665.7	623.7
Total current assets	9,596.4	14,144.2
Property and equipment, net	1,227.8	1,159.3
Goodwill	1,088.0	1,088.0
Other intangible assets, net	825.9	839.9
Deferred tax assets	2,331.1	1,812.1
Operating lease assets	1,356.8	293.6
Long-term marketable securities	5,107.9	2,497.8
Other assets	999.3	895.3
Total assets	$ 22,533.2	$ 22,730.2
Liabilities and Shareholders' Equity		
Current liabilities:		
Accounts payable	$ 413.0	$ 364.9
Accrued expenses	2,788.6	2,655.3
Other current liabilities	363.0	527.2
Total current liabilities	3,564.6	3,547.4
Long-term operating lease liabilities	1,544.4	348.6
Long-term finance lease liabilities	112.8	376.1
Other long-term liabilities	901.8	877.7
Total liabilities	6,123.6	5,149.8
Commitments and contingencies	—	—
Shareholders' equity:		
Preferred stock, $0.01 par value; 1,000,000 shares authorized; none issued and outstanding	—	—
Common stock, $0.01 par value; 500,000,000 shares authorized, 256,940,382 and 257,695,221 shares issued and outstanding, respectively	2.6	2.6
Additional paid-in capital	6,672.4	7,449.7
Accumulated other comprehensive income (loss)	127.8	(14.3)
Retained earnings	9,606.8	10,142.4
Total shareholders' equity	16,409.6	17,580.4
Total liabilities and shareholders' equity	$ 22,533.2	$ 22,730.2

The accompanying notes are an integral part of these consolidated financial statements.

VERTEX PHARMACEUTICALS INCORPORATED
Consolidated Statements of Shareholders' Equity
(in millions)

	Common Stock		Additional Paid-in Capital	Accumulated Other Comprehensive Income (Loss)	Retained Earnings	Total Shareholders' Equity
	Shares	Amount				
Balance at December 31, 2021	254.5	$ 2.5	$ 6,880.8	$ 15.9	$ 3,200.8	$ 10,100.0
Other comprehensive loss, net of tax	—	—	—	(15.1)	—	(15.1)
Net income	—	—	—	—	3,322.0	3,322.0
Common stock withheld for employee tax obligations	(0.7)	(0.0)	(172.0)	—	—	(172.0)
Issuance of common stock under benefit plans	3.2	0.1	187.3	—	—	187.4
Stock-based compensation expense	—	—	490.4	—	—	490.4
Balance at December 31, 2022	257.0	$ 2.6	$ 7,386.5	$ 0.8	$ 6,522.8	$ 13,912.7
Other comprehensive loss, net of tax	—	—	—	(15.1)	—	(15.1)
Net income	—	—	—	—	3,619.6	3,619.6
Repurchases of common stock	(1.3)	(0.0)	(427.6)	—	—	(427.6)
Common stock withheld for employee tax obligations	(0.7)	(0.0)	(226.1)	—	—	(226.1)
Issuance of common stock under benefit plans	2.7	0.0	133.4	—	—	133.4
Stock-based compensation expense	—	—	583.5	—	—	583.5
Balance at December 31, 2023	257.7	$ 2.6	$ 7,449.7	$ (14.3)	$ 10,142.4	$ 17,580.4
Other comprehensive income, net of tax	—	—	—	142.1	—	142.1
Net loss	—	—	—	—	(535.6)	(535.6)
Repurchases of common stock	(2.7)	(0.0)	(1,194.9)	—	—	(1,194.9)
Common stock withheld for employee tax obligations	(0.9)	(0.0)	(405.0)	—	—	(405.0)
Issuance of common stock under benefit plans	2.8	0.0	113.5	—	—	113.5
Stock-based compensation expense	—	—	709.1	—	—	709.1
Balance at December 31, 2024	256.9	$ 2.6	$ 6,672.4	$ 127.8	$ 9,606.8	$ 16,409.6

The accompanying notes are an integral part of these consolidated financial statements.

VERTEX PHARMACEUTICALS INCORPORATED
Consolidated Statements of Cash Flows
(in millions)

	Year Ended December 31,		
	2024	**2023**	**2022**
Cash flows from operating activities:			
Net (loss) income	$ (535.6)	$ 3,619.6	$ 3,322.0
Adjustments to reconcile net (loss) income to net cash (used in) provided by operating activities:			
Stock-based compensation expense	698.5	581.2	491.3
Depreciation and amortization expenses	207.2	181.3	148.3
Deferred income taxes	(348.8)	(536.5)	(275.9)
Losses on equity securities	57.7	0.6	149.1
Decrease in fair value of contingent consideration	(0.5)	(51.6)	(57.5)
Other non-cash items, net	(56.3)	8.4	11.8
Changes in operating assets and liabilities:			
Accounts receivable, net	(99.3)	(84.1)	(358.6)
Inventories	(517.3)	(322.9)	(136.4)
Prepaid expenses and other assets	(200.3)	(545.7)	(326.4)
Accounts payable	49.5	48.7	120.8
Accrued expenses	212.9	429.4	542.5
Other liabilities	39.7	208.9	498.9
Net cash (used in) provided by operating activities	(492.6)	3,537.3	4,129.9
Cash flows from investing activities:			
Purchases of available-for-sale debt securities	(7,438.2)	(3,786.5)	(692.7)
Sales and maturities of available-for-sale debt securities	4,465.6	839.1	920.0
Purchases of property and equipment	(297.7)	(200.4)	(204.7)
Sale of equity securities	—	95.1	—
Net payments related to finite-lived intangible assets	(187.7)	(58.0)	—
Acquisition of available-for-sale debt securities from Alpine Immune Sciences, Inc.	(258.0)	—	—
Payment to acquire ViaCyte, Inc., net of cash acquired	—	—	(295.9)
Other investing activities	(54.0)	(31.0)	(47.8)
Net cash used in investing activities	(3,770.0)	(3,141.7)	(321.1)
Cash flows from financing activities:			
Issuances of common stock under benefit plans	114.6	134.6	186.3
Repurchases of common stock	(1,177.1)	(427.6)	—
Payments in connection with common stock withheld for employee tax obligations	(405.0)	(226.1)	(172.0)
Payments on finance leases	(33.6)	(44.9)	(85.5)
Other financing activities	6.2	1.8	3.5
Net cash used in financing activities	(1,494.9)	(562.2)	(67.7)
Effect of changes in exchange rates on cash	(42.6)	26.9	(29.2)
Net (decrease) increase in cash, cash equivalents and restricted cash	(5,800.1)	(139.7)	3,711.9
Cash, cash equivalents and restricted cash—beginning of period	10,372.3	10,512.0	6,800.1
Cash, cash equivalents and restricted cash—end of period	$ 4,572.2	$ 10,372.3	$ 10,512.0
Supplemental disclosure of cash flow information:			
Cash paid for income taxes	$ 1,082.1	$ 1,677.3	$ 1,057.8
Cash paid for interest	$ 30.5	$ 43.1	$ 52.3
Net payments due to CRISPR Therapeutics AG related to finite-lived intangible assets	$ —	$ 180.0	$ —

The accompanying notes are an integral part of these consolidated financial statements.

A. Nature of Business and Accounting Policies

Business

Vertex Pharmaceuticals Incorporated ("Vertex," "we," "us" or "our") is a global biotechnology company that invests in scientific innovation to create transformative medicines for people with serious diseases, with a focus on specialty markets. We have seven approved medicines: five that treat the underlying cause of cystic fibrosis ("CF"), a life-threatening genetic disease, one that treats severe sickle cell disease ("SCD") and transfusion dependent beta thalassemia ("TDT"), life shortening inherited blood disorders, and one that treats moderate-to-severe acute pain. Our pipeline includes clinical-stage programs in CF, SCD, beta thalassemia, acute and peripheral neuropathic pain, APOL1-mediated kidney disease, IgA nephropathy and other autoimmune renal diseases and cytopenias, type 1 diabetes ("T1D"), myotonic dystrophy type 1 ("DM1"), and autosomal dominant polycystic kidney disease.

Our marketed CF medicines are ALYFTREK (vanzacaftor/tezacaftor/deutivacaftor), which was approved by the U.S. Food and Drug Administration (the "FDA") in December 2024, TRIKAFTA/KAFTRIO (elexacaftor/tezacaftor/ivacaftor and ivacaftor), SYMDEKO/SYMKEVI (tezacaftor/ivacaftor and ivacaftor), ORKAMBI (lumacaftor/ivacaftor) and KALYDECO (ivacaftor).

We have received approval to market CASGEVY (exagamglogene autotemcel), a gene-therapy, for the treatment of SCD or TDT in the United States ("U.S."), the European Union ("E.U."), the United Kingdom ("U.K."), the Kingdom of Saudi Arabia, the Kingdom of Bahrain, the United Arab Emirates, Canada and Switzerland. CASGEVY was initially approved by the FDA in December 2023.

In January 2025, the FDA approved JOURNAVX (suzetrigine), our selective non-opioid NaV1.8 pain signal inhibitor, for the treatment of moderate-to-severe acute pain.

Basis of Presentation

The accompanying consolidated financial statements, which have been prepared in accordance with accounting principles generally accepted in the U.S. ("U.S. GAAP"), reflect the operations of Vertex and our wholly owned subsidiaries. All material intercompany balances and transactions have been eliminated. We operate in one segment, pharmaceuticals. Please refer to Note Q, "Segment Information," for enterprise-wide disclosures regarding our revenues, major customers, significant segment expenses, and long-lived assets by geographic area.

Use of Estimates

The preparation of consolidated financial statements in accordance with U.S. GAAP requires us to make certain estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of our consolidated financial statements, and the amounts of revenues and expenses during the reported periods. We base our estimates on historical experience and various other assumptions, including in certain circumstances future projections that we believe to be reasonable under the circumstances. Actual results could differ from those estimates. Changes in estimates are reflected in reported results in the period in which they become known.

Revenue Recognition

We recognize revenue when a customer obtains control of promised goods or services. We record the amount of revenue that reflects the consideration that we expect to receive in exchange for those goods or services. We apply the following five-step model to determine this amount: (i) identification of the promised goods or services in the contract; (ii) determination of whether the promised goods or services are performance obligations, including whether they are distinct in the context of the contract; (iii) measurement of the transaction price, including the constraint on variable consideration; (iv) allocation of the transaction price to the performance obligations; and (v) recognition of revenue when (or as) we satisfy each performance obligation.

We only apply the five-step model to contracts when it is probable that we will collect the consideration to which we are

entitled in exchange for the goods or services that we transfer to the customer. Once a contract is determined to be within the scope of Accounting Standards Codification ("ASC") 606, *Revenue from Contracts with Customers* at contract inception, we review the contract to determine which performance obligations we must deliver and which of these performance obligations are distinct. We recognize as revenue the amount of the transaction price that is allocated to each performance obligation when that performance obligation is satisfied or as it is satisfied. Generally, our performance obligations are transferred to customers at a point in time, typically upon delivery.

Product Revenues, Net

We sell our products primarily to a limited number of specialty pharmacy and specialty distributors globally, as well as to retail pharmacies, hospitals and clinics internationally. Many of the international hospital and clinics are government-owned or supported. In the U.S., we also sell certain products to major wholesalers. Our customers in the U.S. subsequently resell our products to patients, health care providers, or authorized treatment centers ("ATCs"). In certain markets, we may sell CASGEVY directly to ATCs. Revenue recognition typically occurs upon delivery of our small molecule products, including our CF medicines, and upon infusion of our gene-therapy products, including CASGEVY.

Revenues from product sales are recorded at the net sales price, or "transaction price," which includes estimates of variable consideration that result from (a) invoice discounts for prompt payment and distribution fees, (b) government and private payor rebates, chargebacks, discounts and fees, (c) product returns, and (d) other incentives for certain indirect customers, including costs of co-pay assistance programs for patients. Reserves are established for the estimates of variable consideration based on the amounts earned or to be claimed on the related sales. The reserves are classified as reductions to "Accounts receivable, net" if payable to a customer or "Accrued expenses" if payable to a third-party. Where appropriate, we utilize the expected value method to determine the appropriate amount for estimates of variable consideration based on factors such as our historical experience, current contractual and statutory requirements, specific known market events and trends, industry data and forecasted customer buying and payment patterns. The amount of variable consideration that is included in the transaction price may be constrained and is included in our net product revenues only to the extent that it is probable that a significant reversal in the amount of the cumulative revenue recognized will not occur in a future period. Actual amounts of consideration ultimately received may differ from our estimates. If actual results vary from our estimates, we adjust these estimates, which would affect net product revenue and earnings in the period such variances become known.

Invoice Discounts and Distribution Fees: In the U.S., we may provide invoice discounts on product sales to our customers for prompt payment and pay distribution and administrative fees, such as fees for certain data that customers provide to us. These fees are based on a fixed percentage of sales. We estimate that, based on our experience, our customers will earn these discounts and fees, and deduct the full amount of these discounts and fees from our gross product revenues and accounts receivable at the time such revenues are recognized.

Rebates, Chargebacks, Discounts and Fees: We contract with government agencies and commercial payors (our "Third-party Payors") so that products will be eligible for purchase by, or partial or full reimbursement from, such Third-party Payors. We estimate the rebates, chargebacks, discounts and fees we will provide to Third-party Payors and deduct these estimated amounts from our gross product revenues at the time the revenues are recognized. For each product, we estimate the aggregate rebates, chargebacks and discounts that we will provide to Third-party Payors based upon (i) our contracts with these Third-party Payors, (ii) the government-mandated discounts and fees applicable to government-funded programs, (iii) information obtained from our customers and other third-party data regarding the payor mix for such product and (iv) historical experience.

Product Returns: We typically permit returns if our product is damaged, defective, or otherwise cannot be used by our customer. However, our return policies vary by product and market. We record deductions from our gross product revenues for estimated sales returns in the period the related revenue is recognized and base our estimate for returns on historical experience and known or expected changes in the marketplace specific to each product.

