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, 2019
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 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, 2019 (the last business day of the registrant's most recently completed second fiscal quarter of 2019) was $46.7 billion.

As of January 31, 2020, the registrant had 259,268,593 shares of common stock outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the definitive proxy statement for the 2020 Annual Meeting of Shareholders, which we expect to hold on June 3, 2020, are incorporated by reference into Part III of this Annual Report on Form 10-K.

VERTEX PHARMACEUTICALS INCORPORATED

ANNUAL REPORT ON FORM 10-K

TABLE OF CONTENTS

“We,” “us,” “Vertex” and the “Company” as used in this Annual Report on Form 10-K refer to Vertex Pharmaceuticals Incorporated, a Massachusetts corporation, and its subsidiaries.

“Vertex,” “KALYDECO®,” “ORKAMBI®,” “SYMDEKO®,” “SYMKEVI®” and “TRIKAFTA®” are registered trademarks of Vertex. Other brands, names and trademarks contained in this Annual Report on Form 10-K are the property of their respective owners.

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 development programs, we refer to our compounds by their scientific (or generic) name or VX developmental designation.

PART I

ITEM 1. BUSINESS

OVERVIEW

We invest in scientific innovation to create transformative medicines for people with serious diseases with a focus on specialty markets.

Cystic Fibrosis

Our goal is to develop treatment regimens that will provide benefits to all patients with cystic fibrosis, or CF, and will enhance the benefits that currently are being provided to patients taking our medicines. Our marketed medicines are TRIKAFTA (elexacaftor/tezacaftor/ivacaftor and ivacaftor), SYMDEKO/SYMKEVI (tezacaftor/ivacaftor and ivacaftor), ORKAMBI (lumacaftor/ivacaftor) and KALYDECO (ivacaftor). We obtained approval from the U.S. Food and Drug Administration, or the FDA, for TRIKAFTA, our triple combination regimen, in October 2019. This approval increased the number of patients eligible for our medicines in the U.S. by approximately 6,000 and provided an additional treatment option for many patients who are also eligible for one of our previously approved products. We have submitted a Marketing Authorization Application, or MAA, to the European Medicines Agency, or EMA, for this triple combination regimen. The FDA approval and the MAA filing were based on positive data from Phase 3 clinical trials evaluating the triple combination regimen in patients 12 years of age or older (i) who have a copy of the F508del mutation in their cystic fibrosis transmembrane conductance regulator, or CFTR, gene and a second mutation that results in minimal CFTR function, whom we refer to as F508del/Min patients, and (ii) who have two copies of the F508del mutation, whom we refer to as F508del homozygous patients. Our four medicines are collectively approved to treat approximately 60% of the 75,000 CF patients in North America, Europe and Australia. We are focused on obtaining approval for the triple combination in ex-U.S. markets for patients 12 years of age and older and evaluating our triple combination in younger patients, with the goal of having treatments for up to 90% of patients with CF. We are also pursuing other therapeutic approaches to address the remaining 10% of CF patients.

Research and Development

Our goal is to identify and develop new medicines by combining transformative advances in the understanding of human disease and in the science of therapeutics to advance human health.

Small Molecule Programs

Alpha-1 Antitrypsin Deficiency. In 2019, we initiated a Phase 2 clinical trial to evaluate VX-814, our first investigational small molecule corrector for the treatment of alpha-1 antitrypsin, or AAT, deficiency. We expect to obtain data from this clinical trial in 2020. A Phase 1 clinical trial to evaluate VX-864, our second investigational small molecule corrector for the treatment of AAT deficiency, is ongoing in healthy volunteers.

APOL1-Mediated Kidney Diseases. In 2019, we completed a Phase 1 clinical trial evaluating VX-147 as a small molecule inhibitor of APOL1 function, a causal genetic factor in focal segmental glomerulosclerosis, or FSGS, and other proteinuric kidney diseases. In 2020, we expect to initiate a Phase 2 proof of concept clinical trial to evaluate VX-147.

Pain. We believe that NaV1.8 inhibitors have the potential to provide an effective non-opioid treatment for pain. We expect to begin clinical development of a NaV1.8 inhibitor in the first half of 2020.

Cell and Genetic Therapies

Sickle cell disease and beta-thalassemia. We are co-developing CTX001, an investigational gene-editing treatment for beta-thalassemia and sickle cell disease, with CRISPR Therapeutics AG, or CRISPR. Enrollment is ongoing in our two Phase 1/2 clinical trials to evaluate CTX001. In November 2019, we announced positive interim data from the first two patients with these hemoglobinopathies treated with the investigational CRISPR/Cas9 gene-editing therapy CTX001 in our ongoing trials.

Type 1 Diabetes. In 2019, we established a preclinical program to develop cell-based therapies for type 1 diabetes through our acquisition of Semma Therapeutics, Inc., or Semma.

Duchenne muscular dystrophy, or DMD, and myotonic dystrophy type 1, or DM1. In 2019, we established preclinical genetic therapy programs for DMD and DM1, through our acquisition of Exonics Therapeutics, Inc., or Exonics, and the expansion of our collaboration with CRISPR.

We plan to continue investing in our research and development programs and fostering scientific innovation, including by continuing to identify additional drug candidates through our internal research efforts and investing in business development transactions to access emerging technologies, drugs and drug candidates.

CYSTIC FIBROSIS

Background

CF is a life-shortening genetic disease affecting approximately 75,000 people in North America, Europe and Australia. CF is 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 of the two of the most prevalent mutations, the F508del mutation or the G551D 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. The G551D mutation results in a defect in the CFTR protein in which the defective protein reaches the surface of a cell but does not efficiently transport chloride ions across the cell membrane.

The absence of working CFTR proteins 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 VX-561 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, and elexacaftor, help CFTR proteins reach the cell surface.

Our Medicines

Our medicines, TRIKAFTA, SYMDEKO/SYMKEVI, ORKAMBI and KALYDECO, are collectively approved to treat approximately 60% of the 75,000 CF patients in North America, Europe and Australia. Our approved medicines, including information regarding the indication and age groups for which the medicine is approved, are set forth in the table below.

Product	Scientific Name	Region/Initial Approval	Indication	Eligible Age Group
trikafta®	elexacaftor/tezacaftor/ivacaftor and ivacaftor	U.S. (2019)	CF patients with at least one F508del mutation	12 years of age and older
symdeko®	tezacaftor/ivacaftor and ivacaftor	U.S. (2018)	CF patients (i) homozygous for the F508del mutation or (ii) with at least one mutation that is responsive to tezacaftor/ivacaftor	6 years of age and older
symkevi®	tezacaftor/ivacaftor	European Union (2018)	CF patients (i) homozygous for the F508del mutation or (ii) with one copy of the F508del mutation and one copy of certain mutations that result in residual CFTR activity	12 years of age and older
ORKAMBI®	lumacaftor/ivacaftor	U.S. (2015)	CF patients homozygous for the F508del mutation	2 years of age and older
	lumacaftor/ivacaftor	European Union (2015)	CF patients homozygous for the F508del mutation	2 years of age and older
kalydeco®	ivacaftor	U.S. (2012)	CF patients with G551D and other specified mutations	6 months of age and older
	ivacaftor	European Union (2012)	CF patients with G551D and other specified mutations	6 months of age and older

In addition to the European Union and the United States, we market our products in additional countries, including Australia and Canada. We continuously seek to increase the number of patients eligible to receive our current medicines through label expansions and the approval of new medicines. Activities in support of these efforts include:

TRIKAFTA

- In October 2019, we received approval from the FDA for TRIKAFTA for the treatment of patients with CF 12 years of age and older who have at least one copy of the *F508del* mutation.
- In the fourth quarter of 2019, the MAA we submitted for the triple combination of elexacaftor, tezacaftor, and ivacaftor in patients 12 years of age and older was validated by the EMA.
- A Phase 3 clinical trial evaluating the triple combination of elexacaftor, tezacaftor and ivacaftor in children six to 11 years of age who are F508del homozygous or who have one copy of the F508del mutation and one minimum function mutation is ongoing.

SYMDEKO/SYMKEVI

- In June 2019, we obtained approval for SYMDEKO in the United States for children 6 to 11 years of age.
- In the fourth quarter of 2019, we submitted an application to the EMA to extend the indication of tezacaftor in combination with ivacaftor to patients 6 to 11 years of age.

ORKAMBI

- In January 2019, we obtained approval for ORKAMBI in the European Union for children 2 to 5 years of age.

KALYDECO

- In April 2019, we obtained approval for KALYDECO in the United States for infants 6 to <12 months of age.
- In December 2019, we obtained approval for KALYDECO in the European Union for infants 6 to <12 months of age.

Drug Candidates

- We are evaluating VX-121, an additional next-generation corrector, and VX-561, a potentiator, in Phase 2 clinical development.

RESEARCH AND DEVELOPMENT PROGRAMS

We invest in research and development in order to discover and develop transformative medicines for people with serious diseases. Our strategy is to combine transformative advances in the understanding of human disease and the science of therapeutics in order to identify and develop new medicines. Our approach to drug discovery historically focused on the research and development of small molecule drugs, which has been validated through our success in moving novel small molecule drug candidates into clinical trials and obtaining marketing approvals for TRIKAFTA, KALYDECO, ORKAMBI and SYMDEKO/SYMKEVI for the treatment of CF and INCIVEK (telaprevir) for the treatment of hepatitis C infection. Over the last several years, we have expanded our research capabilities to include additional innovative therapeutic approaches with a focus on cell and genetic therapies, including:

- our collaboration with CRISPR in hemoglobinopathies and other diseases;
- our establishment of preclinical genetic therapy programs for DMD and DM1, through our acquisition of Exonics; and
- our establishment of a preclinical program to develop cell-based therapies for type 1 diabetes through our acquisition of Semma.

The experience we gained developing medicines for CF and our analysis of research and development programs conducted by other companies in our industry have shaped a disciplined strategy that guides our investments in research and development and external innovation that focuses on:

- transformative treatments for life-threatening diseases with a high unmet medical need;

- targets validated as playing a causal role in the human biology of a disease;
- innovative approaches to addressing those targets;
- biological assays and clinical biomarkers that we believe will be predictive of clinical responses; and
- efficient clinical and regulatory paths to bring new medicines to patients.

In addition to continuing our research to identify additional drug candidates for the treatment of CF, we are focusing our research and development efforts on developing products for the treatment of serious diseases including AAT deficiency, APOL1-mediated FSGS, pain, sickle cell disease, beta-thalassemia, DMD, DM1 and type 1 diabetes.

To augment our internal programs, we seek to acquire businesses and technologies and to 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 as well as to access technologies needed to execute on our strategy. We have established such relationships with organizations around the world and intend to extend and leverage that experience to further our research efforts to discover transformational medicines for serious diseases. We will continue to identify and evaluate potential acquisitions and collaborations that may be similar to or different from the transactions that we have engaged in previously.

Small Molecule Programs

Alpha-1 Antitrypsin Deficiency

AAT deficiency is caused by mutations in the SERPINA1 gene that produces AAT protein. To develop AAT deficiency, people must inherit two mutant SERPINA1 alleles (one from each parent). The mutations result in a defect in the AAT protein in which the protein does not fold correctly. This folding defect causes the AAT protein to accumulate in the liver (where it is produced), which can cause liver damage. As a result, the protein fails to reach other organs in adequate quantity and function, particularly in the lungs, where its normal role is to protect them from the digestive effects of certain proteases. The unchecked activity of these proteases can cause auto-digestion of lung tissue and may lead over time to emphysema or chronic pulmonary obstructive disease, and lung infections. Currently, there is no cure or treatment that targets the underlying cause of the disease in both the liver and the lung. Available treatments are aimed at transiently increasing levels of AAT in the blood, but have no effect in the liver. Patients living with AAT deficiency typically experience recurring hospital visits and a shortened life expectancy.

We are seeking to develop medicines to treat AAT deficiency. In the laboratory, we have discovered multiple small molecule correctors that restore normal folding of the mutant AAT protein, with the potential to treat both the liver and lung diseases caused by AAT deficiency. In 2019, we began a Phase 2 clinical trial evaluating VX-814 as a potential treatment for AAT deficiency. In addition, in 2019, we initiated a Phase 1 clinical trial evaluating VX-864, our second investigational small molecule corrector for the treatment of AAT deficiency, in healthy volunteers.

APOL1-Mediated Kidney Diseases

Inherited mutations in the APOL1 gene play a causal role in the biology of FSGS as well as other kidney diseases. FSGS is a rare disease that attacks the kidney's filtering units, causing leakage of protein into the urine followed later by deterioration in kidney function, scarring, and, ultimately, permanent kidney damage. FSGS is a leading cause of nephrotic syndrome in children and kidney failure in adults. We have discovered multiple novel small molecules that inhibit the function of APOL1 protein with the goal of treating APOL1-mediated FSGS. In 2019, we completed a Phase 1 clinical trial for VX-147, our first investigational oral small molecule medicine for the treatment of FSGS and other serious kidney diseases. We expect to begin a Phase 2 clinical trial to evaluate VX-147 in 2020.

Pain

Pain can develop from a variety of pathophysiological and psychological conditions. Patients with pain can suffer from acute pain (for example, following surgery or an injury), neuropathic pain (when there is damage to a nerve), and musculoskeletal pain. Current treatments may not work well or cause significant side effects. In addition, there is the potential for addiction and the practice of over- and mis-utilization, as well as underutilization of current pain medicines.

Vertex has discovered multiple inhibitors of the sodium channel 1.8, or NaV1.8, as potential treatments for pain. Consistent with our research strategy, the Nav1.8 protein is a validated target for pain based both on inherited mutations that cause pain syndromes as well as through our own clinical trial data. Specifically, we have obtained positive results from three separate Phase 2 clinical trials evaluating VX-150, a NaV1.8 inhibitor, in patients with three different pain conditions: acute, neuropathic and musculoskeletal pain. We continue to focus our research and development efforts on discovering, developing and advancing inhibitors of NaV1.8 as a potential treatment for pain. In the first quarter of 2020, we announced the discontinuation of Phase 1 development of VX-961 and that we expect to begin clinical development of an additional molecule in the first half of 2020.

Out-licenses

Our research team has also discovered several additional first-in-class compounds that were out-licensed to collaborators consistent with our corporate strategy. Several of these compounds are continuing in clinical development. Janssen Pharmaceuticals, Inc., or Janssen, is developing pimodivir, a compound we discovered and licensed to Janssen in 2014, as a potential treatment for the influenza A virus. Janssen is conducting Phase 3 clinical trials of pimodivir in combination with standard of care treatment in patients who are hospitalized or are outpatients at a higher risk of influenza-related complications.

Cell and Genetic Therapies

Sickle Cell Disease and Beta-Thalassemia

Sickle cell disease and beta-thalassemia 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 and removes carbon dioxide throughout the body.

Sickle cell disease is caused by the change of a single amino acid in the 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, 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 mutations in hemoglobin 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, with severely affected patients requiring regular blood transfusions, as frequently as every two to four weeks. Blood transfusions eventually cause an unhealthy buildup of iron in the patient, leading to organ damage.

We are co-developing CTX001, an investigational gene-editing treatment, for the treatment of hemoglobinopathies, with CRISPR. We are seeking to develop a CRISPR/Cas9-based therapy to treat both beta-thalassemia and sickle cell disease. In November 2019, we announced positive, interim data from the first two patients with severe hemoglobinopathies treated with the investigational CRISPR/Cas9 gene-editing therapy, CTX001, in ongoing Phase 1/2 clinical trials. One patient with severe sickle cell disease received CTX001 in mid-2019 and data for this patient reflect four months of safety and efficacy follow-up. One patient with transfusion-dependent beta-thalassemia received CTX001 in the first quarter of 2019 and data for this patient reflect nine months of safety and efficacy follow-up. These trials are ongoing and additional patients have been enrolled.

Type 1 Diabetes

Type 1 diabetes, or T1D, is a chronic, metabolic disorder caused by an absence of insulin secretion by the beta cells in the pancreas. In patients with T1D the person's own immune system attacks the insulin-producing islet cells of the pancreas, resulting in a complete lack of insulin. 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), burden of care on patients and families, and long-term vascular complications. In 2019, we acquired a preclinical program to develop cell-based therapies for T1D through our acquisition of Semma. We plan to advance this program into clinical development in T1D patients in late 2020 or early 2021.

Duchenne Muscular Dystrophy

Duchenne Muscular Dystrophy, or DMD, and myotonic dystrophy type 1, or DM1, are inherited diseases that result in the weakening and breakdown of skeletal muscles over time. In 2019, we acquired preclinical programs to develop genetic therapies for DMD and DM1 through our acquisition of Exonics and the expansion of our collaboration with CRISPR.

COMMERCIALIZATION OF OUR MEDICINES

Commercial Organization

Our commercial organization focuses on supporting sales of TRIKAFTA, SYMDEKO/SYMKEVI, ORKAMBI and KALYDECO in the markets where these products have been approved. Our sales and marketing organizations are responsible for promoting products to health care providers and obtaining reimbursement for our products from third-party payors, including governmental organizations in the United States and ex-U.S. markets.

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 United States 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 United States focused on the treatment of CF. In international markets, we have small sales forces that support KALYDECO, ORKAMBI and SYMDEKO/SYMKEVI in jurisdictions where these products are approved.

We market our products through personal interactions with physicians and allied health care professionals. In addition, 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 policy-makers. We also have established programs in the United States that provide our products to qualified uninsured or underinsured patients at no charge or at a reduced charge, based on specific eligibility criteria.

Reimbursement

Sales of our products depend, to a large degree, on the extent to which our products will be covered 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 medical products and services. Additionally, the containment of health care costs has become a priority of federal and state 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.

The Medicare Prescription Drug, Improvement, and Modernization Act of 2003, or the MMA, established the Medicare Part D program to provide 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. 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. However, Part D prescription drug formularies must include drugs within each therapeutic category and class of covered Part D drugs, though not necessarily all the drugs in each category or class. Any formulary used by a Part D prescription drug plan must be developed and reviewed by a pharmacy and therapeutic committee. Government payment for some of the costs of prescription drugs may increase demand for products for which we receive marketing approval. However, any negotiated prices for our products covered by a Part D prescription drug plan likely will be lower than the prices we might otherwise obtain. Moreover, while the MMA applies only to drug benefits for Medicare beneficiaries, private payors often follow Medicare coverage policy and payment limitations in setting their own payment rates. Any reduction in payment that results from the MMA may result in a similar reduction in payments from non-governmental payors.

The American Recovery and Reinvestment Act of 2009 provided funding for the federal government to compare the effectiveness of different treatments for the same illness. A plan for the research was to be developed by the Department of Health and Human Services, or HHS, the Agency for Healthcare Research and Quality and the National Institutes of Health, and periodic reports on the status of the research and related expenditures were to be made to the U.S. Congress. Although the results of the comparative effectiveness studies are not intended to mandate coverage policies for public or private payors, it is not clear what effect, if any, the research will have on the sales of our products. In the future, it is possible that comparative effectiveness research demonstrating benefits of a competitor's product could adversely affect the sales of our products. If third-party payors do not consider our products to be cost-effective compared to other available therapies, they may not cover our products as a benefit under their plans or, if they do, the level of payment may not be sufficient to allow us to sell our products on a profitable basis.

The Patient Protection and Affordable Care Act, or 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 is designed to expand and increase industry rebates for drugs covered under Medicaid programs, impose an annual fee on branded pharmaceutical manufacturers and make changes to the coverage requirements under the Medicare Part D program.

In Europe and many other foreign jurisdictions, the success of our products depends largely on obtaining and maintaining government reimbursement because patients are unable to access prescription pharmaceutical products that are not reimbursed by their governments. Negotiating reimbursement rates in foreign countries can delay the commercialization of a pharmaceutical product and generally results in a reimbursement rate that is lower than the net price that companies can obtain for the same product in the United States.

In some countries, such as Germany, commercial sales of a new product may begin while the reimbursement rate that a company will receive is under discussion. In other countries, a company must complete the reimbursement discussions prior to the commencement of commercial supply of the pharmaceutical product. The requirements governing drug pricing vary widely from country to country. For example, the member states of the European Union can restrict the range of drugs for which their national health insurance systems provide reimbursement and can control the prices of drugs for human use. In addition, many ex-U.S. government payers 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. Recently, many countries in the European Union have increased the amount of mandatory discounts imposed on pharmaceuticals and these efforts could continue as countries attempt to manage healthcare expenditures. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will reimburse our products. Similarly, it could be the case that such countries may only provide for reimbursement on terms that we do not deem adequate. Additionally, reimbursement discussions in ex-U.S. markets may take a significant period of time.

STRATEGIC TRANSACTIONS, COLLABORATIONS AND STRATEGIC INVESTMENTS

As part of our business strategy, we seek to license or acquire drugs, drug candidates, businesses and other technologies that have the potential to complement 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 drug 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

Acquisitions

In July 2019, we acquired Exonics, a privately-held company focused on creating transformative gene-editing therapies to repair mutations that cause DMD and other severe neuromuscular diseases, including DM1. Our acquisition of Exonics enhanced our gene-editing capabilities and supports the potential development of novel therapies for DMD and DM1. In connection with the acquisition, we acquired all of the outstanding equity of Exonics for an upfront payment of approximately $245.0 million plus customary working capital adjustments in cash, and certain potential future payments based primarily upon the successful achievement of specified development and regulatory milestones for the DMD and DM1 programs.

In October 2019, we acquired Semma, a privately-held company focused on the use of stem cell-derived human islets as a potentially curative treatment for T1D. Our acquisition of Semma advanced our cell therapy capabilities and supports the potential development of transformative therapies for T1D. In connection with the acquisition, we acquired all of the outstanding equity of Semma for approximately $950.0 million in cash.

Collaboration and Licensing Arrangements

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 drug candidates. Depending on the terms of the arrangements, we may be responsible for the costs of research activities, 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 resulting from the collaboration. In our co-development and co-commercialization arrangement with CRISPR, we agreed to split costs and revenues associated with the relevant program. Our current in-license agreements include:

- Arbor Biotechnologies, Inc. In 2018, we entered into a collaboration with Arbor Biotechnologies, pursuant to which we are focusing on the discovery of novel proteins, including DNA endonucleases, to advance the development of new gene-editing therapies.
- CRISPR Therapeutics AG. In 2015, we entered into a collaboration with CRISPR for the discovery and development of potential new treatments aimed at the underlying genetic causes of human diseases using CRISPR-Cas9 gene-editing technology. We currently are co-developing CTX001 for the treatment of sickle cell disease and beta-thalassemia and, if successful, have agreed to co-commercialize CTX001. In addition, we have exercised options to exclusively license treatments for specific targets, including CF, that were subject to the research program. In 2019, we obtained exclusive worldwide rights to CRISPR's intellectual property for DMD and DM1 gene-editing products through a new agreement with CRISPR.
- Kymera Therapeutics, Inc. In 2019, we entered into a collaboration with Kymera Therapeutics for the research and development of small molecule protein degraders. Under the collaboration, Kymera conducts research activities in multiple targets, and upon designation of a clinical development candidate for a target, we have the option to exclusively license molecules against the target.
- Moderna Therapeutics, Inc. In 2016, we entered into a collaboration with Moderna Therapeutics, pursuant to which we are seeking to identify and develop messenger ribonucleic acid, or mRNA, therapeutics for the treatment of CF.
- Other Arrangements. In 2019, we entered into collaborations with Molecular Templates, Inc. and Ribometrix, Inc. In 2018, we entered into agreements with Genomics plc, Merck KGaA, Darmstadt, Germany, and X-Chem, Inc. in order to support our research and development efforts.

Out-license Agreements

We have entered into various agreements pursuant to which we have out-licensed rights to certain drug 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 drug candidates and obtain development and commercialization rights to these drug 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. Our current out-license agreements include:

- Janssen Pharmaceuticals, Inc. In 2014, we entered into an agreement with Janssen. Pursuant to this agreement, Janssen Inc. is developing pimodivir for the treatment of influenza. Janssen is evaluating pimodivir in Phase 3 clinical trials in patients with influenza A infection.
- Merck KGaA, Darmstadt, Germany. In 2017, we entered into a Strategic Collaboration and License Agreement with Merck KGaA, Darmstadt, Germany, pursuant to which we granted an exclusive worldwide license to research, develop and commercialize four oncology research and development programs.

Strategic Investments

In connection with our business development activities, we periodically make equity investments in our collaborators. We hold strategic equity investments in public companies including CRISPR, Moderna Therapeutics and Molecular Templates, as well as certain private companies, including Arbor Biotechnologies, Kymera Therapeutics and Ribometrix. We may make additional strategic equity investments in public or private companies in the future.

Cystic Fibrosis Foundation Therapeutics Incorporated

In 2004, we entered into a collaboration agreement with the Cystic Fibrosis Foundation, or CFF, 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 KALYDECO (ivacaftor), ORKAMBI (lumacaftor in combination with ivacaftor) and SYMDEKO/SYMKEVI (tezacaftor in combination with ivacaftor) and royalties ranging from low-single digits to mid-single digits on potential net sales of certain compounds first synthesized and/or tested between March 1, 2014 and August 31, 2016, including elexacaftor. For combination products, such as ORKAMBI, SYMDEKO/SYMKEVI and TRIKAFTA (elexacaftor, tezacaftor, and ivacaftor), sales are allocated equally to each of the active pharmaceutical ingredients in the combination product.

INTELLECTUAL PROPERTY

Patents and other proprietary 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 and products.

Patents provide a period of exclusivity that can make it more difficult for competitors to market and use our technology. We own patents and pending patent applications that relate to compounds, formulations, treatment of diseases, synthetic routes, intermediates 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 in some countries. In addition to patent protection, we have market exclusivity from U.S. and European regulatory agencies for the active pharmaceutical agents and, where applicable, their approved orphan indications for a certain time period. Market exclusivity runs concurrently with patent exclusivity.

The table below sets forth the year of projected expiration for the basic product patents or pending patent applications covering each of our approved products. For products that are combinations of two or more active ingredients, the projected expiration of the latest expiring patent or application covering any of the active pharmaceutical ingredients is provided (lumacaftor for ORKAMBI, tezacaftor for SYMDEKO/SYMKEVI and elexacaftor for TRIKAFTA). Patent term extensions, supplementary protection certificates, 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 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/Drug Candidate	Status of United States Patent (Projected Expiration)	Status of European Union Patent (Projected Expiration)
KALYDECO	Granted (2027)	Granted (2025) [1]
ORKAMBI	Granted (2030)	Granted (2026) [2]
SYMDEKO/SYMKEVI	Granted (2027)	Granted (2028) [3]
TRIKAFTA	Pending (2037)	Pending (2037)

[1] Certain European countries have granted supplementary protection certificates for KALYDECO, which expire in 2027.

[2] Certain European countries have granted supplementary protection certificates for ORKAMBI, which expire in 2030.

[3] Certain European countries have granted supplementary protection certificates for SYMKEVI, which expire in 2033.

In addition to our later-stage programs and marketed products, we actively monitor and file patent applications in the United States and in foreign countries on technology that is in the pre-clinical and early clinical stages. For example, we also own U.S. and foreign patents and patent applications covering the following:

- CF potentiators and correctors and many other related compounds, and the use of those compounds to treat CF.
- Other pre-clinical and clinical drug candidates and the use of such drug 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 own or hold exclusive licenses to several hundred patents in the United States. We own nine issued U.S. patents that cover the active pharmaceutical ingredients in KALYDECO, its marketed formulations, and/or its approved indication. We own 17 issued U.S. patents that cover the active pharmaceutical ingredients in ORKAMBI, its marketed formulations, and/or its approved indication. We own 19 issued U.S. patents that cover the active pharmaceutical ingredients in SYMDEKO, its marketed formulation, and/or its approved indication. We own 18 issued U.S. patents that cover the active pharmaceutical ingredients in TRIKAFTA, its marketed formulation, and/or its approved indication, and the patent application covering elexacaftor is pending in the United States.

We cannot be certain, however, that issued patents will be enforceable or provide adequate protection or that pending patent applications will result in issued patents.

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.

MANUFACTURING

As we market and sell our approved products and advance our drug 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 an international network of third parties to manufacture and distribute our products for commercial sale and post-approval clinical trials and to manufacture and distribute our drug candidates for clinical trials. In addition to establishing supply chains for each new approved product, we need to adapt our supply chain for existing products to include additional formulations that are often required in order to treat younger patients or to increase scale of production for existing products. We currently are focused on ensuring the stability of the supply chains for our current products, including TRIKAFTA.

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 have established our own small-scale manufacturing capabilities in Boston, which we use for clinical trial and commercial supplies.

Our supply chain for sourcing raw materials and manufacturing drug product ready for distribution is a multi-step international endeavor. In general, these raw materials are available from multiple sources. 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. In addition, third parties are used for packaging, warehousing and distribution of products.

Establishing and managing this global supply chain for each of our drugs and drug candidates requires a significant financial commitment and the creation and maintenance of numerous third-party contractual relationships. To ensure the stability of our supply chains, we aim to develop additional sources of manufacture for all steps of our manufacturing processes at the time of, or shortly after, marketing approval. Therefore, at any point in time, we may have a limited number of single source manufacturers for certain steps in our manufacturing processes, particularly for recently launched products.

In order to manufacture our commercial products, we utilize both continuous manufacturing technology as well as batch manufacturing processes. While continuous process manufacturing has been used in many industries, we believe that we are the first company to obtain FDA approval for a fully-continuous drug product manufacturing process.

We have developed systems and processes to track, monitor and oversee our third-party manufacturers' activities, including a quality assurance program intended to ensure that our third-party manufacturers comply with current Good Manufacturing Practices, or GMP. 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.

Compared to the manufacturing processes required for small molecule drugs, the manufacturing processes for genetic and cell-based therapies are typically more complex and challenging, require different systems, equipment and facilities and require different expertise to develop and maintain. In 2019, we gained expertise in these areas through our acquisitions of Exonics and Semma, but in order to successfully develop and commercialize genetic and cell-based therapies, we will need to establish the manufacturing infrastructure, independently or through a third-party network, to manufacture these therapies.

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 drug 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 drug 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 drug 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.

Cystic Fibrosis

A number of companies are seeking to identify and develop drug candidates for the treatment of CF, including public companies such as AbbVie, Eloxx Pharmaceuticals, Proteostasis Therapeutics, and Translate Bio, and several private companies. Our competitors have research and development programs directed at identifying and developing CFTR potentiators, CFTR correctors and drug candidates with other mechanisms of action or that utilize new therapeutic approaches that seek to address the underlying cause of CF. Our competitors are exploring the development of drug candidates primarily as part of combination regimens of small molecules, and some competitors are exploring development of new therapeutic approaches, including nucleic acid-based therapies, which could provide additional treatment options for patients with CF. Our success in rapidly developing and commercializing our products may increase the resources that our competitors allocate to the development of these potential treatments for CF. If one or more competing therapies are successfully developed as a treatment for patients with CF, our revenues from our current products and/or additional CF products, if then approved, could face significant competitive pressure.

Pipeline

In recent years, we have committed significant research resources to and made significant investments in our pipeline of potential new therapies for alpha-1 antitrypsin deficiency, APOL1-mediated kidney diseases, pain, beta-thalassemia, sickle cell disease, muscular dystrophy, T1D, and other diseases. We plan to continue investing in our pipeline, including expanding beyond small molecule therapies and into the discovery and development of gene therapies and cell therapies. Many other pharmaceutical and biotechnology companies are also investing resources for discovery and development of small molecules, gene therapies and cell therapies to treat the same diseases for which we are developing therapies. 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.

GOVERNMENT REGULATION

Our operations and activities are subject to extensive regulation by numerous government authorities in the United States, the European Union and other countries. In the United States, the European Union and other countries, drugs are subject to rigorous regulations governing the testing, manufacture, labeling, storage, record keeping, approval, advertising and promotion of our products. As a result of these regulations, product development and product approval processes are very expensive and time consuming. The regulatory requirements applicable to drug 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 Approval Processes

The process required by the FDA before a drug may be marketed in the United States generally involves the following:

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

Once a drug candidate 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 candidate in humans. Preclinical or nonclinical testing typically continues even after the IND is submitted.

If the FDA accepts the IND, the drug candidate can then be studied in human clinical trials to determine if the drug candidate is safe and effective. These 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 initially is introduced into healthy human subjects and tested for safety, dosage tolerance, absorption, metabolism, distribution and elimination. In the case of some drug candidates for severe or life-threatening diseases, such as cancer, especially when the drug candidate 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 initiated in a limited patient population intended to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the drug candidate for specific targeted diseases 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 candidate and provide an adequate basis for regulatory approval and product labeling.

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 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. All clinical trials must be conducted under the supervision of one or more qualified investigators in accordance with GCP. Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA and more frequently in other situations, including the occurrence of serious adverse events. Information about certain clinical trials must be submitted within specific time-frames to the National Institutes of Health for public dissemination on the *www.clinicaltrials.gov* website.

The results of drug development, preclinical studies and clinical trials, along with descriptions of the manufacturing process, analytical tests conducted on the chemistry of the drug candidate, proposed labeling and other relevant information are submitted to the FDA as part of an NDA requesting approval to market the drug candidate. The FDA reviews each NDA 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 for filing.

Once the submission is accepted for filing, the FDA begins an in-depth review. The FDA reviews an NDA to determine, among other things, whether a drug candidate is safe and effective for its intended use and whether its manufacturing is GMP-compliant to assure and preserve the drug candidate's identity, strength, quality and purity. The FDA may refer the NDA to an advisory committee for review and recommendation as to whether the NDA 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, the FDA will inspect the facility or facilities where the drug candidate is manufactured and tested. Additionally, before approving an NDA, 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, pre-approval 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 in its present form.

Biologics License Application Process

Certain of our drug candidates may be regulated by the FDA under the Food, Drug, and Cosmetic Act, or FDCA, and the Public Health Service Act as biologics. Biologics can present special safety, efficacy and manufacturing challenges that may differ from those present in the regulation of small molecule drugs. As such, while similar to the NDA review process described above, in lieu of filing an NDA, biologics require the submission of a Biologics License Application, or BLA, and approval of such BLA by the FDA prior to being marketed in the U.S.

Expedited Review and Approval

The FDA has developed four distinct approaches to make new drugs 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 or life-threatening 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.

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 that are intended to treat a serious condition and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over available therapy on a clinically significant endpoint. For drugs and biologics that have been designated as Breakthrough Therapies, robust FDA-sponsor interaction and communication can help to identify the most efficient and expeditious path for clinical development while minimizing the number of patients placed in ineffective control regimens.

The FDA may grant "priority review" status to products 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 GMP. In complying with GMP, manufacturers must devote substantial time, money and effort in the areas of production, quality control and quality assurance to maintain 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 enforcement action may be taken, which may include a warning letter 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 standards 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, under the FDCA the sponsor of an approved drug in the United States may not promote that drug for unapproved, or off-label, uses, although a physician may prescribe a drug for an off-label use in accordance with the practice of medicine. 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 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 manufactured or distributed by us 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 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:

- 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 mitigation and evaluation strategy or other safety-related limitations;
- warning letters or "untitled letters";
- product seizures;
- total or partial suspension of production or distribution; or
- injunctions, fines, disgorgement, refusals of government contracts, or civil or criminal penalties.

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 an active ingredient 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. If the NDA 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.

Biologics are also entitled to exclusivity under the Biologics Price Competition and Innovation Act, which was passed as Title VII to the Patient Protection and Affordable Care Act, or the ACA. The law provides a pathway for approval of biosimilars following the expiration of 12 years of exclusivity for the innovator biologic and a potential additional 180 day-extension term for conducting pediatric studies. 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.

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

If a drug candidate that has orphan drug designation subsequently receives the first FDA approval for that drug 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 indication 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 drug candidates for seven years if a competitor first obtains approval of the same product as defined by the FDA or if our drug candidate is determined to be contained within the competitor's product for the same indication or disease. KALYDECO, ORKAMBI, SYMDEKO, and TRIKAFTA have been granted orphan drug exclusivity by the FDA.

Foreign Regulation

We conduct clinical trials and market our products in numerous jurisdictions outside the United States. Most of these jurisdictions have clinical trial, product approval and post-approval regulatory processes that are similar in principle to those in the United States. Thus, whether or not we obtain FDA approval for a drug candidate, we must obtain approval by the comparable regulatory authorities of foreign countries or economic areas, such as the European Union, 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 European Union regulatory systems, a company may submit marketing authorization applications either under a centralized or decentralized procedure. The centralized procedure, which is compulsory for medicines produced by biotechnology or 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 European Union member states. In addition to the centralized procedure, Europe 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.

Other Regulations

Pharmaceutical companies are also subject to various laws pertaining to healthcare "fraud and abuse," including anti-kickback and false claims laws. Anti-kickback laws generally make 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. False claims laws prohibit 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 false claims laws may also arise when a violation of certain laws or regulations related to the underlying products (e.g., violations regarding improper promotional activity 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 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 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 and teaching hospitals and, beginning with disclosures in 2022, to certain non-physician practitioners. 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 United States, 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, or 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, or 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 United Kingdom generally will be subject to the Bribery Act.

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 data privacy and protection, 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 specifically governing the testing, manufacture, and approval of medical devices. Furthermore, the extent of government regulation, which might result from future legislation or administrative action, cannot accurately be predicted.

EMPLOYEES

As of December 31, 2019, we had approximately 3,000 employees. Of these employees, approximately 2,400 were based in the United States and approximately 600 were based outside the United States. Our employees are not covered by a collective bargaining agreement, except for a small number of employees outside the United States.

A key aspect of remaining competitive in our industry is recruiting and retaining employees, including employees with the scientific and technical expertise to conduct our research activities and advance our development programs and commercial expertise to effectively marketing our products. We consider our relations with our employees to be good and over the last several years have successfully recruited talented and diverse employees to support our expanding business. However, we continue to face intense competition for our personnel from our competitors and other companies throughout our industry and from universities and research institutions.

OTHER MATTERS

Financial Information and Significant Customers

The Company operates in one segment, pharmaceuticals. Financial information about our revenue by product and major customers is set forth in Note R, "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-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
Jeffrey M. Leiden, M.D., Ph.D.	64	Chairman of the Board, Chief Executive Officer and President
Reshma Kewalramani, M.D.	47	Executive Vice President and Chief Medical Officer
David Altshuler, M.D., Ph.D.	55	Executive Vice President, Global Research and Chief Scientific Officer
Stuart A. Arbuckle	54	Executive Vice President and Chief Commercial Officer
Carmen Bozic, M.D.	57	Executive Vice President, Global Medicines Development and Medical Affairs
Michael Parini, J.D.	45	Executive Vice President and Chief Legal and Administrative Officer
Amit K. Sachdev, J.D.	52	Executive Vice President and Chief Patient Officer
Charles F. Wagner, Jr.	51	Executive Vice President and Chief Financial Officer
Paul M. Silva	53	Senior Vice President and Corporate Controller
Nia Tatsis, Ph.D.	50	Senior Vice President and Chief Regulatory Officer

Dr. Leiden is our Chairman, Chief Executive Officer and President. In July 2019, we announced that Dr. Leiden would be transitioning to the role of Executive Chair in April 2020. He has held the positions of Chief Executive Officer and President since February 2012 after joining us as CEO Designee in December 2011. He has been a member of our Board of Directors since July 2009, the Chairman of our Board of Directors since May 2012, and served as our lead independent director from October 2010 through December 2011. Dr. Leiden was a Managing Director at Clarus Ventures, a life sciences venture capital firm, from 2006 through January 2012. Dr. Leiden was President and Chief Operating Officer of Abbott Laboratories, Pharmaceuticals Products Group, and a member of the Board of Directors of Abbott Laboratories from 2001 to 2006. From 1987 to 2000, Dr. Leiden held several academic appointments, including the Rawson Professor of Medicine and Pathology and Chief of Cardiology and Director of the Cardiovascular Research Institute at the University of Chicago, the Elkan R. Blout Professor of Biological Sciences at the Harvard School of Public Health, and Professor of Medicine at Harvard Medical School. He is an elected member of both the American Academy of Arts and Sciences and the Institute of Medicine of the National Academy of Sciences. Dr. Leiden serves as a director of Massachusetts Mutual Life Insurance Company, an insurance company. Dr. Leiden was a director and the non-executive Vice Chairman of the board of Shire plc, a specialty biopharmaceutical company, from 2006 to January 2012 and a director of Quest Diagnostics, a medical diagnostics company, from December 2014 to May 2019. Dr. Leiden received his M.D., Ph.D. and B.A. degrees from the University of Chicago.

Dr. Kewalramani is our Executive Vice President and Chief Medical Officer and became a member of our Board of Directors on February 13, 2020. In July 2019, we announced she would be appointed our Chief Executive Officer and President in April 2020. Dr. Kewalramani was our Executive Vice President and Chief Medical Officer since April 2018. She was our Senior Vice President, Late Development from February 2017 until April 2018. From August 2004 to January 2017, she served in roles of increasing responsibility at Amgen Inc., most recently as Vice President, Global Clinical Development, Nephrology & Metabolic Therapeutic Area and as Vice President, U.S. Medical Organization. From 2014 through 2019, Dr. Kewalramani was the industry representative to the FDA's Endocrine and Metabolic Drug Advisory Committee. She completed her internship and residency in Internal Medicine at the Massachusetts General Hospital and her fellowship in Nephrology at the Massachusetts General Hospital and Brigham and Women's Hospital combined program. Dr. Kewalramani holds a B.A. from Boston University and an M.D. from Boston University School of Medicine. Dr. Kewalramani also completed the General Management Program at Harvard Business School and is an alumnus of the school.

Dr. Altshuler has been our Executive Vice President, Global Research and Chief Scientific Officer 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 and Chief Commercial Officer, a position he has held since September 2012. Prior to joining us, Mr. Arbuckle held multiple commercial leadership roles at Amgen, Inc., a 17,000 person biotechnology company, 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 served as a member of the Board of Directors of Cerulean Pharma, Inc. from June 2015 through July 2017 and has served as a member of the Board of Directors of ImmunoGen, Inc. since January 2018 and of Rhythm Pharmaceuticals Inc. since July 2019. Mr. Arbuckle holds a BSc in pharmacology and physiology from the University of Leeds.

Dr. Bozic has been our Executive Vice President, Global Medicines Development and Medical Affairs since October 2019. She was our Senior Vice President and Head of Global Clinical Development from May 2019 to October 2019. Prior to joining Vertex, Dr. Bozic spent more than 20 years at Biogen Inc., 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 Board 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. Parini is our Executive Vice President and Chief Legal and Administrative Officer, a position he has held since January 2017. From January 2016 to January 2017, he was our Executive Vice President and Chief Legal Officer. From 2004 until he joined Vertex, Mr. Parini served in various roles of increasing responsibility at Pfizer Inc., a pharmaceutical company, most recently as Senior Vice President and Associate General Counsel. Prior to Pfizer, Mr. Parini was an attorney at Akin, Gump, Strauss, Hauer & Feld, L.L.P. Mr. Parini holds a B.A. from Georgetown University and a J.D. from the Georgetown University Law Center.

Mr. Sachdev is our Executive Vice President and Chief Patient Officer, a role he has held since October 2019. 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, and has led 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 United States House of Representatives and practiced law at the Chemical Manufacturers Association, and subsequently at the law firm of Ropes & Gray LLP. He has served as a member of the Board of Directors of Eiger BioPharmaceuticals since May 2019. Mr. Sachdev holds a B.S from Carnegie Mellon University and a J.D. from Emory University School of Law.

Mr. Wagner has been our Executive Vice President and Chief Financial Officer since April 2019. Prior to joining 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 information systems, lender relations, and acquisitions and divestiture groups, as well as shared leadership over 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 and chairman of the Audit Committee 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. Mr. Wagner holds a B.S. in accounting from Boston College and a M.B.A from Harvard Business School.

Mr. Silva is our Senior Vice President and Corporate Controller, a position he has held since April 2011. Mr. Silva also served as our interim Chief Financial Officer from January 2019 to April 2019. Mr. Silva joined us in August 2007 as Senior Director, Accounting Operations and was our Vice President and Corporate Controller from September 2008 through April

2011. Prior to joining us, he was the Vice President, Internal Reporting at Iron Mountain Incorporated from July 2006 until August 2007 and a consultant to Iron Mountain's finance department from April 2005 until July 2006. He was the Finance Director of the Bioscience Technologies Division of Thermo Electron Corporation from 2002 to April 2005. Mr. Silva holds a B.S. in accounting from Assumption College.

Dr. Tatsis has been our Senior Vice President, Chief Regulatory Officer since October 2019. She served as our Senior Vice President, Global Regulatory Affairs from September 2017 to October 2019. Prior to joining Vertex, 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. 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.

ITEM 1A. RISK FACTORS

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.

Risks Related to Our Business

All of our product revenues and the vast majority of our total revenues are derived from sales of medicines for the treatment of CF. If we are unable to continue to increase revenues from sales of our CF medicines, our business would be materially harmed and the market price of our common stock would likely decline.

Our net product revenues and the vast majority of our total revenues are derived from the sale of CF medicines. As a result, our future success is dependent upon our ability to increase revenues from sales of our CF medicines. This will require us to gain approval and reimbursement for our triple combination therapy in ex-U.S. markets and successfully develop and commercialize our triple combination therapy for patients with CF less than 12 years of age.

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

- that one or more competing therapies may successfully be developed as a treatment for patients with CF;
- that reimbursement policies of payors and other third parties may make it difficult to obtain reimbursement or 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 and/or CF drug candidates.

If one or more of the above risks were to materialize, if we are otherwise unable to increase or maintain 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 research and development programs for the discovery and development or acquisition of new products would be harmed, which would limit our ability to diversify our revenue base and our stock price would likely be adversely affected.

We are investing significant resources in the research and development of therapies for serious diseases other than CF, and if we are unable to successfully commercialize one or more of these therapies, our business could be materially harmed.

We are investing significant resources in the research and development of medicines for serious diseases including alpha-1 antitrypsin deficiency, APOL1-mediated kidney diseases, pain, beta-thalassemia, sickle cell disease, type 1 diabetes, DMD and DM1. Some of these programs have progressed into early-stage clinical trials, while others are still in pre-clinical development. Product development is highly uncertain and expensive, and product candidates that may appear promising in the early phases of research and development may fail to reach commercial success for many reasons, including the failure to demonstrate acceptable clinical trial results or obtain marketing approval, the inability to manufacture or commercialize the product candidate on economically feasible terms, or the appearance of safety issues. Even if we gain marketing approval for one or more pipeline products, we cannot be sure that we will obtain market acceptance or adequate reimbursement levels from third-party payors or foreign governments for such products.

Additionally, many of the therapies that we are developing in our pipeline target rare diseases with a limited number of patients. There can be no guarantee that we will effectively identify patients that are eligible for enrollment in our clinical trials or treatment with our drug candidates. Even if we do successfully identify eligible patients, the number of patients that our drug candidates are able to treat may turn out to be lower than we expect or new patients may become increasingly difficult to identify, each of which may adversely affect our revenues and materially harm our business. For these and other reasons, we may never be successful in expanding our pipeline and future revenue may continue to depend on sales of our CF medicines.

We have experienced challenges commercializing products outside of the United States, and our future revenues will be dependent on our ability to obtain adequate reimbursement for our products.

In most ex-U.S. markets, the pricing and reimbursement of therapeutic and other pharmaceutical products is subject to governmental control. Given recent global economic pressures and geopolitical uncertainty, government authorities throughout the world are increasingly attempting to limit or regulate the price of drug products. The reimbursement process in ex-U.S. markets can take a significant period of time and reimbursement decisions are made on a country-by-country basis.

Our medicines 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. Particular attention is being paid by payors, including government and private payors, to these types of medicines given the relative higher cost of these products as compared to other types of pharmaceutical products, and countries are increasingly refusing to reimburse costly medicines. We have experienced challenges in obtaining reimbursement for ORKAMBI in various countries outside the United States, including the United Kingdom and France. For example, we obtained reimbursement for ORKAMBI and SYMKEVI in England in the fourth quarter of 2019, four years after ORKAMBI's initial approval in 2015. Our future product revenues, including from ORKAMBI, SYMKEVI, and TRIKAFTA, depend on, among other things, our ability to complete reimbursement discussions in ex-U.S. markets for our products. There is no assurance that coverage and reimbursement will be available outside of the United States for our CF or future medicines, and, even if it is available, whether the timing or the level of reimbursement will be sufficient to allow us to market our medicines. Adverse pricing limitations or a delay in obtaining coverage and reimbursement would decrease our future net product revenues and harm our business.

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

A number of companies are seeking to identify and develop drug candidates for the treatment of CF 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 patients with CF or any of the other diseases 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 drug candidates, our business could be materially adversely affected.

In addition, our business faces competition from major pharmaceutical companies possessing substantially greater financial resources than we possess. We also face competition 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 drugs that we develop in the future may not be able to compete effectively with marketed drugs or new drugs that may be developed by competitors. The risk of competition is particularly important to our company because substantially all of our revenues as well as our most advanced drug candidates are related to the treatment of patients with CF. There are many other companies developing drugs for the same patient populations that we are pursuing. In order 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 drugs.

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 or sales could be suspended, and our business could be materially harmed.

Our products are subject to continuing regulatory oversight, including the review of additional safety information. Drugs 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 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. Three of our commercial products are combination products, and each of our products shares at least one active pharmaceutical ingredient with another of our products. As a result, if any of our cystic fibrosis products were to experience safety issues, our other cystic fibrosis products may be adversely affected. 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.

In addition, we and our third-party manufacturers must comply with GMP 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 GMP 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 drugs, or if patients do not remain on treatment or comply with their prescribed dosing regimen, our product revenues would be materially harmed in future periods.

Our drugs may not gain or maintain market acceptance among physicians and patients. Effectively marketing our drugs and any of our drug candidates, if approved, requires substantial efforts, both prior to launch and after approval. Physicians may elect not to prescribe our drugs, and patients may elect not to take them or may discontinue use of our drugs 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 drug;
- convenience and ease of administration;
- other potential advantages of alternative treatment methods; and
- ineffective sales, marketing and/or distribution support.

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

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.

Our sales of 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 United States and the national health care systems in many international 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 most ex-U.S. markets, the pricing and reimbursement of therapeutic and other pharmaceutical products is subject to governmental control, and such government authorities are increasingly attempting to limit or regulate the price of drug products. In the United States, 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 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.

Third-party payors throughout the world also have been attempting to control drug spending through various other actions. In reimbursement negotiations, many payers are imposing 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. As part of these negotiations, many ex-U.S. government payers also are requiring companies to establish product cost-effectiveness as a condition of reimbursement and companies' data-backed explanations are assessed by government agencies set up for this purpose. These cost-effectiveness reviews may not account for 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 United States, various organizations have started advocating for cost-effectiveness analyses in the United States. If U.S. payors were to adopt such assessments and make negative coverage determinations, it could adversely affect our product revenues.

There is also an increase in laws, regulations, and activity related to drug pricing and drug pricing transparency. In the United States, various states, including Nevada, Maryland, Louisiana, New York, California, Washington, Massachusetts, Connecticut, and Oregon, have passed legislation requiring companies to disclose significant amounts of information, including information relating to drug prices, drug price increases, and spending on research, development, and marketing. Although it is not clear what states ultimately will do with the information collected, some laws were designed to obtain additional product discounts, and we likely will continue to see more state action, which could require further disclosures or other actions.

Complying with these laws requires significant personnel and operational resources and deters focus on our business. Additionally, 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.

In addition, in the United States and some foreign jurisdictions, there have been a number of legislative and regulatory proposals and initiatives to change the health care system in ways that could affect our ability to sell products. For example, in the United States, there have been ongoing federal legislative and administrative efforts as well as legal challenges seeking to repeal, substantially modify or invalidate some or all of the provisions of the ACA. Tax legislation enacted at the end of 2017 eliminated the tax penalty for individuals who do not maintain sufficient health insurance coverage beginning in 2019. The Bipartisan Budget Act of 2018 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%, which started in 2019. There are also a number of bills pending in Congress that would affect drug pricing in the Medicare and Medicaid programs, and HHS recently issued a proposed rule and FDA issued guidance on how pharmaceuticals could be imported into the United States from Canada. As a result, there is uncertainty regarding future changes in the laws and regulations applicable to the health care system and the effect any such changes may have on our business. Some of these proposed and implemented reforms have resulted, or could result, in reduced reimbursement rates and/or more limited access for our current or future products, which would adversely affect our business, operations and financial results.

The increasing availability and use of innovative specialty pharmaceuticals for rare diseases, combined with their relative 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 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.

Any legislation or regulatory changes or relaxation of laws that restrict imports of drugs from other countries, revisions to reimbursement or pharmaceuticals under government programs or general budget control actions also could reduce the net price we receive for our products.

We have limited experience developing genetic and cell-based therapies and could experience challenges with these programs, which could result in delays or prevent the development and commercialization of our genetic and cell-based therapies.

We are investing significant financial and other resources in the research and development of genetic and cell-based therapies. While we have previously successfully developed, manufactured and commercialized several small molecule drugs, we have limited experience with the development, manufacture and commercialization of genetic and cell-based therapies. Development and commercialization of genetic and cell-based therapies are subject to all of the same risks and uncertainties as development and commercializing small molecules. In addition:

- the manufacturing processes for genetic and cell-based therapies are typically more complex and challenging than the manufacturing processes required for small molecule drugs, require different systems, equipment and facilities and require different expertise to develop and maintain;
- there have been a limited number of FDA approvals for genetic therapies to date, the regulatory requirements governing genetic therapies are continuing to evolve and current and future regulatory positions and interpretations could lead to delays with respect to our genetic therapy programs; and
- our cell-based therapies include approaches involving devices, which are subject to additional regulatory requirements.

If we are not able to successfully develop or commercialize genetic or cell-based therapies, we will not realize benefits or generate cash flows based on our investments in these programs.

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 off-label 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 federal False Claims Act and anti-kickback laws, which prohibit off-label product promotion and other similar laws and regulations both in United States and in non-U.S. markets. 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.

The federal anti-kickback law 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. The federal statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on the one hand and prescribers, patients, purchasers and formulary managers on the other hand, and therefore constrains our marketing practices and our various service arrangements with physicians, including physicians who make clinical decisions to use our products. Although there are a number of statutory exemptions and regulatory safe harbors protecting certain common activities from prosecution, the exemptions and safe harbors are drawn narrowly and have been interpreted by courts as such.

Federal false claims laws 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, known as “off-label” uses, that caused claims to be submitted to Medicaid for those off-label 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.

Although physicians are permitted, based on their medical judgment, to prescribe products for indications other than those approved by the FDA, manufacturers are prohibited from promoting their products for such off-label uses. We market our products to eligible CF patients for whom the applicable product has been approved and provide promotional materials and training programs to physicians regarding the use of each product in these patient populations. These eligible patients do not represent all patients with CF. If the FDA determines that our promotional materials, training or other activities constitute off-label promotion, it could request that we modify our training or promotional materials or other activities, conduct corrective advertising or subject us to regulatory enforcement actions, including the issuance of a warning letter, injunction, seizure, civil fine 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 off-label 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 recent years, legislation has been adopted at the federal, state and local level requiring pharmaceutical companies to establish marketing compliance programs, file periodic reports or make periodic public disclosures on sales, marketing, pricing, clinical trials, health care provider payments and other activities. For example, as part of the ACA, the federal government enacted the Physician Payments Sunshine Act (referred to as the Sunshine Act). The Sunshine Act requires pharmaceutical manufacturers to report annually to the Centers for Medicare and Medicaid Services payments or other transfers of value made by that entity to physicians and teaching hospitals (and additional categories of health care practitioners beginning with reports submitted on or after January 1, 2022). We also now have similar reporting obligations throughout the European Union, or the E.U. We expended significant efforts to establish, and are continuing to devote significant resources to maintain and enhance, systems and processes in order 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. 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 governmental entities in the United Sates and other countries in which we market our products, and we believe that this trend will continue. The risk of our being found in violation of these laws is increased by the fact that many of them have not been fully interpreted by the regulatory authorities or the courts, and their provisions are subject to a variety of interpretations. If our past or present operations are found to be in violation of any such laws or any other governmental regulations that may apply to us, 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. Any action against us for violation of these laws, even if we successfully defend against them, also could cause us to incur significant legal expenses and divert our management's attention from the operation of our business.

There is also enhanced scrutiny of company-sponsored patient assistance programs, including insurance premium and co-pay assistance programs and donations to third-party charities that provide such assistance. If we, or our vendors or donation recipients are deemed to fail to comply with relevant laws, regulations or government guidance in the operation of these programs, we could be subject to significant fines and 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 which 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 and a number of other federal and state government pricing programs in the U.S. in order to obtain coverage for our products by certain government health care programs. These programs would generally require us to pay rebates or provide discounts to certain private purchasers or government payers 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 change frequently. We may also 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. Responding to current and future changes may increase our costs and the complexity of compliance, will be time-consuming, and could have a material adverse effect on our results of operations.

We are subject to various and evolving laws and regulations governing the privacy and security of personal information, 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, transmission, storage and use of personal information, 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. For example, the E.U. General Data Protection Regulation, or GDPR, went into effect in May 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. In the United States, California has passed the California Consumer Privacy Act, which went into effect on January 1, 2020, and several states and the federal government are actively considering proposed legislation governing the protection of personal data. Additionally, Brazil has passed the General Data Protection Law (LGPD), which is set to go into effect in August 2020. 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 and our efforts to comply with the evolving data protection rules may be unsuccessful. Each law is also subject to various interpretations by courts and regulatory agencies, creating even more uncertainty.

We must devote significant resources to understanding and complying with this changing landscape. Failure to comply with laws regarding data protection would expose us to risk of enforcement actions taken by data protection authorities, private rights of action in some jurisdictions, and the potential for significant penalties if we are found to be non-compliant. For example, 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, or 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. Even if we are not determined to have violated these laws, government investigations into these issues typically require the expenditure of significant resources and generate negative publicity, which could harm our business and our reputation.

The EMA has adopted a policy on publication of clinical data whereby it will publish clinical reports submitted as part of MAAs for drugs. The EMA aims to publish reports within 60 days after a decision on the application has been made by the European Commission. The ability of third-parties to review and/or analyze the raw data from our clinical trials may increase the risk of patient confidentiality breaches and could result in enhanced scrutiny of our clinical trials results. Such scrutiny could result in misconceptions being spread about our drugs and drug candidates, even if the underlying analysis of such review turns out to be flawed. These publications could also result in the disclosure of information to our competitors that we might otherwise deem confidential, which could harm our competitive position.

The use of social media platforms presents risks and challenges.

Social media is being used by third parties to communicate about our products and drug candidates and the diseases our therapies are designed to treat. We believe that members of the CF community may be more active on social media as compared to other patient populations due to the demographics of this patient population. 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 drug or a drug candidate, which could result in reporting obligations. In addition, our employees may engage on social media in ways that may not comply with our social media policy or 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. Certain data protection regulations, such as the GDPR in the EU, also 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 restrictive regulatory actions or incur other harm to our business, including damage to our reputation.

Risks Related to Development, Clinical Testing and Regulation of Our Products and Drug Candidates

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

Our business depends upon the successful development and commercialization of drug candidates. These drug 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 drug candidates. Discovery and development efforts for new pharmaceutical products, including new combination therapies, are resource-intensive and may take 10 to 15 years or longer for each drug candidate. Despite our efforts, our drug 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 candidate;
- 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 products.

We have recently completed and/or have ongoing or planned clinical trials for several of our drug candidates. The strength of our company's product portfolio and pipeline will depend in large part upon the outcomes of these clinical trials, including clinical trials evaluating our triple combination therapy in younger patients with CF and our earlier-stage clinical trials of potential medicines to treat other diseases. 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 drug candidate or program.

Moreover, clinical data are often susceptible to varying interpretations, and many companies that have believed their drug candidates performed satisfactorily in clinical trials have nonetheless failed to obtain marketing approval of their drug 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 drug candidate.

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 drug candidates may not be predictive of the results we may obtain in later-stage clinical trials or of the likelihood of approval of a drug candidate for commercial sale. In addition, from time to time we report interim data from our clinical trials. Interim data from a clinical trial may not be predictive of final results from the clinical trial.

If we are unable to obtain regulatory approval, we will be unable to commercialize our drug 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 also 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 may seek a Fast Track and/or Breakthrough Therapy designation for some of our drug candidates. Drug candidates that receive one or both 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 drug candidates meets the criteria for Fast Track and/or Breakthrough Therapy designation, the FDA may disagree and instead determine not to make such designation. The receipt of one or both of these designations for a drug candidate does not guarantee a faster development process, review or approval compared to drugs 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 drugs or drug candidates qualifies for Fast Track and/or Breakthrough Therapy designation, the FDA may later decide to withdraw such designation if it determines that the drug or drug candidate no longer meets the conditions for qualification.

Any failure to obtain regulatory approvals for a drug candidate would prevent us from commercializing that drug candidate. Any delay in obtaining required regulatory approvals could materially adversely affect our ability to successfully commercialize a drug candidate. Furthermore, any regulatory approval to market a drug may be subject to limitations that we do not expect on the indicated uses for which we may market the drug. 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 drug 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 United States 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 United States, 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 United States, 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 drug candidate.

If clinical trials are prolonged or delayed, our development timelines for the affected development program could be extended, our costs to develop the drug candidate could increase and the competitive position of the drug 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;
- 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 inconclusive results, unforeseen complications in testing or clinical investigator error;
- inadequate supply or deficient quality of drug 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 scientific results from clinical trials;
- serious and unexpected drug-related side-effects experienced by participants in our clinical trials or by participants in clinical trials being conducted by our competitors to evaluate drug candidates with similar mechanisms of action or structures to drug candidates that we are developing;
- favorable results in testing of our competitors' drug candidates, or FDA or foreign regulatory authority approval of our competitors' drug 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.

Our ability to enroll patients in our clinical trials in sufficient numbers and on a timely basis is subject to a number of factors, including the size of the patient population, the nature of the protocol, the proximity of patients to clinical sites, the availability of effective treatments for the relevant disease, the number of other clinical trials ongoing and competing for patients in the same indication and the eligibility criteria for the clinical trial. In addition, patients may drop out of our clinical trials or may be lost to follow-up medical evaluation after treatment ends, and this could impair the validity or statistical significance of the trials. Delays in patient enrollment or unforeseen drop-out rates may result in increased costs and longer development times.

We, our collaborators, the FDA or other applicable regulatory authorities may suspend clinical trials of a drug 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 drug candidate and our business.

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 drug candidates.

We have a number of regulated processes and systems that are required both prior to and following approval of our drugs and drug 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 drug candidates, or delays in obtaining regulatory approval after filing, if at all. Any later discovery of previously unknown problems or safety issues with approved drugs or manufacturing processes, or failure to comply with regulatory requirements, may result in restrictions on such drugs or manufacturing processes, withdrawal of drugs 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 drugs 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 drugs 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.

Risks Related to Business Development Activities

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.

In order to achieve our long-term business objectives, we seek to license or acquire drugs, drug 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 with a focus on early-stage assets. We have faced and will continue to face significant competition for the acquisition of rights to these types of drugs, drug candidates and other technologies from a variety of other companies, many of which have significantly more financial resources and experience in business development activities than we have. In addition, non-profit organizations may be willing to provide capital to the companies that control additional drugs, drug candidates or technologies, which may provide incentives for companies to advance these drugs, drug candidates or technologies independently. Also, the cost of acquiring, in-licensing or otherwise obtaining rights to such drugs, drug 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 drugs, drug candidates or other technologies on acceptable terms or at all.

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

It is challenging to effectively integrate businesses and technologies that we acquire, including the acquisitions of Semma and Exonics and exclusive licenses that we have acquired from CRISPR, and we may not realize the benefits anticipated from such transactions. Achieving the anticipated benefits of any transaction and successfully integrating acquired businesses or technologies involves a number of risks, including:

- failure to successfully develop and commercialize the acquired drugs, drug 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 drug or drug candidates;
- difficulty in integrating the drugs, drug 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 drug, drug candidate or technology, including but not limited to, 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 but not limited to, 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 benefits of the strategic transaction to the extent anticipated. Additionally, we may later incur impairment charges related to assets acquired in any such transaction. For example, we entered into a strategic collaboration and license agreement with Parion Sciences, Inc., or Parion, to develop ENaC inhibitors in 2015 and incurred an impairment charge related to this collaboration in the third quarter of 2017. In addition, 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 (loss). Future strategic transactions could result in 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.

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

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

- Our collaborators may change the focus of their development and commercialization efforts or may have insufficient resources to effectively develop our drug candidates. The ability of some of our products and drug candidates to reach their potential could be limited if collaborators decrease or fail to increase development or commercialization efforts related to those products or drug candidates. Our collaboration agreements provide our collaborators with a level of discretion in determining the amount and timing of efforts and resources that they will apply to these collaborations.
- Collaboration agreements may have the effect of limiting the areas of research and development that we may pursue, either alone or in collaboration with third parties.
- Collaborators may develop and commercialize, either alone or with others, drugs that are similar to or competitive with the drugs or drug 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 drug candidates, might lead to additional responsibilities for us with respect to drug candidates, or might result in litigation or arbitration. Any such disagreements would divert management attention and resources and 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.

- Our collaboration agreements are subject to termination under various circumstances.

Additionally, if a collaborator were to be involved in a business combination with a third party, it might deemphasize or terminate the development or commercialization of any drug 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.

We may not be able to attract collaborators or external funding for the development and commercialization of certain of our drug candidates.