Other Incentives: Other incentives that we offer include co-pay mitigation rebates that we provide in the U.S. to commercially insured patients who have coverage and who reside in states that permit co-pay mitigation programs. Based upon the terms of our co-pay mitigation programs, we estimate average co-pay mitigation amounts for each of our products to establish appropriate accruals.

We make significant estimates and judgments that materially affect our recognition of net product revenues. We adjust our estimated rebates, chargebacks and discounts based on new information, including information regarding actual rebates, chargebacks and discounts for our products, as it becomes available. Claims by third-party payors for rebates, chargebacks and discounts frequently are submitted to us significantly after the related sales, potentially resulting in adjustments in the period in which the new information becomes known. Our credits to product revenue related to prior period sales have not been significant and primarily related to rebates and discounts.

Our payment terms, which typically range from 30 to 150 days depending on the product and market, are consistent with prevailing market practice. We do not adjust our net product revenues for the effects of a significant financing component for transactions where we expect, at contract inception, the period between our customer obtaining control of our product and when we receive payment to be one year or less.

We exclude taxes collected from customers relating to product sales and remitted to governmental authorities from revenues.

Contract Liabilities

We had contract liabilities of $206.8 million and $170.3 million as of December 31, 2024 and 2023, respectively, primarily related to annual contracts with government-owned and supported customers in international markets that limit the amount of annual reimbursement we can receive for our CF products. Upon exceeding the annual reimbursement amount provided by the customer's contract with us, our CF products are provided free of charge, which is a material right. These contracts include upfront payments and fees. If we estimate that we will exceed the annual reimbursement amount under a contract, we defer a portion of the consideration received for shipments made up to the annual reimbursement limit as a portion of "Other current liabilities." Once the reimbursement limit has been reached, we recognize the deferred amount as revenue when we deliver the free products. Our CF product revenue contracts include performance obligations that are one year or less.

Our contract liabilities at the end of each fiscal year relate to contracts with CF annual reimbursement limits in international markets in which the annual period associated with the contract is not the same as our fiscal year. In these markets we recognize revenues related to performance obligations satisfied in previous years; however, these revenues do not relate to any performance obligations that were satisfied more than 12 months prior to the beginning of the current year. During the years ended December 31, 2024, 2023 and 2022, we recorded $170.3 million, $159.6 million and $171.7 million, respectively, of CF product revenues that were recorded as contract liabilities at the beginning of the year.

Concentration of Credit Risk

Financial instruments that potentially subject us to concentration of credit risk consist principally of cash equivalents and marketable securities. We place these investments with highly rated financial institutions, and, by policy, limit the amount of credit exposure to any one financial institution. We also maintain a foreign currency hedging program that includes foreign currency forward contracts with several counterparties. We have not experienced any credit losses related to these financial instruments and do not believe we are exposed to any significant credit risk related to these instruments.

We are also subject to credit risk from our accounts receivable related to our product sales and collaborators. We evaluate the creditworthiness of each of our customers and have determined that all our material customers are creditworthy. To date, we have not experienced significant losses with respect to the collection of our accounts receivable. We believe that our allowances, which are not significant to our consolidated financial statements, are adequate at December 31, 2024. Please refer to Note Q, "Segment Information," for further information.

Cash and Cash Equivalents

We consider all highly liquid investments with original maturities of three months or less at the date of purchase to be cash equivalents.

Marketable Securities

As of December 31, 2024, our marketable securities consisted of investments in available-for-sale debt securities and corporate equity securities with readily determinable fair values. We classify marketable securities with current maturities of less than one year as current assets on our consolidated balance sheets. The remainder of our marketable securities are classified as long-term assets within "Long-term marketable securities" on our consolidated balance sheets. The fair value of these securities is based on quoted prices for identical or similar assets.

We record unrealized gains (losses) on available-for-sale debt securities as a component of "Accumulated other comprehensive income (loss)," which is a separate component of shareholders' equity on our consolidated balance sheets, until such gains and losses are realized. Realized gains and losses, if any, are determined using the specific identification method.

For available-for-sale debt securities in unrealized loss positions, we are required to assess whether to record an allowance for credit losses using an expected loss model. A credit loss is limited to the amount by which the amortized cost of an investment exceeds its fair value. A previously recognized credit loss may be decreased in subsequent periods if our estimate of fair value for the investment increases. To determine whether to record a credit loss, we consider issuer specific credit ratings and historical losses as well as current economic conditions and our expectations for future economic conditions.

We record changes in the fair value of our investments in corporate equity securities to "Other expense, net" in our consolidated statements of income. Realized gains and losses, which are also included in "Other expense, net," are determined on an original weighted-average cost basis.

Accounts Receivable

We deduct invoice discounts for prompt payment and fees for distribution services from our accounts receivable based on our experience that our customers will earn these discounts and fees. Our estimates for our allowance for credit losses, which has not been significant to date, is determined based on existing contractual payment terms, historical payment patterns, current economic conditions and our expectation for future economic conditions.

Stock-based Compensation Expense

We expense the fair value of employee restricted stock units and other forms of stock-based employee compensation over the associated employee service period on a straight-line basis. Stock-based compensation expense is determined based on the fair value of the award at the grant date and is adjusted each period to reflect actual forfeitures and the outcomes of certain performance conditions.

For awards with performance conditions in which the award does not vest unless the performance condition is met, we recognize expense if, and to the extent that, we estimate that achievement of the performance condition is probable. If we conclude that vesting is probable, we recognize expense from the date we reach this conclusion through the estimated vesting date.

We provide to employees who have rendered a certain number of years of service to Vertex and meet certain age requirements, partial or full acceleration of vesting of these equity awards, subject to certain conditions including a notification period, upon a termination of employment other than for cause. Approximately 5% of our employees were eligible for partial or full acceleration of any of their equity awards as of December 31, 2024. We recognize stock-based compensation expense related to these awards over a service period reflecting qualified employees' eligibility for partial or full acceleration of vesting.

Please refer to Note N, "Stock-based Compensation Expense," for tables displaying our stock-based compensation expense by type of award and by line item within our consolidated statements of income.

Cost of Sales

Our cost of sales primarily includes royalty expenses, cost of product sales, intangible asset amortization expenses, and other items related to our manufacturing processes, adjusted by CRISPR Therapeutics AG's ("CRISPR") share of the net commercial profits or losses for CASGEVY. Please refer to Note B, "Collaboration, License and Other Arrangements," for further information on our royalties related to our CF products and our agreements with CRISPR related to the treatment of net commercial profits or losses for CASGEVY.

Shipping and handling costs incurred for inventory purchases are capitalized and recorded upon sale in "Cost of sales" in our consolidated statements of income. Shipping and handling costs incurred for product shipments are recorded as incurred in "Cost of sales" in our consolidated statements of income.

Research and Development Expenses

Research and development expenses are comprised of costs we incur in performing research and development activities, including salary and benefits; stock-based compensation expense; outsourced services and other direct expenses, including clinical trial, pharmaceutical development and drug supply costs; intangible asset impairment charges; and infrastructure costs, including facilities costs and depreciation expense. We recognize research and development expenses as incurred. We capitalize nonrefundable advance payments we make for research and development activities and expense the payments as the related goods are delivered or the related services are performed.

Acquired In-process Research and Development Expenses

Our research and development activities include upfront, contingent milestone, and other payments pursuant to our business development transactions, including collaborations, licenses of third-party technologies, and asset acquisitions. In-process research and development that is acquired in a transaction that does not qualify as a business combination under U.S. GAAP and that does not have an alternative future use is recorded to "Acquired in-process research and development expenses" ("AIPR&D") in our consolidated statements of income in the period in which it is acquired.

In transactions that do not qualify as a business combination, we present the cost to acquire AIPR&D within our "Cash flows from operating activities" in our consolidated statements of cash flows.

Inventories

We value our inventories at the lower-of-cost or net realizable value. We determine the cost of our inventories, which include amounts related to materials and manufacturing overhead, on a first-in, first-out basis. We perform an assessment of the recoverability of our capitalized inventory during each reporting period and write down any excess and obsolete inventories to their net realizable value in the period in which the impairment is first identified.

We capitalize inventories prior to regulatory approval when we consider the related product candidate to have a high likelihood of regulatory approval and expect to recover the related costs. In making this determination, we evaluate, among other factors, the status of regulatory submissions and communications with regulatory authorities, information regarding the product candidate's safety and efficacy, and the outlook for commercial sales, including the existence of any competition.

Property and Equipment

Property and equipment are recorded at cost, net of accumulated depreciation. Depreciation expense is recorded using the straight-line method over the estimated useful life of the related asset generally as follows:

Description	Estimated Useful Life
Buildings and improvements	15 to 40 years
Laboratory equipment, other equipment and furniture	7 to 10 years
Leasehold improvements; assets under finance leases	The shorter of the useful life of the assets or the estimated remaining term of the associated lease
Computers and software	3 to 5 years

Maintenance and repairs to an asset that do not improve or extend its life are expensed as incurred. When assets are retired or otherwise disposed of, the assets and related accumulated depreciation are eliminated from the accounts and any resulting gain or loss is reflected in our consolidated statements of income. We perform an assessment of the fair value of the assets if indicators of impairment are identified during a reporting period and record the assets at the lower of the net book value or the fair value of the assets.

We capitalize costs incurred to develop software for internal use during the application development stage, which are depreciated over the useful life of the related asset.

Cloud Computing Service Contracts

We classify costs incurred to implement cloud computing service contracts as "Other assets" on our consolidated balance sheets. Amortization is recorded over the noncancellable term of the cloud computing service contract, plus any optional renewal periods that are reasonably certain to be exercised.

Leases

We determine whether an arrangement contains a lease at inception. If a lease is identified in an arrangement, we recognize a right-of-use asset and liability on our consolidated balance sheet and determine whether the lease should be classified as a finance or operating lease. We do not recognize assets or liabilities for leases with lease terms of less than 12 months.

A lease qualifies as a finance lease if any of the following criteria are met at the inception of the lease: (i) there is a transfer of ownership of the leased asset to Vertex by the end of the lease term, (ii) we hold an option to purchase the leased asset that we are reasonably certain to exercise, (iii) the lease term is for a major part of the remaining economic life of the leased asset, (iv) the present value of the sum of lease payments equals or exceeds substantially all of the fair value of the leased asset, or (v) the nature of the leased asset is specialized to the point that it is expected to provide the lessor no alternative use at the end of the lease term. All other leases are recorded as operating leases.

Finance and operating lease assets and liabilities are recognized at the lease commencement date based on the present value of the lease payments over the lease term using the discount rate implicit in the lease. If the rate implicit is not readily determinable, we utilize our incremental borrowing rate at the lease commencement date. Operating lease assets are further adjusted for prepaid or accrued lease payments. Operating lease payments are expensed using the straight-line method as an operating expense over the lease term. Finance lease assets are amortized to depreciation expense using the straight-line method over the shorter of the useful life of the related asset or the lease term. Finance lease payments are bifurcated into (i) a portion that is recorded as imputed interest expense and (ii) a portion that reduces the finance liability associated with the lease.

For our real estate leases, we account for lease and fixed non-lease components together as a single lease component. For our embedded leases with contract manufacturing organizations, we account for the lease component separately from the non-lease components. Variable lease payments are expensed as incurred. If a lease includes an option to extend or terminate the lease, we reflect the option in the lease term if it is reasonably certain we will exercise the option.

Finance leases are recorded in "Property and equipment, net," "Other current liabilities" and "Long-term finance lease liabilities," and operating leases are recorded in "Operating lease assets," "Other current liabilities" and "Long-term operating lease liabilities" on our consolidated balance sheets.

Income Taxes

Our provision for income taxes is accounted for under the asset and liability method and includes federal, state, local and foreign taxes.

Deferred tax assets and liabilities are recognized for the estimated future tax consequences of temporary differences between the financial statement carrying amounts and the income tax bases of assets and liabilities. Deferred tax assets and liabilities are measured using enacted tax rates expected to apply to taxable income in the year in which the temporary differences are expected to be recovered or settled. A valuation allowance is applied against any net deferred tax asset if,

based on the available evidence, it is more likely than not that some or all of the deferred tax assets will not be realized. On a periodic basis, we reassess the valuation allowance on our deferred income tax assets weighing positive and negative evidence to assess the recoverability of our deferred tax assets. We include, among other things, our recent financial performance and our future projections in this periodic assessment.

We record liabilities related to uncertain tax positions by prescribing a minimum recognition threshold and measurement attribute for the financial statement recognition and measurement of a tax position taken or expected to be taken in a tax return. We evaluate our uncertain tax positions on a quarterly basis and consider various factors, including, but not limited to, changes in tax law, the measurement of tax positions taken or expected to be taken in our tax returns, and changes in facts or circumstances related to a tax position. We adjust our liabilities to reflect any subsequent changes in the relevant facts and circumstances surrounding the uncertain positions. We accrue interest and penalties related to unrecognized tax benefits as a component of our "Provision for income taxes."

As part of the U.S. Tax Cut and Jobs Act of 2017, we are subject to a territorial tax system, under which we must establish an accounting policy to provide for tax on Global Intangible Low Taxed Income ("GILTI") earned by certain foreign subsidiaries. We have elected to treat the impact of GILTI as a current tax expense in our "Provision for income taxes."

Fair Value of Contingent Consideration

We base our estimates of the probability of achieving the milestones relevant to the fair value of contingent payments on industry data and our knowledge of the programs and viability of the programs. Estimates included in the discounted cash flow models pertaining to contingent payments also include: (i) estimates regarding the timing of the relevant development and commercial milestones and royalties, and (ii) and appropriate discount rates. We record any increases or decreases in the fair value of our contingent payments to "Change in fair value of contingent consideration" in our consolidated statements of income. We record our contingent consideration liabilities at fair value on our consolidated balance sheets as "Other current liabilities" or "Other long-term liabilities" depending on when we estimate we will pay them. Please refer to Note D, "Fair Value Measurements," for further information.

In-process Research and Development Assets

We record the fair value of in-process research and development assets as of the transaction date of a business combination on our consolidated balance sheets as "Other intangible assets, net." These assets are used in research and development activities but have not yet reached technological feasibility, which occurs when we complete the research and development efforts by obtaining regulatory approval to market an underlying product candidate. We characterize in-process research and development assets on our consolidated balance sheets as indefinite-lived intangible assets until either they achieve regulatory approval and become finite-lived intangible assets, or the assets are impaired. Upon completion of the associated research and development efforts, we will determine the remaining estimated life of the marketed product and begin amortizing the carrying value of the assets over this period. If the assets become impaired or are abandoned, the carrying value is written down to fair value, and we record an impairment charge in the period in which the impairment occurs. We test in-process research and development assets for impairment on an annual basis as of October 1, and more frequently if indicators are present or changes in circumstances suggest that impairment may exist.

The fair value of our in-process research and development assets is determined using either the multi-period excess earnings or the relief from royalty methods of the income approach. Each method requires us to make: (i) assumptions regarding the probability of obtaining marketing approval for a product candidate; (ii) estimates of future cash flows from potential product sales with respect to a product candidate; and (iii) appropriate discount and tax rates. The multi-period excess earnings method also requires us to estimate the timing of and the expected costs to develop and commercialize a product candidate. The relief from royalty method also requires us to estimate the after-tax royalty savings expected from ownership of a product candidate that we acquired.

Finite-lived Intangible Assets

We record finite-lived intangible assets at cost, net of accumulated amortization, on our consolidated balance sheets as "Other intangible assets, net." Most of these assets relates to our marketed products and may include, among other things,

completed research and development projects that were previously reflected on our consolidated balance sheets as in-process research and development assets, or rights to developed technology associated with in-licenses, regulatory approval milestones due to our collaborators, or other payments. We amortize our finite-lived intangible assets related to our marketed products using the straight-line method within "Cost of sales" over the remaining estimated life of the assets beginning in the period in which regulatory approval is achieved or the assets are acquired and continuing through the period that we no longer have either exclusive rights to market the products associated with the assets or in-license rights to the intellectual property underlying the assets.

We test our finite-lived intangible assets for impairment if indicators are present or changes in circumstances suggest that the carrying value of the assets may not be recoverable. If we determine that the carrying value of a finite-lived intangible asset may not be recoverable, we compare the carrying value of the asset's group to the undiscounted cash flows that we expect the asset group to generate. When we determine that a finite-lived intangible asset has become impaired, we write down the carrying value of the asset to its fair value and record an impairment charge in the period in which the impairment occurs.

Goodwill

The difference between the purchase price and the fair value of assets acquired and liabilities assumed in a business combination is allocated to goodwill. Goodwill is evaluated for impairment by reporting unit on an annual basis as of October 1, and more frequently if indicators are present or changes in circumstances suggest that impairment may exist. As noted in *Basis of Presentation* above, we have one operating segment, pharmaceuticals, which is our only reporting unit.

Hedging Activities

We recognize the fair value of our foreign currency forward contracts that are designated and qualify as hedging instruments pursuant to U.S. GAAP as either assets or liabilities on our consolidated balance sheets. Changes in the fair value of these instruments are recorded each period in "Accumulated other comprehensive income (loss)" as unrealized gains and losses until the forecasted underlying transaction occurs. Unrealized gains and losses on these foreign currency forward contracts are included in "Prepaid expenses and other current assets" or "Other assets," and "Other current liabilities" or "Other long-term liabilities," respectively, on our consolidated balance sheets depending on the remaining period until their contractual maturity. Realized gains and losses for the effective portion of such contracts are recognized in "Product revenues, net" in our consolidated statement of income in the same period that we recognize the product revenues that were impacted by the hedged foreign exchange rate changes. We classify the cash flows from hedging instruments in the same category as the cash flows from the hedged items.

Certain of our hedging instruments are subject to master netting arrangements to reduce the risk arising from such transactions with our counterparties. We present unrealized gains and losses on our foreign currency forward contracts on a gross basis within our consolidated balance sheets.

We also enter into foreign currency forward contracts, typically with contractual maturities of approximately one month designed to mitigate the effect of changes in foreign exchange rates on monetary assets and liabilities including intercompany balances. These contracts are not designated as hedging instruments pursuant to U.S. GAAP. Realized gains and losses for such contracts are recognized in "Other expense, net" in our consolidated statements of income each period.

Comprehensive Income (Loss)

Comprehensive income (loss) consists of net income (loss) and other comprehensive income (loss), which includes foreign currency translation adjustments and unrealized gains and losses on foreign currency forward contracts and our available-for-sale debt securities. For purposes of comprehensive income disclosures, we record provisions for or benefits from income taxes related to the unrealized gains and losses on foreign currency forward contracts and our available-for-sale debt securities. We record provisions for or benefits from income taxes related to our cumulative translation adjustment only for those undistributed earnings in our foreign subsidiaries that we do not intend to permanently reinvest.

Foreign Currency Translation and Transactions

The majority of our operations occur in entities that have the U.S. dollar denominated as their functional currency. The assets and liabilities of our entities with functional currencies other than the U.S. dollar are translated into U.S. dollars at exchange rates in effect at the end of the year. Revenue and expense amounts for these entities are translated using the average exchange rates for the period. Changes resulting from foreign currency translation are included in "Accumulated other comprehensive income (loss)." Net foreign currency exchange transaction losses, which are included in "Other expense, net" on our consolidated statements of income, were $27.3 million, $24.6 million and $15.1 million for 2024, 2023 and 2022, respectively. These net foreign currency exchange losses are presented net of the impact of the foreign currency forward contracts designed to mitigate their effect on our consolidated statements of income.

Share Repurchase Programs

Repurchases of our common stock are recorded as reductions to "Common Stock" and "Additional paid-in capital" pursuant to our established accounting policy. Repurchases in excess of the par value will be recorded as reductions to "Retained earnings" in the event that "Additional paid-in capital" is reduced to zero.

Net Income (Loss) Per Common Share

Basic net income (loss) per common share is based upon the weighted-average number of common shares outstanding during the period. Diluted net income (loss) per common share utilizing the treasury-stock method is based upon the weighted-average number of common shares outstanding during the period plus additional weighted-average common equivalent shares outstanding during the period when the effect is dilutive. Potentially dilutive shares result from the assumed (i) vesting of restricted stock units ("RSUs") and performance-based restricted stock units ("PSUs"), and (ii) exercise of outstanding stock options. The proceeds of such vestings or exercises are assumed to have been used to repurchase outstanding stock using the treasury-stock method.

Recently Adopted Accounting Standards

Segment Reporting

In 2023, the Financial Accounting Standards Board ("FASB") issued Accounting Standards Update ("ASU") 2023-07, *Segment Reporting (Topic 280): Improvements to Reportable Segment Disclosures* ("ASU 2023-07"), which requires public entities to disclose significant segment expenses and other segment items. ASU 2023-07 also requires public entities to provide in interim periods all disclosures about a reportable segment's profit or loss and assets that are currently required annually. ASU 2023-07 became effective for the annual period starting on January 1, 2024, and for the interim periods starting on January 1, 2025. We have disclosed significant segment expenses, other segment items, and our measure of segment profit or loss in Note Q, "Segment Information."

Recently Issued Accounting Standards

Income Tax Disclosures

In 2023, the FASB issued ASU 2023-09, *Income Taxes (Topic 740): Improvements to Income Tax Disclosures* ("ASU 2023-09"), which requires public entities to disclose in their rate reconciliation table additional categories of information about federal, state and foreign income taxes and to provide more details about the reconciling items in some categories if items meet a quantitative threshold. ASU 2023-09 becomes effective for the annual period starting on January 1, 2025. We anticipate that the adoption of ASU 2023-09 will expand our income tax footnote disclosures, including a more detailed effective tax rate reconciliation.

Disaggregation of Income Statement Expenses

In 2024, the FASB issued ASU 2024-03, *Income Statement—Reporting Comprehensive Income—Expense Disaggregation Disclosures (Subtopic 220-40): Disaggregation of Income Statement Expenses* ("ASU 2024-03"), which requires public entities, among other items, to disclose in a tabular format, on an annual and interim basis, purchases of inventory, employee compensation, depreciation, intangible asset amortization and depletion for each income statement line item that contains those expenses. ASU 2024-03 becomes effective for the annual period starting on January 1, 2027 and interim periods starting on January 1, 2028. We are in the process of analyzing the impact that the adoption of ASU 2024-03 will have on our disclosures.

B. Collaboration, License and Other Arrangements

We have entered into numerous business development agreements with third parties to collaborate on research, development and commercialization programs, license technologies, or acquire assets. Our AIPR&D included $4.6 billion, $527.1 million and $115.5 million in 2024, 2023 and 2022, respectively, related to upfront, contingent milestone, or other payments pursuant to our business development transactions, including asset acquisitions, collaborations, and licenses of third-party technologies. In 2024, our AIPR&D included $4.4 billion associated with our asset acquisition of Alpine Immune Sciences, Inc. ("Alpine") as discussed below.

Asset Acquisitions

Alpine Immune Sciences, Inc. - povetacicept

On May 20, 2024, we acquired all of the issued and outstanding shares of common stock of Alpine, a publicly traded biotechnology company focused on discovering and developing innovative, protein-based immunotherapies for approximately $5.0 billion in cash. We funded the Alpine acquisition with our cash and cash equivalents.

Alpine's lead molecule, povetacicept, is a highly potent and effective dual antagonist of B cell activating factor ("BAFF") and a proliferation-inducing ligand ("APRIL"). As of the acquisition date, povetacicept was in Phase 2 development and had shown potential best-in-class efficacy in IgA nephropathy ("IgAN"), a serious, progressive, autoimmune disease of the kidney that can lead to end-stage-renal disease. Due to its mechanism of action as a dual BAFF/APRIL antagonist, povetacicept also holds the potential to benefit patients with other serious autoimmune diseases of the kidney, such as membranous nephropathy and lupus nephritis. We accounted for the Alpine transaction as an asset acquisition because povetacicept represented substantially all of the fair value of the gross assets that we acquired. As a result, $4.4 billion of fair value attributed to povetacicept was expensed to AIPR&D in 2024.

We paid total cash of $5.0 billion at the acquisition date, which included $4.8 billion to acquire Alpine and $197.6 million for cash-settled unvested Alpine equity awards. The $197.6 million represented post-acquisition expense, which was recorded as $165.0 million of "Research and development expenses" and $32.6 million of "Selling, general and administrative expenses."

The total cash paid to acquire Alpine, allocation of consideration to the assets acquired and liabilities assumed and AIPR&D was as follows:

		(in millions)
Cash consideration to acquire Alpine's outstanding common stock	$	4,536.9
Cash consideration for Alpine's vested and unvested equity awards		420.6
Total cash consideration paid to Alpine		4,957.5
Less: Expense related to unvested equity awards		(197.6)
Transaction costs		40.7
Total consideration allocated	$	4,800.6
Cash and cash equivalents	$	31.9
Current marketable securities		209.5
Long-term marketable securities		48.5
Deferred tax asset		105.5
Total other assets		19.5
Total liabilities		(37.5)
Total identifiable assets acquired, net		377.4
Acquired in-process research and development expense		4,423.2
Total consideration allocated	$	4,800.6

Septerna, Inc. - Novel G Protein-coupled Receptor Program

In 2023, pursuant to an asset purchase agreement, we acquired a novel G protein-coupled receptor ("GPCR") program from Septerna, Inc. We determined that substantially all the fair value acquired was concentrated in the GPCR in-process research and development asset, which did not constitute a business, and for which we determined there was no alternative future use. As a result, we recorded $47.5 million to AIPR&D in 2023.

Catalyst Biosciences, Inc. - Complement 3 Degrader Program

In 2022, pursuant to an asset purchase agreement, we acquired from Catalyst Biosciences, Inc.'s a portfolio of protease medicines that target the complement system and related intellectual property, including CB 2782-PEG, which is a pre-clinical complement component 3 degrader program for geographic atrophy in dry age-related macular degeneration. We determined that substantially all the fair value acquired was concentrated in the CB-2782 PEG in-process research and development assets, which did not constitute a business, and for which we determined there was no alternative future use. As a result, we recorded our $60.0 million upfront payment to AIPR&D in 2022.

In-license Agreements

We have entered into several in-license agreements to advance and obtain access to technologies and services related to our research and early-development activities. We are generally required to make an upfront payment upon execution of our license agreements; development, regulatory and commercialization milestones payments upon the achievement of certain product research, development and commercialization objectives; and royalty payments on future sales, if any, of commercial products resulting from our collaborations.

Pursuant to the terms of our in-license agreements, our collaborators typically lead the discovery efforts and we lead all preclinical, development and commercialization activities associated with the advancement of any product candidates and fund all expenses.

We typically can terminate our in-license agreements by providing advance notice to our collaborators. Our license agreements may be terminated by either party for a material breach by the other, subject to notice and cure provisions. Unless earlier terminated, these license agreements generally remain in effect until the date on which the royalty term and all payment obligations with respect to all products in all countries have expired.

CRISPR Therapeutics AG

CRISPR-Cas9 Gene-editing Therapies Agreements

In 2015, we entered into a strategic collaboration, option and license agreement (the "CRISPR Agreement") with CRISPR and its affiliates to collaborate on the discovery and development of potential new treatments aimed at the underlying genetic causes of human diseases using CRISPR-Cas9 gene-editing technology. We had the exclusive right to license certain targets. In 2019, we elected to exclusively license three targets, including CF, pursuant to the CRISPR Agreement. For each of the three targets that we elected to license, CRISPR has the potential to receive up to an additional $410.0 million in development, regulatory and commercial milestones as well as royalties on resulting net product sales.