As part of our ongoing strategy, we may seek additional collaborative arrangements or external funding for certain of our development programs and/or seek to expand existing collaborations to cover additional commercialization and/or development activities. We have a number of research programs and early-stage clinical development programs, some of which are being developed in collaboration with a third party. For example, we have an ongoing collaboration with Janssen, pursuant to which Janssen is developing pimodivir, a drug candidate for the treatment of influenza we discovered. At any time, we may determine that in order to continue development of a drug candidate or program or successfully commercialize a drug we need to identify a collaborator or amend or expand an existing collaboration. 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 drug candidate, the costs and complexities of manufacturing and delivering such drug 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. Potentially, and depending on the circumstances, we may desire that a collaborator either agree to fund portions of a drug development program led by us, or agree to provide all of the funding and directly lead the development and commercialization of a program. 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. If we elect to fund and undertake development or commercialization activities on our own, we may need to obtain additional expertise and additional capital, which may not be available to us on acceptable terms or at all. If we are unable to enter into acceptable collaborative relationships, one or more of our development programs could be delayed or terminated and the possibility of our receiving a return on our investment in the program could be impaired.

Risks Related to Third-Party Manufacturing and Reliance on Third Parties

We depend on third-party manufacturers to manufacture our products and the materials we require for our clinical trials. We may not be able to maintain these relationships and could experience supply disruptions outside of our control.

We rely on a worldwide network of third-party manufacturers to manufacture our drugs for commercial use and our drug candidates for clinical trials. As a result of our reliance on these third-party manufacturers and suppliers, we could be subject to significant supply disruptions outside of our control. Our supply chain for sourcing raw materials and manufacturing drug product ready for distribution 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. Third parties are used for packaging, warehousing and distribution of products. Establishing and managing this global supply chain requires a significant financial commitment and the creation and maintenance of numerous third-party contractual relationships. Although we attempt to manage the business relationships with companies in our supply chain, we do not have control over their operations. 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 or any other performance failure by any third-party manufacturer on which we rely. Any supply disruptions could disrupt sales of our products and/or the timing of our clinical trials.

We require a supply for our medicines for commercial sale and a supply of our drug candidates for use in our clinical trials. While we have developed some internal capabilities, a majority of the manufacturing steps needed to produce our drug candidates and drug products are performed through a third-party manufacturing network. To ensure the stability of our supply chains we aim to develop additional sources of manufacture for all steps of our manufacturing processes at the time of, or shortly after, marketing approval. Therefore, at any point in time, we may have a limited number of single source manufacturers for certain steps in our manufacturing processes, particularly for recently launched products.

If we or our third-party manufacturers become unable 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 drug products could delay the completion of clinical trials and affect timelines for regulatory filings. There can be no assurance that we will be able to establish and maintain secondary manufacturers for all of our drug candidates and drug 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 drug 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 in order to have our products or drug 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 contract research organizations 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 CFF, 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 requires 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.

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, drug 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 drug 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 Intellectual Property

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

We have numerous issued patents and pending patent applications in the United States, 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 drugs, 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.

Due to evolving legal standards relating to the patentability, validity and enforceability of patents covering pharmaceutical 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. Recent patent reform legislation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents in the U.S. The Leahy-Smith America Invents Act, or the Leahy-Smith Act, includes a number of significant changes to United States patent law. These include provisions that affect the way patent applications are prosecuted and may also affect patent litigation. The United States Patent Office developed new regulations and procedures to govern administration of the Leahy-Smith Act, and many of the substantive changes to patent law associated with the Leahy-Smith Act, and in particular, the first to file provisions, became effective in March 2013. The first to file provisions limit the rights of an inventor who is the first to invent an invention but is not the first to file an application claiming that invention. 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 invent, or the first to file patent applications on, our products or drug candidates or their use. If a third party also has filed a U.S. patent application relating to our drugs or drug candidates, their uses, or a similar invention, we may have to participate in legal or administrative proceedings to determine priority of invention. For applications governed by the Lahey-Smith Act, if a third-party has an earlier filed U.S. patent application relating to our drugs or drug candidates, their uses, or a similar invention, we may be unable to obtain an issued patent from our application.

The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability. Our patents may be challenged by third parties, resulting in the patent being deemed invalid, unenforceable or narrowed in scope, or the third party may circumvent any such issued patents. Also, our pending patent applications may not issue, and we may not receive any additional patents. Our patents might not contain claims that are sufficiently broad to prevent others from utilizing our technologies. For instance, the issued patents relating to our drugs or drug candidates may be limited to a particular molecule or molecules and may not cover similar molecules that have similar clinical properties. Consequently, our competitors may independently develop competing products that do not infringe our patents or other intellectual property. In addition, if the breadth or strength of protection provided by our patents and patent applications is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize current or future products.

The laws of many foreign jurisdictions do not protect intellectual property rights to the same extent as in the United States and many companies in our segment of the pharmaceutical industry have encountered significant difficulties in protecting and defending such rights in foreign jurisdictions. If we encounter such difficulties in protecting or are otherwise precluded from effectively protecting our intellectual property rights in foreign jurisdictions, our business could be substantially harmed.

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

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

There is considerable uncertainty within our industry about the validity, scope and enforceability of many issued patents in the United States and elsewhere in the world, and, to date, the law and practice remains in substantial 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 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 drugs or to remove our drugs from the market. Any litigation, including litigation related to Abbreviated New Drug Applications, or 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 financial statements.

To the extent that valid present or future third-party patents or other intellectual property rights cover our drugs, drug candidates or technologies, we or our strategic collaborators may seek licenses or other agreements from the holders of such rights in order 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 drugs. 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

Risks associated with operating in foreign countries could materially adversely affect our business.

We have expanded our international operations over the past several years in order to market our CF 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 as well as patient-level clinical trial data and have expanded protections related to personal data and provided for increased sanctions for violations. Collectively, our expansion and these new requirements are adding to our compliance costs and expose us to potential sanctions for failing to meet the enhanced safeguards and reporting demands 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. 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. 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;
- collectibility 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;
- complying with local laws and regulations, which are interpreted and enforced differently across jurisdictions and 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 United States;
- reliance on third-party vendors 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.

Our revenues are subject to foreign exchange rate fluctuations due to the global nature of our operations. Although we have foreign currency forward contracts to hedge forecasted product revenues denominated in foreign currencies, our efforts to reduce currency exchange losses 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.

If we fail to manage our operations effectively, 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:

- implement and clearly communicate our corporate-wide strategies;
- enhance our operational and financial infrastructure, including our controls over records and information;
- enhance our operational, financial and management processes, including our cross-functional decision-making processes and our budget prioritization systems;
- train and manage our global employee base; and
- enhance our compliance and legal resources.

Our business faces potential risks relating to the United Kingdom's withdrawal from the European Union.

Our European headquarters and European research facility are located in the United Kingdom, or the U.K., and a significant portion of our ex-U.S. net product revenues are derived from sales in the U.K. On January 31, 2020, the U.K. formally withdrew from the E.U. ("Brexit") and began a transition period set to end on December 31, 2020. During the transition period, the U.K. and the E.U. will negotiate their future relationship, including the terms of trade. The effects of Brexit will depend on any agreements the U.K. makes to retain access to E.U. markets, either during the transitional period or more permanently. Brexit could lead to legal uncertainty and potentially divergent national laws and regulations as the U.K. determines which E.U. laws to replace or replicate. Given the lack of comparable precedent, it is unclear what financial, trade, regulatory and legal implications the withdrawal of the U.K. from the E.U. would have and how such withdrawal would affect us. Any of these effects of Brexit, among others, could adversely affect our business, financial condition and operating results.

Our business has a substantial risk of product liability claims and other litigation liability. If we do not obtain appropriate levels of insurance, any potential claims could adversely affect our business.

We are or may be involved in various legal proceedings, including securities/shareholder matters and claims related to product liability, intellectual property 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 but not limited to 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.

With respect to product liability and clinical trial risks, in the ordinary course of business we are subject to liability claims and lawsuits, including potential class actions, alleging that our products or drug candidates have caused, or could cause, serious adverse events or other injury. 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 resulting from a claim brought successfully against us 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 and integrity of such confidential information. The size and complexity of our information technology and information security systems makes such systems potentially vulnerable to service interruptions and to security breaches. 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 in an attempt 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, cyber-attacks are increasing in their frequency, sophistication and intensity, and have become increasingly difficult to detect. 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, our liability insurance may not be sufficient in type or amount to cover us against claims related to security breaches, cyber-attacks or other related liabilities.

If we fail to attract and retain skilled employees or manage our upcoming executive transition, 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 marketing and commercialization of medicines. We have entered into employment agreements with some executives and provide stock-related compensation benefits to all of our key employees that vest over time and therefore induce them to remain with us. 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 — such as restricted stock units and stock options — can be significantly affected by movements in our stock price, 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. 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 in Massachusetts can make it difficult to attract employees from other parts of the country to our Massachusetts headquarters. 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.

On April 1, 2020, Dr. Jeffrey Leiden will transition to the role of Executive Chairman and Dr. Reshma Kewalramani will become our President and Chief Executive Officer. No assurance can be made about the impact that this transition in management will have on our business.

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 provide adequate coverage against 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.

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, 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 a business continuity plan 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.

Risks Related to Holding Our Common Stock

Our stock price may fluctuate.

Market prices for securities of companies such as ours are highly volatile. From January 1, 2019 to December 31, 2019, our common stock traded between $160.95 and $225.66 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 our net product revenues and operating expenses for completed periods and guidance regarding future periods;
- announcements of FDA actions with respect to our drugs or our competitors' drugs, or regulatory filings for our drug candidates or those of our competitors, or announcements of interim or final results of clinical trials or nonclinical studies relating to our drugs, drug candidates or those of our competitors;
- developments in domestic and international governmental policy or regulation, for example, relating to drug pricing or intellectual property rights;
- 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.

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 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 level 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 related to business development activities, changes in the fair value of our strategic investments, impairment charges, charges for excess and obsolete inventories, changes in the fair value of derivative instruments and the consolidation or deconsolidation of variable interest entities. Our revenues also are subject to foreign exchange rate fluctuations due to the global nature of our operations. Although we have foreign currency forward contracts to hedge forecasted product revenues denominated in foreign currencies, our efforts to reduce currency exchange losses 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 drug candidates or competitive products or potentially competitive drug candidates can substantially affect investors' perceptions regarding our future prospects. We, our collaborators and our competitors periodically provide updates regarding drug 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 drug candidates, competitive products or potentially competitive drug candidates. The timing of the release of information by us regarding our drug 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.

Changes in tax laws, regulations and treaties could affect our future taxable income.

We are subject to taxation in numerous countries, states and other jurisdictions. As a result, 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, the results of 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 significantly different from previous periods or our current expectations

We continue to assess the impact of various tax reform proposals and modifications to existing tax treaties in all jurisdictions where we have operations to determine the potential effect on our business and any assumptions we have made about our future taxable income. We cannot predict whether any specific proposals will be enacted, the terms of any such proposals or what effect, if any, such proposals would have on our business if they were to be enacted.

Recommendations from the Organization for Economic Co-operation and Development that are part of the base erosion and profit shifting, or BEPS, framework could result in changes in tax laws in countries where we do business and adversely affect our provision for income taxes and our current rate. If these recommendations (or other changes in law) were adopted by the countries in which we do business, it could adversely affect our provision for income tax and our current rate.

We may need to raise additional capital that may not be available.

We may need to raise additional capital in the future. Any potential public offering, private placement or debt financing may or may not be similar to the transactions that we entered into in the past. Any debt financing may be on terms that, among other things, include conversion features that could result in dilution to our then-existing security holders and restrict our ability to pay interest and dividends—although we do not intend to pay dividends for the foreseeable future. Any equity financings would result in dilution to our then-existing security holders. If adequate funds are not available on acceptable terms, or at all, we may be required to curtail significantly or discontinue one or more of our research, drug discovery or development programs, including clinical trials, incur significant cash exit costs, or attempt to obtain funds through arrangements with collaborators or others that may require us to relinquish rights to certain of our technologies, drugs or drug candidates. Based on many factors, including general economic conditions, additional financing may not be available on acceptable terms, if at all.

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

In September 2019, we entered into a credit agreement providing for a $500 million revolving facility. The credit agreement provides that, subject to the satisfaction of certain conditions, we may request that the borrowing capacity under the credit agreement be increased by an additional $500.0 million. All outstanding borrowings under the credit agreement mature on September 17, 2024. If we borrow under our current credit agreements or any future credit agreement, 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 (i) a consolidated leverage ratio covenant and (ii) a consolidated interest coverage ratio covenant, in each case to be measured on a quarterly basis. 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, pay dividends, repurchase capital stock 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 owing under the credit agreement and/or our capital 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.

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

As of December 31, 2019, we had 259.0 million shares of common stock issued and outstanding. As of December 31, 2019, we also had outstanding options to purchase 6.3 million shares of common stock with a weighted-average exercise price of$134.92 per share. Outstanding vested options are likely to be exercised if the market price of our common stock exceeds the applicable exercise price, and, in the future, we expect to issue additional options and restricted stock units to directors and employees. 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.

Our Board of Directors has authorized a share repurchase program of up to $500 million to repurchase shares of our common stock. Our stock repurchases will depend upon, among other factors, 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 anti-takeover provisions and are subject to Massachusetts corporate laws that may frustrate any attempt to remove or replace our current management or effectuate a business combination involving Vertex.

Our corporate charter and by-law provisions and Massachusetts state laws may discourage certain types of transactions involving an actual or potential change of control of Vertex that might be beneficial to us or our security holders. Our by-laws grant the directors a right to adjourn annual meetings of shareholders, and certain provisions of our by-laws may be amended only with an 80% shareholder vote. 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 prohibits us from engaging in specified business combinations, unless the combination is approved or consummated in a prescribed manner, and prohibits voting by any shareholder who acquires 20% or more of our voting stock without shareholder approval. As a result, shareholders or other parties may find it more difficult to remove or replace our current management.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K and, in particular, the description of our Business set forth in Item 1, the Risk Factors set forth in this Item 1A and our Management's Discussion and Analysis of Financial Condition and Results of Operations set forth in Item 7 contain or incorporate a number of forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended, including statements regarding:

- our expectations regarding the amount of, timing of and trends with respect to our revenues, costs and expenses and other gains and losses, including those related to our net product revenues;
- our expectations regarding the timing and structure of clinical trials of our drugs and drug candidates, the expected timing of our receipt of data from our ongoing and planned clinical trials and regulatory authority filings and submissions for our drugs or drug candidates;
- our ability to obtain reimbursement for our medicines in ex-U.S. markets and our ability to otherwise successfully market our medicines or any drug candidates for which we obtain regulatory approval;
- the data that will be generated by ongoing and planned clinical trials and the ability to use that data to advance compounds, continue development or support regulatory filings;
- our beliefs regarding the support provided by clinical trials and preclinical and nonclinical studies of our drug candidates for further investigation, clinical trials or potential use as a treatment;
- our plan to continue investing in our research and development programs and our strategy to develop our drug candidates, alone or with third party-collaborators;
- the establishment, development and maintenance of collaborative relationships;
- potential business development activities;
- potential fluctuations in foreign currency exchange rates;
- our ability to use our research programs to identify and develop new drug candidates to address serious diseases and significant unmet medical needs; and
- our liquidity and our expectations regarding the possibility of raising additional capital.

Any or all of our forward-looking statements in this Annual Report on Form 10-K may turn out to be wrong. They can be affected by inaccurate assumptions or by known or unknown risks and uncertainties. Many factors mentioned in this Annual Report on Form 10-K will be important in determining future results. Consequently, no forward-looking statement can be guaranteed. Actual future results may vary materially from expected results. We also provide a cautionary discussion of risks and uncertainties under "Risk Factors" above in this Item 1A. These are factors and uncertainties that we think could cause our actual results to differ materially from expected results. Other factors and uncertainties besides those listed there could also adversely affect us.

Without limiting the foregoing, the words “believes,” “anticipates,” “plans,” “intends,” “expects” and similar expressions are intended to identify forward-looking statements. There are a number of factors and uncertainties that could cause actual events or results to differ materially from those indicated by such forward-looking statements, many of which are beyond our control, including the factors and uncertainties set forth under “Risk Factors” above in this Item 1A. In addition, the forward-looking statements contained herein represent our estimate only as of the date of this filing and should not be relied upon as representing our estimate as of any subsequent date. While we may elect to update these forward-looking statements at some point in the future, we specifically disclaim any obligation to do so to reflect actual results, changes in assumptions or changes in other factors affecting such forward-looking 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, 2019 regarding our filings under the Securities Exchange Act of 1934, as amended, that have not been resolved.

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. These leases commenced in December 2013 and will extend until December 2028. We have an option to extend the term of the leases for an additional ten years.

Additional United States and Worldwide Locations

In addition to our corporate headquarters, we lease an aggregate of approximately 488,000 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.

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

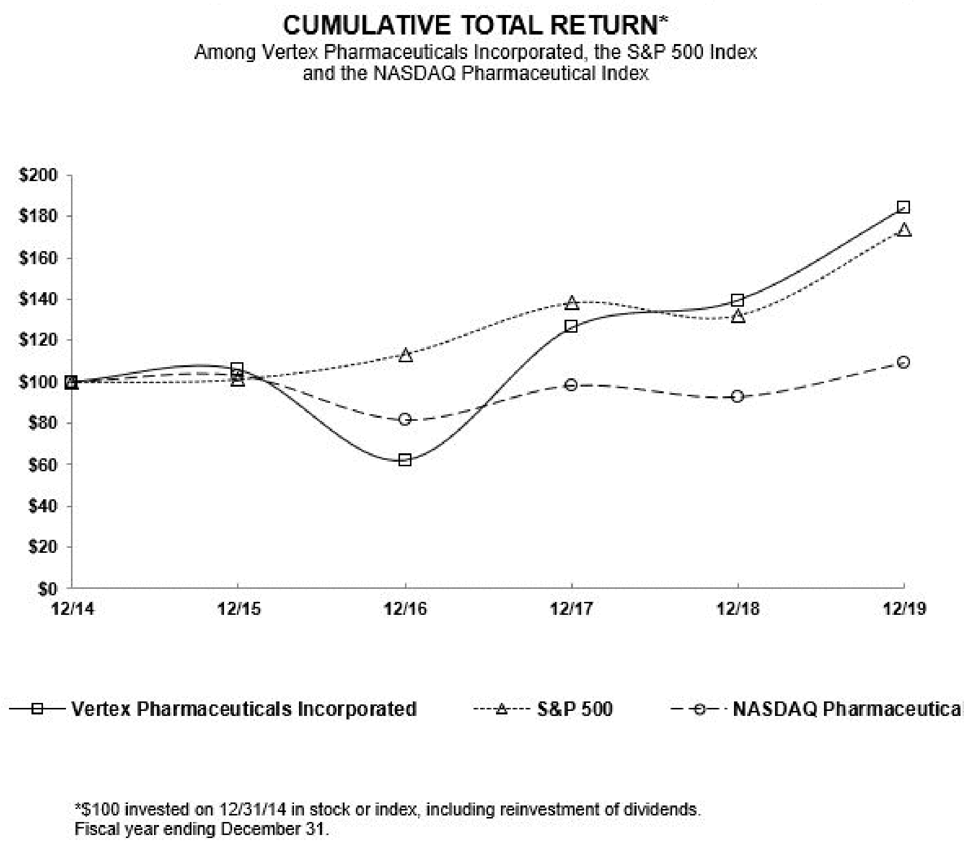
Market Information

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

Shareholders

As of January 31, 2020, there were 1,102 holders of record of our common stock.

Performance Graph



We became part of the Standard & Poor's 500 ("S&P 500®") Stock Index in 2013.

Dividends

We currently expect that any future earnings will be retained for use in our business. Any future determination to declare cash dividends will be subject to the discretion of our board of directors and applicable law and will depend on various factors, including our results of operations, financial condition, prospects and any other factors deemed relevant by our board of directors. In addition, our credit agreement limits our ability to pay cash dividends on our common stock.

Issuer Repurchases of Equity Securities

In January 2018, we announced a share repurchase program (the "2018 Share Repurchase Program"), under which we were authorized to repurchase up to $500.0 million of our common stock by December 31, 2019. As of June 30, 2019, we had repurchased the entire $500.0 million of common stock that was authorized under the 2018 Share Repurchase Program. In July 2019, we approved a new share repurchase program (the "2019 Share Repurchase Program"), pursuant to which we are authorized to repurchase up to $500.0 million of our common stock between August 1, 2019 and December 31, 2020.

The table set forth below shows repurchases of securities by us during the three months ended December 31, 2019, including shares repurchased under our 2019 Share Repurchase Program and a small number of restricted shares repurchased by us from employees pursuant to our equity programs. As of December 31, 2019, we had repurchased $36.0 million of common stock under the share repurchase program and had remaining available $464.0 million to repurchase additional shares pursuant to this program.

Period	Total Number of Shares Purchased (1)		Average Price Paid per Share	Total Number of Shares Purchased as Part of Publicly Announced Plans or Programs (2)		Maximum Number (or approximate dollar value) of Shares that May Yet be Purchased Under the Plans or Programs (2)
Oct. 1, 2019 to Oct. 31, 2019	143,306	$	167.47	142,835	$	464,000
Nov. 1, 2019 to Nov. 30, 2019	815	$	0.01	—	$	464,000
Dec. 1, 2019 to Dec. 31, 2019	148	$	0.01	—	$	464,000
Total	144,269	$	166.35	142,835	$	464,000

(1) Consists of 142,835 shares repurchased pursuant to our 2019 Share Repurchase Program (described in footnote 2 below) at an average price of $168.02 per share and 1,434 restricted shares repurchased for $0.01 per share from our employees pursuant to our equity plans. While we have restricted shares that are continuing to vest under our equity plans that are subject to repurchase rights upon termination of service, we have transitioned our equity program to granting restricted stock units. Unvested restricted stock units are forfeited upon termination of service and do not result in an issuer repurchase that would be reflected in this table.

(2) Under our 2019 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. The approximate dollar value of shares that may yet be repurchased is based solely on shares that may be repurchased under the share repurchase program and excludes any shares that may be repurchased under our employee equity programs.

ITEM 6. SELECTED FINANCIAL DATA

The following unaudited selected consolidated financial data are derived from our audited consolidated financial statements. These data should be read in conjunction with our audited consolidated financial statements and related notes that are included elsewhere in this Annual Report on Form 10-K and with "Management's Discussion and Analysis of Financial Condition and Results of Operations" included in Item 7.

	Year Ended December 31,				
	2019	2018	2017	2016	2015
Consolidated Statements of Operations Data:	(in thousands, except per share amounts)				
Product revenues, net	$ 4,160,726	$ 3,038,325	$ 2,165,480	$ 1,683,632	$ 1,000,324
Collaborative and royalty revenues	2,095	9,272	323,172	18,545	32,012
Total revenues	4,162,821	3,047,597	2,488,652	1,702,177	1,032,336
Total costs and expenses (1)	2,965,255	2,412,447	2,365,409	1,692,241	1,499,215
Provision for (benefit from) income taxes (2)	218,109	(1,486,862)	(107,324)	16,665	30,381
Net income (loss) attributable to Vertex	$ 1,176,810	$ 2,096,896	$ 263,484	$ (112,052)	$ (556,334)
Diluted income (loss) from continuing operations per share attributable to Vertex common shareholders	$ 4.51	$ 8.09	$ 1.04	$ (0.46)	$ (2.31)
Shares used in per diluted share calculations	260,673	259,185	253,225	244,685	241,312

	As of December 31,				
	2019	2018	2017	2016	2015
Consolidated Balance Sheet Data:	(in thousands)				
Cash, cash equivalents and marketable securities	$ 3,808,294	$ 3,168,242	$ 2,088,666	$ 1,434,557	$ 1,042,462
Deferred tax assets (2)	1,190,815	1,499,672	—	—	—
Total assets	8,318,465	6,245,898	3,546,014	2,896,787	2,498,587
Total current liabilities	1,334,827	1,120,290	807,260	792,537	506,167
Long-term debt obligations, excluding current portion	—	—	—	—	223,863
Long-term finance leases	538,576	581,550	583,902	521,335	515,534
Other long-term liabilities	359,818	108,853	112,546	244,724	159,395
Total shareholders' equity	6,085,244	4,435,203	2,042,306	1,338,191	1,093,628

(1) Total costs and expenses included (i) in 2017, an intangible asset impairment charges of $255.3 million, and (ii) in 2019, 2018 and 2017, collaborative license and asset acquisition expenses of $318.3 million, $111.9 million and $168.7 million, respectively. See Note B, "Collaborative Arrangements."

(2) In 2018, we released the valuation allowance on the majority of our net operating losses and other deferred tax assets resulting in a benefit from income taxes of $1.56 billion in the fourth quarter of 2018 and we recorded a $1.50 billion deferred tax asset on our consolidated balance sheet as of December 31, 2018. In 2019, we began recording a provision for income taxes on our pre-tax income approximating statutory rates. See Note P, "Income Taxes." In 2017, we recorded a benefit from income taxes related to the impairment of intangible assets. See Note K, "Intangible Assets and Goodwill."

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

OVERVIEW

We invest in scientific innovation to create transformative medicines for people with serious diseases with a focus on specialty markets. We continue to focus on developing and commercializing therapies for the treatment of cystic fibrosis, or CF, and in 2019 we obtained approval in the United States, or U.S., for TRIKAFTA (elexacaftor/tezacaftor/ivacaftor and ivacaftor). We are broadening our pipeline through internal research efforts and accessing external innovation through business development transactions.

We have four approved medicines that treat the underlying cause of CF, which is a life-threatening genetic disease. In October 2019, TRIKAFTA , our triple-combination regimen, was approved by the United States Food and Drug Administration, or FDA, for the treatment of patients with CF 12 years of age or older who have at least one *F508del* mutation in the cystic fibrosis transmembrane conductance regulator, or CFTR, gene. This approval increased the number of patients eligible for our medicines in the U.S. by approximately 6,000 and provided an additional treatment option for many patients who are also eligible for one of our previously approved products. We have submitted a Marketing Authorization Application, or MAA, to the European Medicines Agency, or EMA, for this triple combination regimen. Our four medicines are collectively approved to treat approximately 60% of the 75,000 CF patients in North America, Europe and Australia. We are focused on obtaining approval for the triple combination in ex-U.S. markets for patients 12 years of age and older and evaluating our triple combination in younger patients, with the goal of having treatments for up to 90% of patients with CF. We are also pursuing other therapeutic approaches to address the remaining 10% of CF patients.

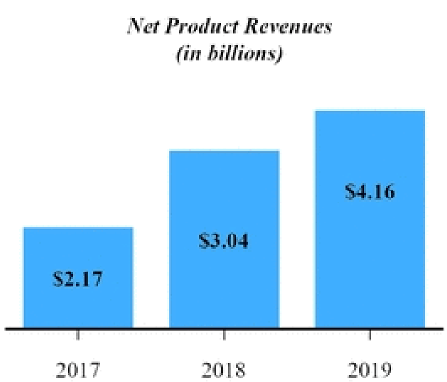
Our small molecule programs include programs focused on developing treatments for alpha-1 antitrypsin, or AAT, deficiency, APOL1-mediated kidney diseases and pain. We are evaluating CTX001, a genetic therapy as a potential treatment for sickle cell disease and beta-thalassemia, in a Phase 1/2 clinical trial in collaboration with CRISPR Therapeutics AG, or CRISPR. In 2019, through a series of strategic transactions, we established preclinical genetic therapy programs for Duchenne muscular dystrophy, or DMD, and myotonic dystrophy type 1, or DM1, and a preclinical program to develop cell-based therapies for type 1 diabetes, or T1D.

Financial Highlights

Over the last three years, our product revenues have increased significantly and we have limited the growth of our expenses, which has allowed us to create significant operating margins and reinvest in our business.

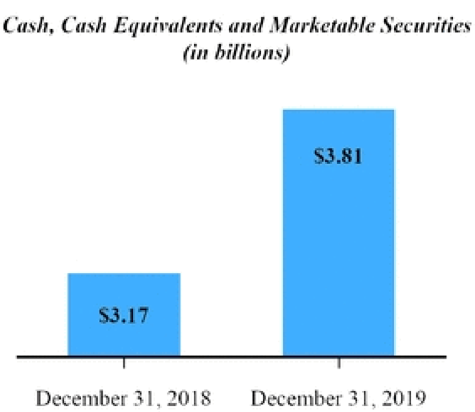
Revenues

Over the last three years, our net product revenues have increased as we obtained approvals for TRIKAFTA and SYMDEKO/SYMKEVI and expanded access to our medicines.



Expenses

Our combined R&D and SG&A expenses increased from$1.97 billion in 2018 to $2.41 billion in 2019 primarily due to research expenses associated with our business development activities. In 2019, cost of sales was approximately 13.2% of our net product revenues.



Balance Sheet

Business Highlights

Cystic Fibrosis

- Obtained approval in October 2019 from the FDA for TRIKAFTA for treatment of patients with CF 12 years of age and older who have at least one *F508del* mutation.
- TRIKAFTA was approved approximately three months after we submitted the NDA for the triple combination regimen and within four years of discovery of the final component of the triple combination regimen.
- Submitted a MAA to the European Medicines Agency, or EMA, for the triple combination of elexacaftor, tezacaftor and ivacaftor in patients 12 years of age and older.
- Conducting a Phase 3 clinical trial evaluating elexacaftor/tezacaftor/ivacaftor and ivacaftor in children 6 to 11 years of age who have two *F508del* mutations or one *F508del* mutation and one minimal function mutation.
- Obtained a positive opinion from the EMA's Committee for Medicinal Products for Human Use for KALYDECO for infants as young as six months old.
- Obtained reimbursement of ORKAMBI and/or SYMDEKO/SYMKEVI for eligible patients in several important ex-U.S. markets, including England, France, Australia, Scotland and Spain.

Pipeline

- *AAT Deficiency:* We initiated a Phase 2 proof-of-concept clinical trial for VX-814, our first investigational oral small molecule corrector for the treatment of alpha-1 antitrypsin, or AAT, deficiency, in order to evaluate VX-814 in patients with AAT deficiency who have two copies of the Z mutation. A Phase 1 clinical trial of VX-864, a second investigational small molecule corrector for the treatment of AAT deficiency, is ongoing in healthy volunteers.
- *APOL1-mediated Kidney Disease:* In the fourth quarter of 2019, we completed a Phase 1 clinical trial evaluating VX-147, our first investigational oral small molecule for the treatment of APOL1-mediated focal segmental glomerulosclerosis, or FSGS, and other serious kidney diseases, in healthy volunteers. We plan to initiate a Phase 2 proof-of-concept clinical trial in 2020 to evaluate the reduction in protein levels with VX-147 in FSGS patients.
- *Sickle Cell Disease and Beta-Thalassemia:* Enrollment is ongoing in Phase 1/2 clinical trials evaluating CTX001 for the treatment of severe sickle cell disease and beta-thalassemia. Along with our collaborator, CRISPR, we announced positive, interim data from the first two patients with these hemoglobinopathies treated with the investigational CRISPR/Cas9 gene-editing therapy CTX001 in the ongoing Phase 1/2 trials. We expect to provide additional data for this program in 2020.
- *Pain:* We plan to initiate clinical development of a novel NaV1.8 inhibitor for the treatment of pain in the first half of 2020.
- *Type 1 diabetes:* Acquired cell-based therapy programs that we are advancing as potential treatments for T1D by acquiring Semma Therapeutics. We plan to advance this program into clinical development in T1D patients in late 2020 or early 2021.
- *DMD and DM1:* Acquired Exonics and expanded our collaboration with CRISPR in July 2019, in order to support a pre-clinical program to develop treatments for DMD and DM1.

Research

We are continuing to invest in our research programs and fostering scientific innovation in order to identify and develop transformative medicines. Our strategy is to combine transformative advances in the understanding of human disease and the science of therapeutics in order to identify and develop new medicines. We believe that pursuing research in diverse areas allows us to balance the risks inherent in drug development and may provide drug 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.

Drug Discovery and Development

Discovery and development of a new pharmaceutical product is a difficult and lengthy process that requires significant financial resources along with extensive technical and regulatory expertise. Potential drug candidates are subjected to rigorous evaluations, driven in part by stringent regulatory considerations, designed to generate information concerning efficacy, side-effects, proper dosage levels and a variety of other physical and chemical characteristics that are important in determining whether a drug candidate should be approved for marketing as a pharmaceutical product. Most chemical compounds that are investigated as potential drug candidates never progress into development, and most drug candidates that do advance into development never receive marketing approval. Because our investments in drug candidates are subject to considerable risks, we closely monitor the results of our discovery, research, clinical trials and nonclinical studies and frequently evaluate our drug development 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 abrupt 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.