In 2017, we entered into a joint development and commercialization agreement with CRISPR (the "CRISPR JDCA"), which we amended and restated in 2021, pursuant to the terms of the CRISPR Agreement. Under the CRISPR JDCA, we and CRISPR were co-developing and preparing to co-commercialize CASGEVY for the treatment of hemoglobinopathies, including treatments for SCD and TDT.

Pursuant to the CRISPR JDCA, we lead global development, manufacturing and commercialization of CASGEVY, with support from CRISPR. We also conduct all research, development, manufacturing and commercialization activities relating to other product candidates and products under the CRISPR JDCA throughout the world subject to CRISPR's reserved right to conduct certain activities.

CASGEVY was approved by the FDA in December 2023 for the treatment of SCD. In connection with this approval, we made a $200.0 million milestone payment to CRISPR in January 2024, which we accrued to "Other current liabilities" and recorded within "Other intangible assets, net" on our consolidated balance sheet as of December 31, 2023. Please refer to Note J, "Goodwill and Other Intangible Assets," for further information. Subsequent to receiving marketing approval for CASGEVY, we continue to lead the research and development activities under the CRISPR JDCA, subject to CRISPR's reserved right to conduct certain activities. We are reimbursed by CRISPR for its 40% share of these research and development activities, subject to certain adjustments, and we record this reimbursement from CRISPR as a credit within "Research and development expenses." We also share with CRISPR 40% of the net commercial profits or losses incurred with respect to CASGEVY, subject to certain adjustments, which is recorded to "Cost of sales." The net commercial profits or losses equal the sum of the product revenues, cost of sales and selling, general and administrative expenses that we have recognized related to the CRISPR JDCA. In 2024, we recognized net reimbursements from CRISPR pursuant to the CRISPR JDCA as credits to "Cost of sales" of $73.5 million related to CRISPR's share of the CRISPR JDCA's net commercial loss, and to "Research and development expenses" of $31.6 million, related to CRISPR's share of the CRISPR JDCA's research and development activities.

Prior to receiving marketing approval from the FDA for CASGEVY in December 2023, we accounted for the CRISPR JDCA as a cost-sharing arrangement, with costs incurred related to CASGEVY allocated 60% to us and 40% to CRISPR, subject to certain adjustments. In 2023 and 2022, we recognized net reimbursements from CRISPR as credits to "Research and development expenses" of $61.9 million and $30.5 million, respectively, and to "Selling, general and administrative expenses" of $32.0 million and $24.2 million, respectively, related to CRISPR's share of the CRISPR JDCA's operating expenses.

CRISPR-Cas9 Gene-editing Hypoimmune Cell Therapies Agreement

In 2023, we entered into a non-exclusive license agreement (the "CRISPR T1D Agreement") for the use of CRISPR's CRISPR-Cas9 gene-editing technology to accelerate the development of our hypoimmune cell therapies for T1D. Pursuant to the CRISPR T1D Agreement, we made a $100.0 million upfront payment to CRISPR, and we determined that substantially all the fair value of our upfront payment was attributable to in-process research and development, for which there is no alternative future use, and that no substantive processes were acquired that would constitute a business. In the second quarter

of 2023, we achieved a research milestone that resulted in a $70.0 million payment to CRISPR. We recorded the upfront payment and the research milestone, totaling $170.0 million, to AIPR&D in 2023. In 2024, we achieved additional research milestone totaling $35.0 million, which were recorded to AIPR&D. CRISPR is eligible to receive up to an additional $125.0 million in research, development, regulatory and commercial milestones, as well as royalties on resulting net product sales.

Orna Therapeutics

In December 2024, we entered into a strategic collaboration and license agreement (the "Orna Agreement") with Orna Therapeutics ("Orna") to utilize Orna's novel and proprietary lipid nanoparticle delivery solutions to enhance our efforts in developing next generation gene-editing therapies for patients with SCD and TDT. Under the terms of the agreement, we made a $40.0 million upfront payment to Orna and paid an additional $25.0 million for a convertible promissory note in connection with the agreement. Orna is eligible to receive up to $635.0 million in research, development, regulatory and commercial milestones for SCD or TDT products that may result from the collaboration agreement. Orna is also eligible to receive up to $365.0 million in option and milestone payments for each additional indication that we elect to license pursuant to the Orna Agreement. Orna will also receive royalties on net product sales for SCD and TDT and each additional indication we license pursuant to the Orna Agreement. We determined that substantially all the fair value of the upfront payment was attributable to in-process research and development, for which there was no alternative future use and that no substantive processes were acquired that would constitute a business. As a result, we recorded the upfront payment to AIPR&D. We recorded the convertible promissory note at amortized cost within "Other assets" after concluding that its fair value approximated its contractual value.

Entrada Therapeutics, Inc.

In 2023, we closed a strategic collaboration and license agreement (the "Entrada Agreement") with Entrada Therapeutics, Inc. ("Entrada") focused on discovering and developing intracellular therapeutics for DM1. Upon closing, we made an upfront payment of $225.1 million to Entrada, and purchased $24.9 million of Entrada's common stock in connection with the Entrada Agreement. We determined that substantially all the fair value of our upfront payment was attributable to in-process research and development, for which there was no alternative future use, and that no substantive processes were acquired that would constitute a business. In 2024 and 2023, Entrada also earned milestones of $75.0 million and $17.5 million, respectively. As a result, we recorded $75.0 million and $242.6 million in total to AIPR&D in 2024 and 2023, respectively. We recorded the investment in Entrada's common stock at fair value on our consolidated balance sheet within "Marketable securities." Entrada is eligible to receive up to an additional $335.0 million in research, development, regulatory and commercial milestones for any products that may result from the Entrada Agreement, as well as royalties on resulting net product sales.

Moderna, Inc.

In 2016, we entered into a strategic collaboration and licensing agreement with Moderna, Inc. ("Moderna"), pursuant to which the parties are seeking to identify and develop messenger ribonucleic acid ("mRNA") therapeutics encoding cystic fibrosis transmembrane conductance regulator for the treatment of CF. Moderna is eligible to receive up to $270.0 million in development and regulatory milestones as well as royalties on net product sales related to this agreement.

Additional In-License Agreements and Other Arrangements

In addition to the agreements described above, we recorded upfront, option and milestone payments totaling $55.2 million in 2024, $67.0 million in 2023 and $55.5 million in 2022 to AIPR&D related to additional in-license agreements and other business development transactions that we do not consider to be individually significant to our consolidated financial statements. For each of these transactions, we determined that substantially all the fair value of the consideration for each individual agreement was attributable to in-process research and development, for which we did not have any alternative future use, and no substantive processes were acquired that would constitute a business.

Please refer to Note D, "Fair Value Measurements," and Note E, "Marketable Securities and Equity Investments," for further information regarding our investments in our collaborators.

Editas Medicine, Inc.

In December 2023, we entered into a sublicense agreement (the "Editas Agreement") with Editas Medicine, Inc. ("Editas") to obtain a non-exclusive license for Editas CRISPR/Cas9 gene-editing technology related to SCD and TDT, including CASGEVY. Pursuant to the Editas Agreement, we made a $50.0 million upfront payment to Editas and Editas is eligible to receive an additional $50.0 million license payment upon the resolution of certain contingencies related to Editas' license to the technology. Editas is also eligible to receive commercial milestones based on certain annual CASGEVY sales thresholds. Pursuant to the CRISPR JDCA described above, CRISPR reimbursed us for 40%, or $20.0 million, of the upfront payment, and would also reimburse us for 40% of the additional contingent $50.0 million license payment, subject to certain adjustments. We recorded the net $30.0 million upfront payment related to our sublicense for Editas' developed technology to "Other intangible assets, net" on our consolidated balance sheet as of December 31, 2023.

Out-license Agreements

We have entered into licensing agreements pursuant to which we have out-licensed rights to certain product candidates to third-party collaborators. Pursuant to these out-license agreements, our collaborators may become responsible for all costs related to the continued development of such product candidates and obtain development and commercialization rights to these product candidates, either globally or within certain geographic regions. Depending on the terms of the agreements, our collaborators may be required to make upfront payments, milestone payments upon the achievement of certain product research, development and regulatory objectives and may also be required to pay royalties on future sales, if any, of commercial products resulting from the collaboration. The termination provisions associated with these collaborations are generally the same as those described above related to our in-license agreements.

Zai Lab Limited

In January 2025, we entered into a collaboration agreement with Zai Lab Limited ("Zai") for the development and commercialization of povetacicept in mainland China, Hong Kong SAR, Macau SAR, Taiwan region and Singapore. Under this collaboration, Zai will help advance the povetacicept clinical trials and make the regulatory submissions in the licensed territories. Zai will also be responsible for commercialization activities in the licensed territories, if povetacicept becomes an approved product. Under the terms of the agreement, we will receive a $10.0 million upfront payment in the first quarter of 2025, as well as certain regulatory milestone payments and tiered royalties, on future net sales of povetacicept in the region of focus for Zai.

Cystic Fibrosis Foundation

In 2004, we entered into a collaboration agreement with the Cystic Fibrosis Foundation, as successor in interest to the Cystic Fibrosis Foundation Therapeutics, Inc., to support research and development activities. Pursuant to the collaboration agreement, as amended, we have agreed to pay tiered royalties ranging from single digits to sub-teens on covered compounds first synthesized and/or tested during a research term on or before February 28, 2014, including ivacaftor, lumacaftor and tezacaftor and royalties ranging from low-single digits to mid-single digits on net sales of certain compounds first synthesized and/or tested between March 1, 2014 and August 31, 2016, including elexacaftor. We do not have any royalty obligations on compounds first synthesized and tested on or after September 1, 2016. For combination products, such as ORKAMBI, SYMDEKO/SYMKEVI, TRIKAFTA/KAFTRIO, and ALYFTREK sales are allocated equally to each of the active pharmaceutical ingredients in the combination product, and royalties are then paid for any royalty-bearing components included in the combination. We record expenses related to these royalty obligations to "Cost of sales."

C. Earnings Per Share

The following table sets forth the computation of basic and diluted net (loss) income per common share for the periods ended:

	Year ended December 31,		
	2024	2023	2022
	(in millions, except per share amounts)		
Net (loss) income	$ (535.6)	$ 3,619.6	$ 3,322.0
Basic weighted-average common shares outstanding	257.9	257.7	256.1
Effect of potentially dilutive securities:			
Restricted stock units (including PSUs)	—	1.6	1.6
Stock options	—	1.2	1.4
Employee stock purchase program	—	0.0	0.0
Diluted weighted-average common shares outstanding	257.9	260.5	259.1
Basic net (loss) income per common share	$ (2.08)	$ 14.05	$ 12.97
Diluted net (loss) income per common share	$ (2.08)	$ 13.89	$ 12.82

We did not include the securities in the following table in the computation of the diluted net (loss) income per common share because the effect would have been anti-dilutive during each period:

	Year ended December 31,		
	2024	2023	2022
	(in millions)		
Unvested restricted stock units (including PSUs)	0.8	0.1	0.2
Stock options	0.4	0.0	0.0

D. Fair Value Measurements

The following fair value hierarchy is used to classify assets and liabilities based on observable inputs and unobservable inputs used to determine the fair value of our financial assets and liabilities:

Level 1: Quoted prices in active markets for identical assets or liabilities. An active market for an asset or liability is a market in which transactions for the asset or liability occur with sufficient frequency and volume to provide pricing information on an ongoing basis.

Level 2: Observable inputs other than Level 1 inputs. Examples of Level 2 inputs include quoted prices in active markets for similar assets or liabilities and quoted prices for identical assets or liabilities in markets that are not active.

Level 3: Unobservable inputs based on our assessment of the assumptions that market participants would use in pricing the asset or liability.

Our investment strategy is focused on capital preservation. We invest in instruments that meet the credit quality standards outlined in our investment policy, which also limits the amount of credit exposure to any one issue or type of instrument. We utilize foreign currency forward contracts intended to mitigate the effect of changes in foreign exchange rates on our consolidated statements of income.

The following tables set forth our financial assets and liabilities subject to fair value measurements by level within the fair value hierarchy:

	As of December 31, 2024				As of December 31, 2023			
		Fair Value Hierarchy				Fair Value Hierarchy		
	Total	Level 1	Level 2	Level 3	Total	Level 1	Level 2	Level 3
	(in millions)							
Financial instruments carried at fair value (asset positions):								
Cash equivalents	$ 1,687.1	$ 613.3	$ 1,073.8	$ —	$ 7,033.9	$ 5,397.3	$ 1,636.6	$ —
Marketable securities:								
Corporate equity securities	36.6	36.6	—	—	46.0	46.0	—	—
U.S. Treasury securities	1,602.0	1,566.8	35.2	—	546.5	546.5	—	—
U.S. government agency securities	240.5	—	240.5	—	425.2	—	425.2	—
Asset-backed securities	1,244.2	—	1,244.2	—	306.0	—	306.0	—
Certificates of deposit	—	—	—	—	33.7	—	33.7	—
Corporate debt securities	3,525.9	—	3,525.9	—	1,802.8	—	1,802.8	—
Commercial paper	5.0	—	5.0	—	186.8	—	186.8	—
Prepaid expenses and other current assets:								
Foreign currency forward contracts	130.1	—	130.1	—	1.8	—	1.8	—
Other assets:								
Foreign currency forward contracts	12.4	—	12.4	—	—	—	—	—
Total financial assets	$ 8,483.8	$ 2,216.7	$ 6,267.1	$ —	$ 10,382.7	$ 5,989.8	$ 4,392.9	$ —
Financial instruments carried at fair value (liability positions):								
Other current liabilities:								
Foreign currency forward contracts	$ —	$ —	$ —	$ —	$ (33.7)	$ —	$ (33.7)	$ —
Other long-term liabilities:								
Contingent consideration	(76.9)	—	—	(76.9)	(77.4)	—	—	(77.4)
Total financial liabilities	$ (76.9)	$ —	$ —	$ (76.9)	$ (111.1)	$ —	$ (33.7)	$ (77.4)

Please refer to Note E, “Marketable Securities and Equity Investments,” for the carrying amount and related unrealized gains (losses) by type of investment. Our cash equivalents primarily include money market funds and time deposits.

Fair Value of Corporate Equity Securities

We classify our investments in publicly traded corporate equity securities as “Marketable securities” on our consolidated balance sheets. Generally, our investments in the common stock of publicly traded companies are valued based on Level 1 inputs because they have readily determinable fair values. However, certain of our investments in publicly traded companies have been or continue to be valued based on Level 2 inputs due to transfer restrictions associated with these investments.

As of December 31, 2024, one of our investments in publicly traded corporate equity securities was subject to a contractual sales restriction with a total fair value of $14.0 million, which expired in February 2025.

Please refer to Note E, “Marketable Securities and Equity Investments,” for further information on these investments.

Fair Value of Contingent Consideration

In 2019, we acquired Exonics Therapeutics, Inc. (“Exonics”), a privately held company focused on creating transformative gene-editing therapies to repair mutations that cause Duchenne muscular dystrophy and other severe neuromuscular diseases, including DM1. Our Level 3 contingent consideration liabilities are related to $678.3 million of development and regulatory milestones potentially payable to former Exonics equity holders. We base our estimates of the probability of achieving the milestones relevant to the fair value of contingent payments on industry data attributable to gene therapies and our knowledge of the progress and viability of the programs. The discount rates used in the valuation model for

contingent payments, which were between 4.9% and 5.1% as of December 31, 2024, represent a measure of credit risk and market risk associated with settling the liabilities.

The following table represents a rollforward of the fair value of our contingent consideration liabilities:

	Year Ended December 31, 2024
	(in millions)
Balance at December 31, 2023	$ 77.4
Decrease in fair value of contingent payments	(0.5)
Balance at December 31, 2024	$ 76.9

Significant judgment is used in determining the appropriateness of these assumptions at each reporting period. Due to the uncertainties associated with development and commercialization of product candidates in the pharmaceutical industry and the effects of changes in other assumptions including discount rates, we expect our estimates regarding the fair value of contingent consideration to continue to change in the future, resulting in adjustments to the fair value of our contingent consideration liabilities, and the effect of any such adjustments could be material.

E. Marketable Securities and Equity Investments

A summary of our cash equivalents and marketable securities, which are recorded at fair value, is shown below:

	As of December 31, 2024				As of December 31, 2023			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
	(in millions)							
Cash equivalents	$ 1,687.1	$ —	$ —	$ 1,687.1	$ 7,033.9	$ —	$ —	$ 7,033.9
Marketable securities:								
U.S. Treasury securities	$ 1,603.9	$ 3.6	$ (5.5)	$ 1,602.0	$ 544.5	$ 3.0	$ (1.0)	$ 546.5
U.S. government agency securities	240.5	0.5	(0.5)	240.5	424.8	0.9	(0.5)	425.2
Asset-backed securities	1,239.6	5.1	(0.5)	1,244.2	304.9	1.4	(0.3)	306.0
Certificates of deposit	—	—	—	—	33.7	0.0	(0.0)	33.7
Corporate debt securities	3,519.4	10.6	(4.1)	3,525.9	1,794.0	10.5	(1.7)	1,802.8
Commercial paper	5.0	0.0	(0.0)	5.0	186.8	0.1	(0.1)	186.8
Total marketable available-for-sale debt securities	6,608.4	19.8	(10.6)	6,617.6	3,288.7	15.9	(3.6)	3,301.0
Corporate equity securities	72.1	3.0	(38.5)	36.6	72.1	—	(26.1)	46.0
Total marketable securities	6,680.5	22.8	(49.1)	6,654.2	3,360.8	15.9	(29.7)	3,347.0
Total cash equivalents and marketable securities	$ 8,367.6	$ 22.8	$ (49.1)	$ 8,341.3	$ 10,394.7	$ 15.9	$ (29.7)	$ 10,380.9

Amounts in the table above at fair value were classified on our consolidated balance sheets as follows:

	December 31,	
	2024	2023
	(in millions)	
Cash and cash equivalents	$ 1,687.1	$ 7,033.9
Marketable securities	1,546.3	849.2
Long-term marketable securities	5,107.9	2,497.8
Total	$ 8,341.3	$ 10,380.9

Marketable available-for-sale debt securities by contractual maturity were as follows:

	December 31,	
	2024	2023
	(in millions)	
Matures within one year	$ 1,509.7	$ 803.2
Matures after one year through five years	5,034.4	2,495.6
Matures after five years	73.5	2.2
Total	$ 6,617.6	$ 3,301.0

We did not record any allowances for credit losses to adjust the fair value of our marketable available-for-sale debt securities in 2024, 2023 or 2022. Additionally, we did not record any realized gains or losses that were material to our consolidated statements of income in 2024, 2023 or 2022. As of December 31, 2024, we held marketable available-for-sale debt securities with a total fair value of $2.2 billion that were in unrealized loss positions totaling $10.6 million. Included in this amount were marketable available-for sale debt securities with a total fair value of $19.1 million and total unrealized loss of $0.1 million that had been in unrealized loss positions for greater than twelve months. We intend to hold these investments until maturity and do not expect to incur realized losses on these investments when they mature.

We record changes in the fair value of our investments in corporate equity securities to "Other expense, net" in our consolidated statements of income. During the three years ended December 31, 2024, our net unrealized losses on corporate equity securities with readily determinable fair values held at the conclusion of each period were as follows:

	Year ended December 31,		
	2024	2023	2022
	(in millions)		
Net unrealized losses	$ (9.5)	$ (7.5)	$ (149.1)

In 2023, we received proceeds of $95.1 million related to the sale of the common stock of a publicly traded company, which had a total original cost basis of $57.3 million. In 2024 and 2022, we did not sell any common stock of publicly traded companies.

As of December 31, 2024, the carrying value of our equity investments without readily determinable fair values, which are recorded in "Other assets" on our consolidated balance sheets, was $64.8 million. During 2024, we reduced the carrying value of our equity investments without readily determinable fair values by $48.2 million based on observable changes in price.

F. Accumulated Other Comprehensive Income (Loss)

The following table summarizes the changes in accumulated other comprehensive income (loss) by component:

		Unrealized Holding Gains (Losses), Net of Tax		
	Foreign Currency Translation Adjustment	On Available-For-Sale Debt Securities	On Foreign Currency Forward Contracts	Total
		(in millions)		
Balance at December 31, 2021	$ (13.6)	$ (0.5)	$ 30.0	$ 15.9
Other comprehensive (loss) income before reclassifications	(11.4)	(3.3)	138.9	124.2
Amounts reclassified from accumulated other comprehensive income (loss)		3.7	(143.0)	(139.3)
Net current period other comprehensive (loss) income	(11.4)	0.4	(4.1)	(15.1)
Balance at December 31, 2022	$ (25.0)	$ (0.1)	$ 25.9	$ 0.8
Other comprehensive income (loss) before reclassifications	26.1	9.7	(27.2)	8.6
Amounts reclassified from accumulated other comprehensive income (loss)			(23.7)	(23.7)
Net current period other comprehensive income (loss)	26.1	9.7	(50.9)	(15.1)
Balance at December 31, 2023	$ 1.1	$ 9.6	$ (25.0)	$ (14.3)
Other comprehensive income (loss) before reclassifications	8.6	(4.4)	163.8	168.0
Amounts reclassified from accumulated other comprehensive income (loss)	—	1.9	(27.8)	(25.9)
Net current period other comprehensive income (loss)	8.6	(2.5)	136.0	142.1
Balance at December 31, 2024	$ 9.7	$ 7.1	$ 111.0	$ 127.8

G. Hedging

Foreign currency forward contracts - Designated as hedging instruments

We maintain a hedging program intended to mitigate the effect of changes in foreign exchange rates for a portion of our forecasted product revenues denominated in certain foreign currencies. The program includes foreign currency forward contracts that are designated as cash flow hedges under U.S. GAAP having contractual durations from one to eighteen months. We recognize realized gains and losses for the effective portion of such contracts in "Product revenues, net" in our consolidated statements of income in the same period that we recognize the product revenues that were impacted by the hedged foreign exchange rate changes.

We formally document the relationship between foreign currency forward contracts (hedging instruments) and forecasted product revenues (hedged items), as well as our risk management objective and strategy for undertaking various hedging activities, which includes matching all foreign currency forward contracts that are designated as cash flow hedges to forecasted transactions. We also formally assess, both at the hedge's inception and on an ongoing basis, whether the foreign currency forward contracts are highly effective in offsetting changes in cash flows of hedged items on a prospective and retrospective basis. If we were to determine that a (i) foreign currency forward contract is not highly effective as a cash flow hedge, (ii) foreign currency forward contract has ceased to be a highly effective hedge or (iii) forecasted transaction is no longer probable of occurring, we would discontinue hedge accounting treatment prospectively. We measure effectiveness based on the change in fair value of the forward contracts and the fair value of the hypothetical foreign currency forward contracts with terms that match the critical terms of the risk being hedged. As of December 31, 2024, all hedges were determined to be highly effective.

We consider the impact of our counterparties' credit risk on the fair value of the foreign currency forward contracts. As of December 31, 2024 and December 31, 2023, credit risk did not change the fair value of our foreign currency forward contracts.

The following table summarizes the notional amount in U.S. dollars of our outstanding foreign currency forward contracts designated as cash flow hedges under U.S. GAAP:

	As of December 31,	
	2024	2023
Foreign Currency	**(in millions)**	
Euro	$ 1,977.4	$ 1,720.6
Canadian dollar	322.0	229.5
British pound sterling	301.7	225.0
Australian dollar	179.2	153.3
Swiss Franc	79.7	63.9
Total foreign currency forward contracts	$ 2,860.0	$ 2,392.3

Foreign currency forward contracts - Not designated as hedging instruments

We also enter into foreign currency forward contracts, typically with contractual maturities of approximately one month, which are designed to mitigate the effect of changes in foreign exchange rates on monetary assets and liabilities, including intercompany balances. These contracts are not designated as hedging instruments under U.S. GAAP. We recognize realized gains and losses for such contracts in "Other expense, net" in our consolidated statements of income each period. As of December 31, 2024, the notional amount of our outstanding foreign currency forward contracts where hedge accounting under U.S. GAAP is not applied was $367.0 million.

During the three years ended December 31, 2024, we recognized the following related to foreign currency forward contracts in our consolidated statements of income:

	Year ended December 31,		
	2024	2023	2022
	(in millions)		
Designated as hedging instruments - Reclassified from AOCI			
Product revenues, net	$ 35.7	$ 30.2	$ 182.5
Not designated as hedging instruments			
Other income (expense), net	$ 11.7	$ 4.4	$ (9.9)
Total reported in the Consolidated Statements of Income			
Product revenues, net	$ 11,020.1	$ 9,869.2	$ 8,930.7
Other expense, net	$ (86.1)	$ (22.8)	$ (164.8)

The following table summarizes the fair value of our outstanding foreign currency forward contracts designated as cash flow hedges under U.S. GAAP included on our consolidated balance sheets:

As of December 31, 2024			
Assets		Liabilities	
Classification	Fair Value	Classification	Fair Value
	(in millions)		
Prepaid expenses and other current assets	$ 130.1	Other current liabilities	$ —
Other assets	12.4	Other long-term liabilities	—
Total assets	$ 142.5	Total liabilities	$ —

As of December 31, 2023			
Assets		Liabilities	
Classification	Fair Value	Classification	Fair Value
	(in millions)		
Prepaid expenses and other current assets	$ 1.8	Other current liabilities	$ (33.7)

As of December 31, 2024, we expect the amounts that are related to foreign exchange forward contracts designated as cash flow hedges under U.S. GAAP recorded in “Prepaid expenses and other current assets” and “Other current liabilities” to be reclassified to earnings within twelve months.

As discussed in “Note A, “Nature of Business and Accounting Policies,” we present the fair value of our foreign currency forward contracts on a gross basis within our consolidated balance sheets. The following table summarizes the potential effect of offsetting derivatives by type of financial instrument designated as cash flow hedges under U.S. GAAP on our consolidated balance sheets:

	As of December 31, 2024				
Foreign currency forward contracts	Gross Amounts Recognized	Gross Amounts Offset	Gross Amounts Presented	Gross Amounts Not Offset	Legal Offset
	(in millions)				
Total assets	$ 142.5	$ —	$ 142.5	$ —	$ 142.5
Total liabilities	—	—	—	—	—

	As of December 31, 2023				
	Gross Amounts Recognized	Gross Amounts Offset	Gross Amounts Presented	Gross Amounts Not Offset	Legal Offset
Foreign currency forward contracts			(in millions)		
Total assets	$ 1.8	$ —	$ 1.8	$ (1.8)	$ —
Total liabilities	(33.7)	—	(33.7)	1.8	(31.9)

H. Inventories

"Inventories" consisted of the following:

	As of December 31,	
	2024	2023
	(in millions)	
Raw materials	$ 252.0	$ 78.7
Work-in-process	768.8	525.1
Finished goods	184.6	135.0
Total	$ 1,205.4	$ 738.8

During the first quarter of 2024, following positive results for our Phase 3 trials related to JOURNAVX, we began capitalizing inventories produced in preparation for our planned product launch. As of December 31, 2024, we had $204.6 million of JOURNAVX inventories capitalized. In January 2025, we received approval from the FDA to market JOURNAVX in the U.S. Prior to 2024, we expensed inventoriable and related costs associated with JOURNAVX as "Research and development expenses."