If we believe that data from a completed registration program support approval of a drug candidate, we submit an NDA to the FDA requesting approval to market the drug candidate in the United States and seek analogous approvals from comparable regulatory authorities in jurisdictions outside the United States. To obtain approval, we must, among other things, demonstrate with evidence gathered in nonclinical studies and well-controlled clinical trials that the drug candidate is safe and effective for the disease it is intended to treat and that the manufacturing facilities, processes and controls for the manufacture of the drug candidate are adequate. The FDA and ex-U.S. regulatory authorities have substantial discretion in deciding whether or not a drug candidate should be granted approval based on the benefits and risks of the drug candidate in the treatment of a particular disease, and could delay, limit or deny regulatory approval. If regulatory delays are significant or regulatory approval is limited or denied altogether, our financial results and the commercial prospects for the drug candidate involved will be harmed.

Regulatory Compliance

Our marketing of pharmaceutical products is subject to extensive and complex laws and regulations. We have a corporate compliance program designed to actively identify, prevent and mitigate risk through the implementation of compliance policies and systems and through the promotion of a culture of compliance. Among other laws, regulations and standards, we are subject to various U.S. federal and state laws, and comparable laws in other jurisdictions, pertaining to health care fraud and abuse, including anti-kickback and false claims laws, and laws prohibiting the promotion of drugs for unapproved or off-label uses. Anti-kickback laws generally make it illegal for a prescription drug manufacturer 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. False claims laws prohibit anyone from knowingly or willfully presenting for payment to third-party payors, including Medicare and Medicaid, 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. We are subject to laws and regulations that regulate the sales and marketing practices of pharmaceutical manufacturers, as well as laws such as the U.S. Foreign Corrupt Practices Act, which govern our international business practices with respect to payments to government officials. In addition, we are subject to various data protection and privacy laws and regulations in the U.S., E.U., Canada, Australia and other jurisdictions. We expect to continue to devote substantial resources to maintain, administer and expand these compliance programs globally.

Reimbursement

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. We dedicate substantial management and other resources in order to obtain and maintain appropriate levels of reimbursement for our products from third-party payors, including governmental organizations in the United States and ex-U.S. markets.

In the United States, we have worked successfully with third party-payors in order to promptly obtain appropriate levels of reimbursement for our first three CF medicines and have begun working with these stakeholders to obtain reimbursement for TRIKAFTA. 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 our medicines provide by treating the underlying cause of cystic fibrosis and continue to provide access to our medicines.

In Europe and other ex-U.S. markets, we seek government reimbursement for our medicines on a country-by-country basis. This is necessary for each new medicine, as well as, in most countries, label expansions for our current medicines. We successfully obtained reimbursement for KALYDECO in each significant ex-U.S. market within two years of approval. We experienced significant challenges in obtaining reimbursement for ORKAMBI in certain ex-U.S. markets. In the fourth quarter of 2019, we obtained reimbursement for ORKAMBI and SYMKEVI in the United Kingdom and ORKAMBI in France, four years after ORKAMBI's initial approval in 2015. With this approval, we now have obtained reimbursement for ORKAMBI or SYMKEVI in most of our significant ex-U.S. markets. In some ex-U.S. markets, including Ireland, Denmark and Australia, our reimbursement agreements include innovative arrangements that provide a pathway to access and rapid reimbursement for certain future CF medicines. We recently filed a MAA with the EMA for the triple combination regimen of elexacaftor, tezacaftor and ivacaftor and, if approved, we would need to seek government reimbursement on a country-by-country basis, in most European markets. In December 2019, we reached an agreement with the government in Ireland to expand the existing reimbursement agreement to include the triple combination regimen pending approval by the EMA.

Strategic Transactions

Acquisitions

As part of our business strategy, we seek to acquire drugs, drug candidates and other technologies and businesses that have the potential to complement our ongoing research and development efforts. In 2019, we invested significantly in business development transactions designed to augment our pipeline. We expect to continue to identify and evaluate potential acquisitions that may be similar to or different from the transactions that we have engaged in previously.

In July 2019, we acquired Exonics, a privately-held company focused on creating transformative gene-editing therapies to repair mutations that cause DMD and other severe neuromuscular diseases, including DM1. Our acquisition of Exonics enhanced our gene-editing capabilities and supports the potential development of novel therapies for DMD and DM1. In connection with the acquisition, we acquired all of the outstanding equity of Exonics for an upfront payment of approximately $245.0 million plus customary working capital adjustments in cash, and certain potential future payments based primarily upon the successful achievement of specified development and regulatory milestones for the DMD and DM1 programs.

In October 2019, we acquired Semma, a privately-held company focused on the use of stem cell-derived human islets as a potentially curative treatment for type 1 diabetes. Our acquisition of Semma advanced our cell therapy capabilities and supports the potential development of transformative therapies for T1D. In connection with the acquisition, we acquired all of the outstanding equity of Semma for approximately $950.0 million in cash.

Both of these acquisitions were accounted for as business combinations. As of the acquisition date for each transaction, the cash payments, as well as the fair value of contingent consideration for Exonics, were allocated primarily to goodwill and the fair value of several in-process research and development assets that we acquired. The fair value of contingent consideration related to Exonics was recorded as a liability and will be adjusted on a quarterly basis in the future. As a result, these acquisitions are primarily reflected in additional assets and liabilities on our consolidated balance sheet. Operating expenses incurred by Exonics and Semma after the acquisition dates and specific expenses associated with the acquisitions are reflected in our consolidated statement of operations for 2019.

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

Collaboration and Licensing Arrangements

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

In-License Agreements

We have entered into collaborations with biotechnology and pharmaceutical companies in order to acquire rights or to license drug candidates or technologies that enhance our pipeline and/or our research capabilities. Over the last several years, we entered into collaboration agreements with:

- Arbor Biotechnologies, Inc., or Arbor, pursuant to which we are collaborating on the discovery of novel proteins, including DNA endonucleases, to advance the development of new gene-editing therapies.

- CRISPR, pursuant to which we have been collaborating since 2015 on the discovery and development of potential new treatments aimed at the underlying genetic causes of human diseases using CRISPR-Cas9 gene-editing technology. In 2019, we obtained the exclusive worldwide rights to CRISPR's intellectual property for DMD and DM1 gene-editing products through a new agreement with CRISPR.
- Kymera Therapeutics, or Kymera, pursuant to which we are looking to advance small molecule protein degraders against multiple targets.
- Molecular Templates, Inc., pursuant to which we are collaborating on the discovery and development of novel targeted conditioning regimens to enhance the hematopoietic stem cell transplant process.

Generally, when we in-license a technology or drug 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 research and development expenses; however, depending on many factors, including the structure of the collaboration, the significance of the drug candidate that we license to the collaborator's operations and the other activities in which our collaborators are engaged, the accounting for these transactions can vary significantly. Our research and development expenses included $318.3 million in 2019, $111.9 million in 2018 and $168.7 million in 2017 related to upfront and milestone payments pursuant to our collaboration agreements.

Upfront payments and expenses incurred in connection with the collaborations listed above are being expensed as research or development expenses because the collaboration represents a small portion of each of these collaborator's overall business. In contrast, Parion Sciences, Inc., or Parion, and BioAxone Biosciences, Inc., or BioAxone, with whom we previously collaborated, were historically accounted for as variable interest entities, or VIEs, and included in our consolidated financial statements. In 2017 and 2018, we determined that the requirements for consolidation were no longer met with respect to Parion and BioAxone, respectively. As a result, we deconsolidated Parion and BioAxone from our consolidated financial statements as of September 30, 2017 and December 31, 2018, respectively, and did not consolidate any VIEs in 2019.

A collaborator that we account for as a VIE may engage in activities unrelated to our collaboration. The revenues and expenses unrelated to the programs we in-license from our VIEs have historically been immaterial to our consolidated financial statements. With respect to each of Parion and BioAxone, the activities unrelated to our collaborations with these entities represented approximately 2% or less of our total revenues and total expenses on an annual basis during the periods that we consolidated these collaborators.

Out-License Agreements

We also have out-licensed internally-developed programs to collaborators who are leading the development of these programs. These out-license arrangements include our agreements with:

- Janssen Pharmaceuticals, Inc., or Janssen, which is evaluating pimodivir in Phase 3 clinical trials for the treatment of influenza; and
- Merck KGaA, Darmstadt, Germany, which licensed oncology research and development programs from us in early 2017.

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.

Please refer to Note B, "Collaborative Arrangements," for further information regarding our VIEs, in-license agreements and out-license agreements.

Strategic Investments

In connection with our business development activities, we have periodically made equity investments in our collaborators. As of December 31, 2019, we held strategic equity investments in several public companies, including CRISPR, and certain private companies, and we plan to make additional strategic equity investments in the future. While we invest the majority of our cash, cash equivalents and marketable securities in instruments that meet specific credit quality standards and limit our exposure to any one issue or type of instrument, our strategic investments are maintained and managed separately from our other cash, cash equivalents and marketable securities.

Until December 31, 2017, changes in the fair value of these strategic investments were reflected on our consolidated balance sheet, but did not affect our net income until the related gains or losses were realized. As a result of accounting guidance, effective January 1, 2018, changes in the fair value of equity investments with readily determinable fair values (including publicly traded securities such as CRISPR) were recorded to other income (expense), net in our consolidated statement of operations in 2019 and 2018. For equity investments without readily determinable fair values including equity investments in private companies, each reporting period we are required to re-evaluate the carrying value of the investment, which may result in other income (expense).

In 2019 and 2018, we recorded within other income (expense), net gains of$197.6 million and $2.6 million related to changes in the fair value of our strategic investments and from sales of certain investments. To the extent that we continue to hold strategic investments, particularly strategic investments in publicly traded companies, we will record other income (expense) related to these strategic investments on a quarterly basis. Due to the high volatility of stocks in the biotechnology industry, we expect the value of these strategic investments to fluctuate and that the increases or decreases in the fair value of these strategic investments will continue to have material impacts on our net income (expense) and our profitability on a quarterly and/or annual basis.

RESULTS OF OPERATIONS

	2019	2018	2017	2019/2018 Comparison Increase/(Decrease) $	%	2018/2017 Comparison Increase/(Decrease) $	%
	(in thousands)			(in thousands, except percentages)			
Revenues	$ 4,162,821	$ 3,047,597	$ 2,488,652	$ 1,115,224	37%	$ 558,945	22%
Operating costs and expenses	2,965,255	2,412,447	2,365,409	552,808	23%	47,038	2%
Income from operations	1,197,566	635,150	123,243	562,416	89%	511,907	415%
Other non-operating income (expense), net	197,353	(25,116)	32,917	**	**	**	**
Provision for income taxes	218,109	(1,486,862)	(107,324)	**	**	**	**
Net income attributable to Vertex	$ 1,176,810	$ 2,096,896	$ 263,484	$ (920,086)	**	$ 1,833,412	**
Net income per diluted share attributable to Vertex common shareholders	$ 4.51	$ 8.09	$ 1.04				
Diluted shares used in per share calculations	260,673	259,185	253,225				

** Not meaningful

Net Income and Income from Operations

Our income from operations increased to$1.20 billion in 2019 compared to $635.2 million in 2018 and $123.2 million in 2017, primarily as a result ofthe approval of SYMDEKO/SYMKEVI in 2018 and TRIKAFTA in 2019, and continued strong net product revenues from KALYDECO and ORKAMBI. The increased net product revenues were partially offset by increased operating costs and expenses primarily attributable to increased cost of sales due to increased net product revenues and increased research expenses associated with our business development activities.

Net income attributable to Vertex in 2018 included a one-time non-cash benefit from income taxes of $1.56 billion resulting from our release of our valuation allowance. As a result of this one-time cash benefit in 2018, net income attributable to Vertex was higher in 2018 than 2019 and 2017.

Earnings Per Share

In 2019, 2018 and 2017, net income attributable to Vertex was$4.51, $8.09, $1.04, respectively, per diluted share. The higher diluted earnings per share in 2018 as compared to 2019 and 2017 was due primarily to the benefit from income taxes as a result of the release of our valuation allowance, which increased net income attributable to Vertex by $6.03 per diluted share in 2018.

Revenues

	2019	2018	2017	2019/2018 Comparison Increase/(Decrease) $	%	2018/2017 Comparison Increase/(Decrease) $	%
	(in thousands)			(in thousands, except percentages)			
Product revenues, net	$ 4,160,726	$ 3,038,325	$ 2,165,480	$ 1,122,401	37 %	$ 872,845	40 %
Collaborative and royalty revenues	2,095	9,272	323,172	(7,177)	(77)%	(313,900)	(97)%
Total revenues	$ 4,162,821	$ 3,047,597	$ 2,488,652	$ 1,115,224	37 %	$ 558,945	22 %

Product Revenues, Net

	2019	2018	2017
	(in thousands)		
TRIKAFTA	$ 420,105	$ —	$ —
SYMDEKO/SYMKEVI	1,417,668	768,657	—
ORKAMBI	1,331,891	1,262,166	1,320,850
KALYDECO	991,062	1,007,502	844,630
Product revenues, net	$ 4,160,726	$ 3,038,325	$ 2,165,480

In 2019, our net product revenues increased by $1.12 billion as compared to 2018. In 2018, our net product revenues increased by $872.8 million as compared to 2017. The increase in total net product revenues in 2019 was primarily due to the increasing number of patients being treated with SYMDEKO/SYMKEVI, the October 2019 approval of TRIKAFTA in the United States, label expansions for KALYDECO and ORKAMBI and expanded access to our medicines in ex-U.S. markets. In 2019, 2018 and 2017, our net product revenues included product revenues of $1.1 billion, $682.4 million, and 501.8 million, respectively, from ex-U.S. markets.

We expect that our net product revenues will increase in2020 due to increasing numbers of patients being treated with our medicines as a result of the approval of TRIKAFTA, label expansions for our previously approved products and expanded access to our medicines. TRIKAFTA increases the number of patients eligible for our medicines by providing the first treatment option for a significant number of patients with CF, and provides a new treatment option for many patients who are eligible for one of our previously approved medicines. As a result, the approval of TRIKAFTA in the United States is resulting in increased net product revenues as well as a shift of net product revenues from our previously approved products to TRIKAFTA.

TRIKAFTA

TRIKAFTA was approved by the FDA in October 2019. TRIKAFTA net product revenues were $420.1 million in 2019, all of which were recognized in the fourth quarter of 2019. We recently submitted a MAA to the EMA for the triple combination regimen of elexacaftor, tezacaftor and ivacaftor. We expect TRIKAFTA net product revenues will increase significantly in 2020 as compared to 2019.

SYMDEKO/SYMKEVI

SYMDEKO/SYMKEVI net product revenues were $1.42 billion in 2019 as compared to $768.7 million in 2018. SYMDEKO was approved by the FDA in February 2018 and SYMKEVI was approved in the European Union in November 2018. In the fourth quarter of 2019, some patients in the United States began switching from SYMDEKO to TRIKAFTA.

ORKAMBI

ORKAMBI net product revenues were $1.33 billion in 2019, $1.26 billion in 2018 and $1.32 billion in 2017. We have continued to increase the number of patients eligible for ORKAMBI through label expansions and additional ex-U.S. reimbursement arrangements. These increases in eligible patients have been offset by a portion of the patients who were being treated with ORKAMBI switching to SYMDEKO/SYMKEVI or TRIKAFTA.

From 2015 into the fourth quarter of 2019, we distributed ORKAMBI through early access programs in France. Upon adopting ASC 606, *Revenue from Contracts with Customers*, in the first quarter of 2018, we began recognizing a portion of the amounts collected related to shipments of ORKAMBI through early access programs as net product revenues, based on an estimated transaction price that reflected the consideration we expected to retain that would not be subject to a significant reversal in amounts recognized. Prior to adopting ASC 606, we had not recognized any net product revenues from sales of ORKAMBI in France because the price was not fixed or determinable at the time of delivery. Upon reaching an agreement with the French government for ORKAMBI in the fourth quarter of 2019, including the final amount for ORKAMBI distributed through early access programs, we recognized an adjustment to increase net product revenues related to prior period shipments of ORKAMBI distributed through early access programs of $155.8 million. Please refer to “Critical Accounting Policies - Revenue Recognition” below for a discussion of our accounting treatment for our early access program for ORKAMBI in France.

KALYDECO

KALYDECO net product revenues were $991.1 million in 2019, $1.01 billion in 2018 and $844.6 million in 2017. KALYDECO net product revenues in 2019 were similar to KALYDECO net product revenues in 2018. The increases in 2018 as compared to 2017 were primarily due to additional patients being treated with KALYDECO as we completed reimbursement discussions in various ex-U.S. jurisdictions and as we increased the number of patients eligible to receive KALYDECO through label expansions.

Collaborative and Royalty Revenues

Our collaborative and royalty revenues were $2.1 million, $9.3 million and $323.2 million in 2019, 2018 and 2017, respectively. In 2017, our collaborative and royalty revenues included (i) $230.0 million in revenues related to a one-time upfront payment earned in 2017 from Merck KGaA, Darmstadt, Germany, (ii) a $25.0 million milestone related to our license agreement with Janssen for the treatment of influenza and (iii) $40.0 million in revenues related to upfront and milestone payments earned by one of our VIEs pursuant to a license agreement entered into with a third party. We were not a party to the license agreement between the VIE and the third party, and we had no economic interest in either the license or these milestone payments. In 2017 through 2019, our collaborative and royalty revenues also include a small amount of revenues related to a cash payment we received in 2008 when we sold our rights to certain HIV royalties and reimbursements for research and development activities related to our collaborative arrangements.

Our collaborative revenues have historically fluctuated significantly from one period to another and may continue to fluctuate in the future. Our future royalty revenues will be dependent on if, and when, our collaborators, including Janssen and Merck KGaA, Darmstadt, Germany are able to successfully develop drug candidates that we have out-licensed to them.

Operating Costs and Expenses

				2019/2018 Comparison Increase/(Decrease)		2018/2017 Comparison Increase/(Decrease)	
	2019	2018	2017	$	%	$	%
		(in thousands)		(in thousands, except percentages)			
Cost of sales	$ 547,758	$ 409,539	$ 275,119	$ 138,219	34%	$ 134,420	49%
Research and development expenses	1,754,540	1,416,476	1,324,625	338,064	24%	91,851	7%
Sales, general and administrative expenses	658,498	557,616	496,079	100,882	18%	61,537	12%
Change in fair value of contingent consideration	4,459	—	—	4,459	**	—	**
Restructuring (income) expenses	—	(184)	14,246	184	**	(14,430)	**
Intangible asset impairment charges	—	29,000	255,340	(29,000)	**	(226,340)	**
Total costs and expenses	$ 2,965,255	$ 2,412,447	$ 2,365,409	$ 552,808	23%	$ 47,038	2%

** Not meaningful

Cost of Sales

Our cost of sales primarily consists of the cost of producing inventories that corresponded to product revenues for the reporting period, plus the third-party royalties payable on our net sales of our products. Pursuant to our agreement with the CFF, our tiered third-party royalties on sales of TRIKAFTA, SYMDEKO/SYMKEVI, KALYDECO and ORKAMBI, calculated as a percentage of net sales, range from the single digits to the sub-teens. As a result of the tiered royalty rate, which resets annually, our cost of sales as a percentage of net product revenues are lower at the beginning of each calendar year.

Over the last several years, our cost of sales has been increasing primarily due to increased net product revenues. Our costs of sales as a percentage of net product revenues has been approximately 13% for each of 2019, 2018 and 2017. In 2020, we expect our total cost of sales will increase due to expected increases in our net product revenues and our cost of sales as a percentage of total net product revenues will be similar to our cost of sales as a percentage of total net product revenues in 2019.

Research and Development Expenses

	2019	2018	2017	2019/2018 Comparison Increase/(Decrease) $	2019/2018 Comparison Increase/(Decrease) %	2018/2017 Comparison Increase/(Decrease) $	2018/2017 Comparison Increase/(Decrease) %
	(in thousands)			(in thousands, except percentages)			
Research expenses	$ 732,772	$ 438,360	$ 311,206	$ 294,412	67%	$ 127,154	41 %
Development expenses	1,021,768	978,116	1,013,419	43,652	4%	(35,303)	(3)%
Total research and development expenses	$ 1,754,540	$ 1,416,476	$ 1,324,625	$ 338,064	24%	$ 91,851	7 %

Our research and development expenses include internal and external costs incurred for research and development of our drugs and drug candidates and expenses related to certain technology that we acquire or license through business development transactions. 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 drugs or drug candidates, because the employees within our research and development groups typically are deployed across multiple research and development programs. These internal costs are significantly greater than our external costs, such as the costs of services provided to us by clinical research organizations and other outsourced research, which we allocate by individual program. All research and development costs for our drugs and drug candidates are expensed as incurred.

Over the past three years, we have incurred $4.5 billion in research and development expenses associated with drug discovery and development. The successful development of our drug 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 drug 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 drug candidates to market are not available.

In 2017, 2018 and 2019, costs related to our CF programs represented the largest portion of our development costs. Any estimates regarding development and regulatory timelines for our drug 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 revenue and cash flow.

Research Expenses

	2019	2018	2017	2019/2018 Comparison Increase/(Decrease) $	2019/2018 Comparison Increase/(Decrease) %	2018/2017 Comparison Increase/(Decrease) $	2018/2017 Comparison Increase/(Decrease) %
	(in thousands)			(in thousands, except percentages)			
Research Expenses:							
Salary and benefits	$ 134,642	$ 87,773	$ 81,229	$ 46,869	53%	$ 6,544	8%
Stock-based compensation expense	69,417	62,925	60,122	6,492	10%	2,803	5%
Outsourced services and other direct expenses	116,575	89,355	85,319	27,220	30%	4,036	5%
Collaboration and asset acquisition expenses	307,828	111,600	8,425	196,228	**	103,175	**
Infrastructure costs	104,310	86,707	76,111	17,603	20%	10,596	14%
Total research expenses	$ 732,772	$ 438,360	$ 311,206	$ 294,412	67%	$ 127,154	41%

** Not meaningful

We expect to continue to invest in our research programs with a focus on identifying drug candidates with the goal of creating transformative medicines for serious diseases. Our research expenses increased by 67% in 2019 as compared to 2018 primarily as a result of a $196.2 million increase associated with our business development activities, as well as increased expenses related to additional headcount and increased infrastructure costs. In 2019, our business development activities included collaborative upfront and option payments to CRISPR, Kymera and Molecular Templates, which are reflected in "Collaboration and asset acquisition expenses" in the table above. The increase in salary and benefits in 2019 was primarily related to costs associated with our acquisitions of Exonics and Semma. In 2018, our research expenses increased as compared to 2017 primarily due to $111.6 million in expenses associated with our business development activities, including collaborative upfront payments of $65.0 million to Merck KGaA, Darmstadt, Germany and $30.0 million to Arbor.

Development Expenses

	2019	2018	2017	2019/2018 Comparison Increase/(Decrease) $	%	2018/2017 Comparison Increase/(Decrease) $	%
	(in thousands)			(in thousands, except percentages)			
Development Expenses:							
Salary and benefits	$ 249,860	$ 220,128	$ 208,769	$ 29,732	14 %	$ 11,359	5 %
Stock-based compensation expense	155,141	140,187	121,778	14,954	11 %	18,409	15 %
Outsourced services and other direct expenses	425,149	471,338	397,155	(46,189)	(10)%	74,183	19 %
Collaboration and asset acquisition expenses	10,440	250	160,250	10,190	**	(160,000)	**
Infrastructure costs	181,178	146,213	125,467	34,965	24 %	20,746	17 %
Total development expenses	$ 1,021,768	$ 978,116	$ 1,013,419	$ 43,652	4 %	$ (35,303)	(3)%

** Not meaningful

Our development expenses increased by $43.7 million, or 4%, in 2019 as compared to 2018 and decreased by $35.3 million, or 3%, in 2018 as compared to 2017. The increase in 2019 as compared to 2018 was primarily due to increased headcount and infrastructure costs to support our advancing pipeline and increased milestones related to our collaborative agreements, partially offset by decreased expenses related to our CF programs. The decrease in 2018 as compared to 2017 was primarily due to increased costs associated with clinical trial expenses, including Phase 3 clinical trials evaluating elexacaftor as part of our triple combination regimen, which were more than offset by a $160.0 million payment to Concert Pharmaceuticals Inc. in connection with the acquisition of VX-561 in 2017 for which there were no comparable expenses in 2018.

Sales, General and Administrative Expenses

	2019	2018	2017	2019/2018 Comparison Increase/(Decrease) $	%	2018/2017 Comparison Increase/(Decrease) $	%
	(in thousands)			(in thousands, except percentages)			
Sales, general and administrative expenses	$ 658,498	$ 557,616	$ 496,079	$ 100,882	18%	$ 61,537	12%

Sales, general and administrative expenses increased by 18% in 2019 as compared to 2018, and by 12% in 2018 as compared to 2017. These increases were primarily due to increased global support for our medicines and incremental investment to support the launch of our triple combination regimen. We expect our sales, general and administrative expenses to continue to increase in 2020.

Contingent Consideration

In 2019, the increase in the fair value of contingent consideration of$4.5 million was due to changes in market interest rates and the time value of money related to the contingent development and regulatory milestone payments resulting from our acquisition of Exonics. There were no similar amounts in 2018 or 2017. 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 changes in market interest rates.

Restructuring Expenses

We did not record any restructuring expenses in 2019. Restructuring income was insignificant in 2018. In 2017, we recorded restructuring expenses of$14.2 million, primarily related to our decision to consolidate our research activities into our Boston, Milton Park and San Diego locations and to close our research site in Canada.

Intangible Asset Impairment Charge

In 2018, we recorded a $29.0 million impairment charge related to VX-210 that was licensed from BioAxone in 2014. In 2017, we recorded a $255.3 million impairment charge related to Parion's pulmonary ENaC platform that we licensed from Parion in 2015 and a benefit from income taxes of $97.7 million related to this impairment charge. Both of these impairment charges, and the related benefits from income taxes, were attributable to non-controlling interest because we consolidated these entities as VIEs. There were no corresponding intangible asset impairment charges in 2019.

Other Non-Operating Income (Expense), Net

Interest Income

Interest income increased from $11.7 million in 2017 to $38.4 million in 2018 and$63.7 million in 2019, primarily due to an increase in our cash equivalents and marketable securities and prevailing market interest rates. Our future interest income will be dependent on the amount of, and prevailing market interest rates on, our outstanding cash equivalents and marketable securities.

Interest Expense

Interest expense was $58.5 million in 2019, $72.5 million in 2018 and $69.3 million in 2017. The majority of our interest expense in these periods was related to imputed interest expense associated with our leased corporate headquarters in Boston and our research site in San Diego. On January 1, 2019, we adopted ASC 842, *Leases*, which resulted in a reduction in our imputed interest expense associated with these leases beginning in 2019. Our future interest expense will be dependent on whether, and to what extent, we borrow amounts under our credit facility.

Other Income (Expense), Net

In 2019, we recorded net other income of$192.2 million primarily related to changes in the fair value of our strategic investments. In 2018, we recorded net other expense of $0.8 million. In 2017, we recorded net other expense of $81.4 million primarily related to the deconsolidation of Parion.

In 2019 and 2018, our other income (expense), net included realized and unrealized gains totaling$197.6 million and $2.6 million, respectively, related to our strategic investments. 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 investments.

Noncontrolling Interest (VIEs)

In 2019, we had no noncontrolling interest because we did not consolidate any VIEs into our consolidated statement of operations. In 2018 and 2017, the net loss attributable to noncontrolling interest recorded on our consolidated statements of operations reflects Parion (through September 30, 2017) and BioAxone's (through December 31, 2018) net loss for the reporting period, adjusted for any changes in the noncontrolling interest holders' claim to net assets, including contingent milestone, royalty and option payments. A summary of net loss attributable to noncontrolling interest related to our VIEs for 2018 and 2017 is as follows:

	2018	2017
	(in thousands)	
Loss attributable to noncontrolling interest before benefit from income taxes and changes in fair value of contingent payments	$ 31,191	$ 223,379
Benefit from income taxes	(3,668)	(114,090)
(Increase) decrease in fair value of contingent payments	(17,730)	62,560
Net loss attributable to noncontrolling interest	$ 9,793	$ 171,849

In 2018, the net loss attributable to noncontrolling interest was primarily related to the $29.0 million impairment charge related to VX-210 offset by an increase in the fair value of the contingent payments payable by us to BioAxone of $17.7 million. In 2017, the net loss attributable to noncontrolling interest was primarily related to the $255.3 million impairment charge related to Parion's pulmonary ENaC platform, a decrease in fair value of the contingent payments payable by us to Parion of $69.6 million upon deconsolidation and a benefit from income taxes of $126.2 million related to these charges.

Income Taxes

In 2017 and 2018, we were profitable from a U.S. federal income tax perspective and used a portion of our net operating losses to offset this income since becoming profitable. Until the fourth quarter of 2018, we maintained a valuation allowance on the majority of our net operating losses and other deferred tax assets. Due to this valuation allowance, we did not record a significant provision for income taxes in 2017 and the nine months ended September 30, 2018. In the fourth quarter of 2018, we released the valuation allowance, resulting in a non-cash credit to net income of $1.56 billion. Further information on the release of the valuation allowance and significant judgments related to its release can be found below in "Critical Accounting Policies - Income Taxes."

In 2019, we recorded a provision for income taxes of$218.1 million. Starting in 2019, we began recording a provision for income taxes approximating statutory rates on our pre-tax income and continued to utilize our net operating losses to offset income. Our effective tax rate for 2019 is lower than the U.S. statutory rate primarily due to excess tax benefits related to stock-based compensation and research and development tax credits partially offset by a change in our valuation allowance as well as the tax impact of our officers' compensation. Due to our ability to offset our pre-tax income against previously benefited net operating losses, we expect the majority of our tax provision to represent a non-cash expense until our net operating losses have been fully utilized.

In 2017, we recorded a benefit from income taxes of $107.3 million, primarily due to a total benefit from income taxes of $114.1 million attributable to noncontrolling interest related to the impairment of Parion's pulmonary ENaC platform and decrease in the fair value of the contingent payments payable by us to Parion.

LIQUIDITY AND CAPITAL RESOURCES

The following table summarizes the components of our financial condition as of December 31,2019 and 2018:

	2019	2018	Increase/(Decrease) $	Increase/(Decrease) %
	(in thousands, except percentages)			
Cash, cash equivalents and marketable securities	$ 3,808,294	$ 3,168,242	$ 640,052	20 %
Working Capital:				
Total current assets	$ 4,822,829	$ 3,843,109	$ 979,720	25 %
Total current liabilities	(1,334,827)	(1,120,292)	(214,535)	(19)%
Total working capital	$ 3,488,002	$ 2,722,817	$ 765,185	28 %

As of December 31, 2019, total working capital was $3.5 billion, which represented an increase of $765.2 million from $2.7 billion as of December 31, 2018. The most significant items that increased total working capital in 2019 were $1.6 billion of cash provided by operations and $343.2 million of cash received from issuances of common stock under our employee benefit plans and partially offset by $1.2 billion of cash used to acquire Exonics and Semma and $192.0 million of cash used to repurchase shares of our common stock.

Sources of Liquidity

As of December 31, 2019, we had cash, cash equivalents and marketable securities of $3.8 billion, which represented an increase of $640.1 million from $3.2 billion as of December 31, 2018. We intend to rely on our existing cash, cash equivalents and marketable securities together with cash flows from product sales as our primary source of liquidity.

We may borrow up to $500.0 million pursuant to a revolving credit facility that we entered into in 2019. We may repay and reborrow amounts under the revolving credit agreement without penalty. Subject to certain conditions, we may request that the borrowing capacity under this credit agreement be increased by an additional $500.0 million, up to a total of $1.0 billion. Other possible sources of future liquidity include commercial debt, public and private offerings of our equity and debt securities, strategic sales of assets or businesses and financial transactions. Negative covenants in our credit agreement may prohibit or limit our ability to access these sources of liquidity.

Future Capital Requirements

We have significant future capital requirements including:

- significant expected operating expenses to conduct research and development activities and to operate our organization; and

- substantial facility and capital lease obligations, including leases for two buildings in Boston, Massachusetts that continue through 2028.

In addition:

- We have entered into certain collaboration agreements with third parties that include the funding of certain research, development and commercialization efforts with the potential for future milestone and royalty payments by us upon the achievement of pre-established developmental and regulatory targets and/or commercial targets, and we may enter into additional business development transactions, including acquisitions, collaborations and equity investments, that require additional capital.

- We have reached an agreement with the French government and will repay a portion of the amounts we have collected under the ORKAMBI early access programs in France to the French government in 2020 based on the difference between the invoiced amount and the final amount for ORKAMBI distributed through these programs as reflected in the structure of the agreement with the French government.

- To the extent we borrow amounts under the credit agreement we entered into in 2019, we would be required to repay any outstanding principal amounts in 2024.

As of December 31, 2019, $464.0 million remained available to fund repurchases under the 2019 Share Repurchase Program that we announced in July 2019.

We expect that cash flows from our products together with our current cash, cash equivalents and 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 the amounts of future revenues generated by our products, and the potential introduction of one or more of our other drug candidates to the market, the level of our business development activities and the number, breadth, cost and prospects of our research and development programs.

Financing Strategy

We may 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.

CONTRACTUAL COMMITMENTS AND OBLIGATIONS

The following table sets forth our commitments and obligations as of December 31, 2019:

	Payments Due by Period				
	2020	2021-2022	2023-2024	2025 and later	Total
	(in thousands)				
Fan Pier Leases	$ 66,540	$ 145,177	$ 150,560	$ 311,884	$ 674,161
Finance leases, excluding Fan Pier Leases	17,724	31,355	25,499	113,367	187,945
Operating leases	14,598	49,778	67,451	368,597	500,424
Research and development costs	51,934	565	18	—	52,517
Total contractual commitments and obligations	$ 150,796	$ 226,875	$ 243,528	$ 793,848	$ 1,415,047

Leases

We lease two buildings that are located at Fan Pier in Boston, Massachusetts. We commenced lease payments on these two buildings in December 2013 and the initial lease periods end in December 2028. We also lease office and laboratory space in San Diego, California. We commenced lease payments for this building in the second quarter of 2019 pursuant to a 16 year lease. The future minimum rental payments that we are obligated to pay related to the San Diego building are included in "Finance leases, excluding Fan Pier Leases," which also reflects leases of equipment that are accounted for as finance leases. The remainder of our real estate leases are reflected in "Operating leases" in the table above.

Research and Development Costs

The amounts reflected in "Research and development costs" do not include certain payments we anticipate making to clinical research organizations, or CROs, because these contracts are cancelable, at our option, with notice. However, we historically have not cancelled such contracts. As of December 31, 2019, we had accrued $40.2 million related to these contracts for costs incurred for services provided through December 31, 2019, and we have approximately $200.6 million in cancelable future commitments based on existing contracts as of December 31, 2019. These amounts reflect planned expenditures based on existing contracts and do not reflect any future modifications to, or terminations of, existing contracts or anticipated or potential new contracts.

Collaborative Arrangements and Asset Acquisitions

We have entered into certain research and development collaboration agreements with third parties and acquired certain assets that include the funding of certain development, manufacturing and commercialization efforts with the potential for future milestone and royalty payments by us upon the achievement of pre-established developmental, regulatory and/or commercial targets. Our obligation to fund these efforts is contingent upon continued involvement in the programs and/or the lack of any adverse events that could cause the discontinuance of the programs. These payments include:

- *CFF:* We pay royalties, which are included in cost of sales, to CFF on sales of our CF products.
- *Research and Development Milestones:* The majority of our in-license agreements and our acquisitions have milestone and royalty payments payable by us upon the successful achievement of pre-established developmental, regulatory and/or commercial targets or net sales. Contingent payments under these agreements become due and payable only upon achievement of certain milestones and are not included in the contractual obligations table above.

Tax-related Obligations

We exclude liabilities pertaining to uncertain tax positions from our summary of contractual obligations as we cannot make a reliable estimate of the period of cash settlement with the respective taxing authorities. As of December 31, 2019, our liabilities associated with uncertain tax positions were $33.9 million.

Other Funding Commitments

Our table detailing contractual commitments and obligations does not include severance payment obligations to certain of our executive officers in the event of a not-for-cause employment termination under existing employment contracts. We will provide information regarding these obligations annually in our proxy statement for our annual meeting of shareholders.

In addition, we began distributing ORKAMBI through early access programs in France in 2015. We received payment from the French government based on the invoiced amount and remained in reimbursement discussions for ORKAMBI in France until November 2019, when we reached an agreement for historical and future shipments of ORKAMBI with the French government. Based on the structure of the agreement with the French government, we will pay the difference between the amounts collected based on the invoiced amount and the final amount for ORKAMBI distributed through early access programs to the French government in 2020.

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 United States. 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; and
- income taxes.

Our accounting policies, including the ones discussed below, are more fully described in the Notes to our consolidated financial statements, including Note A, “Nature of Business and Accounting Policies,” included in this Annual Report on Form 10-K.

Revenue Recognition

Product Revenues, Net

We generate product revenues from sales in the United States and in international markets. We sell our products principally to a limited number of specialty pharmacy and specialty distributors in the United States, which account for the largest portion of our total revenues, and make international sales primarily to specialty distributors and retail chains, as well as hospitals and clinics, many of which are government-owned or supported customers, collectively, our customers. Our customers in the United States subsequently resell our products to patients and health care providers. 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 recognize net product revenues from sales of our products when our customers obtain control of our products, which typically occurs upon delivery to our customers. 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 is related to government and private payor rebates, chargebacks, discounts and fees, collectively rebates. The value 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. In order 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 on new information, including information regarding actual rebates for our products, as it becomes available. 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. Our credits to revenue related to prior period sales, excluding the adjustment to the transaction price for ORKAMBI distributed through early access programs in France, have not been significant (typically less than 1% of gross product revenues) and primarily related to U.S. rebates.

The following table summarizes activity related to our accruals for rebates (including our refund liability to the French government related to ORKAMBI distributed through early access programs in France as described below) for the three years ended December 31, 2019:

	(in thousands)
Balance as of December 31, 2016	$ 81,927
Provision related to current year sales	176,996
Adjustments related to prior year(s) sales	(8,943)
Credits/payments made	(137,765)
Balance as of December 31, 2017	$ 112,215
Provision related to current year sales and the adoption of ASC 606	684,299
Adjustments related to prior year(s) sales	(22,099)
Credits/payments made	(229,361)
Balance as of December 31, 2018	$ 545,054
Provision related to current year sales	655,980
Adjustments related to prior year(s) sales	(95,480)
Credits/payments made	(469,832)
Balance as of December 31, 2019	$ 635,722

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. Upon exceeding the annual reimbursement amount, products are provided free of charge, which is a material right. 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." The deferred amount is recognized as revenue when the free products are shipped. In order to estimate the portion of the consideration received to recognize as revenue and the portion of the amount to defer, 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.

French Early Access Programs

In 2015, we began distributing ORKAMBI through early access programs in France and remained engaged in reimbursement discussions with the French government for ORKAMBI, including ORKAMBI distributed through early access programs, until November 2019, when we reached an agreement with the French government. From the time we began distributing ORKAMBI through early access programs in France, we have expected that the difference between the amounts collected based on the invoiced amount and the final amount for ORKAMBI distributed through these programs would be returned to the French government. Our refund liability related to the early access programs in France is classified in “Accrued expenses” on our consolidated balance sheets.

Pursuant to the revenue recognition accounting guidance that was applicable until December 31, 2017, our ORKAMBI net product revenues for 2015, 2016 and 2017 did not include any net product revenues from sales of ORKAMBI in France. Upon adopting ASC 606, in the first quarter of 2018, we began recognizing ORKAMBI net product revenues in France based on a transaction price that reflected our estimate of consideration we expected to retain that would not be subject to a significant reversal in amounts recognized, which resulted in revenue representing a portion of the invoiced amount. We recognized ORKAMBI net product revenues from shipments of ORKAMBI in France based on this estimate from the first quarter of 2018 through the third quarter of 2019.

Upon reaching an agreement with the French government for ORKAMBI, including the final amount for ORKAMBI distributed through early access programs in France in the fourth quarter of 2019, we updated the transaction price related to ORKAMBI distributed through early access programs and recognized net product revenues of $155.8 million related to these shipments, which occurred from 2015 through the date of our agreement with the French government, because the final amount for these shipments exceeded our previous estimate.

Acquisitions

We are required to make several significant judgments and estimates in order to calculate the purchase price for our business combinations and then allocate it 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. Once recorded, these assets are subject to quarterly impairment analysis and our contingent consideration liability is adjusted quarterly, which requires similar judgments and estimates.

Intangible Assets

In 2019, we recorded in-process research and development assets related to our acquisitions of Exonics and Semma totaling $400.0 million on our consolidated balance sheet. Each of these assets is accounted for as an indefinite-lived intangible asset and is maintained on our consolidated balance sheet until either the project underlying it is completed or the asset becomes impaired. When we determine that an asset has become impaired or we abandon a project, we write down the carrying value of the related intangible asset to its fair value and record an impairment charge in the period in which the impairment occurs. In 2018 and 2017, we recorded full impairment charges of $29.0 million and $255.3 million for the in-process research and development assets that had previously been recorded on our consolidated balance sheets related to our collaborations with BioAxone and Parion, respectively.

To determine the fair value of our in-process research and development assets, we utilize the multi-period excess earnings method of the income approach, which requires us to make estimates of the probability of technical and regulatory success, development cost assumptions, revenue projections and growth rates, commercial cost estimates and appropriate discount rates. These assumptions require significant management judgment and reasonable changes in the assumptions can cause material changes to the fair value of the intangible assets. Due to the pre-clinical nature of Exonics and Semma’s programs, these significant assumptions could be affected by future economic and market conditions.

Contingent Consideration

As of December 31, 2019, we recorded $176.5 million of liabilities on our consolidated balance sheet attributable to the fair value of the contingent development and regulatory payments that we may owe to Exonics’ former equity holders upon the achievement of certain events. Our acquisition of Semma did not include similar contingent payments; therefore, we are not required to record contingent consideration liabilities related to our acquisition of Semma.

We record an increase or a decrease in the fair value of the contingent consideration liability on our consolidated balance sheet and in our consolidated statement of operations on a quarterly basis. We determine the fair value of our contingent consideration liability 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. Significant judgment is used 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 liability. Due to the pre-clinical nature of Exonics' DMD and DM1 programs, these significant assumptions could be affected by future economic and market conditions.

Goodwill

In 2019, we recorded goodwill of$554.6 million and $397.1 million related to our acquisitions of Semma and Exonics, respectively. 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 the fair value of our in-process research and development assets and contingent consideration liabilities.

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 are engaged in research and development activities and incurred significant net operating losses for a number of years before recently becoming profitable. Since we started generating profits, we have used a portion of our net operating losses and maintained a valuation allowance on the majority of our net operating losses and other deferred tax assets until December 31, 2018. Accordingly, we did not report any tax benefits relating to our net operating loss carryforwards and income tax credit carryforwards that are available for utilization in future periods. As of December 31, 2018, we released the valuation allowance on the majority of our net operating losses and other deferred tax assets resulting in a non-cash benefit from income taxes of $1.56 billion in the fourth quarter of 2018.

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. In the fourth quarter of 2018, we reassessed our valuation allowances and considered positive evidence including significant cumulative consolidated and U.S. income over the three years ended December 31, 2018, revenue growth, clinical program progression, including the advancement and clinical trial data from our triple combination regimens, and expectations regarding future profitability, and negative evidence, including potential impact of competition on our projections and cumulative losses in the jurisdictions. After assessing both the positive evidence and the negative evidence, we released the valuation allowance on the majority of our net operating losses and other deferred tax assets as of December 31, 2018.

Significant judgment is required in making these assessments to maintain or reverse 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. The determination to release the majority of our valuation allowances increased our net income by $1.56 billion, or $6.03 per share in 2018. In 2019, we recorded a significant provision for income tax, which was the result of utilizing previously benefitted deferred tax assets.

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 2019.

ITEM 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

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 until it is required to fund operations, including our research and development activities. None of these market risk-sensitive instruments are held for trading purposes. We do not have derivative financial instruments in our investment portfolio.

Interest Rate Risk

We invest our cash in a variety of financial instruments, principally securities issued by the U.S. government and its agencies, investment-grade corporate bonds and commercial paper, and money market funds. These investments are denominated in U.S. Dollars. All of our interest-bearing securities are subject to interest rate risk and could decline 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. Due to the conservative nature of these instruments, we do not believe that we have a material exposure to interest rate risk. If interest rates were to increase or decrease by 1%, the fair value of our investment portfolio would increase or decrease by an immaterial amount.

In 2019, we entered into a credit agreement. Loans under the credit agreement bear interest, at our option, at either a base rate or a Eurocurrency rate, in each case plus an applicable margin. The applicable margin on base rate loans ranges from 0.125% to 0.50% and the applicable margin on Eurocurrency loans ranges from 1.125% to 1.50%, 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). We do not believe that changes in interest rates related to the credit agreement would have a material effect on our financial statements. As of December 31, 2019, we had no principal or interest outstanding. A portion of our “Interest expense” in 2020 will be dependent on whether, and to what extent, we borrow amounts under the existing facility.

Foreign Exchange Market Risk

As a result of our foreign operations, we face exposure to movements in foreign currency exchange rates, primarily the Euro and British Pound against the U.S. Dollar. The current exposures arise primarily from cash, accounts receivable, intercompany receivables and payables, payables and accruals and inventories. Both positive and negative effects to our net revenues from international product sales from movements in exchange rates are partially mitigated by the natural, opposite effect that exchange rates have on our international operating costs and expenses.

We have a foreign currency management program with the objective of reducing the effect of exchange rate fluctuations on our operating results and forecasted revenues and expenses denominated in foreign currencies. We currently have cash flow hedges for the Euro, British Pound, Canadian Dollar 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, 2019, we held foreign exchange forward contracts that were designated as cash flow hedges with notional amounts totaling $728.4 million and had a net fair value of $2.4 million recorded 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. Assuming that the December 31, 2019 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, 2019 would change by approximately $72.8 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 (loss) income” on our consolidated balance sheet 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.

ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA

The information required by this Item 8 is contained on pages F-1 through F-59 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. The Company’s chief executive officer and chief financial officer, after evaluating the effectiveness of the Company’s 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) as of the end of the period covered by this Annual Report on Form 10-K, have concluded that, based on such evaluation, the Company’s disclosure controls and procedures were effective. In designing and evaluating the disclosure controls and procedures, the Company’s 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 the Company’s management necessarily was required to apply its judgment in evaluating the cost-benefit relationship of possible controls and procedures.

(2) Management’s Annual Report on Internal Control Over Financial Reporting. The management of the Company 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 Securities Exchange Act of 1934, as amended, as a process designed by, or under the supervision of, the Company’s principal executive and principal financial officers and effected by the Company’s 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. The Company’s internal control over financial reporting includes those policies and procedures that:

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

The Company’s management assessed the effectiveness of the Company’s internal control over financial reporting as ofDecember 31, 2019. In making this assessment, it 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 its assessment, the Company’s management has concluded that, as of December 31, 2019, the Company’s internal control over financial reporting is effective based on those criteria.

On July 16, 2019 and October 10, 2019, the Company completed its acquisition of Exonics Therapeutics, Inc. (“Exonics”) and Semma Therapeutics, Inc. (“Semma”), respectively. As a result, management has excluded the operations of Exonics and Semma from its assessment of internal control over financial reporting. The total and net assets of Exonics and Semma excluded from management’s assessment represent less than 1% of the Company’s related consolidated financial statement amounts, as of and for the year ended December 31, 2019. The total costs and expenses of each of Exonics and Semma excluded from management’s assessment represent 1.4%, of the Company’s related consolidated financial statement amounts, as of and for the year ended December 31, 2019.

The Company’s independent registered public accounting firm, Ernst & Young LLP, issued an attestation report on the Company’s internal control over financial reporting. See Section 4 below.

(3) Changes in Internal Controls. The Company’s management has extended its oversight and monitoring processes that support internal control over financial reporting to include operations of Exonics and Semma. The Company’s management is continuing to integrate the acquired operations of Exonics and Semma into the Company’s overall internal control over financial reporting process. However, management has excluded Exonics and Semma from its assessment of internal controls over financial reporting set forth above.

During the quarter ended December 31, 2019, there were no other changes in the Company’s internal control over financial reporting that materially affected, or are reasonably likely to materially affect, the Company’s 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, 2019, 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, 2019, based on the COSO criteria.

As indicated in the accompanying Management's Annual Report on Internal Control Over Financial Reporting, management's assessment of and conclusion on the effectiveness of internal control over financial reporting did not include the internal controls of Semma Therapeutics, Inc. and Exonics Therapeutics, Inc., which are included in the 2019 consolidated financial statements of the Company and constituted less than 1% of the Company's total and net assets, respectively, as of December 31, 2019 and 1.4% of the Company's total costs and expenses for the year then ended. Our audit of internal control over financial reporting of the Company also did not include an evaluation of the internal control over financial reporting of Semma Therapeutics, Inc. and Exonics Therapeutics, Inc.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the consolidated balance sheets of Vertex Pharmaceuticals Incorporated as of December 31, 2019 and 2018, the related consolidated statements of operations, comprehensive income (loss), shareholders' equity and noncontrolling interest, and cash flows for each of the three years in the period ended December 31, 2019, and the related notes and our report dated February 13, 2020 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 of 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, 2020

ITEM 9B. OTHER INFORMATION

On February 13, 2020, Dr. Kewalramani was elected to our Board of Directors. Under her employment agreement, Dr. Kewalramani had been scheduled to join our Board of Directors on April 1, 2020. In addition, there are no transactions involving the Company and Dr. Kewalramani that would be required to be disclosed pursuant to Item 404(a) of Regulation S-K.

PART III

Portions of our definitive Proxy Statement for the 2020 Annual Meeting of Shareholders, or 2020 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 2020 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 2020 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.

ITEM 11. EXECUTIVE COMPENSATION

The information required by this Item 11 will be included in the 2020 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 2020 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 2020 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 2020 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
Plan of Acquisition					
2.1	Agreement and Plan of Merger, dated as of August 30, 2019, by and among Vertex Pharmaceuticals Incorporated, Vertex Disc Inc., Semma Therapeutics, Inc., and Shareholder Representative Services LLC, solely in its capacity as agent for the Equityholders.†		10-Q (Exhibit 2.1)	October 31, 2019	000-19319
2.2	Agreement and Plan of Merger, dated as of June 6, 2019, among Vertex Pharmaceuticals Incorporated, VXP Merger Sub, Inc., Exonics Therapeutics, Inc. and Shareholder Representative Services LLC, solely in its Capacity as Shareholders' Representative, as amended by the Amendment to Agreement and Plan of Merger, dated as of June 12, 2019, among Vertex Pharmaceuticals Incorporated, VXP Merger Sub, Inc., Exonics Therapeutics, Inc. and Shareholder Representative Services LLC, solely in its Capacity as Shareholders' Representative.†		10-Q (Exhibit 10.1)	August 1, 2019	000-19319
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.		10-Q (Exhibit 3.2)	July 26, 2018	000-19319
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/A (Exhibit 10.2)	August 19, 2011	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-K (Exhibit 10.9)	March 16, 2006	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

Exhibit Number	Exhibit Description	Filed with this report	Incorporated by Reference herein from—Form or Schedule	Filing Date/ Period Covered	SEC File/ Reg. Number
10.4	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)	August 9, 2011	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-K (Exhibit 10.05)	February 23, 2017	000-19319
Leases					
10.6	Lease, dated May 5, 2011, between Fifty Northern Avenue LLC and Vertex Pharmaceuticals Incorporated.†		10-Q (Exhibit 10.4)	August 9, 2011	000-19319
10.7	Lease, dated May 5, 2011, between Eleven Fan Pier Boulevard LLC and Vertex Pharmaceuticals Incorporated.†		10-Q (Exhibit 10.5)	August 9, 2011	000-19319
Financing Agreements					
10.8	Credit Agreement, dated as of September 17, 2019, by and among Vertex Pharmaceuticals Incorporated, Bank of America, N.A. and the other lenders party thereto.		10-Q (Exhibit 10.1)	October 31, 2019	000-19319
Equity Plans					
10.9	Amended and Restated 2006 Stock and Option Plan.*		10-Q (Exhibit 10.1)	October 25, 2018	000-19319
10.10	Form of Stock Option Agreement under Amended and Restated 2006 Stock and Option Plan (granted prior to July 30, 2013).*		8-K (Exhibit 10.2)	May 15, 2006	000-19319
10.11	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
10.12	Amended and Restated 2013 Stock and Option Plan.*		DEF 14A (Appendix A)	April 26, 2019	000-19319
10.13	Form of Non-Qualified Stock Option Agreement under 2013 Stock and Option Plan.*		10-K (Exhibit 10.17)	February 13, 2015	000-19319
10.14	Form of Restricted Stock Agreement under 2013 Stock and Option Plan.*		10-K (Exhibit 10.18)	February 13, 2015	000-19319
10.15	Form of Restricted Stock Unit Agreement under 2013 Stock and Option Plan (U.S.).*		10-K (Exhibit 10.25)	February 16, 2016	000-19319
10.16	Form of Restricted Stock Unit Agreement under 2013 Stock and Option Plan (International).*		10-K (Exhibit 10.19)	February 13, 2015	000-19319
10.17	Form of Restricted Stock Unit Agreement Under 2013 Stock and Option Plan.*	X			
10.18	Non-Employee Director Deferred Compensation Plan.*		10-K (Exhibit 10.27)	February 16, 2016	000-19319
10.19	Vertex Pharmaceuticals Incorporated Employee Stock Purchase Plan.*		DEF 14A (Appendix B)	April 26, 2019	000-19319
Agreements with Executive Officers and Directors					
10.20	Amended and Restated Employment Agreement, dated November 30, 2016, by and between Vertex Pharmaceuticals Incorporated and Jeffrey M. Leiden, M.D., Ph.D*		8-K (Exhibit 10.1)	December 2, 2016	000-19319
10.21	Employee Non-disclosure, Non-competition and Inventions Agreement between Jeffrey M. Leiden and Vertex, dated December 14, 2011.*		10-K (Exhibit 10.35)	February 22, 2012	000-19319
10.22	Amendment No. 1, dated as of July 24, 2019, to the Amended and Restated Employment Agreement, dated November 30, 2016, by and between Vertex Pharmaceuticals Incorporated and Jeffrey M. Leiden, M.D., PhD.*		8-K (Exhibit 10.3)	July 25, 2019	000-19319
10.23	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
10.24	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
10.25	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
10.26	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
10.27	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
10.28	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

Exhibit Number	Exhibit Description	Filed with this report	Incorporated by Reference herein from—Form or Schedule	Filing Date/ Period Covered	SEC File/ Reg. Number
10.29	Employment Agreement, dated as of November 14, 2015, between Vertex Pharmaceuticals Incorporated and Michael Parini.*		10-K (Exhibit 10.40)	February 23, 2017	000-19319
10.30	Change of Control Agreement, dated as of November 9, 2015, between Vertex Pharmaceuticals Incorporated and Michael Parini.*		10-K (Exhibit 10.41)	February 23, 2017	000-19319
10.31	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
10.32	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
10.33	Employment Agreement, dated March 28, 2019, by and between Vertex Pharmaceuticals Incorporated and Charles F. Wagner, Jr.*		10-Q (Exhibit 10.1)	May 1, 2019	000-19319
10.34	Change of Control Agreement, dated as of March 28, 2019, by and between Vertex Pharmaceuticals Incorporated and Charles F. Wagner, Jr.*		10-Q (Exhibit 10.2)	May 1, 2019	000-19319
10.35	Amended and Restated Change of Control Agreement, dated as of May 18, 2012, between Vertex Pharmaceuticals Incorporated and Paul M. Silva.*	X			
10.36	Amended and Restated Employment Agreement, dated as of November 8, 2004, between Vertex Pharmaceuticals Incorporated and Ian F. Smith.*		10-Q (Exhibit 10.13)	November 9, 2004	000-19319
10.37	Amendment No. 1 to Amended and Restated Employment Agreement between Ian F. Smith and Vertex Pharmaceuticals Incorporated, dated December 29, 2008.*		10-K (Exhibit 10.66)	February 17, 2009	000-19319
10.38	Vertex Employee Compensation Plan.*		10-K (Exhibit 10.46)	February 15, 2018	000-19319
10.39	Vertex Pharmaceuticals Non-Employee Board Compensation.*		10-K (Exhibit 10.39)	February 13, 2019	000-19319
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			
32.1	Certification of the Chief Executive Officer and the Chief Financial Officer under Section 906 of the Sarbanes-Oxley Act of 2002.	X			
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			

* 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, 2020	By:	/s/ Jeffrey M. Leiden
		Jeffrey M. Leiden *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/ Jeffrey M. Leiden Jeffrey M. Leiden	Chair of the Board, President and Chief Executive Officer (Principal Executive Officer)	February 13, 2020
/s/ Charles F. Wagner, Jr. Charles F. Wagner, Jr.	Executive Vice President and Chief Financial Officer (Principal Financial Officer)	February 13, 2020
/s/ Paul M. Silva Paul M. Silva	Senior Vice President and Corporate Controller (Principal Accounting Officer)	February 13, 2020
/s/ Reshma Kewalramani Reshma Kewalramani	Executive Vice President, Chief Medical Officer and Director	February 13, 2020
/s/ Sangeeta N. Bhatia Sangeeta N. Bhatia	Director	February 13, 2020
/s/ Lloyd Carney Lloyd Carney	Director	February 13, 2020
/s/ Alan Garber Alan Garber	Director	February 13, 2020
/s/ Terrence C. Kearney Terrence C. Kearney	Director	February 13, 2020
/s/ Yuchun Lee Yuchun Lee	Director	February 13, 2020
/s/ Margaret G. McGlynn Margaret G. McGlynn	Director	February 13, 2020
/s/ Bruce I. Sachs Bruce I. Sachs	Director	February 13, 2020
/s/ William D. Young William D. Young	Director	February 13, 2020

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, 2019 and 2018, the related consolidated statements of operations, comprehensive income (loss), shareholders' equity and noncontrolling interest, and cash flows for each of the three years in the period ended December 31, 2019, 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, 2019 and 2018, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2019, 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, 2019, 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, 2020 expressed an unqualified opinion thereon.

Adoption of New Accounting Standards

ASU No. 2014-09

As discussed in Note A to the consolidated financial statements, the Company changed its method for recognizing revenue as a result of the adoption of Accounting Standard Update (ASU) No. 2014-09, Revenue from Contracts with Customers (Topic 606), and the amendments in ASUs 2015-14, 2016-08, 2016-10 and 2016-12 effective January 1, 2018.

ASU No. 2016-01

As discussed in Note A to the consolidated financial statements, on January 1, 2018, the Company changed its method of presenting changes in the fair value of its investments in corporate equity securities as a result of the adoption of ASU No. 2016-01, Financial Instruments (Subtopic 825-10): Recognition and Measurement of Financial Assets and Financial Liabilities.

ASU No. 2016-02

As discussed in Note A to the consolidated financial statements, the Company changed its method for lease accounting as a result of the adoption of ASU No. 2016-02, Leases (Topic 842), and the related amendments effective January 1, 2019.

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) related to accounts or disclosures that are material to the financial statements and (2) involved our especially challenging, subjective or complex judgments. The communication of 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.

	Revenue Recognition - Payor Mix Impact on Measuring Variable Consideration
Description of the Matter	As discussed in Note A to the Company's consolidated financial statements, the Company records product sales at the net sales price, or "transaction price," which requires the Company to make several significant estimates regarding the net sales price. The most significant estimates relate to government rebates, chargebacks, discounts and fees, collectively rebates. Due to the delay in receipt of claims by third-party payors, the Company estimates the percentage of prescriptions that will be covered by each third-party payor, which is referred to as the payor mix. Rebate accruals inclusive of estimated amounts due for claims not yet received or processed are recorded within accrued expenses on the Company's consolidated balance sheet. Auditing the measurement of the Company's net product revenues was especially complex and judgmental due to the significant estimation required in determining the amount of consideration that will be collected net of estimates for payor rebates. In particular, the net sales price is affected by assumptions in payor behavior such as changes in payor mix, payor collections, current customer contractual requirements, and experience with ultimate collection from third-party payors.
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 the underlying assumptions and inputs used by management to estimate amounts due to third-party payors and the completeness and accuracy of the data used in the estimates. We also tested the Company's controls to assess the completeness and accuracy of the current and historical data that supports the estimate. Our audit procedures to test the Company's recognition of net product revenues included, among others, assessing the methodology used to determine the estimate and testing the significant assumptions and the underlying data used by the Company in its analysis, which included historical claims data. To assess the payor mix assumptions we tested contracted rates, historical claims and payment data and related trends, and other relevant factors. We also assessed the historical accuracy of the Company's estimates of third-party payor rebates.

Accounting for the Impacts of Business Combinations

Description of the Matter	As described in Note C and Note E to the Company’s consolidated financial statements, the Company closed two business combinations during 2019; the acquisition of all outstanding shares of Exonics Therapeutics, Inc. (“Exonics”) for upfront consideration of $266.3 million and contingent milestones of up to $728.0 million and the acquisition of all outstanding shares of Semma Therapeutics, Inc. (“Semma”) for total upfront consideration of $936.8 million. Assets and liabilities recognized as part of the business combinations are recorded at fair value with $13.0 million and $387.0 million of in-process-research development intangible assets recognized for Exonics at July 16, 2019 and Semma at October 10, 2019, respectively, and $172.0 million recognized at July 16, 2019 for the contingent consideration liability for Exonics. The contingent liability for Exonics is remeasured to fair value at each reporting period and the amount recorded at December 31, 2019 was $176.5 million. Auditing the Company's accounting for its acquisitions of Exonics and Semma was especially complex due to the significant estimation and judgment required by management in determining the fair value of in-process-research and development intangible assets acquired for Exonics and Semma and the contingent consideration liability for Exonics. The significant estimation was primarily due to the judgmental nature of the inputs to the valuation models used to measure the fair value of the in-process research and development intangible assets and contingent consideration, as well as the sensitivity of the respective fair values to the underlying significant assumptions. The Company used the multi-period excess earnings method of the income approach to measure the fair value of the in-process-research and development intangible assets acquired and a probability weighted discounted cash flow method of the income approach to measure the fair value of contingent consideration. The significant assumptions used to estimate the fair value of the in-process-research and development intangible assets acquired included the estimated probability of technical and regulatory success rates, development cost assumptions, revenue projections and growth rates, commercial cost estimates and discount rates. The significant assumptions used to estimate the fair value of contingent consideration included the estimated timing of regulatory and commercial milestone achievement and the corresponding estimated probability of technical and regulatory success rates applied by management. Given the pre-clinical nature of the assets acquired, these significant assumptions are forward-looking and could be affected by future economic and market conditions.
How We Addressed the Matter in Our Audit	We obtained an understanding, evaluated the design and tested the operating effectiveness of the controls over the Company’s accounting for acquisitions. Our testing of controls included controls over the valuation of the intangible assets acquired and contingent consideration, including the valuation models used and the underlying assumptions used to develop such estimates, and controls over the completeness and accuracy of the data used to develop the estimates. To test the estimated fair value of the intangible assets and contingent consideration, we performed audit procedures that included, among others, evaluating the Company's use of the income approach (the multi-period excess earnings method and probability weighted discounted cash flow method), testing the significant assumptions used in the model, as described above, and assessing the completeness and accuracy of the underlying data. We compared the significant assumptions to current industry, and market data, to the assumptions used to value similar assets in other acquisitions and to other guideline companies within the same industry. We involved our valuation professionals to assist with our evaluation of the methodology used by the Company and significant assumptions included in the fair value estimates.