I. Property and Equipment

"Property and equipment, net" consisted of the following:

	As of December 31,	
	2024	2023
	(in millions)	
Buildings and improvements	$ 461.2	$ 928.6
Laboratory equipment, other equipment and furniture	684.5	579.1
Leasehold improvements	737.6	474.6
Computers and software	376.2	332.8
Land	33.1	33.1
Total property and equipment, gross	2,292.6	2,348.2
Less: accumulated depreciation	(1,064.8)	(1,188.9)
Total property and equipment, net	$ 1,227.8	$ 1,159.3

During 2024, we amended the leases associated with our corporate headquarters, resulting in a change to our accounting classification for the leases from finance leases to operating leases. The decrease in "Buildings and Improvements" in the table above is primarily attributable to these amendments. Please refer to Note L, "Leases," for further information.

We recorded depreciation expense of $160.4 million, $167.8 million and $148.3 million in 2024, 2023 and 2022, respectively, which includes our finance lease amortization.

J. Goodwill and Other Intangible Assets

Intangible Assets

"Other intangible assets, net" consisted of the following:

		As of December 31, 2024			As of December 31, 2023		
	Estimated Useful lives	Gross Carrying Amount	Accumulated Amortization	Net Carrying Amount	Gross Carrying Amount	Accumulated Amortization	Net Carrying Amount
		(in millions, except useful lives)					
In-process research and development	Indefinite	$ 603.6	$ —	$ 603.6	$ 603.6	$ —	$ 603.6
Finite-lived intangible assets - marketed products	10 to 12 yrs.	238.0	(21.9)	216.1	238.0	(1.7)	236.3
Finite-lived intangible assets - assembled workforce	3 yrs.	7.7	(1.5)	6.2	—	—	$ —
Total other intangible assets, net		$ 849.3	$ (23.4)	$ 825.9	$ 841.6	$ (1.7)	$ 839.9

In 2023, we recorded a total of $238.0 million of finite-lived intangible assets following the regulatory approval of CASGEVY in several markets, which we are amortizing on a straight-line basis over the longer of the last underlying patents to expire or the period that we have exclusive rights to market CASGEVY. We recorded intangible asset amortization expense of $20.2 million and $1.7 million to "Cost of sales" related to these assets in in 2024 and 2023, respectively.

As of December 31, 2024, the estimated future amortization of our finite-lived intangible assets was as follows:

Year	Estimated Amortization Expense
	(in millions)
2025	$ 22.7
2026	$ 22.7
2027	$ 21.3
2028	$ 20.2
2029	$ 20.2

In 2022, we recorded a $13.0 million impairment of an in-process research and development intangible asset to "Research and development expenses" due to a decision to revise the scope of certain acquired gene-editing programs.

Goodwill

As of December 31, 2024 and 2023, we had goodwill of $1.1 billion on our consolidated balance sheets.

K. Additional Balance Sheet & Cash Flow Information

"Prepaid expenses and other current assets" consisted of the following:

	As of December 31,	
	2024	2023
	(in millions)	
Tax-related prepaid and receivables	$ 357.0	$ 429.0
Prepaid expenses	102.2	108.6
Fair value of cash flow hedges	130.1	1.8
Other	76.4	84.3
Total	$ 665.7	$ 623.7

"Accrued expenses" consisted of the following:

	As of December 31,	
	2024	2023
	(in millions)	
Product revenue accruals	$ 1,618.9	$ 1,716.4
Payroll and benefits	352.1	295.0
Research, development and commercial contract costs	319.2	265.2
Royalty payable	271.0	237.6
Tax related accruals	161.1	99.5
Other	66.3	41.6
Total	$ 2,788.6	$ 2,655.3

"Other current liabilities" consisted of the following:

	As of December 31,	
	2024	2023
	(in millions)	
Milestones payable	$ 32.5	$ 222.5
Contract liabilities	206.8	170.3
Operating lease liabilities	87.1	33.1
Finance lease liabilities	5.2	50.6
Other	31.4	50.7
Total	$ 363.0	$ 527.2

"Other long-term liabilities" consisted of the following:

	As of December 31,	
	2024	2023
	(in millions)	
Tax-related liabilities	$ 698.6	$ 681.4
Contingent consideration	76.9	77.4
Other	126.3	118.9
Total	$ 901.8	$ 877.7

Cloud Computing Service Contracts

As of December 31, 2024 and 2023, "Other assets" included $62.6 million and $58.9 million, respectively, related to costs incurred to implement cloud computing service contracts. We recorded amortization associated with cloud computing service contracts of $25.2 million and $11.8 million in 2024 and 2023, respectively. We did not have amortization associated with cloud computing service contracts in 2022.

Cash, Cash Equivalents and Restricted Cash Presented in Consolidated Statements of Cash Flows

The cash, cash equivalents and restricted cash balances at the beginning and ending of each period presented in our consolidated statements of cash flows consisted of the following:

	As of December 31,			
	2024	2023	2022	2021
	(in millions)			
Cash and cash equivalents	$ 4,569.6	$ 10,369.1	$ 10,504.0	$ 6,795.0
Prepaid expenses and other current assets	2.6	3.2	8.0	5.1
Cash, cash equivalents and restricted cash per consolidated statements of cash flows	$ 4,572.2	$ 10,372.3	$ 10,512.0	$ 6,800.1

Our restricted cash, if any, is included in "Prepaid expenses and other current assets" and "Other assets" on our consolidated balance sheets.

L. Leases

Operating Leases

Our operating leases relate to the majority of our real estate leases and each of our embedded leases with contract manufacturing organizations.

Corporate Headquarters

In 2011, we entered into two lease agreements, pursuant to which we lease approximately 1.1 million square feet of office and laboratory space in two buildings in Boston, Massachusetts for a term of 15 years (our "Corporate Headquarters"). In August 2024, we amended the existing lease agreements to, among other terms, extend the lease termination dates from December 2028 to June 2044 (the "Amendments"). We have the option to extend the amended leases for up to two additional ten-year periods.

The Amendments did not grant us any additional rights of use not contemplated in the existing lease agreements. As a result, we have accounted for the Amendments as modifications that extend the terms of the existing leases and reassessed the classification of the leases as of their effective dates. We remeasured the lease liabilities using our incremental borrowing rate

as of the effective date of the Amendments and classified the leases associated with our Corporate Headquarters as operating leases because none of the finance lease criteria were met. As of December 31, 2024, the adjusted right-of-use assets associated with our Corporate Headquarters, totaling $840.0 million, were recorded within "Operating lease assets" and the long-term portion of the remeasured lease liabilities of $1.0 billion were recorded within "Long-term operating lease liabilities."

Prior to the Amendments, we classified the leases associated with our Corporate Headquarters as finance leases because the present value of the sum of the lease payments exceeded substantially all of the fair value of our Corporate Headquarters at lease inception. As of December 31, 2023, our Corporate Headquarters were recorded as assets with net book values of $177.0 million within "Property and equipment, net" and long-term liabilities of $258.1 million within "Long-term finance lease liabilities."

As of December 31, 2024 and 2023, the amounts recorded within "Other current liabilities" related to our Corporate Headquarters were not material to our condensed consolidated balance sheets.

Jeffrey Leiden Center for Cell and Genetic Therapies

In 2019, we entered into an agreement to lease approximately 269,000 square feet of office and laboratory space near our corporate headquarters in Boston, Massachusetts for a term of 16 years. Base rent payments commenced in 2021 and will continue through November 2036. We utilize the initial period as our lease term. We have an option to extend the lease term for up to two additional ten-year periods.

Embedded Leases with Contract Manufacturing Organizations

We have several embedded leases with contract manufacturing organizations related to the manufacturing and commercialization of our products, which are classified as operating leases and have remaining lease terms up to 8 years as of December 31, 2024.

Finance Leases

As of December 31, 2024, our finance leases primarily relate to our research site in San Diego and land related to a facility that we own.

San Diego Lease

In 2015, we entered into a lease agreement pursuant to which we lease approximately 170,000 square feet of office and laboratory space in San Diego, California for a term of 16 years (the "San Diego Lease"). Base rent payments commenced in 2019 and will continue through May 2034. We utilize this initial period as our lease term. We have an option to extend the lease term for up to two additional five-year terms. The San Diego Lease is classified as a finance lease because the present value of the sum of its lease payments exceeded substantially all of the fair value of the research site at lease inception.

Please refer to our accounting policy, *Leases*, in Note A, "Nature of Business and Accounting Policies," for further information on the accounting treatment for our finance and operating leases.

Aggregate Lease Information

The components of lease cost recorded in our consolidated statements of income were as follows:

	Year ended December 31,		
	2024	2023	2022
	(in millions)		
Operating lease cost	$ 103.9	$ 47.8	$ 35.3
Finance lease cost			
Amortization of leased assets	30.9	42.7	51.0
Interest on lease liabilities	25.2	38.8	43.5
Variable lease cost	43.6	44.6	39.8
Sublease income	(1.6)	(2.7)	(2.7)
Net lease cost	$ 202.0	$ 171.2	$ 166.9

Our variable lease cost during 2024, 2023 and 2022 primarily related to operating expenses, taxes and insurance associated with our real estate leases.

Our leases are included on our consolidated balance sheets as follows:

	As of December 31,	
	2024	2023
	(in millions)	
Operating leases		
Operating lease assets	$ 1,356.8	$ 293.6
Total operating lease assets	$ 1,356.8	$ 293.6
Other current liabilities	$ 87.1	$ 33.1
Long-term operating lease liabilities	1,544.4	348.6
Total operating lease liabilities	$ 1,631.5	$ 381.7
Finance leases		
Property and equipment, net	$ 57.9	$ 272.8
Total finance lease assets	$ 57.9	$ 272.8
Other current liabilities	$ 5.2	$ 50.6
Long-term finance lease liabilities	112.8	376.1
Total finance lease liabilities	$ 118.0	$ 426.7

Maturities of our finance and operating lease liabilities as of December 31, 2024 were as follows:

Year	Operating Leases	Finance Leases	Total
		(in millions)	
2025	$ 167.3	$ 10.2	$ 177.5
2026	158.7	11.4	170.1
2027	157.9	11.8	169.7
2028	154.7	12.2	166.9
2029	102.8	12.5	115.3
Thereafter	1,997.8	130.9	2,128.7
Total lease payments	2,739.2	189.0	2,928.2
Less: tenant allowance	(199.2)	—	(199.2)
Less: amount representing interest	(908.5)	(71.0)	(979.5)
Present value of lease liabilities	$ 1,631.5	$ 118.0	$ 1,749.5

The weighted-average remaining lease terms and discount rates related to our leases were as follows:

	As of December 31,	
	2024	2023
Weighted-average remaining lease term (in years)		
Operating leases	15.58	11.24
Finance leases	22.17	10.06
Weighted-average discount rate		
Operating leases	4.61 %	2.42 %
Finance leases	4.58 %	8.20 %

Supplemental cash flow information related to our leases was as follows:

	Year ended December 31,		
	2024	2023	2022
		(in millions)	
Cash paid for amounts included in the measurement of lease liabilities			
Operating cash flows from operating leases	$ 113.5	$ 62.8	$ 50.8
Operating cash flows from finance leases	$ 25.7	$ 38.4	$ 42.5
Financing cash flows from finance leases	$ 33.6	$ 44.9	$ 85.5
Right-of-use assets obtained in exchange for lease obligations			
Operating leases	$ 1,120.9	$ 2.4	$ 58.6

The right-of-use assets of $1.1 billion that are included in the table above for 2024 were obtained in exchange for operating lease obligations of $1.3 billion, including $847.9 million of right-of-use operating lease assets and $1.0 billion of operating lease obligations related to the Amendments for our Corporate Headquarters. The Amendments also resulted in a reduction to our finance leases of $275.3 million and a net reduction to our property and equipment of $107.5 million.

M. Common Stock, Preferred Stock and Equity Plans

Common Stock and Preferred Stock

We are authorized to issue 500.0 million shares of common stock. Holders of common stock are entitled to one vote per share. Holders of common stock are entitled to receive dividends, if and when declared by our Board of Directors, and to share ratably in our assets legally available for distribution to our shareholders in the event of liquidation. Holders of common stock have no preemptive, subscription, redemption or conversion rights. The holders of common stock do not have cumulative voting rights.

We are authorized to issue 1.0 million shares of preferred stock in one or more series and to fix the powers, designations, preferences and relative participating, option or other rights thereof, including dividend rights, conversion rights, voting rights, redemption terms, liquidation preferences and the number of shares constituting any series, without any further vote or action by our shareholders. As of December 31, 2024 and 2023, we had no shares of preferred stock issued or outstanding.

Share Repurchase Programs

In February 2023, our Board of Directors approved a share repurchase program, pursuant to which we are authorized to repurchase up to $3.0 billion of our common stock. This program does not have an expiration date and can be discontinued at any time. In 2024 and 2023, we repurchased 2.7 million and 1.3 million shares of our common stock, respectively, under this program for an aggregate of $1.2 billion and $427.6 million, respectively. As of December 31, 2024, we had $1.4 billion remaining authorization under this program.

Stock and Option Plans

The purpose of each of our stock and option plans is to attract, retain and motivate our employees, consultants and directors. Awards granted under these plans can be nonstatutory stock options ("NSOs"), incentive stock options ("ISOs"), RSUs including PSUs, restricted stock ("RSs"), or other equity-based awards, as specified in the individual plans.