/s/ Ernst & Young LLP

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

Boston, Massachusetts
February 13, 2020

VERTEX PHARMACEUTICALS INCORPORATED

Consolidated Statements of Operations

(in thousands, except per share amounts)

	Year Ended December 31,		
	2019	**2018**	**2017**
Revenues:			
Product revenues, net	$ 4,160,726	$ 3,038,325	$ 2,165,480
Collaborative and royalty revenues	2,095	9,272	323,172
Total revenues	4,162,821	3,047,597	2,488,652
Costs and expenses:			
Cost of sales	547,758	409,539	275,119
Research and development expenses	1,754,540	1,416,476	1,324,625
Sales, general and administrative expenses	658,498	557,616	496,079
Change in fair value of contingent consideration	4,459	—	—
Restructuring (income) expenses	—	(184)	14,246
Intangible asset impairment charges	—	29,000	255,340
Total costs and expenses	2,965,255	2,412,447	2,365,409
Income from operations	1,197,566	635,150	123,243
Interest income	63,678	38,352	11,748
Interest expense	(58,502)	(72,471)	(69,298)
Other income (expense), net	192,177	(790)	(81,382)
Income (loss) before provision for (benefit from) income taxes	1,394,919	600,241	(15,689)
Provision for (benefit from) income taxes	218,109	(1,486,862)	(107,324)
Net income	1,176,810	2,087,103	91,635
Loss attributable to noncontrolling interest	—	9,793	171,849
Net income attributable to Vertex	$ 1,176,810	$ 2,096,896	$ 263,484
Amounts per share attributable to Vertex common shareholders:			
Net income:			
Basic	$ 4.58	$ 8.24	$ 1.06
Diluted	$ 4.51	$ 8.09	$ 1.04
Shares used in per share calculations:			
Basic	256,728	254,292	248,858
Diluted	260,673	259,185	253,225

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

VERTEX PHARMACEUTICALS INCORPORATED

Consolidated Statements of Comprehensive Income (Loss)

(in thousands)

	Year ended December 31,		
	2019	**2018**	**2017**
Net income	$ 1,176,810	$ 2,087,103	$ 91,635
Changes in other comprehensive (loss) income:			
Unrealized holding gains on marketable securities, net of tax of zero, zero and $(2.7) million, respectively	1,039	58	6,954
Unrealized (losses) gains on foreign currency forward contracts, net of tax of $7.0 million, $(7.1) million and $3.4 million, respectively	(14,003)	27,438	(26,530)
Foreign currency translation adjustment	10,332	8,855	(13,169)
Total changes in other comprehensive (loss) income	(2,632)	36,351	(32,745)
Comprehensive income	1,174,178	2,123,454	58,890
Comprehensive loss attributable to noncontrolling interest	—	9,793	171,849
Comprehensive income attributable to Vertex	$ 1,174,178	$ 2,133,247	$ 230,739

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

VERTEX PHARMACEUTICALS INCORPORATED

Consolidated Balance Sheets

(in thousands, except share and per share amounts)

	December 31,	
	2019	**2018**
Assets		
Current assets:		
Cash and cash equivalents	$ 3,109,322	$ 2,650,134
Marketable securities	698,972	518,108
Accounts receivable, net	633,518	409,688
Inventories	167,502	124,360
Prepaid expenses and other current assets	213,515	140,819
Total current assets	4,822,829	3,843,109
Property and equipment, net	745,080	812,005
Goodwill	1,002,158	50,384
Intangible assets	400,000	—
Deferred tax assets	1,190,815	1,499,672
Other assets	157,583	40,728
Total assets	$ 8,318,465	$ 6,245,898
Liabilities and Shareholders' Equity		
Current liabilities:		
Accounts payable	$ 87,610	$ 110,987
Accrued expenses	1,116,912	958,899
Other current liabilities	130,305	50,406
Total current liabilities	1,334,827	1,120,292
Long-term finance lease liabilities	538,576	581,550
Long-term contingent consideration	176,500	—
Other long-term liabilities	183,318	108,853
Total liabilities	2,233,221	1,810,695
Commitments and contingencies	—	—
Shareholders' equity:		
Preferred stock, $0.01 par value; 1,000 shares authorized; none issued and outstanding	—	—
Common stock, $0.01 par value; 500,000 shares authorized, 258,993 and 255,172 shares issued and outstanding, respectively	2,589	2,546
Additional paid-in capital	7,937,606	7,421,476
Accumulated other comprehensive (loss) income	(1,973)	659
Accumulated deficit	(1,852,978)	(2,989,478)
Total shareholders' equity	6,085,244	4,435,203
Total liabilities and shareholders' equity	$ 8,318,465	$ 6,245,898

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

VERTEX PHARMACEUTICALS INCORPORATED

Consolidated Statements of Shareholders' Equity and Noncontrolling Interest

(in thousands)

	Common Stock			Accumulated Other Comprehensive Income (Loss)				
	Shares	Amount	Additional Paid-in Capital		Accumulated Deficit	Total Vertex Shareholders' Equity	Noncontrolling Interest	Total Shareholders' Equity
Balance, December 31, 2016	248,301	$ 2,450	$ 6,506,795	$ 21,173	$ (5,373,836)	$ 1,156,582	$ 181,609	$ 1,338,191
Cumulative effect adjustment for adoption of new accounting guidance	—	—	9,371	—	(9,371)	—	—	—
Other comprehensive loss, net of tax	—	—	—	(32,745)	—	(32,745)	—	(32,745)
Net income (loss)	—	—	—	—	263,484	263,484	(171,849)	91,635
Issuance of common stock under benefit plans	4,952	62	345,554	—	—	345,616	57	345,673
Stock-based compensation expense	—	—	295,642	—	—	295,642	—	295,642
VIE noncontrolling interest upon deconsolidation	—	—	—	—	—	—	3,910	3,910
Balance, December 31, 2017	253,253	$ 2,512	$ 7,157,362	$ (11,572)	$ (5,119,723)	$ 2,028,579	$ 13,727	$ 2,042,306
Cumulative effect adjustment for adoption of new accounting guidance	—	—	—	(24,120)	33,349	9,229	—	9,229
Other comprehensive income, net of tax	—	—	—	36,351	—	36,351	—	36,351
Net income (loss)	—	—	—	—	2,096,896	2,096,896	(9,793)	2,087,103
Repurchases of common stock	(2,094)	(21)	(350,022)	—	—	(350,043)	—	(350,043)
Issuance of common stock under benefit plans	4,013	55	288,480	—	—	288,535	—	288,535
Stock-based compensation expense	—	—	325,656	—	—	325,656	—	325,656
VIE noncontrolling interest upon deconsolidation	—	—	—	—	—	—	(3,540)	(3,540)
Other VIE activity	—	—	—	—	—	—	(394)	(394)
Balance, December 31, 2018	255,172	$ 2,546	$ 7,421,476	$ 659	$ (2,989,478)	$ 4,435,203	$ —	$ 4,435,203
Cumulative effect adjustment for adoption of new accounting guidance	—	—	—	—	(40,310)	(40,310)	—	(40,310)
Other comprehensive loss, net of tax	—	—	—	(2,632)	—	(2,632)	—	(2,632)
Net income	—	—	—	—	1,176,810	1,176,810	—	1,176,810
Repurchases of common stock	(1,074)	(10)	(192,005)	—	—	(192,015)	—	(192,015)
Issuance of common stock under benefit plans	4,895	53	345,926	—	—	345,979	—	345,979
Stock-based compensation expense	—	—	362,209	—	—	362,209	—	362,209
Balance, December 31, 2019	258,993	$ 2,589	$ 7,937,606	$ (1,973)	$ (1,852,978)	$ 6,085,244	$ —	$ 6,085,244

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

VERTEX PHARMACEUTICALS INCORPORATED

Consolidated Statements of Cash Flows

(in thousands)

	Year Ended December 31,		
	2019	**2018**	**2017**
Cash flows from operating activities:			
Net income	$ 1,176,810	$ 2,087,103	$ 91,635
Adjustments to reconcile net income to net cash provided by operating activities:			
Stock-based compensation expense	360,489	325,047	293,236
Depreciation expense	106,941	72,420	61,397
Deferred income taxes (including benefit from valuation allowance release in 2018)	167,387	(1,512,325)	(120,513)
Gains on equity securities	(197,597)	(2,558)	—
Increase in fair value of contingent consideration	4,459	—	—
Intangible asset impairment charges	—	29,000	255,340
Acquired in-process research and development	—	—	160,000
Deconsolidation of VIE	—	1,077	76,644
Other non-cash items, net	16,942	32,502	14,439
Changes in operating assets and liabilities:			
Accounts receivable, net	(225,587)	(108,152)	(71,759)
Inventories	(64,047)	(31,965)	(47,484)
Prepaid expenses and other assets	35,440	16,684	(111,063)
Accounts payable	(22,785)	36,554	8,753
Accrued expenses	172,881	302,755	255,178
Other liabilities	37,997	22,144	(20,861)
Net cash provided by operating activities	1,569,330	1,270,286	844,942
Cash flows from investing activities:			
Payments to acquire businesses, net of cash acquired	(1,154,212)	—	—
Purchases of available-for-sale debt securities	(537,196)	(431,918)	(532,581)
Maturities of available-for-sale debt securities	475,924	431,576	369,214
Sale of equity securities	94,936	—	—
Expenditures for property and equipment	(75,451)	(95,524)	(99,421)
Investment in equity securities	(39,319)	(83,471)	—
Investment in note receivable	—	(15,000)	—
Decrease in restricted cash due to deconsolidation of VIE	—	(7,896)	(61,602)
Purchase of in-process research and development	—	—	(160,000)
Other investing activities	—	75	1,061
Net cash used in investing activities	(1,235,318)	(202,158)	(483,329)
Cash flows from financing activities:			
Issuances of common stock under benefit plans	343,244	289,293	344,840
Repurchases of common stock	(192,015)	(350,043)	—
Payments on finance leases	(39,185)	—	—
Advance from collaborator	12,500	7,500	12,500
Proceeds related to capital lease and construction financing lease obligations	10,046	20,840	34,666
Repayments of advanced funding	(5,866)	(5,027)	(4,266)
Payments on capital lease and construction financing lease obligations	—	(33,388)	(19,336)
Payments on revolving credit facility	—	—	(300,000)
Other financing activities	(1,951)	(394)	—
Net cash provided by (used in) financing activities	126,773	(71,219)	68,404
Effect of changes in exchange rates on cash	1,643	(6,182)	5,802
Net increase in cash, cash equivalents and restricted cash	462,428	990,727	435,819
Cash, cash equivalents and restricted cash—beginning of period	2,658,253	1,667,526	1,231,707
Cash, cash equivalents and restricted cash—end of period	$ 3,120,681	$ 2,658,253	$ 1,667,526
Supplemental disclosure of cash flow information:			
Cash paid for interest	$ 55,554	$ 66,458	$ 68,696
Cash paid for income taxes	$ 24,730	$ 12,402	$ 6,414
Capitalization of costs related to construction financing lease obligation	$ —	$ 3,389	$ 40,855

Issuances of common stock from employee benefit plans receivable	$	2,820	$	86	$	844

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

VERTEX PHARMACEUTICALS INCORPORATED

Notes to Consolidated Financial Statements

A. Nature of Business and Accounting Policies

Business

Vertex Pharmaceuticals Incorporated ("Vertex" or the "Company") invests in scientific innovation to create transformative medicines for serious diseases. The Company's business is focused on developing and commercializing therapies for the treatment of cystic fibrosis ("CF") and advancing research and development programs in other indications. The Company's marketed products are TRIKAFTA (elexacaftor/tezacaftor/ivacaftor and ivacaftor), SYMDEKO/SYMKEVI (tezacaftor in combination with ivacaftor), ORKAMBI (lumacaftor in combination with ivacaftor) and KALYDECO (ivacaftor), which are approved to treat patients with CF who have specific mutations in their cystic fibrosis transmembrane conductance regulator ("CFTR") gene.

As of December 31, 2019, the Company had cash, cash equivalents and marketable securities of$3.8 billion. The Company expects that cash flows from the sales of its products, together with the Company's cash, cash equivalents and marketable securities, will be sufficient to fund its operations for at least the next twelve months.

The Company is subject to risks common to companies in its industry including, but not limited to, the dependence on revenues from its CF products, competition, uncertainty about clinical trial outcomes and regulatory approvals, uncertainties relating to pharmaceutical pricing and reimbursement, uncertainty related to international expansion, uncertain protection of proprietary technology, the need to comply with government regulations, share price volatility, dependence on collaborative relationships and potential product liability.

Basis of Presentation

The accompanying consolidated financial statements, which have been prepared in accordance with accounting principles generally accepted in the United States of America ("GAAP"), reflect the operations of (i) the Company, (ii) its wholly-owned subsidiaries and (iii) consolidated variable interest entities ("VIEs"). In 2017, the Company deconsolidated Parion Sciences, Inc. ("Parion"), a VIE the Company had consolidated since 2015. In 2018, the Company deconsolidated BioAxone Biosciences, Inc. ("BioAxone"), a VIE the Company had consolidated since 2014. As of December 31, 2019 and 2018, the Company did not have any consolidated VIEs. All material intercompany balances and transactions have been eliminated. The Company operates in one segment, pharmaceuticals. Please refer to Note R, "Segment Information," for enterprise-wide disclosures regarding the Company's revenues, major customers and long-lived assets by geographic area. The Company has reclassified certain items from the prior year's consolidated financial statements to conform to the current year's presentation.

Use of Estimates

The preparation of consolidated financial statements in accordance with GAAP requires management 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 the consolidated financial statements, and the amounts of revenues and expenses during the reported periods. Significant estimates in these consolidated financial statements have been made in connection with (i) determining the transaction price of revenues, (ii) accounting for acquisitions, including intangible assets, goodwill and contingent consideration and (iii) evaluating deferred tax asset valuation allowances and the provision for income taxes. The Company bases its estimates on historical experience and various other assumptions, including in certain circumstances future projections that management believes 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

Pursuant to Accounting Standards Codification ("ASC") 606, *Revenue from Contracts with Customers* ("ASC 606"), the Company recognizes revenue when a customer obtains control of promised goods or services. The Company records the amount of revenue that reflects the consideration that it expects to receive in exchange for those goods or services. The Company applies the following five-step model in order 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) the Company satisfies each performance obligation.

The Company only applies the five-step model to contracts when it is probable that it will collect the consideration to which it is entitled in exchange for the goods or services that it transfers to the customer. Once a contract is determined to be within the scope of ASC 606 at contract inception, the Company reviews the contract to determine which performance obligations it must deliver and which of these performance obligations are distinct. The Company recognizes 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, the Company's performance obligations are transferred to customers at a point in time, typically upon delivery.

Product Revenues, Net

The Company sells its products principally to a limited number of specialty pharmacy and specialty distributors in the United States, which account for the largest portion of its total revenues, and makes international sales primarily to specialty distributors and retail chains, as well as hospitals and clinics, many of which are government-owned or supported (collectively, its "Customers"). The Company's Customers in the United States subsequently resell the products to patients and health care providers. In accordance with ASC 606, the Company recognizes net product revenues from sales when the Customers obtain control of the Company's products, which typically occurs upon delivery to the Customer. The Company's payment terms are approximately 30 days in the United States and consistent with prevailing practice in international markets.

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 and (c) costs of co-pay assistance programs for patients, as well as other incentives for certain indirect customers. 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, the Company utilizes the expected value method to determine the appropriate amount for estimates of variable consideration based on factors such as the Company's 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 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 the Company's estimates. If actual results vary from the Company's estimates, the Company adjusts these estimates, which would affect net product revenue and earnings in the period such variances become known.

Invoice Discounts and Distribution Fees: The Company generally provides invoice discounts on product sales to its Customers for prompt payment and pays fees for distribution services, such as fees for certain data that Customers provide to the Company. The Company estimates that, based on its experience, its Customers will earn these discounts and fees, and deducts the full amount of these discounts and fees from its gross product revenues and accounts receivable at the time such revenues are recognized.

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

Other Incentives: Other incentives that the Company offers include co-pay mitigation rebates provided by the Company to commercially insured patients who have coverage and who reside in states that permit co-pay mitigation programs. Based upon the terms of the Company's co-pay mitigation programs, the Company estimates average co-pay mitigation amounts for each of its products in order to establish appropriate accruals.

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

The Company excludes taxes collected from Customers relating to product sales and remitted to governmental authorities from revenues.

Contract Liabilities

The Company recorded contract liabilities of $62.3 million and $24.9 million as of December 31, 2019 and 2018, respectively, related to annual contracts with government-owned and supported customers in international markets that limit the amount of annual reimbursement the Company can receive. Upon exceeding the annual reimbursement amount, products are provided free of charge, which is a material right. These contracts include upfront payments and fees. The Company defers a portion of the consideration received for shipments made up to the annual reimbursement limit as a portion of "Other current liabilities." The deferred amount is recognized as revenue when the free products are shipped. The Company's product revenue contracts include performance obligations that are one year or less.

The Company's contract liabilities at the end of each fiscal year relate to contracts with annual reimbursement limits in international markets in which the annual period associated with the contract is not the same as the Company's fiscal year. In these markets the Company recognizes 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 year ended December 31, 2019, the Company recorded $24.9 million of revenues that were recorded as contract liabilities at the beginning of the year.

French Early Access Programs

Pursuant to ASC 605, *Revenue Recognition* ("ASC 605"), which was applicable until December 31, 2017, the Company only recognized revenues from product sales if it determined that the price was fixed or determinable at the time of delivery. If the Company determined that the price was not fixed or determinable, it deferred the recognition of revenues. If the Company was able to determine that the price was fixed or determinable, it recognized the net product revenues associated with the units.

In 2015, the Company began distributing ORKAMBI through early access programs in France and remained engaged in reimbursement discussions with the French government until November 2019, when the Company reached an agreement with the French government for ORKAMBI, including ORKAMBI distributed through early access programs. From the time the Company began distributing ORKAMBI through early access programs in France, it expected the difference between the amounts collected based on the invoiced amount and the final amount for ORKAMBI distributed through early access programs would be returned to the French government. As a result, the Company has classified a refund liability related to the early access programs in France within "Accrued expenses" on its consolidated balance sheets.

Pursuant to the revenue recognition accounting guidance that was applicable until December 31, 2017, the Company's ORKAMBI net product revenues for 2015, 2016 and 2017 did not include any net product revenues from sales of ORKAMBI in France because the price was not fixed or determinable at the time of delivery. Upon adopting ASC 606 in 2018, the Company recorded an $8.3 million cumulative effect adjustment to "Accumulated deficit" primarily related to shipments of ORKAMBI under the early access programs in France. The Company determined the amount of the adjustment based upon (i) the status of reimbursement discussions in France upon adoption, (ii) its estimate of the amount of consideration it expected to retain related to ORKAMBI sales in France that occurred on or prior to December 31, 2017 that would not be subject to a significant reversal in amounts recognized and (iii) recognition of costs previously deferred related to the ORKAMBI sales in France. Please refer to *Recent Accounting Pronouncements* included in this Note A, "Nature of Business and Accounting Policies," below for more information regarding the revenue recognition guidance adopted as of January 1, 2018.

For ORKAMBI sales in France that occurred after December 31, 2017 under the early access programs, the Company recognized net product revenues based on a transaction price that reflected the Company's estimate of consideration it expected to retain that would not be subject to a significant reversal in amounts recognized. When determining if variable consideration should be constrained, the Company considers whether there are factors outside its control that could result in a significant reversal of revenue. In making these assessments, the Company considers the likelihood and magnitude of a potential reversal of revenue. The Company recognized ORKAMBI net product revenues from sales in France based on this estimate from the first quarter of 2018 through the third quarter of 2019. Upon reaching an agreement with the French government for ORKAMBI, including ORKAMBI distributed through early access programs in November 2019, the Company updated the transaction price to reflect the final amount for ORKAMBI distributed through early access programs. As a result, the Company recognized net product revenues of $155.8 million related to prior period ORKAMBI early access program sales in the fourth quarter of 2019 because the updated transaction price for ORKAMBI distributed through these programs exceeded the Company's previous estimate of the consideration it expected to retain that would not be subject to a significant reversal in amounts recognized. Additionally, the Company's refund liability no longer requires estimation as of December 31, 2019 and will be paid to the French government in 2020.

Collaborative and Royalty Revenues

The Company recognizes collaborative revenues generated through collaborative research, development and/or commercialization agreements. The terms of these agreements typically include payment to the Company related to one or more of the following: nonrefundable, upfront license fees; development and commercial milestones; funding of research and/or development activities; and royalties on net sales of licensed products. Revenue is recognized upon satisfaction of a performance obligation by transferring control of a good or service to the collaborator.

For each collaborative research, development and/or commercialization agreement that results in revenue, the Company identifies all material performance obligations, which may include a license to intellectual property and know-how, research and development activities and/or transition activities. In order to determine the transaction price, in addition to any upfront payment, the Company estimates the amount of variable consideration at the outset of the contract either utilizing the expected value or most likely amount method, depending on the facts and circumstances relative to the contract. The Company constrains (reduces) the estimate of variable consideration such that it is probable that a significant reversal of previously recognized revenue will not occur throughout the life of the contract. When determining if variable consideration should be constrained, management considers whether there are factors outside the Company's control that could result in a significant reversal of revenue. In making these assessments, the Company considers the likelihood and magnitude of a potential reversal of revenue. These estimates are re-assessed each reporting period as required.

Once the estimated transaction price is established, amounts are allocated to the performance obligations that have been identified. The transaction price is generally allocated to each separate performance obligation on a relative standalone selling price basis. In order to account for these agreements, the Company must develop assumptions that require judgment to determine the standalone selling price, which may include (i) the probability of obtaining marketing approval for the drug candidate, (ii) estimates regarding the timing of and the expected costs to develop and commercialize the drug candidate, (iii) estimates of future cash flows from potential product sales with respect to the drug candidate and (iv) appropriate discount and tax rates. Standalone selling prices used to perform the initial allocation are not updated after contract inception. The Company does not include a financing component to its estimated transaction price at contract inception unless it estimates that certain performance obligations will not be satisfied within one year.

Upfront License Fees: If a license to the Company's intellectual property is determined to be distinct from the other performance obligations identified in an arrangement, the Company recognizes revenue from the related nonrefundable, upfront license fees based on the relative standalone selling price prescribed to the license compared to the total selling price of the arrangement. The revenue is recognized when the license is transferred to the collaborator and the collaborator is able to use and benefit from the license. For licenses that are not distinct from other obligations identified in the arrangement, the Company utilizes judgment to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time. If the combined performance obligation is satisfied over time, the Company applies an appropriate method of measuring progress for purposes of recognizing revenue from nonrefundable, upfront license fees. The Company evaluates the measure of progress each reporting period and, if necessary, adjusts the measure of performance and related revenue recognition.

Development and Regulatory Milestone Payments: Depending on facts and circumstances, the Company may conclude that it is appropriate to include certain milestones in the estimated transaction price or that it is appropriate to fully constrain the milestones. A milestone payment is included in the transaction price in the reporting period that the Company concludes that it is probable that recording revenue in the period will not result in a significant reversal in amounts recognized in future periods. This may result in revenues from certain milestones and a corresponding contract asset being recorded in a reporting period before the milestone is achieved. Milestone payments that have not been included in the transaction price to date are fully constrained until the Company concludes that their achievement is probable and that recognition of the related revenue will not result in a significant reversal in amounts recognized in future periods. The Company re-evaluates the probability of achievement of such development milestones and any related constraint each reporting period and adjusts its estimate of the overall transaction price, including the amount of collaborative revenue that it has recorded, if necessary. The Company has not recorded any significant development or regulatory milestone revenues the three years ended December 31, 2019.

Research and Development Activities/Transition Services: If the Company is entitled to reimbursement from its collaborators for specified research and development expenses, it accounts for the related services that it provides as separate performance obligations if it determines that these services represent a material right. The Company also determines whether the reimbursement of research and development expenses should be accounted for as collaborative revenues or an offset to research and development expenses in accordance with the provisions of gross or net revenue presentation. The Company recognizes the corresponding revenues or records the corresponding offset to research and development expenses as it satisfies the related performance obligations.

Sales-based Milestone and Royalty Payments: The Company's collaborators may be required to pay the Company sales-based milestones or royalties on future sales of commercial products. The Company recognizes revenues related to sales-based milestone and royalties upon the later to occur of (i) achievement of the collaborator's underlying sales or (ii) satisfaction of any performance obligation(s) related to these sales, in each case assuming the license to the Company's intellectual property is deemed to be the predominant item to which the sales-based milestones and/or royalties relate. The Company has not recorded any sales-based milestones or royalties revenues during the three years ended December 31, 2019.

Concentration of Credit Risk

Financial instruments that potentially subject the Company to concentration of credit risk consist principally of money market funds and marketable securities. The Company places these investments with highly rated financial institutions, and, by policy, limits the amounts of credit exposure to any one financial institution. These amounts at times may exceed federally insured limits. The Company also maintains a foreign currency hedging program that includes foreign currency forward contracts with several counterparties. The Company has not experienced any credit losses related to these financial instruments and does not believe it is exposed to any significant credit risk related to these instruments.

The Company also is subject to credit risk from its accounts receivable related to its product sales and collaborators. The Company evaluates the creditworthiness of each of its customers and has determined that all of its material customers are creditworthy. To date, the Company has not experienced significant losses with respect to the collection of its accounts receivable. The Company believes that its allowance for doubtful accounts was adequate at December 31, 2019. Please refer to Note R, “Segment Information,” for further information.

Cash and Cash Equivalents

The Company considers all highly liquid investments with original maturities ofthree months or less at the date of purchase to be cash equivalents.

Marketable Securities

As of December 31, 2019, the Company’s marketable securities consisted of investments in available-for-sale debt securities, including government-sponsored enterprise securities, corporate debt securities and commercial paper, and corporate equity securities with readily determinable fair values. The Company classifies marketable securities available to fund current operations as current assets on its consolidated balance sheets. Marketable securities are classified as long-term assets on the consolidated balance sheets if (i) they have been in an unrealized loss position for longer than one year and (ii) the Company has the ability and intent to hold them (a) until the carrying value is recovered and (b) such holding period may be longer than one year. The Company’s marketable securities are stated at fair value. The fair value of these securities is based on quoted prices for identical or similar assets.

The Company records unrealized gains (losses) on available-for-sale debt securities as a component of “Accumulated other comprehensive (loss) income,” which is a separate component of shareholders’ equity on its consolidated balance sheet, until such gains and losses are realized.

Pursuant to the adoption of Accounting Standards Update (“ASU”) 2016-01,*Recognition and Measurement of Financial Assets and Financial Liabilities* (“ASU 2016-01”) on January 1, 2018, the Company began recording changes in the fair value of its investments in corporate equity securities to “Other income (expense), net” in the Company’s consolidated statements of operations. Prior to its adoption of ASU 2016-01 in 2018, the Company recorded changes in the fair value of its investments in corporate equity securities to “Accumulated other comprehensive (loss) income.”

The Company reviews investments in marketable debt securities for other-than-temporary impairment whenever the fair value of an investment is less than the amortized cost and evidence indicates that an investment’s carrying amount is not recoverable within a reasonable period of time. To determine whether an impairment is other-than-temporary, the Company considers whether it has an intent to sell, or whether it is more likely than not that the Company will be required to sell, the investment before recovery of the investment’s amortized cost basis. Evidence considered in this assessment includes reasons for the impairment, compliance with the Company’s investment policy, the severity and the duration of the impairment and changes in value subsequent to year-end. If a decline in the fair value is considered other-than-temporary, based on available evidence, the unrealized loss is transferred from other comprehensive income (loss) to the consolidated statements of operations.

Realized gains and losses are determined using the specific identification method and are included in “Other income (expense), net” in the consolidated statements of operations.

Accounts Receivable

The Company deducts invoice discounts for prompt payment and fees for distribution services from its accounts receivable based on its experience that the Company’s Customers will earn these discounts and fees. The Company’s estimates for its allowance for doubtful accounts, which have not been significant to date, are determined based on existing contractual payment terms and historical payment patterns.

Stock-based Compensation Expense

The Company expenses the fair value of employee stock options 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, the Company recognizes expense if, and to the extent that, the Company estimates that achievement of the performance condition is probable. If the Company concludes that vesting is probable, it recognizes expense from the date it reaches this conclusion through the estimated vesting date.

The Company provides to employees who have rendered a certain number of years' to the Company 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 the Company's employees were eligible for partial or full acceleration of any of their equity awards as ofDecember 31, 2019. The Company recognizes stock-based compensation expense related to these awards over a service period reflecting qualified employees' eligibility for partial or full acceleration of vesting.

Research and Development Expenses

The Company expenses as incurred all research and development expenses, including amounts funded by research and development collaborations. The Company capitalizes nonrefundable advance payments made by the Company for research and development activities and expenses the payments as the related goods are delivered or the related services are performed.

Research and development expenses are comprised of costs incurred by the Company in performing research and development activities, including salary and benefits; stock-based compensation expense; outsourced services and other direct expenses, including clinical trial and pharmaceutical development costs; collaboration and asset acquisition payments; expenses associated with drug supplies that are not being capitalized; and infrastructure costs, including facilities costs and depreciation expense.

Inventories

The Company values its inventories at the lower-of-cost or net realizable value. The Company determines the cost of its inventories, which includes amounts related to materials and manufacturing overhead, on a first-in, first-out basis. The Company performs an assessment of the recoverability of capitalized inventory during each reporting period, and writes down any excess and obsolete inventories to their net realizable value in the period in which the impairment is first identified. Shipping and handling costs incurred for inventory purchases are capitalized and recorded upon sale in "Cost of sales" in the consolidated statements of operations. Shipping and handling costs incurred for product shipments are recorded as incurred in "Cost of sales" in the consolidated statements of operations.

The Company capitalizes inventories produced in preparation for initiating sales of a drug candidate when the related drug candidate is considered to have a high likelihood of regulatory approval and the related costs are expected to be recoverable through sales of the inventories. In determining whether or not to capitalize such inventories, the Company evaluates, among other factors, information regarding the drug candidate's safety and efficacy, the status of regulatory submissions and communications with regulatory authorities and the outlook for commercial sales, including the existence of current or anticipated competitive drugs and the availability of reimbursement. In addition, the Company evaluates risks associated with manufacturing the drug candidate and the remaining shelf-life of the inventories.

Property and Equipment

Property and equipment are recorded at cost. Depreciation expense is recorded using the straight-line method over the estimated useful life of the related asset, generally seven to ten years for furniture and equipment, three to five years for computers and software and for leasehold improvements, the shorter of the useful life of the improvements or the estimated remaining life of the associated lease. Maintenance and repairs to an asset that do not improve or extend its life are charged to operations. 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 the Company's consolidated statements of operations. The Company performs an assessment of the fair value of the assets if indicators of impairment are identified during a reporting period and records the assets at the lower of the net book value or the fair value of the assets.

The Company capitalizes internal costs incurred to develop software for internal use during the application development stage. Amortization of capitalized internally developed software costs is recorded in depreciation expense over the useful life of the related asset.

Leases

The Company adopted ASU 2016-02, Leases (Topic 842) ("ASC 842") as of January 1, 2019. Under ASC 842, the Company determines whether the arrangement contains a lease at the inception of an arrangement. If a lease is identified in an arrangement, the Company recognizes a right-of-use asset and liability on its consolidated balance sheet and determines whether the lease should be classified as a finance or operating lease. The Company does 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 the Company by the end of the lease term, (ii) the Company holds an option to purchase the leased asset that it is 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, the Company utilizes its 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.

The Company does not separate lease and non-lease components when determining which lease payments to include in the calculation of its lease assets and liabilities. Variable lease payments are expensed as incurred. If a lease includes an option to extend or terminate the lease, the Company reflects the option in the lease term if it is reasonably certain it 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 "Other assets," "Other current liabilities" and "Other long-term liabilities" on the Company's consolidated balance sheet.

Prior to the adoption of ASC 842 on January 1, 2019, the Company applied build-to-suit accounting and was the deemed owner of its leased corporate headquarters in Boston and research site in San Diego, for which it was recognizing depreciation expense over the buildings' useful lives and imputed interest on the corresponding construction financing lease obligations. The Company also recorded leases for equipment as capital leases pursuant to the accounting guidance that was effective until December 31, 2018.

The assets and liabilities associated with the Company's capital lease agreements were recorded at the present value of the minimum lease payments at the inception of the lease agreement. The assets were depreciated using the straight-line method over the shorter of the useful life of the related asset or the remaining life of the associated lease. Amortization of capital lease assets was included in depreciation expense.

Income Taxes

Deferred tax assets and liabilities are recognized for the expected future tax consequences of temporary differences between the financial statement carrying amounts and the income tax bases of assets and liabilities. 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, the Company reassesses the valuation allowance on its deferred income tax assets weighing positive and negative evidence to assess the recoverability of its deferred tax assets. The Company includes, among other things, its recent financial performance and its future projections in this periodic assessment.

The Company records 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. The Company does not believe any such uncertain tax positions currently pending will have a material adverse effect on its consolidated financial statements.

Variable Interest Entities

The Company reviews each collaboration agreement pursuant to which it licenses assets owned by a collaborator in order to determine whether or not it has a variable interest via the license agreement with the collaborator and if the variable interest is a variable interest in the collaborator as a whole. In assessing whether the Company has a variable interest in the collaborator as a whole, the Company considers and makes judgments regarding the purpose and design of the entity, the value of the licensed assets to the collaborator, the value of the collaborator's total assets and the significant activities of the collaborator. If the Company has a variable interest in the collaborator as a whole, the Company assesses whether or not the Company is the primary beneficiary of that VIE based on a number of factors, including (i) which party has the power to direct the activities that most significantly affect the VIE's economic performance, (ii) the parties' contractual rights and responsibilities pursuant to the collaboration agreement and (iii) which party has the obligation to absorb losses of or the right to receive benefits from the VIE that could be significant to the VIE. If the Company determines it is the primary beneficiary of a VIE at the onset of the collaboration agreement, the collaboration is treated as a business combination and the Company consolidates the financial statements of the VIE into the Company's consolidated financial statements. On a quarterly basis, the Company evaluates whether it continues to be the primary beneficiary of any consolidated VIEs. If the Company determines that it is no longer the primary beneficiary of a consolidated VIE, or no longer has a variable interest in the VIE, it deconsolidates the VIE in the period that the determination is made.

Fair Value of In-process Research and Development Assets and Contingent Payments

The present-value models the Company uses to estimate the fair values of in-process research and development assets and contingent payments pursuant to collaborations and acquisitions incorporate significant assumptions.

The Company's discounted cash flow models pertaining to in-process research and development assets include: (i) assumptions regarding the probability of obtaining marketing approval for a drug candidate; (ii) the timing of and the expected costs to develop and commercialize a drug candidate; (iii) estimates of future cash flows from potential product sales with respect to a drug candidate; and (iv) appropriate discount and tax rates.

The Company bases its estimates of the probability of achieving the milestones relevant to the fair value of contingent payments, which could include milestone, royalty and option payments, on industry data. Estimates included in the discounted cash flow models pertaining to contingent payments also include: (i) estimate regarding the timing of the relevant development and commercial milestones and royalties, (ii) and appropriate discount rates. Please refer to Note E, "Fair Value Measurements," for further information.

In-process Research and Development Assets

The Company records the fair value of in-process research and development assets as of the transaction date of a business combination. Each of these assets is accounted for as an indefinite-lived intangible asset and is maintained on the Company's consolidated balance sheet until either the project underlying it is completed or the asset becomes impaired. If the asset becomes impaired or is abandoned, the carrying value of the related intangible asset is written down to its fair value, and an impairment charge is recorded in the period in which the impairment occurs. If a project is completed, the carrying value of the related intangible asset is amortized as a part of "Cost of sales" over the remaining estimated life of the asset beginning in the period in which the project is completed. In-process research and development assets are tested 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.

In-process research and development that is acquired in a transaction that does not qualify as a business combination under GAAP and that does not have an alternative future use is expensed in the period in which it is acquired.

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 on an annual basis as of October 1, and more frequently if indicators are present or changes in circumstances suggest that impairment may exist.

Deconsolidation

Upon the occurrence of certain events and on a regular basis, the Company evaluates whether it no longer has a controlling interest in its subsidiaries, including consolidated VIEs. If the Company determines it no longer has a controlling interest, the subsidiary is deconsolidated. The Company records a gain or loss on deconsolidation based on the difference on the deconsolidation date between (i) the aggregate of (a) the fair value of any consideration received, (b) the fair value of any retained noncontrolling investment in the former subsidiary and (c) the carrying amount of any noncontrolling interest in the subsidiary being deconsolidated, less (ii) the carrying amount of the former subsidiary's assets and liabilities.

Discontinued Operations

The Company assesses whether a deconsolidation is required to be presented as discontinued operations in its consolidated financial statements on the deconsolidation date. This assessment is based on whether or not the deconsolidation represents a strategic shift that has or will have a major effect on the Company's operations or financial results. If the Company determines that a deconsolidation requires presentation as a discontinued operation on the deconsolidation date, or at any point during the one year period following such date, it will present the former subsidiary as a discontinued operation in current and comparative period financial statements.

Embedded Derivatives

Embedded derivatives are required to be bifurcated from the host instruments and recorded at fair value if the derivatives are not clearly and closely related to the host instruments on the date of issuance. The Company did not have any material embedded derivatives that required bifurcation recorded on its consolidated balance sheets as of December 31, 2019 and 2018, respectively.

Hedging Activities

The Company recognizes the fair value of hedging instruments that are designated and qualify as hedging instruments pursuant to GAAP, foreign currency forward contracts, as either assets or liabilities on the consolidated balance sheets. Changes in the fair value of these instruments are recorded each period in "Accumulated other comprehensive (loss) income" 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 the Company's 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 the consolidated statement of operations in the same period that it recognizes the product revenues that were impacted by the hedged foreign exchange rate changes. The Company classifies the cash flows from hedging instruments in the same category as the cash flows from the hedged items.

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

The Company also enters into foreign currency forward contracts with contractual maturities of less thanone 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 GAAP. Realized gains and losses for such contracts are recognized in “Other income (expense), net” in the consolidated statement of operations each period.

Restructuring Expenses

The Company records costs and liabilities associated with exit and disposal activities based on estimates of fair value in the period the liabilities are incurred. The Company’s exit and disposal activities have primarily been associated with the Company’s facilities, but also have included the termination of employees in some cases. The Company’s initial estimate of its liabilities for net ongoing costs associated with its facility obligations are recorded at fair value on the cease use date. On a quarterly basis, the Company evaluates and adjusts these liabilities as appropriate for changes in circumstances. Changes to the Company’s estimate of these liabilities are recorded as additional restructuring expenses (credits). These costs are included in “Restructuring (income) expenses” on the Company’s consolidated statements of operations.

The Company has adopted several plans to restructure its facilities and operations for which it has incurred restructuring expenses. The only significant restructuring event during the three years ended December 31, 2019 commenced in February 2017 upon the Company’s decision to consolidate its research activities into its Boston, Milton Park and San Diego locations. The Company closed its research site in Canada as a result of this decision affecting approximately 70 positions. The Company’s lease for its research site in Canada expired in October 2018. As of December 31, 2019 and 2018, the Company has no restructuring liabilities recorded on its consolidated balance sheet and does not anticipate any additional charges related to this restructuring event in the future.

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 certain marketable securities. For purposes of comprehensive income (loss) disclosures, the Company records provisions for or benefits from income taxes related to the unrealized gains and losses on foreign currency forward contracts and certain marketable securities. The Company does not record provisions for or benefits from income taxes related to the cumulative translation adjustment, as the Company intends to permanently reinvest undistributed earnings in its foreign subsidiaries.

Foreign Currency Translation and Transactions

The majority of the Company’s operations occur in entities that have the U.S. dollar denominated as their functional currency. The assets and liabilities of the Company’s entities with functional currencies other than the U.S. dollar are translated into U.S. dollars at rates of exchange 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. Net unrealized gains and losses resulting from foreign currency translation are included in “Accumulated other comprehensive (loss) income.” Net foreign currency exchange transaction losses, which are included in “Other income (expense), net” on the Company’s consolidated statement of operations, were $5.2 million, $1.1 million and $5.5 million for 2019, 2018 and 2017, 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 the Company’s consolidated statement of operations.

Net Loss Per Share Attributable to Vertex Common Shareholders

Basic and diluted net loss per share attributable to Vertex common shareholders are presented in conformity with the two-class method required for participating securities. Under the two-class method, earnings are allocated to (i) Vertex common shares, excluding unvested restricted stock, and (ii) participating securities, based on their respective weighted-average shares outstanding for the period. Shares of unvested restricted stock granted under the Company’s Amended and Restated 2006 Stock and Option Plan have the non-forfeitable right to receive dividends on an equal basis with other outstanding common stock. As a result, these unvested shares of restricted stock are considered participating securities under the two-class method. Potentially dilutive shares result from the assumed exercise of outstanding stock options (the proceeds of which are then assumed to have been used to repurchase outstanding stock using the treasury stock method).

Basic net loss per share attributable to Vertex common shareholders is based upon the weighted-average number of common shares outstanding during the period, excluding restricted stock that has been issued but is not yet vested. Diluted net loss per share attributable to Vertex common shareholders 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.

Recently Adopted Accounting Standards

Leases

In 2016, the Financial Accounting Standards Board ("FASB") issued ASC 842, which amends a number of aspects of lease accounting and requires entities to recognize right-of-use assets and liabilities on the balance sheet. ASC 842 became effective on January 1, 2019.

Until December 31, 2018, the Company applied build-to-suit accounting and was the deemed owner of its leased corporate headquarters in Boston and research site in San Diego, for which it was recognizing depreciation expense over the buildings' useful lives and imputed interest on the corresponding construction financing lease obligations. Under the amended guidance that became effective January 1, 2019, the Company accounts for these buildings as finance leases, resulting in increased depreciation expense over the respective lease terms of approximately 15 years, which are significantly shorter than the buildings' useful lives of 40 years. The amended guidance also results in a reduction in imputed interest expense in the initial years of each finance lease term.

In July 2018, the FASB issued ASU 2018-11, *Leases (Topic 842): Targeted Improvements* ("ASU 2018-11"), which offered a transition option to entities adopting ASC 842. Under ASU 2018-11, entities could elect to apply ASC 842 using a modified-retrospective adoption approach resulting in a cumulative effect adjustment to accumulated deficit at the beginning of the year in which the new lease standard is adopted, rather than adjustments to the earliest comparative period presented in their financial statements. The Company adopted ASC 842 using the modified-retrospective method. As of January 1, 2019, the Company recorded a cumulative effect adjustment to increase its "Accumulated deficit" by $40.3 million related to the adjustments to its build-to-suit leases described in the previous paragraph.

The Company elected the package of transition practical expedients for leases that commenced prior to January 1, 2019, allowing it not to reassess (i) whether any expired or existing contracts contain leases, (ii) the lease classification for any expired or existing leases and (iii) the initial indirect costs for any existing leases.

Additionally, the Company recorded, upon adoption of ASC 842 on January 1, 2019, operating lease assets of $61.7 million and corresponding liabilities of $71.9 million related to its real estate leases that are not treated as finance leases under ASC 842. The difference between these assets and liabilities was primarily attributable to prepaid or accrued lease payments. The Company also reclassified amounts that were recorded as "Capital lease obligations, current portion" and "Capital lease obligations, excluding current portion" as of December 31, 2018 to "Other current liabilities" and "Long-term finance lease liabilities," respectively, on January 1, 2019. These adjustments had no impact on the Company's consolidated statement of operations and had no impact on the Company's accumulated deficit.

The cumulative effect of applying ASC 842 on the Company's consolidated balance sheet as of January 1, 2019 was as follows:

	Balance as of December 31, 2018 ^	Adjustments	Balance as of January 1, 2019
Assets		(in thousands)	
Prepaid expenses and other current assets	$ 140,819	$ (2,930)	$ 137,889
Property and equipment, net	812,005	(53,920)	758,085
Deferred tax assets	1,499,672	11,236	1,510,908
Other assets	—	61,674	61,674
Total assets	$ 6,245,898	$ 16,060	$ 6,261,958
Liabilities and Shareholders' Equity			
Capital lease obligations, current portion	$ 9,817	$ (9,817)	$ —
Other current liabilities	40,589	34,304	74,893
Capital lease obligations, excluding current portion	19,658	(19,658)	—
Construction financing lease obligation, excluding current portion	561,892	(561,892)	—
Long-term finance lease liabilities	—	569,487	569,487
Other long-term liabilities	26,280	43,946	70,226
Accumulated deficit	(2,989,478)	(40,310)	(3,029,788)
Total liabilities and shareholders' equity	$ 6,245,898	$ 16,060	$ 6,261,958

^ As reported in the Company's 2018 Annual Report on Form 10-K.

"Other assets" and "Other long-term liabilities" in the table above relate primarily to the Company's operating leases. Please refer to Note M, "Leases," for further information regarding the Company's leases as well as certain disclosures required by ASC 842.

Derivatives and Hedging

In 2017, the FASB issued ASU 2017-12, *Derivatives and Hedging (Topic 815)* ("ASU 2017-12"), which helps simplify certain aspects of hedge accounting and enables entities to more accurately present their risk management activities in their financial statements. ASU 2017-12 became effective January 1, 2019. The adoption of ASU 2017-12 did not have a significant effect on the Company's consolidated financial statements.

Revenue Recognition

In 2014, the FASB issued ASC 606. The new guidance became effective January 1, 2018. ASC 606 applies a more principles-based approach to recognizing revenue. Under ASC 606, revenue is recognized when a customer obtains control of promised goods or services in an amount that reflects the consideration that an entity expects to receive in exchange for those goods or services. In addition, the standard requires disclosure of the nature, amount, timing, and uncertainty of revenue and cash flows arising from contracts with customers. The Company adopted ASC 606 on January 1, 2018 using the modified-retrospective adoption method for all contracts that were not completed as of the date of adoption. Under the modified-retrospective method, the Company recognized the cumulative effect of applying the standard within "Accumulated deficit" on its consolidated balance sheet as of January 1, 2018.

For all reporting periods, the Company has not disclosed the value of unsatisfied performance obligations for all product revenue contracts with an original expected length of one year or less, which is an optional exemption that is permitted under the adoption rules.

Based on the Company's review of existing customer contracts as of January 1, 2018, it concluded that the only significant impact that the adoption of ASC 606 had on its financial statements related to shipments of ORKAMBI under early access programs in France. Prior to the adoption of ASC 606, the Company did not recognize revenue on the proceeds received from sales of ORKAMBI under early access programs in France because the price was not fixed or determinable based on the status of ongoing pricing discussions. As of January 1, 2018, the Company recorded a cumulative effect adjustment to its accumulated deficit of $8.3 million related to the adoption of ASC 606, which primarily represented the Company's estimated amount of consideration it expected to retain related to these shipments that would not be subject to a significant reversal in amounts recognized, net of costs previously deferred related to these shipments. Please refer to "Product Revenues, Net" above for further information related to the impact of the new revenue recognition on these sales.

The impact of adoption on the Company's consolidated statement of operations for the year ended December 31, 2018 was as follows:

	Year Ended December 31, 2018		
	As Reported under ASC 606	Balances without Adoption of ASC 606	Effect of Change Higher/(Lower)
	(in thousands)		
Product revenues, net	$ 3,038,325	$ 3,019,484	$ 18,841
Cost of sales	409,539	402,925	6,614
Income from operations	635,150	622,923	12,227
Net income attributable to Vertex	$ 2,096,896	$ 2,084,669	$ 12,227
Amounts per share attributable to Vertex common shareholders:			
Net income:			
Basic	$ 8.24	$ 8.20	$ 0.04
Diluted	$ 8.09	$ 8.04	$ 0.05

ASC 606 did not have an aggregate impact on the Company's net cash provided by operating activities, but resulted in offsetting changes in certain assets and liabilities presented within net cash provided by operating activities in the Company's consolidated statement of cash flows.

Equity Investments

In 2016, the FASB issued ASU 2016-01, which amended guidance related to the recording of financial assets and financial liabilities. Under ASU 2016-01, equity investments (except those accounted for under the equity method of accounting or those that result in consolidation of an investee) are measured at fair value with changes in fair value recognized in net income (loss). However, an entity has the option to measure equity investments without readily determinable fair values at (i) fair value or (ii) cost adjusted for changes in observable prices minus impairment. Changes in measurement under either alternative are recognized in net income (loss). ASU 2016-01 became effective January 1, 2018 and required the modified-retrospective adoption method. As of January 1, 2018, the Company held publicly traded equity investments and equity investments accounted for under the cost method. As a result, in 2018, the Company recorded a $25.1 million cumulative effect adjustment to "Accumulated deficit" related to its publicly traded equity investments equal to the unrealized gain, net of tax, that was recorded in "Accumulated other comprehensive (loss) income" as of December 31, 2017. The adoption of ASU 2016-01 had no effect on the Company's equity investments accounted for under the cost method because the original cost basis of these investments was recorded on the Company's consolidated balance sheet as of December 31, 2017. In 2019 and 2018, the Company recorded net unrealized gains of $132.5 million and $2.6 million, respectively, to "Other income (expense), net" in its consolidated statement of operations related to the change in fair value of its equity investments.

Intra-Entity Transfers

In 2016, the FASB issued ASU 2016-16, *Intra-Entity Transfers of Assets Other Than Inventory* ("ASU 2016-16"), which removes the previous exception in GAAP prohibiting an entity from recognizing current and deferred income tax expenses or benefits related to the transfer of assets, other than inventory, within the consolidated entity. The exception to defer the recognition of any tax impact on the transfer of inventory within the consolidated entity until it is sold to a third party remains unaffected. ASU 2016-16 became effective January 1, 2018. In 2018, upon adoption of ASU 2016-16, the Company recorded a deferred tax asset and corresponding full valuation allowance of $204.7 million equal to the unamortized cost of intellectual property rights transferred to the United Kingdom in 2014 multiplied by an appropriate statutory rate. There was no cumulative effect adjustment to "Accumulated deficit" using the modified-retrospective adoption method.

Goodwill

In 2017, the FASB issued ASU 2017-04,*Intangibles - Goodwill and Other (Topic 350)*("ASU 2017-04") related to measurements of goodwill. ASU 2017-04 modifies the concept of impairment from the condition that exists when the carrying amount of goodwill exceeds its implied fair value to the condition that exists when the carrying amount of a reporting unit exceeds its fair value, which eliminates Step 2 from the goodwill impairment test. An entity would recognize an impairment charge for the amount by which the carrying amount exceeds the reporting unit's fair value; however, the loss recognized should not exceed the total amount of goodwill allocated to the related reporting unit. The Company early adopted ASU 2017-04 and utilized this approach for annual and interim goodwill impairment tests conducted after January 1, 2018. The adoption of ASU 2017-04 did not have a significant effect on the Company's consolidated financial statements.

Cash Flows - Restricted Cash

In 2016, the FASB issued ASU 2016-18, *Statement of Cash Flows (Topic 230) Restricted Cash* ("ASU 2016-18"), which requires that a statement of cash flows explain the change during the period in the total of cash, cash equivalents and restricted cash. Therefore, amounts described as restricted cash should be included with cash and cash equivalents when reconciling the beginning of period and end of period amounts shown on the statement of cash flows. ASU 2016-18 became effective January 1, 2018 and was effective on a retrospective basis. The cash, cash equivalents and restricted cash balances for the years ended December 31, 2019 through 2016, which are presented in the Company's consolidated statements of cash flows subsequent to the adoption ofASU 2016-18, consisted of the following:

	As of December 31,			
	2019	2018	2017	2016
	(in thousands)			
Cash and cash equivalents	$ 3,109,322	$ 2,650,134	$ 1,665,412	$ 1,183,945
Prepaid expenses and other current assets	8,004	4,910	2,114	47,762
Other assets	3,355	3,209	—	—
Cash, cash equivalents and restricted cash per statement of cash flows	$ 3,120,681	$ 2,658,253	$ 1,667,526	$ 1,231,707

The Company's restricted cash, if any, is included in "Prepaid expenses and other current assets" and "Other assets" in its consolidated balance sheets. As of December 31, 2017 and 2016, the Company recorded BioAxone's cash and cash equivalents as "Prepaid expenses and other current assets" because the Company did not have any interest in or control over BioAxone's cash and cash equivalents.

Stock-Based Compensation - Improvements

In 2016, the FASB issued ASU 2016-09,*Compensation—Stock Compensation (Topic 718) Improvements to Employee Share-Based Payment Accounting* ("ASU 2016-09"), which simplifies the accounting for employee share-based payment transactions, including the accounting for income taxes, forfeitures, and statutory tax withholding requirements, as well as classification in the statement of cash flows. ASU 2016-09 became effective January 1, 2017. ASU 2016-09 eliminated the requirement that excess tax benefits were realized as a reduction in current taxes payable before the associated tax benefit could be recognized as an increase in additional paid-in capital. This created a deferred tax asset of $410.8 million relating to federal and state net operating losses ("NOLs") that were fully reserved by an equal increase in the Company's valuation allowance as of January 1, 2017. The Company recorded deferred tax assets of $404.7 million relating to federal NOLs and $6.1 million relating to state NOLs, both of which were offset by a full valuation allowance. Upon adoption, the Company also elected to change its accounting policy to account for forfeitures of options and awards as they occur. The change was applied on a modified-retrospective basis with a cumulative effect adjustment to increase "Accumulated deficit" by $9.4 million as of January 1, 2017. This change also resulted in an increase to the deferred tax asset of $3.4 million, which was offset by a full valuation allowance. As a result, there was no cumulative effect adjustment to accumulated deficit related to income taxes. The provisions related to the recognition of excess tax benefits in the Company's consolidated statement of operations and classification in the consolidated statement of cash flows were adopted prospectively, and as such, the prior periods were not retrospectively adjusted.

Recently Issued Accounting Standards

Internal-Use Software

In 2018, the FASB issued ASU 2018-15,*Intangibles—Goodwill and Other—Internal-Use Software (Subtopic 350-40): Customer's Accounting for Implementation Costs Incurred in a Cloud Computing Arrangement That Is a Service Contract* ("ASU 2018-15"), which clarifies the accounting for implementation costs in cloud computing arrangements. ASU 2018-15 was effective on January 1, 2020. The Company expects the adoption of ASU 2018-15 will result in an insignificant amount of additional assets recorded on its consolidated balance sheet.

Fair Value Measurement

In 2018, the FASB issued ASU 2018-13,*Fair Value Measurement (Topic 820): Disclosure Framework-Changes to the Disclosure Requirements for Fair Value Measurement* ("ASU 2018-13"), which modifies the disclosure requirements for fair value measurements. ASU 2018-13 was effective on January 1, 2020. The Company expects the adoption of ASU 2018-13 will result in additional disclosures related to its assets and liabilities that are valued based on Level 3 inputs.

Credit Losses

In 2016, the FASB issued ASU 2016-13, Financial Instruments - Credit Losses (Topic 326): Measurement of Credit Losses on Financial Instruments ("ASU 2016-13"), which requires entities to record expected credit losses for certain financial instruments, including trade receivables, as an allowance that reflects the entity's current estimate of credit losses expected to be incurred. For available-for-sale debt securities in unrealized loss positions, ASU 2016-13 requires allowances to be recorded instead of reducing the amortized cost of the investment. ASU 2016-13 was effective on January 1, 2020. The Company does not expect the adoption of ASU 2016-13 to have a significant impact on its consolidated financial statements.

B. Collaborative Arrangements

The Company has entered into numerous agreements pursuant to which it collaborates with third parties on research, development and commercialization programs, including in-license and out-license agreements.

In-license Agreements

The Company has entered into a number of license agreements in order to advance and obtain access to technologies and services related to its research and early-development activities. The Company is generally required to make an upfront payment upon execution of the license agreement; 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 the collaboration.

Pursuant to the terms of its in-license agreements, the Company's collaborators typically lead the discovery efforts and the Company leads all preclinical, development and commercialization activities associated with the advancement of any drug candidates and funds all expenses.

The Company typically can terminate its in-license agreements by providing advance notice to its collaborators; the required length of notice is dependent on whether any product developed under the license agreement has received marketing approval. The Company's 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

In 2015, the Company entered into a strategic collaboration, option and license agreement (the "CRISPR Agreement") with CRISPR Therapeutics AG and its affiliates ("CRISPR") 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. The Company had the exclusive right to license certain CRISPR Cas9-based targets. In the fourth quarter of 2019, the Company paid an aggregate of $30.0 million to exclusively license three CRISPR-Cas9-based targets, including CF, pursuant to the CRISPR Agreement. The Company recorded the $30.0 million total option payment to "Research and development expenses" in the fourth quarter of 2019. For each of the three targets that the Company 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 net product sales.

In 2017, the Company entered into a co-development and co-commercialization agreement with CRISPR pursuant to the terms of the CRISPR Agreement, under which the Company and CRISPR are co-developing and will co-commercialize CTX001 (the "CTX001 Co-Co Agreement") for the treatment of hemoglobinopathy, including treatments for sickle cell disease and beta-thalassemia. As part of the collaboration, the Company and CRISPR share equally all development costs and potential worldwide revenues related to potential hemoglobinopathy treatments, including treatments for beta-thalassemia and sickle cell disease. The Company concluded that the CTX001 Co-Co Agreement is a cost-sharing arrangement, which results in the net impact of the arrangement being recorded in "Research and development expenses" in its consolidated statements of operations. During the years ended December 31, 2019 and 2018, the net expense related to the CTX001 Co-Co Agreement was $30.1 million and $19.7 million, respectively. Net expense related to the CTX001 Co-Co Agreement during the year ended December 31, 2017 was not significant.

In July 2019, the Company entered into a separate strategic collaboration and license agreement (the "CRISPR DMD/DM1 Agreement") with CRISPR. Pursuant to this agreement, the Company received an exclusive worldwide license to CRISPR's existing and future intellectual property for duchenne muscular dystrophy ("DMD") and myotonic dystrophy type 1 ("DM1") and the Company made an upfront payment of $175.0 million to CRISPR. The Company concluded that it did not have any alternative future use for the acquired in-process research and development and recorded the upfront payment to "Research and development expenses" in the third quarter of 2019. CRISPR has the potential to receive up to $825.0 million in research, development, regulatory and commercial milestones for the DMD and DM1 programs as well as royalties on net product sales. CRISPR has the option to co-develop and co-commercialize all

DM1 products globally and forego the milestones and royalties associated with the DM1 program. The Company will fund all expenses associated with the collaboration except for research costs for specified guide RNA research conducted by CRISPR, which the Company and CRISPR will share equally.

Please refer to Note F, "Marketable Securities and Equity Investments," for information regarding the Company's investment in CRISPR's common stock.

Kymera Therapeutics Inc.

In May 2019, the Company entered into a strategic research and development collaboration agreement with Kymera Therapeutics Inc. ("Kymera") to advance small molecule protein degraders against multiple targets. Kymera's proprietary platform technology is being applied in the collaboration activities in exchange for an upfront payment of $50.0 million. The Company has the exclusive right to license up to six protein targets, for each of which Kymera may receive up to $170.0 million in payments, including development, regulatory and commercial milestones as well as royalties on net product sales. In addition to the upfront payment, the Company purchased $20.0 million of Kymera's preferred stock. The Company determined that the fair value of its investment in Kymera's preferred stock, which does not have a readily determinable fair value, approximated $20.0 million and classified the investment in "Other assets."

The Company determined that substantially all of the fair value of the Kymera collaboration agreement was attributable to in-process research and development and no substantive processes were acquired that would constitute a business. The Company concluded that it did not have any alternative future use for the acquired in-process research and development and recorded the $50.0 million upfront payment to "Research and development expenses."

Other In-License Agreements

In addition to the collaborative arrangements described above, the Company has entered into additional in-license agreements that it does not consider to be individually significant to its financial statements. In addition to the payments described above, the Company recorded upfront, option and milestone payments totaling $63.3 million in 2019, $46.9 million in 2018 and $8.7 million in 2017 to "Research and development expenses," which included a $25.9 million upfront payment to Molecular Templates, Inc. ("Molecular") in 2019 and a $30.0 million upfront payment to Arbor Biotechnologies, Inc. ("Arbor") in 2018.

For Molecular and Arbor and several other in-license agreements that are not individually significant to the Company's financial statements. The Company determined that substantially all of the fair value of each individual agreement was attributable to in-process research and development and no substantive processes were acquired that would constitute a business. The Company concluded that it did not have any alternative future use for the acquired in-process research and development associated with the agreements and recorded the related portion of the upfront payments to "Research and development expenses." Please refer to Note E, "Fair Value Measurements," and Note F, "Marketable Securities and Equity Investments," for further information regarding the Company's investments in its collaborators.

Variable Interest Entities (VIEs)

The Company licensed rights to certain drug candidates from these third-party collaborators, which has resulted in the consolidation of the third-parties' financial statements into the Company's consolidated financial statements as VIEs for certain periods of time. The Company deconsolidated the financial statements of Parion as of September 30, 2017 and BioAxone as of December 31, 2018 from its consolidated financial statements. As of December 31, 2018, and continuing through 2019, the Company had no consolidated VIEs reflected in its financial statements. Please refer to Note K, "Intangible Assets and Goodwill," for further information regarding the impairment of Parion's pulmonary ENaC platform and BioAxone's VX-210 program that were related to these collaborations.

Parion Sciences, Inc.

In 2015, the Company entered into a strategic collaboration and license agreement (the "Parion Agreement") with Parion to develop investigational epithelial sodium channel ("ENaC") inhibitors for the potential treatment of CF and all other pulmonary diseases. The Parion Agreement was terminated in January 2020. Following execution of the Parion Agreement, the Company determined that it had a variable interest in Parion via the Parion Agreement, and that the variable interest represented a variable interest in Parion as a whole because the fair value of the ENaC inhibitors represented more than half of the total fair value of Parion's assets. The Company also concluded that it was the primary beneficiary as it had the power to direct the activities that most significantly affect the economic performance of Parion and that it had the obligation to absorb losses and right to receive benefits that potentially could be significant to Parion. Accordingly, the Company consolidated Parion's financial statements beginning in June 2015.

In the second quarter of 2017, Parion signed a license agreement with an affiliate of Shire plc related to the development of a drug candidate for the potential treatment of dry eye disease; however, the Company continued to consolidate Parion as a VIE because it determined that there was no substantive change in the design of Parion subsequent to Parion's agreement with Shire. Based on the consolidation of Parion's financial statements, during the year ended December 31, 2017, the Company recognized $40.0 million of collaborative revenues and (ii) a tax provision of $14.8 million, both of which were attributable to noncontrolling interest related to payments that Parion received from Shire in the year ended December 31, 2017.

As of September 30, 2017, the Company determined that the $255.3 million fair value of Parion's pulmonary ENaC platform had declined significantly based on data received in September 2017 from a Phase 2 clinical trial of VX-371 that did not meet its primary efficacy endpoint. Based on this data, the Company evaluated the fair value of Parion's pulmonary ENaC platform using the discounted cash flow approach from the perspective of a market participant and determined that the fair value of the intangible asset was zero as of September 30, 2017. The Company recorded a $255.3 million impairment charge in the third quarter of 2017. After evaluating the results of the clinical trial and based on the decrease in the fair value of Parion's pulmonary ENaC platform relative to Parion's other activities, the Company determined that it was no longer the primary beneficiary of Parion as it no longer had the power to direct the significant activities of Parion. Accordingly, the Company deconsolidated Parion as of September 30, 2017. The impairment charge, the decrease in the fair value of the contingent payments payable by the Company to Parion of $69.6 million and the benefit from income taxes of $126.2 million resulting from these charges that were recorded in the third quarter of 2017 were attributable to noncontrolling interest. The benefit from income taxes consisted of benefits of $97.7 million attributable to the impairment charge and $28.5 million attributable to the decrease in the fair value of contingent payments. The net effect of these charges and impact of the deconsolidation was a loss of $7.1 million recorded in "Other income (expense), net" attributable to Vertex in the consolidated statement of operations for the year ended December 31, 2017.

BioAxone Biosciences, Inc.

In 2014, the Company entered into a license and collaboration agreement (the "BioAxone Agreement") with BioAxone, which resulted in the consolidation of BioAxone as a VIE beginning in October 2014.

In October 2018, the Company announced it would stop clinical development of VX-210 and terminate the Phase 2b clinical trial of VX-210 based on the recommendation of the clinical trial's Data Safety Monitoring Board and the Company's review of interim data. In December 2018, the Company notified BioAxone of its intent to terminate the BioAxone Agreement and executed a release that immediately allowed BioAxone to control development of its neurological programs other than VX-210 without the Company's consent. As a result of this decision, the Company recorded a $29.0 million impairment charge related to VX-210 that was attributable to noncontrolling interest.

As a result, the Company deconsolidated BioAxone as of December 31, 2018 because it determined that it no longer was the primary beneficiary of BioAxone as it no longer had the power to direct the significant activities of BioAxone. The net impact of the deconsolidation was not material to the Company's consolidated statement of operations.

The Company concluded that the deconsolidations of Parion and BioAxone, based on clinical data that did not meet expectations, were not developments that represented a significant strategic shift or had a material impact on the Company's overall operations and financial results or its plans to focus on developing and commercializing therapies for the treatment of CF and advancing its research and development programs in additional diseases. Therefore, the Company did not present the results related to Parion and BioAxone as discontinued operations in its consolidated statements of operations for the three years ended December 31, 2019.

Aggregate VIE Financial Information

An aggregate summary of net loss attributable to noncontrolling interest related to the Company's VIEs for the years ended December 31, 2018 and 2017 was as follows:

	2018	2017
	(in thousands)	
Loss attributable to noncontrolling interest before benefit from income taxes and changes in fair value of contingent payments	$ 31,191	$ 223,379
Benefit from income taxes	(3,668)	(114,090)
(Increase) decrease in fair value of contingent payments	(17,730)	62,560
Net loss attributable to noncontrolling interest	$ 9,793	$ 171,849

The increase in the noncontrolling interest holders' claim to net assets with respect to the fair value of the contingent payments for the year ended December 31, 2018 was primarily due to the expiration of the Company's option to purchase BioAxone that increased the probability that a $10.0 million license continuation fee for VX-210 would be paid. The decrease in the noncontrolling interest holders' claim to net assets with respect to the fair value of the contingent payments for the year ended December 31, 2017 was primarily due to the decrease in the fair value of Parion's pulmonary ENaC platform described above.

Out-license Agreements

The Company has entered into licensing agreements pursuant to which it has out-licensed rights to certain drug candidates to third-party collaborators. Pursuant to these out-license agreements, the Company's collaborators become responsible for all costs related to the continued development of such drug candidates and obtain development and commercialization rights to these drug candidates. Depending on the terms of the agreements, the Company's collaborators may be required to make upfront payments, milestone payments upon the achievement of certain product research and development 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 the Company's in-license agreements.

Merck KGaA, Darmstadt, Germany

In January 2017, the Company entered into a strategic collaboration and license agreement (the "Oncology Agreement") with Merck KGaA, Darmstadt, Germany (the "Licensee"). Pursuant to the Oncology Agreement, the Company granted the Licensee an exclusive worldwide license to research, develop and commercialize four oncology research and development programs including two clinical-stage programs targeting DNA damage repair: its ataxia telangiectasia and Rad3-related protein kinase inhibitor program, or ATR program, including VX-970 and VX-803, and its DNA-dependent protein kinase inhibitor program, or DNA-PK program, including VX-984. In addition, the Company granted the Licensee exclusive, worldwide rights to two pre-clinical programs.