Shares issued under all of our plans are funded through the issuance of new shares. The following table contains information about our equity plans:

			As of December 31, 2024	
Title of Plan	**Group Eligible**	**Type of Award Granted**	**Awards Outstanding**	**Additional Awards Authorized for Grant**
			(in thousands)	
2013 Stock and Option Plan	Employees, Non-employee Directors and Consultants	NSO, RS, RSU and PSU	5,130	13,758
2006 Stock and Option Plan	Employees, Non-employee Directors and Consultants	NSO, RS and RSU	14	—
		Total	5,144	13,758

Restricted Stock Units (excluding PSUs)

The following table summarizes our restricted stock unit activity during the year ended December 31, 2024:

	Restricted Stock Units (excluding PSUs)	
	Number of Shares	Weighted-average Grant-date Fair Value
	(in thousands)	(per share)
Unvested at December 31, 2023	2,962	$ 287.41
Granted	1,375	$ 444.98
Vested	(1,482)	$ 271.97
Cancelled	(167)	$ 354.27
Unvested at December 31, 2024	2,688	$ 372.54

The total fair value of restricted stock units that vested during 2024, 2023 and 2022 (measured based on the market price of our common stock on the date of vesting) was $666.0 million, $433.4 million and $372.5 million, respectively.

Performance-based RSUs (PSUs)

The potential range of shares issuable pursuant to our PSU awards range from 0% to 200% of the target shares based on financial and non-financial measures. For the majority of our PSU awards, 50% of PSUs that could be earned have a one-year performance period with the amount actually earned dependent upon our financial performance and with vesting of the earned shares in three equal installments over a three-year period. For these same PSU awards, the remaining 50% of PSUs that could be earned have approximately a three-year performance period with the amount earned dependent upon the achievement of multiple clinical development milestones and with the earned shares cliff vesting at the end of the performance period.

The following table summarizes our PSU activity during the year ended December 31, 2024:

	Performance-Based RSU	
	Number of Units	Weighted-average Grant-date Fair Value
	(in thousands)	(per share)
Unvested at December 31, 2023 (1)	1,195	$ 247.12
Granted (2)	476	$ 444.55
Vested	(773)	$ 231.64
Cancelled	(36)	$ 317.18
Unvested at December 31, 2024	862	$ 346.01

(1) “Unvested” represents our PSUs at target to the extent performance has not been certified plus the actual number of shares that continue to be subject to service conditions for which the performance has been achieved and certified.

(2) “Granted” represents (i) the target number of shares issuable for grants during 2024 and (ii) any change in the number of shares issuable pursuant to outstanding PSUs based on performance certification during 2024.

The total fair value of PSUs that vested during 2024, 2023 and 2022 (measured on the date of vesting) was $347.1 million, $160.4 million and $98.7 million, respectively.

Stock Options

All options granted under our 2013 Stock and Option Plan (“2013 Plan”) and 2006 Stock and Option Plan (“2006 Plan”) were granted with an exercise price equal to the fair value of the underlying common stock on the date of grant. As of December 31, 2024, we are only authorized to make new equity awards under our 2013 Plan. Under the 2013 Plan, no stock

options can be awarded with an exercise price less than the fair market value on the date of grant. All options awarded under our stock and option plans expire not more than 10 years from the grant date. In each of the three years ended December 31, 2024, we only granted stock options to certain of our non-employee directors.

The following table summarizes information related to the outstanding and exercisable options during the year ended December 31, 2024:

	Stock Options	Weighted-average Exercise Price	Weighted-average Remaining Contractual Life	Aggregate Intrinsic Value
	(in thousands)	(per share)	(in years)	(in millions)
Outstanding at December 31, 2023	1,940	$ 151.37		
Granted	14	$ 399.71		
Exercised	(360)	$ 139.07		
Outstanding at December 31, 2024	1,594	$ 156.36	3.21	$ 392.6
Exercisable at December 31, 2024	1,594	$ 156.36	3.21	$ 392.6

The aggregate intrinsic value in the table above represents the total pre-tax amount, net of exercise price, that would have been received by option holders if all option holders had exercised all options with an exercise price lower than the market price on the last business day of 2024, which was $402.70 based on the closing price of our common stock on that date.

The total intrinsic value (the amount by which the fair market value exceeded the exercise price) of stock options exercised during 2024, 2023 and 2022 was $112.8 million, $128.4 million and $157.2 million, respectively. The total cash we received as a result of stock option exercises during 2024, 2023 and 2022 was $50.0 million, $80.8 million and $144.6 million, respectively.

The following table summarizes information about stock options outstanding as of December 31, 2024, which were all exercisable:

	Options Outstanding and Exercisable		
Range of Exercise Prices	Number Outstanding	Weighted-average Remaining Contractual Life	Weighted-average Exercise Price
	(in thousands)	(in years)	(per share)
$86.52–$100.00	393	1.73	$ 88.40
$100.01–$150.00	87	1.00	$ 124.37
$150.01–$200.00	1,019	3.60	$ 172.71
$200.01–$399.71	95	7.14	$ 290.47
Total	1,594	3.21	$ 156.36

Employee Stock Purchase Plan

We have an employee stock purchase plan (the "ESPP"). The ESPP permits eligible employees to enroll in a twelve-month offering period comprising two six-month purchase periods. Participants may purchase shares of our common stock, through payroll deductions, at a price equal to 85% of the fair market value of the common stock on the first day of the applicable twelve-month offering period, or the last day of the applicable six-month purchase period, whichever is lower. Purchase dates under the ESPP occur on or about May 14 and November 14 of each year. As of December 31, 2024, there were 1.1 million shares of common stock authorized for issuance pursuant to the ESPP.

In 2024, the following shares were issued to employees under the ESPP:

	Year Ended December 31, 2024
Number of shares (in thousands)	204
Average price paid per share	$ 310.73

Employee Benefits

We have a 401(k) retirement plan (the "Vertex 401(k) Plan") in which substantially all of our permanent U.S. employees are eligible to participate. Participants may contribute up to 60% of their annual compensation to the Vertex 401(k) Plan, subject to statutory limitations. We may declare discretionary matching contributions to the Vertex 401(k) Plan. We pay matching contributions in the form of cash. In ex-U.S. markets, we have similar benefit plans. In 2024, 2023 and 2022, we recorded approximately $52.3 million, $43.6 million and $36.4 million of expense related to these plans, respectively.

N. Stock-based Compensation Expense

We recognize share-based payments to employees as compensation expense using the fair value method. The fair value of restricted stock units, including PSUs, is based on the intrinsic value on the date of grant. The fair value of shares purchased pursuant to the ESPP and stock options is calculated using the Black-Scholes option pricing model. Stock-based compensation expense, measured at the grant date based on the fair value of the award, is typically recognized ratably over the requisite service period.

During the three years ended December 31, 2024, we recognized the following stock-based compensation expense:

	Year ended December 31,		
	2024	2023	2022
	(in millions)		
Stock-based compensation expense by type of award:			
Restricted stock units (including PSUs)	$ 689.1	$ 563.7	$ 456.1
ESPP share issuances	18.2	15.8	16.7
Stock options	1.8	4.0	17.6
Stock-based compensation expense related to inventories	(10.6)	(2.3)	0.9
Total stock-based compensation expense included in "Total costs and expenses"	$ 698.5	$ 581.2	$ 491.3
Stock-based compensation expense by line item:			
Cost of sales	$ 7.5	$ 7.5	$ 9.4
Research and development expenses	425.8	354.9	297.9
Selling, general and administrative expenses	265.2	218.8	184.0
Total stock-based compensation expense included in "Total costs and expenses"	698.5	581.2	491.3
Income tax effect	(251.6)	(167.5)	(144.1)
Total stock-based compensation expense, net of tax	$ 446.9	$ 413.7	$ 347.2

We capitalize a portion of our stock-based compensation expense to inventories, all of which is attributable to employees who support the manufacturing of our products.

The following table sets forth our unrecognized stock-based compensation expense as of December 31, 2024, by type of award and the weighted-average period we expect to recognize the expense:

	As of December 31, 2024	
	Unrecognized Expense	Weighted-average Recognition Period
	(in millions)	(in years)
Type of award:		
Restricted stock units (including PSUs)	$ 716.6	1.93
ESPP share issuances	11.9	0.62
Total unrecognized stock-based compensation expense	$ 728.5	

Restricted Stock Units and Performance-based Restricted Stock Units

We award restricted stock units with service conditions, which are generally the vesting periods of the awards.

As described in Note M, "Common Stock, Preferred Stock and Equity Plans," we grant the majority of our PSUs to certain members of senior management. Our financial-based PSUs to senior management vest in three equal installments over a three-year period and are expensed ratably over that same period based upon an assessment of the likely level of achievement. Our non-financial based PSUs to senior management cliff vest at the end of approximately a three-year performance period and are expensed on a straight-line basis over that same period based upon an assessment of the likely level of achievement.

Employee Stock Purchase Plan

The weighted-average fair value of each purchase right granted during 2024, 2023 and 2022 was $117.89, $90.91 and $79.36, respectively. The following table reflects the weighted-average assumptions used in our Black-Scholes option pricing model:

	Year ended December 31,		
	2024	2023	2022
Expected stock price volatility	29.37%	28.52%	33.55%
Risk-free interest rate	4.63%	5.13%	4.05%
Expected term (in years)	0.73	0.71	0.71
Expected annual dividends	—	—	—

Stock Options

We issued stock options to our non-employee directors with total grant date fair values of $2.0 million or less in each of the three years ended December 31, 2024.

O. Income Taxes

We are subject to U.S. federal, state, and foreign income taxes. The components of income before provision for income taxes consisted of the following:

	Year ended December 31,		
	2024	2023	2022
	(in millions)		
United States	$ (1,369.7)	$ 3,089.1	$ 3,257.0
Foreign	1,618.2	1,290.7	975.4
Income before provision for income taxes	$ 248.5	$ 4,379.8	$ 4,232.4

The components of our provision for income taxes consisted of the following:

	Year ended December 31,		
	2024	2023	2022
	(in millions)		
Current taxes:			
Federal	$ 704.9	$ 900.4	$ 779.0
State	118.2	46.2	34.9
Foreign	309.8	350.1	372.4
Total current taxes	1,132.9	1,296.7	1,186.3
Deferred taxes:			
Federal	(438.7)	(569.9)	(404.0)
State	(48.7)	(21.9)	(11.0)
Foreign	138.6	55.3	139.1
Total deferred taxes	(348.8)	(536.5)	(275.9)
Provision for income taxes	$ 784.1	$ 760.2	$ 910.4

Unremitted Earnings

As of December 31, 2024, we do not consider a portion of the earnings of our foreign subsidiaries to be indefinitely reinvested. Upon repatriation of the non-indefinitely invested earnings in the form of distributions or otherwise, we could be subject to immaterial U.S. federal withholding taxes payable to various foreign countries and income taxes in certain states. There are no material deferred taxes recorded on the excess of financial statement reporting over the tax basis of our investments in our foreign subsidiaries. Any permanently reinvested basis differences could reverse if we sell our foreign subsidiaries or various other events occur, none of which were considered probable as of December 31, 2024. The tax liabilities described above would not be material to our consolidated financial statements.

Effective Tax Rate Reconciliation

A reconciliation between the U.S. federal statutory rate of 21% and our effective tax rate was as follows:

	Year ended December 31,		
	2024	2023	2022
Federal statutory tax rate	21.0 %	21.0 %	21.0 %
State taxes, net of federal benefit	29.5 %	0.3 %	0.6 %
Foreign income tax rate differential	21.3 %	(0.6)%	(0.3)%
U.S. tax on foreign earnings, net of credits	(12.6)%	0.7 %	1.9 %
Foreign derived intangible income deduction	(28.3)%	(1.7)%	(1.4)%
Tax credits	(102.9)%	(6.0)%	(2.2)%
Stock compensation (benefit), shortfalls and cancellations	(25.5)%	(0.8)%	(0.8)%
Uncertain tax positions	11.3 %	3.4 %	2.7 %
Non-deductible AIPR&D	373.8 %	— %	— %
Other	27.9 %	1.1 %	0.0 %
Effective tax rate	315.5 %	17.4 %	21.5 %

Our 315.5% effective tax rate for 2024 was materially different than the U.S. statutory rate primarily due to the $4.4 billion of non-deductible AIPR&D resulting from our acquisition of Alpine, which significantly lowered our pre-tax income. The non-deductible AIPR&D was partially offset by a benefit from a research and development tax credit study that was completed in 2024 and excess tax benefits related to stock-based compensation.

Our 17.4% effective tax rate for 2023 was lower than the U.S. statutory rate primarily due to a benefit from a research and development tax credit study that was completed in 2023 and excess tax benefits related to stock-based compensation, partially offset by changes in uncertain tax positions.

Our 21.5% effective tax rate for 2022 was higher than the U.S. statutory rate primarily due to an increase in our uncertain tax positions associated with intercompany transfer pricing matters offset by excess tax benefits related to stock-based compensation, tax credits and changes in our estimated prior-year tax liabilities.

Deferred Tax Assets and Liabilities

Deferred tax assets and liabilities are determined based on the difference between financial statement and tax bases using enacted tax rates in effect for the year in which the differences are expected to reverse. The components of the deferred taxes were as follows:

	As of December 31,	
	2024	2023
	(in millions)	
Deferred tax assets:		
Tax credit carryforwards	$ 298.3	$ 261.0
Intangible assets	769.3	799.2
Stock-based compensation	164.2	144.1
Finance lease liabilities	25.9	92.1
Operating lease assets	333.5	72.5
R&D capitalization	1,404.1	919.3
Other	166.1	146.6
Gross deferred tax assets	3,161.4	2,434.8
Valuation allowance	(272.9)	(266.6)
Total deferred tax assets	2,888.5	2,168.2
Deferred tax liabilities:		
Property and equipment	(110.8)	(145.1)
Acquired intangibles	(132.7)	(130.2)
Operating lease liabilities	(271.9)	(55.6)
Other	(42.0)	(25.2)
Total deferred tax liabilities	(557.4)	(356.1)
Net deferred tax assets	$ 2,331.1	$ 1,812.1

On a periodic basis, we reassess the valuation allowance on our deferred income tax assets, weighing positive and negative evidence to assess the recoverability of our deferred tax assets. As of December 31, 2024, we maintained a valuation allowance of $272.9 million related primarily to U.S. state tax attributes.

In addition to deferred tax assets and liabilities, we have recorded deferred charges related to intra-entity sales of inventory. As of December 31, 2024 and 2023, the total deferred charges were $279.3 million and $185.8 million, respectively.

As of December 31, 2024, we had net operating loss ("NOL") carryforwards of $152.3 million, which are subject to annual utilization limitations for U.S. federal income tax purposes. In 2027, our definite lived U.S. federal NOLs of $19.5 million will begin to expire, while the remaining portion may be carried forward indefinitely. For U.S. state income tax purposes, we had NOL carryforwards of $463.8 million and tax credit carryforwards of $380.1 million. The state NOL and tax credit carryforwards begin to expire in 2025. For foreign income tax purposes, we had NOL carryforwards of $40.2 million and tax credit carryforwards of $17.9 million. The foreign NOL carryforwards may be carried forward indefinitely, with the exception of $8.3 million that will expire in 2041. The foreign tax credit carryforwards will begin to expire in 2025.

Unrecognized Tax Benefits

Unrecognized tax benefits were as follows:

	Year ended December 31,		
	2024	2023	2022
	(in millions)		
Balance at beginning of the period	$ 615.9	$ 459.6	$ 147.2
Increases related to current period tax positions	119.2	116.0	128.3
Increases related to prior period tax positions	4.6	62.5	205.3
Decreases related to prior period tax positions	(1.9)	(14.4)	(14.4)
Statute of limitations expiration	(16.6)	(8.1)	(4.5)
Settlement with tax authorities	(14.5)	—	—
Foreign currency translation adjustment	(0.5)	0.3	(2.3)
Balance at end of period	$ 706.2	$ 615.9	$ 459.6

During 2024, we increased our gross unrecognized tax benefits by $90.3 million, primarily associated with intercompany transfer pricing matters. The unrecognized tax benefits were recorded as a $1.6 million increase to our gross deferred tax assets and a $91.9 million gross tax liability.

During 2023, we increased our gross unrecognized tax benefits by $156.3 million, primarily associated with intercompany transfer pricing matters. This unrecognized tax benefit was recorded as a $3.7 million increase to our gross deferred tax assets and a $160.0 million gross tax liability.

During 2022, we increased our gross unrecognized tax benefits by $312.4 million, primarily associated with intercompany transfer pricing matters. This unrecognized tax benefit was recorded as a $29.7 million reduction to our gross deferred tax assets and a $282.7 million gross tax liability.

As of December 31, 2024, we have classified $48.2 million, $22.3 million, and $635.7 million of our unrecognized tax benefits as credits to “Deferred tax assets,” “Accrued expenses” and “Other long-term liabilities,” respectively, on our consolidated balance sheet.

Included in our unrecognized tax benefits as of December 31, 2024, 2023 and 2022, we had $341.4 million, $288.7 million and $208.5 million (net of the federal benefit on state issues), respectively, of unrecognized tax benefits, which would affect our effective income tax rate if recognized.

We recognize potential interest and penalties related to unrecognized tax benefits in our provision for income taxes. In 2024, we recognized total net interest and penalty credits of $41.5 million to our interest and penalty expenses. In 2023 and 2022, we recognized total net interest and penalty expenses of $84.9 million, and $36.6 million, respectively. As of December 31, 2024 and 2023, our accrual for interest and penalties was $82.6 million and $124.1 million, respectively.

The U.S. Internal Revenue Service and other local and foreign tax authorities routinely examine our tax returns, including intercompany transfer pricing, and it is reasonably possible that we will adjust the value of our uncertain tax positions related these matters and other issues as we receive additional information from various taxing authorities, including reaching settlements with such authorities. In the case of intercompany transfer pricing, it is reasonably possible that taxing authorities do not agree with each other on the reallocation of income or the valuation of intellectual property, in which case we could be subject to double taxation, despite bilateral treaty agreements available to prevent this. In 2023, we came to settlement with the U.K.’s HM Revenue & Customs (“HMRC”) with respect to our tax positions for 2015 through 2020 and subsequently received Closure Notices for those periods in 2024. Due to the nature of the adjustments, we have asserted our rights under the U.S./U.K. Income Tax Convention pursuant to the mutual agreement procedures for the relief of double taxation for these matters.

As a result of various audit closures, settlements and statutes of limitations, we estimate that it is reasonably possible that our gross unrecognized tax benefits could decrease by up to $74.3 million in the next 12 months due to statute of limitations expirations.

We file U.S. federal income tax returns and income tax returns in various state, local and foreign jurisdictions. We have various income tax audits ongoing at any time throughout the world. Except for jurisdictions where we have NOLs or tax credit carryforwards, we are no longer subject to any tax assessment from tax authorities for years prior to 2014 in jurisdictions that have a material impact on our consolidated financial statements.

In December 2022, E.U. member states reached an agreement to implement the minimum tax component ("Pillar Two") of the Organization for Economic Co-operation and Development's (the "OECD's"), global international tax reform initiative with effective dates of January 1, 2024 and 2025. In July 2023, the OECD published Administrative Guidance proposing certain safe harbors that effectively extend certain effective dates to January 1, 2027. The assessment of our potential 2024 exposure for the global per-country minimum tax of 15%, based on our forecasted 2024 results, is immaterial to our condensed consolidated financial statements as the effective tax rates in most of the jurisdictions in which we operate are above 15%.

P. Commitments and Contingencies

2022 Credit Facility

In July 2022, Vertex and certain of its subsidiaries entered into a $500.0 million unsecured revolving facility (the "Credit Agreement") with Bank of America, N.A., as administrative agent and the lenders referred to therein (the "Lenders"), which matures on July 1, 2027. The Credit Agreement was not drawn upon at closing and we have not drawn upon it to date. Amounts drawn pursuant to the Credit Agreement, if any, will be used for general corporate purposes. Subject to satisfaction of certain conditions, we may request that the borrowing capacity for the Credit Agreement be increased by an additional $500.0 million. Additionally, the Credit Agreement provides a sublimit of $100.0 million for letters of credit.

Any amounts borrowed under the Credit Agreement will bear interest, at our option, at either a base rate or a Secured Overnight Financing Rate ("SOFR"), in each case plus an applicable margin. Under the Credit Agreement, the applicable margins on base rate loans range from 0.000% to 0.500% and the applicable margins on SOFR loans range from 1.000% to 1.500%, in each case based on our consolidated leverage ratio (the ratio of our total consolidated funded indebtedness to our consolidated EBITDA for the most recently completed four fiscal quarter period).

Any amounts borrowed pursuant to the Credit Agreement are guaranteed by certain of our existing and future domestic subsidiaries, subject to certain exceptions.

The Credit Agreement contains customary representations and warranties and affirmative and negative covenants, including a financial covenant to maintain subject to certain limited exceptions, a consolidated leverage ratio of 3.50 to 1.00, subject to an increase to 4.00 to 1.00 following a material acquisition. As of December 31, 2024, we were in compliance with the covenants described above. The Credit Agreement also contains customary events of default. In the case of a continuing event of default, the administrative agent would be entitled to exercise various remedies, including the acceleration of amounts due under outstanding loans.

Direct costs related to the Credit Agreement are recorded over its term and were not material to our financial statements.

Guaranties and Indemnifications

As permitted under Massachusetts law, our Articles of Organization and By-laws provide that we will indemnify certain of our officers and directors for certain claims asserted against them in connection with their service as an officer or director. The maximum potential amount of future payments that we could be required to make under these indemnification provisions is unlimited. However, we have purchased directors' and officers' liability insurance policies that could reduce our monetary exposure and enable us to recover a portion of any future amounts paid. No indemnification claims currently are outstanding, and we believe the estimated fair value of these indemnification arrangements is minimal.

We customarily agree in the ordinary course of our business to indemnification provisions in agreements with clinical trial investigators and sites in our product development programs, sponsored research agreements with academic and not-for-profit institutions, various comparable agreements involving parties performing services for us, and our real estate leases. We also customarily agree to certain indemnification provisions in our drug discovery, development and commercialization collaboration agreements. With respect to our clinical trials and sponsored research agreements, these indemnification provisions typically apply to any claim asserted against the investigator or the investigator's institution relating to personal injury or property damage, violations of law or certain breaches of our contractual obligations arising out of the research or clinical testing of our compounds or product candidates. With respect to lease agreements, the indemnification provisions typically apply to claims asserted against the landlord relating to personal injury or property damage caused by us, to violations of law by us or to certain breaches of our contractual obligations. The indemnification provisions appearing in our collaboration agreements are similar to those for the other agreements discussed above, but in addition provide some limited indemnification for our collaborator in the event of third-party claims alleging infringement of intellectual property rights. In each of the cases above, the indemnification obligation generally survives the termination of the agreement for some extended period, although we believe the obligation typically has the most relevance during the contract term and for a short period of time thereafter. The maximum potential amount of future payments that we could be required to make under these provisions is generally unlimited. We have purchased insurance policies covering personal injury, property damage and general liability that reduce our exposure for indemnification and would enable us in many cases to recover all or a portion of any future amounts paid. We have never paid any material amounts to defend lawsuits or settle claims related to these indemnification provisions. Accordingly, we believe the estimated fair value of these indemnification arrangements is minimal.

Legal Matters

We are subject to claims and legal proceedings in the ordinary course of our business activities. If we determine that it is probable that future expenditures will be made for a particular matter and such expenditures can be reasonably estimated, we accrue a loss contingency based on our best estimate of the probable range of loss. We accrue the minimum amount within the probable range of loss if no amount within the range is more likely than another. If we determine that future expenditures are not probable, or probable but not reasonably estimated, we do not accrue a loss contingency. If we determine that a material loss is reasonably possible and the range of loss can be estimated, we disclose the possible range of loss. On a quarterly basis, we evaluate developments with these claims and legal proceedings that could result in a loss contingency accrual, or an increase or decrease to a previously accrued loss contingency. There were no material loss contingencies accrued as of December 31, 2024 or 2023.

Other Contingencies

We also have certain contingent liabilities that arise in the ordinary course of our business activities. We accrue for such contingent liabilities when it is probable that future expenditures will be made and such expenditures can be reasonably estimated. Other than our contingent consideration liabilities discussed in Note D, "Fair Value Measurements," there were no material contingent liabilities accrued as of December 31, 2024 or 2023.

Q. Segment Information

Segment reporting is prepared on the same basis that our chief executive officer, who is our chief operating decision maker ("CODM"), manages the business, makes operating decisions and assesses performance. We operate in one segment, pharmaceuticals. We have selected net income (loss) as our reported measure of segment profit or loss because it is regularly provided to our CODM, allows our CODM to allocate resources because it encapsulates the results of our processes that generate revenues and expenses, and is important to the users of our financial statements. Enterprise-wide disclosures about revenues, significant customers, significant segment expenses, and property and equipment, net by location are presented below.

Revenues by Product

Product revenues, net consisted of the following:

	Year ended December 31,		
	2024	2023	2022
	(in millions)		
TRIKAFTA/KAFTRIO	$ 10,238.6	$ 8,944.7	$ 7,686.8
Other product revenues	781.5	924.5	1,243.9
Total product revenues, net	$ 11,020.1	$ 9,869.2	$ 8,930.7

In 2024, "Other product revenues" included CASGEVY product revenues of $10.0 million.

Product Revenues by Geographic Location

Net product revenues are attributed to countries based on the location of the customer and consisted of the following:

	Year ended December 31,		
	2024	2023	2022
	(in millions)		
United States	$ 6,684.9	$ 6,040.4	$ 5,699.3
Outside of the United States			
Europe	3,453.9	3,109.0	2,705.5
Other	881.3	719.8	525.9
Total product revenues outside of the United States	4,335.2	3,828.8	3,231.4
Total product revenues, net	$ 11,020.1	$ 9,869.2	$ 8,930.7

Significant Customers

Gross product revenues and accounts receivable from each of our customers who individually accounted for 10% or more of total gross product revenues and/or 10% or more of total accounts receivable consisted of the following:

	Percent of Total Gross Product Revenues			Percent of Accounts Receivable	
	Year Ended December 31,			As of December 31,	
	2024	2023	2022	2024	2023
McKesson Corporation	26 %	26 %	25 %	17 %	23 %
Accredo Health Group, Inc.	11 %	11 %	12 %	<10%	<10%
Walgreen Co.	<10%	<10%	10 %	<10%	<10%
Lloyds Pharmacy*	<10%	<10%	<10%	13 %	10 %

*A wholly owned subsidiary of McKesson Corporation in the U.K. until 2022.

Significant Segment Expenses

Significant segment expenses are set forth in the following table:

	Year ended December 31,		
	2024	2023	2022
	(in millions)		
Product revenues, net	$ 11,020.1	$ 9,869.2	$ 8,930.7
Costs and expenses:			
Cost of sales - products	516.3	349.2	260.5
Cost of sales - royalty	1,014.2	913.0	819.8
Research expenses	804.5	705.6	626.7
Development expenses	2,825.8	2,457.3	1,913.6
Acquired in-process research and development expenses	4,628.4	527.1	115.5
Selling and other commercial expenses	838.5	592.4	468.9
General and administrative expenses	625.8	544.2	475.8
Interest income	(598.1)	(614.7)	(144.6)
Other Segment items [(1)]	116.2	15.3	162.1
Provision for income taxes	784.1	760.2	910.4
Net (loss) income	$ (535.6)	$ 3,619.6	$ 3,322.0

(1) Other segment items included in "Net (loss) income" primarily include changes in the fair value of contingent consideration, interest expense and changes in the fair value of equity investments.

Long-lived Assets by Location

Long-lived assets by location consisted of the following:

	As of December 31,	
	2024	2023
	(in millions)	
United States	$ 2,392.4	$ 1,359.7
Outside of the United States		
United Kingdom	176.6	77.3
Other	15.6	15.9
Total long-lived assets outside of the United States	192.2	93.2
Total long-lived assets	$ 2,584.6	$ 1,452.9