The Oncology Agreement provided for an upfront payment from the Licensee to the Company of $230.0 million. The Company evaluated the deliverables, primarily consisting of a license to the four programs and the obligation to complete certain fully-reimbursable research and development and transition activities as directed by the Licensee, pursuant to the Oncology Agreement, under the multiple element arrangement accounting guidance that was applicable in 2017. The Company concluded that the license had stand-alone value from the research and development and transition activities based on the resources and know-how possessed by the Licensee, and thus concluded that there are two units of accounting in the arrangement. The Company determined the relative selling price of the units of accounting based on the Company's best estimate of selling price. The Company utilized key assumptions to determine the best estimate of selling price for the license, which included future potential net sales of licensed products, development timelines, reimbursement rates for personnel costs, discount rates, and estimated third-party development costs. The Company utilized a discounted cash flow model to determine its best estimate of selling price for the license and determined the best estimate of selling price for the research and development and transition activities based on what it would sell the services for separately. Given the significance of the best estimate of selling price for the license as compared to the best estimate of selling price for the research and development and transition services, reasonable changes in the assumptions used in the discounted cash flow model would not have a significant impact on the relative selling price allocation. Based on this analysis, the Company recognized the $230.0 million upfront payment upon delivery of the license as well as research and development and transition activities during the year ended December 31, 2017. The Company records the reimbursement for the research and development and transition activities in its consolidated statements of operations as collaborative revenue primarily due to the fact that it is the primary obligor in the arrangement. The Company's activities related to the research and development and transition activities under the Oncology Agreement were substantially complete as of December 31, 2017.

In December 2018, the Company entered into an agreement with Merck KGaA, Darmstadt, Germany (the "DNA-PK Agreement") whereby the Company licensed the two lead Vertex DNA-PK compounds from its DNA-PK program for use in the field of gene integration for six specific indications. In exchange for this exclusive worldwide license to research, develop and commercialize the DNA-PK program for the specified indications within the field of gene integration, the Company made an upfront payment of $65.0 million. Merck KGaA, Darmstadt, Germany has the potential to receive additional milestones, primarily related to approval and reimbursement in various markets, as well as royalties on net product sales.

The Company evaluated the DNA-PK Agreement and concluded it represents a modification of the Oncology Agreement pursuant to ASC 606. As of December 2018, when the Company entered into the DNA-PK Agreement, the Company had completed its obligations under the Oncology Agreement, but the Oncology Agreement was an open contract pursuant to ASC 606 since the Company could receive future royalty payments from the commercialization of the licensed programs under the Oncology Agreement.

In applying ASC 606, the Company determined that the license granted under the DNA-PK Agreement is distinct from the license granted by the Company under the Oncology Agreement since the license to the two lead Vertex DNA-PK compounds is capable of being distinct as the Company is able to benefit from the license via its ability to internally develop and commercialize the two lead Vertex DNA-PK compounds in the six named indications in the field of gene-editing, and the license is not dependent on Merck KGaA, Darmstadt, Germany providing any specialized services to the Company. In addition, the license to the two lead Vertex DNA-PK compounds granted to the Company under the DNA-PK Agreement is distinct from the license granted by the Company under the Oncology Agreement as the rights conveyed in the licenses differ and both parties have the ability to commercially benefit from the licenses on their own. Furthermore, the consideration attributable to the license of the two lead Vertex DNA-PK compounds represents fair value. Therefore, the Company determined it should account for the DNA-PK Agreement as a separate agreement.

The Company determined that substantially all of the fair value of the DNA-PK Agreement was attributable to a single in-process research and development asset that did not constitute a business. The Company concluded that it did not have any alternative future use for the acquired in-process research and development and recorded the $65.0 million payment to "Research and development expenses" accordingly.

Janssen Pharmaceuticals, Inc.

In 2014, the Company entered into an agreement with Janssen Pharmaceuticals, Inc. ("Janssen"). Pursuant to the agreement, Janssen has an exclusive worldwide license to develop and commercialize certain drug candidates for the treatment of influenza, including pimodivir. The Company recognized a $25.0 million milestone in 2017, based on a Phase 3 clinical trial that Janssen initiated.

Cystic Fibrosis Foundation

The Company has a research, development and commercialization agreement that was originally entered into in 2004 with Cystic Fibrosis Foundation ("CFF"), as successor in interest to the Cystic Fibrosis Foundation Therapeutics, Inc. This agreement was most recently amended in 2016 (the "2016 Amendment"). Pursuant to the agreement, as amended, the Company agreed to pay royalties ranging from low-single digits to mid-single digits on potential sales of certain compounds first synthesized and/or tested between March 1, 2014 and August 31, 2016, including elexacaftor, and 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 KALYDECO (ivacaftor), ORKAMBI (lumacaftor in combination with ivacaftor) and SYMDEKO/SYMKEVI (tezacaftor in combination with ivacaftor). For combination products, such as ORKAMBI, SYMDEKO/SYMKEVI and TRIKAFTA (elexacaftor, tezacaftor, and ivacaftor), sales are allocated equally to each of the active pharmaceutical ingredients in the combination product.

Pursuant to the 2016 Amendment, the Company received an upfront payment of$75.0 million and is receiving development funding fromCFF of up to $6.0 million annually. The Company concluded that the upfront payment plus any future development funding represent a form of financing pursuant to ASC 730 and thus records the amounts as a liability on the consolidated balance sheet, primarily reflected in “Other long-term liabilities.” The Company reduces this liability over the estimated royalty term of the agreement and reflects the reductions as an offset to “Cost of sales” and as “Interest expense.”

C. Acquisitions

Business Acquisitions

Exonics Therapeutics, Inc.

On July 16, 2019, the Company completed its acquisition of Exonics Therapeutics, Inc. (“Exonics”), a privately held biotechnology company focused on creating transformative gene-editing therapies to repair mutations that cause DMD and other severe neuromuscular diseases, including DM1. The Company acquired Exonics for an upfront payment of approximately $245.0 million, customary working capital adjustments and approximately $70.0 million in deferred payments. Exonics’ equity holders may receive an additional $728.0 million upon the successful achievement of specified development and regulatory milestones for the DMD and DM1 programs.

The Company concluded that Exonics’ intellectual property, assembled workforce and scientific expertise, has the potential to produce therapies for patients with DMD and DM1; therefore, it accounted for the acquisition as a business combination. The Company determined that the purchase price related to the Exonics business combination was $438.4 million, which consisted of (i) the upfront payment as adjusted for customary working capital adjustments, and (ii) the estimated fair value related to $678.3 million of contingent development and regulatory milestones attributable to the purchase of Exonics’ outstanding shares on July 16, 2019. The remaining portion, or $49.7 million, of the development and regulatory milestones and the $70.0 million in deferred payments were determined to be compensatory, as they relate to post-acquisition services, and will be expensed to “Research and development expenses” as incurred.

The purchase price consisted of the following:

	(in thousands)
Upfront payment (adjusted for customary working capital adjustments)	$ 266,315
Fair value of contingent development and regulatory payments	172,041
Total purchase price	$ 438,356

The Company’s methodology for determining the fair value of the contingent development and regulatory payments is described inNote E, “Fair Value Measurements.”

The Company allocated the purchase price to the following assets acquired and liabilities assumed:

	July 16, 2019 (in thousands)
Cash and cash equivalents	$ 19,535
Goodwill	397,141
Intangible asset	13,000
Net other assets	8,680
Total purchase price	$ 438,356

The “Goodwill” represents the difference between the fair value of the consideration transferred and the fair value of the assets and liabilities acquired. The goodwill was attributable to Exonics’ technological expertise, assembled workforce, the potential additional therapeutic programs that may be discovered utilizing Exonics’ DMD and DM1 programs and synergies from combining these programs with the Company's current gene-editing capabilities through its collaboration with CRISPR. None of the goodwill is expected to be deductible for income tax purposes. The "Intangible asset" is a single in-process research and development asset related to Exonics' DMD and DM1 programs. The Company concluded that the intangible asset was a single asset based on similarities between the DMD and DM1 programs including (i) their pre-clinical stage of development, (ii) the development activities and technologies necessary to further develop them, which will be managed on a combined basis, (iii) anticipated pricing and (iv) patient populations. The fair value of the intangible asset was determined through a discounted cash flow analysis utilizing Level 3 fair value inputs related to the development and commercialization of therapies for DMD and DM1. As of December 31, 2019, the Company's accounting for the Exonics business combination is complete.

Semma Therapeutics, Inc.

On October 10, 2019, the Company completed its acquisition of Semma Therapeutics, Inc. ("Semma"), a privately held biotechnology company primarily focused on the use of stem cell-derived human islets as a potentially curative treatment for type 1 diabetes. The Company acquired Semma in exchange for a purchase price of $936.8 million.

The Company allocated the purchase price to the following assets acquired and liabilities assumed:

	October 10, 2019 (in thousands)	
Cash and cash equivalents	$	29,331
Property and equipment, net		17,111
Goodwill		554,633
Intangible assets		387,000
Deferred tax liability		(54,160)
Net other assets		2,849
Total purchase price	$	936,764

The "Goodwill" represents the difference between the fair value of the consideration transferred and the fair value of the assets and liabilities acquired. The goodwill was attributable to the technological expertise in cell therapy of Semma's assembled workforce, the potential synergies from combining Semma's proprietary platform with the Company's clinical development capabilities and the potential additional therapeutic programs that may be discovered utilizing Semma's proprietary platform. None of the goodwill is expected to be deductible for income tax purposes.

The "Intangible assets" are in-process research and development assets of$379.0 million and $8.0 million related to Semma's pre-clinical treatments for device-assisted cells and naked islets, respectively. Semma produces human pancreatic beta cells, or islets, that could potentially help type 1 diabetes patients produce appropriate levels of insulin and safely control hypoglycemia. The "naked islets treatment" is intended for a small portion of the type 1 diabetes patient population who are already receiving immunosuppression therapy and can receive the islets without their immune system destroying them. For the majority of type 1 diabetes patients, who are not receiving immunosuppression therapy, Semma is seeking to develop a "device-assisted cells treatment" alternative, which includes a novel device that is designed to encapsulate and protect the islets from the immune system. The device could potentially enable durable implantation without the need for ongoing immunosuppressive therapy.

The Company determined that device-assisted cells and the naked islets were two separate assets based on, among other things, (i) the separate type 1 diabetes patient populations expected to receive the treatments and (ii) the clinical and regulatory risks and costs associated with developing the islets versus developing and manufacturing the device.

The fair values of the intangible assets were determined through a discounted cash flow analysis utilizing Level 3 fair value inputs including (i) assumptions regarding the probability of obtaining marketing approval for the treatments;(ii) estimates regarding the timing of and the expected costs to develop and commercialize the treatments; (iii) estimates of future cash flows from potential product sales with respect to treatments; and (iv) appropriate discount and tax rates.

The Company's "Deferred tax liability" in the table above is recorded as a reduction to "Deferred tax assets" on the Company's consolidated balance sheet.

As of December 31, 2019, the Company's accounting for the Exonics and Semma business combinations is complete. The Company has not provided pro forma information because the operations of Exonics and Semma did not have a material effect on its consolidated financial statements. The Company's consolidated financial statements reflect the operations of Exonics and Semma as of December 31, 2019 and for the periods from July 16, 2019 and October 10, 2019 to December 31, 2019, respectively.

Asset Acquisition

Concert Pharmaceuticals

In 2017, the Company acquired certain CF assets including VX-561 (the "Concert Assets") from Concert Pharmaceuticals Inc. ("Concert") pursuant to an asset purchase agreement (the "Concert Agreement"). VX-561 is an investigational CFTR potentiator that has the potential to be used as part of combination regimens of CFTR modulators to treat CF. Pursuant to the Concert Agreement, the Company paid Concert $160.0 million in cash for the Concert Assets. If VX-561 is approved as part of a combination regimen to treat CF, Concert could receive up to an additional $90.0 million in milestones based on regulatory approval in the United States and reimbursement in the United Kingdom, Germany or France. The Company determined that substantially all of the fair value of the Concert Agreement was attributable to a single in-process research and development asset, VX-561, which did not constitute a business. The Company concluded that it did not have any alternative future use for the acquired in-process research and development asset. Thus, the Company recorded the $160.0 million upfront payment to "Research and development expenses" in 2017. The total cost of the transaction was $165.1 million including $5.1 million of transaction costs that were recorded to "Sales, general and administrative expenses."

D. Earnings Per Share

Basic net income per share attributable to Vertex common shareholders is based upon the weighted-average number of common shares outstanding during the period, excluding restricted stock, restricted stock units and performance-based restricted stock units, or "PSUs," that have been issued but are not yet vested. Diluted net income per share attributable to Vertex common shareholders 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.

The following table sets forth the computation of basic and diluted net income per share for the periods ended:

	2019	2018	2017
	(in thousands, except per share amounts)		
Basic net income attributable to Vertex per common share calculation:			
Net income attributable to Vertex common shareholders	$ 1,176,810	$ 2,096,896	$ 263,484
Less: Undistributed earnings allocated to participating securities	—	(501)	(293)
Net income attributable to Vertex common shareholders—basic	$ 1,176,810	$ 2,096,395	$ 263,191
Basic weighted-average common shares outstanding	256,728	254,292	248,858
Basic net income attributable to Vertex per common share	$ 4.58	$ 8.24	$ 1.06
Diluted net income attributable to Vertex per common share calculation:			
Net income attributable to Vertex common shareholders	$ 1,176,810	$ 2,096,896	$ 263,484
Less: Undistributed earnings allocated to participating securities	—	(492)	(288)
Net income attributable to Vertex common shareholders—diluted	$ 1,176,810	$ 2,096,404	$ 263,196
Weighted-average shares used to compute basic net income per common share	256,728	254,292	248,858
Effect of potentially dilutive securities:			
Stock options	2,231	2,913	2,797
Restricted stock and restricted stock units (including PSUs)	1,700	1,963	1,542
Employee stock purchase program	14	17	28
Weighted-average shares used to compute diluted net income per common share	260,673	259,185	253,225
Diluted net income attributable to Vertex per common share	$ 4.51	$ 8.09	$ 1.04

The Company did not include the securities in the following table in the computation of the net income per share attributable to Vertex common shareholders calculations because the effect would have been anti-dilutive during each period.

	2019	2018	2017
		(in thousands)	
Stock options	2,833	2,217	3,554
Unvested restricted stock and restricted stock units (including PSUs)	6	5	411

E. Fair Value Measurements

The fair value of the Company's financial assets and liabilities reflects the Company's estimate of amounts that it would have received in connection with the sale of the assets or paid in connection with the transfer of the liabilities in an orderly transaction between market participants at the measurement date. In connection with measuring the fair value of its assets and liabilities, the Company seeks to maximize the use of observable inputs (market data obtained from sources independent from the Company) and to minimize the use of unobservable inputs (the Company's assumptions about how market participants would price assets and liabilities). The following fair value hierarchy is used to classify assets and liabilities based on the observable inputs and unobservable inputs used in order to value the 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 the Company's assessment of the assumptions that market participants would use in pricing the asset or liability.

The Company's investment strategy is focused on capital preservation. The Company invests in instruments that meet the credit quality standards outlined in the Company's investment policy. This policy also limits the amount of credit exposure to any one issue or type of instrument. The Company maintains strategic investments separately from the investment policy that governs its other cash, cash equivalents and marketable securities as described in Note F, "Marketable Securities and Equity Investments." As of December 31, 2019, the Company's investments were in money market funds, government-sponsored enterprise securities, corporate debt securities, commercial paper and corporate equity securities. Additionally, the Company utilizes foreign currency forward contracts intended to mitigate the effect of changes in foreign exchange rates on its consolidated statement of operations.

As of December 31, 2019, the Company's financial assets and liabilities that were subject to fair value measurements were valued using both observable and unobservable inputs. The Company's financial assets valued based on Level 1 inputs consisted of money market funds, government-sponsored enterprise securities and corporate equity securities. The Company's financial assets and liabilities valued based on Level 2 inputs consisted of certain corporate equity securities as described below, corporate debt securities, commercial paper, which consisted of investments in highly-rated investment-grade corporations and foreign currency forward contracts with reputable and creditworthy counterparties. As discussed further below, the Company's financial liabilities valued based on Level 3 inputs consisted of acquisition related contingent milestones. During 2019, 2018 and 2017, the Company did not record any other-than-temporary impairment charges related to its financial assets.

The following tables set forth the Company's financial assets and liabilities subject to fair value measurements (and does not include $2.3 billion and $1.4 billion of cash as of December 31, 2019 and 2018, respectively):

	Fair Value Measurements as of December 31, 2019			
		Fair Value Hierarchy		
	Total	Level 1	Level 2	Level 3
	(in thousands)			
Financial instruments carried at fair value (asset position):				
Cash equivalents:				
Money market funds	$ 791,039	$ 791,039	$ —	$ —
Corporate debt securities	6,070	—	6,070	—
Commercial paper	29,472	—	29,472	—
Marketable securities:				
Corporate equity securities	282,084	261,797	20,287	—
Government-sponsored enterprise securities	12,733	12,733	—	—
Corporate debt securities	301,799	—	301,799	—
Commercial paper	102,356	—	102,356	—
Prepaid expenses and other current assets:				
Foreign currency forward contracts	9,725	—	9,725	—
Total financial assets	$ 1,535,278	$ 1,065,569	$ 469,709	$ —
Financial instruments carried at fair value (liability position):				
Other current liabilities:				
Foreign currency forward contracts	$ (5,533)	$ —	$ (5,533)	$ —
Long-term contingent consideration	(176,500)	—	—	(176,500)
Other long-term liabilities:				
Foreign currency forward contracts	(1,821)	—	(1,821)	—
Total financial liabilities	$ (183,854)	$ —	$ (7,354)	$ (176,500)

	Fair Value Measurements as of December 31, 2018			
		Fair Value Hierarchy		
	Total	Level 1	Level 2	Level 3
	(in thousands)			
Financial instruments carried at fair value (asset position):				
Cash equivalents:				
Money market funds	$ 1,226,603	$ 1,226,603	$ —	$ —
U.S. Treasury securities	5,966	5,966	—	—
Government-sponsored enterprise securities	7,123	7,123	—	—
Commercial paper	58,268	—	58,268	—
Marketable securities:				
Corporate equity securities	167,323	153,733	13,590	—
U.S. Treasury securities	6,026	6,026	—	—
Government-sponsored enterprise securities	10,704	10,704	—	—
Corporate debt securities	233,665	—	233,665	—
Commercial paper	100,390	—	100,390	—
Prepaid expenses and other current assets:				
Foreign currency forward contracts	19,023	—	19,023	—
Other assets:				
Foreign currency forward contracts	1,514	—	1,514	—
Total financial assets	$ 1,836,605	$ 1,410,155	$ 426,450	$ —
Financial instruments carried at fair value (liability position):				
Other current liabilities:				
Foreign currency forward contracts	$ (340)	$ —	$ (340)	$ —
Other long-term liabilities:				
Foreign currency forward contracts	(108)	—	(108)	—
Total financial liabilities	$ (448)	$ —	$ (448)	$ —

Please refer to Note F, “Marketable Securities and Equity Investments,” for the carrying amount and related unrealized gains (losses) by type of investment.

Fair Value of Corporate Equity Securities

The Company maintains strategic investments in corporate equity securities separately from the investment policy that governs its other cash, cash equivalents and marketable securities. The Company classifies its investments in publicly traded companies as “Marketable securities” on its consolidated balance sheets. Generally, the Company’s investments in the common stock of these publicly traded companies are valued based on Level 1 inputs because they have readily determinable fair values. However, certain of the Company’s 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. During the year ended December 31, 2019, the Company transferred the fair value of one of its strategic investments in a publicly traded company from Level 2 to Level 1 upon the expiration of transfer restrictions associated with this investment. Please refer to Note F, “Marketable Securities and Equity Investments,” for further information on these investments.

Fair Value of Contingent Consideration

The Company’s contingent consideration liabilities, which are related to development and regulatory milestones potentially payable to Exonics’ former equity holders, are classified as Level 3 within the valuation hierarchy. The Company bases its estimates of the probability of achieving the milestones relevant to the fair value of contingent payments on industry data attributable to rare diseases. The discount rates used in the valuation model for contingent payments represent a measure of credit risk and market risk associated with settling the liabilities. 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 a drug candidate in the pharmaceutical industry, the Company's estimates regarding the fair value of contingent consideration will change in the future, resulting in adjustments to the fair value of the Company’s contingent consideration liabilities, and the effect of any such adjustments could be material.

The following table represents a rollforward of the fair value of the Company’s contingent consideration liabilities:

	Year Ended December 31, 2019
	(in thousands)
Balance at December 31, 2018	$ —
Contingent consideration related to acquisition of Exonics	172,041
Increase in fair value of contingent payments	4,459
Balance at December 31, 2019	$ 176,500

The “Increase in fair value of contingent payments” in the table above was due to changes in market interest rates and the time value of money.

Fair Value of Intangible Asset

The fair value of the Company’s in-process research and development intangible assets, which totaled$400.0 million as of December 31, 2019, was determined through discounted cash flow models utilizing Level 3 fair value inputs. Please refer to Note C, “Acquisitions,” for further information on the key assumptions utilized to determine the fair value of the in-process research and development assets that the Company acquired as a result of its acquisitions of Semma and Exonics in 2019.

F. Marketable Securities and Equity Investments

A summary of the Company's cash equivalents and marketable securities, which are recorded at fair value (and do not include $2.3 billion and $1.4 billion of cash as of December 31, 2019 and 2018, respectively), is shown below:

	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
	(in thousands)			
As of December 31, 2019				
Cash equivalents:				
Money market funds	$ 791,039	$ —	$ —	$ 791,039
Corporate debt securities	6,070	—	—	6,070
Commercial paper	29,470	3	(1)	29,472
Total cash equivalents	826,579	3	(1)	826,581
Marketable securities:				
Government-sponsored enterprise securities	12,689	44	—	12,733
Corporate debt securities	301,458	391	(50)	301,799
Commercial paper	102,240	121	(5)	102,356
Total marketable debt securities	416,387	556	(55)	416,888
Corporate equity securities	113,829	168,255	—	282,084
Total marketable securities	$ 530,216	$ 168,811	$ (55)	$ 698,972
As of December 31, 2018				
Cash equivalents:				
Money market funds	$ 1,226,603	$ —	$ —	$ 1,226,603
U.S. Treasury securities	5,967	—	(1)	5,966
Government-sponsored enterprise securities	7,124	—	(1)	7,123
Commercial paper	58,271	—	(3)	58,268
Total cash equivalents	1,297,965	—	(5)	1,297,960
Marketable securities:				
U.S Treasury securities	6,026	—	—	6,026
Government-sponsored enterprise securities	10,704	—	—	10,704
Corporate debt securities	234,088	27	(450)	233,665
Commercial paper	100,498	—	(108)	100,390
Total marketable debt securities	351,316	27	(558)	350,785
Corporate equity securities	133,157	40,619	(6,453)	167,323
Total marketable securities	$ 484,473	$ 40,646	$ (7,011)	$ 518,108

Available-for-sale debt securities were classified on the Company's consolidated balance sheets as follows:

	As of December 31,	
	2019	2018
	(in thousands)	
Cash and cash equivalents	$ 826,581	$ 1,297,960
Marketable securities	416,888	350,785
Total	$ 1,243,469	$ 1,648,745

Available-for-sale debt securities by contractual maturity were as follows:

	As of December 31,	
	2019	2018
	(in thousands)	
Matures within one year	$ 1,137,942	$ 1,647,500
Matures after one year through five years	105,527	1,245
Total	$ 1,243,469	$ 1,648,745

The Company has a limited number of available-for-sale debt securities in insignificant loss positions as of December 31, 2019, which it does not intend to sell and has concluded it will not be required to sell before recovery of the amortized costs for the investments at maturity. The Company did not record any charges for other-than-temporary declines in the fair value of available-for-sale debt securities or gross realized gains or losses in 2019, 2018 or 2017.

As of December 31, 2019 and 2018, the total fair value of the Company's strategic investments in the common stock of publicly traded companies, which was primarily related to its investment in CRISPR, was $282.1 million and $167.3 million, respectively, and was classified as "Marketable securities" on its consolidated balance sheets.

Pursuant to the adoption of ASU 2016-01 on January 1, 2018, the Company began recording changes in the fair value of its investments in strategic corporate equity securities, which are primarily attributable to its investment in CRISPR, to "Other income (expense), net" in the Company's consolidated statements of operations. Prior to its adoption of ASU 2016-01, the Company recorded changes in the fair value of its investments in corporate equity securities to "Accumulated other comprehensive (loss) income" on its consolidated balance sheet until the related gains or losses were realized. The Company continues to record unrealized gains (losses) on available-for-sale debt securities as a component of "Accumulated other comprehensive (loss) income" until such gains and losses are realized.

During the year ended December 31, 2019 and 2018, the Company recorded unrealized gains of $132.5 million and $2.6 million, respectively, which were primarily related to the Company's strategic investment in CRISPR. As noted above, unrealized gains or losses were recorded to "Accumulated other comprehensive (loss) income" during the year ended December 31, 2017.

During the year ended December 31, 2019, the Company recorded realized gains of $65.1 million related to sales of CRISPR's common stock. The Company utilized a weighted-average cost basis to calculate the realized gain. There were no sales of CRISPR's common stock in the years ended December 31, 2018 or 2017.

As of December 31, 2019, the carrying value of the Company's equity investments without readily determinable fair values, which are recorded in "Other assets" on its consolidated balance sheets, was $40.8 million.

G. Accumulated Other Comprehensive Income (Loss)

The following table summarizes the changes in accumulated other comprehensive income (loss) by component:

	Foreign Currency Translation Adjustment	Unrealized Holding Gains (Losses), Net of Tax: On Available-For-Sale Debt Securities	On Equity Securities	On Foreign Currency Forward Contracts	Total
			(in thousands)		
Balance at December 31, 2016	$ (7,862)	$ (10)	$ 17,531	$ 11,514	$ 21,173
Other comprehensive (loss) income before reclassifications	(13,169)	(584)	7,538	(29,175)	(35,390)
Amounts reclassified from accumulated other comprehensive income (loss)	—	—	—	2,645	2,645
Net current period other comprehensive (loss) income	(13,169)	(584)	7,538	(26,530)	(32,745)
Balance at December 31, 2017	$ (21,031)	$ (594)	$ 25,069	$ (15,016)	$ (11,572)
Other comprehensive income before reclassifications	8,855	58	—	25,664	34,577
Amounts reclassified from accumulated other comprehensive income (loss)	—	—	—	1,774	1,774
Net current period other comprehensive income	8,855	58	—	27,438	36,351
Amounts reclassified to accumulated deficit pursuant to adoption of new accounting standard	949	—	(25,069)	—	(24,120)
Balance as of December 31, 2018	$ (11,227)	$ (536)	$ —	$ 12,422	$ 659
Other comprehensive income before reclassifications	10,332	1,039	—	11,513	22,884
Amounts reclassified from accumulated other comprehensive income (loss)	—	—	—	(25,516)	(25,516)
Net current period other comprehensive income (loss)	10,332	1,039	—	(14,003)	(2,632)
Balance as of December 31, 2019	$ (895)	$ 503	$ —	$ (1,581)	$ (1,973)

H. Hedging

Foreign currency forward contracts - Designated as hedging instruments

The Company maintains a hedging program intended to mitigate the effect of changes in foreign exchange rates for a portion of the Company’s forecasted product revenues denominated in certain foreign currencies. The program includes foreign currency forward contracts that are designated as cash flow hedges under GAAP having contractual durations from one to eighteen months. The Company recognizes realized gains and losses for the effective portion of such contracts in “Product revenues, net” in its consolidated statements of operations in the same period that it recognizes the product revenues that were impacted by the hedged foreign exchange rate changes.

The Company formally documents the relationship between foreign currency forward contracts (hedging instruments) and forecasted product revenues (hedged items), as well as the Company’s 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. The Company also formally assesses, 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 the Company 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, the Company would discontinue hedge accounting treatment prospectively. The Company measures 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, 2019, all hedges were determined to be highly effective.

Prior to the adoption of ASU 2017-12 on January 1, 2019, the Company did not record any ineffectiveness related to its foreign currency forward contracts that were designated as hedging instruments in the years ended December 31, 2018 and 2017. ASU 2017-12 eliminated the requirement to separately measure and report hedge ineffectiveness.

The Company considers the impact of its counterparties' credit risk on the fair value of the foreign currency forward contracts. As of December 31, 2019 and December 31, 2018, credit risk did not change the fair value of the Company's foreign currency forward contracts.

The following table summarizes the notional amount of the Company's outstanding foreign currency forward contracts designated as cash flow hedges under GAAP:

	As of December 31,	
	2019	2018
Foreign Currency	(in thousands)	
Euro	$ 501,197	$ 335,179
Australian dollar	89,705	52,820
British pound sterling	87,032	73,460
Canadian dollar	50,452	43,759
Total foreign currency forward contracts	$ 728,386	$ 505,218

Foreign currency forward contracts - Not designated as hedging instruments

The Company also enters into foreign currency forward contracts with contractual maturities of less thanone month that 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 GAAP. The Company recognizes realized gains and losses for such contracts in "Other income (expense), net" in its consolidated statements of operations each period. As of December 31, 2019, the notional amount of the Company's outstanding foreign currency forward contracts where hedge accounting under GAAP is not applied was $412.1 million.

During the three years ended December 31, 2019, the Company recognized the following related to foreign currency forward contacts in its consolidated statements of operations:

	December 31,		
	2019	2018	2017
	(in thousands)		
Designated as hedging instruments - Reclassified from AOCI			
Product revenues, net	$ 32,546	$ (1,252)	$ 768
Not designated as hedging instruments			
Other income (expense), net	$ 4,838	$ 623	$ 14,129
Total reported in the Consolidated Statement of Operations			
Product revenues, net	$ 4,160,726	$ 3,038,325	$ 2,165,480
Other income (expense), net	$ 192,177	$ (790)	$ (81,382)

The following table summarizes the fair value of the Company's outstanding foreign currency forward contracts designated as cash flow hedges under GAAP included on its consolidated balance sheets:

As of December 31, 2019						
Assets			**Liabilities**			
Classification	**Fair Value**		**Classification**	**Fair Value**		
	(in thousands)					
Prepaid expenses and other current assets	$	9,725	Other current liabilities	$	(5,533)	
Other assets		—	Other long-term liabilities		(1,821)	
Total assets	$	9,725	Total liabilities	$	(7,354)	

As of December 31, 2018					
Assets			**Liabilities**		
Classification	**Fair Value**		**Classification**	**Fair Value**	
	(in thousands)				
Prepaid expenses and other current assets	$	19,023	Other current liabilities	$	(340)
Other assets		1,514	Other long-term liabilities		(108)
Total assets	$	20,537	Total liabilities	$	(448)

As of December 31, 2019, the Company expects amounts that are related to foreign exchange forward contracts designated as cash flow hedges under GAAP recorded in "Prepaid expenses and other current assets" and "Other current liabilities" to be reclassified to earnings within twelve months.

The following table summarizes the potential effect of offsetting derivatives by type of financial instrument designated as cash flow hedges under GAAP on the Company's consolidated balance sheets:

	As of December 31, 2019				
	Gross Amounts Recognized	**Gross Amounts Offset**	**Gross Amounts Presented**	**Gross Amounts Not Offset**	**Legal Offset**
Foreign currency forward contracts	**(in thousands)**				
Total assets	$ 9,725	$ —	$ 9,725	$ (7,354)	$ 2,371
Total liabilities	(7,354)	—	(7,354)	7,354	—

	As of December 31, 2018				
	Gross Amounts Recognized	**Gross Amounts Offset**	**Gross Amounts Presented**	**Gross Amounts Not Offset**	**Legal Offset**
Foreign currency forward contracts	**(in thousands)**				
Total assets	$ 20,537	$ —	$ 20,537	$ (448)	$ 20,089
Total liabilities	(448)	—	(448)	448	—

I. Inventories

Inventories consisted of the following:

	As of December 31,	
	2019	**2018**
	(in thousands)	
Raw materials	$ 26,247	$ 9,677
Work-in-process	107,021	87,944
Finished goods	34,234	26,739
Total	$ 167,502	$ 124,360

J. Property and Equipment

Property and equipment, net consisted of the following:

	As of December 31,	
	2019	2018
	(in thousands)	
Buildings	$ 648,003	$ 657,438
Furniture and equipment	317,567	280,908
Software	167,547	162,601
Leasehold improvements	241,178	103,428
Computers	63,325	59,073
Total property and equipment, gross	1,437,620	1,263,448
Less: accumulated depreciation	(692,540)	(451,443)
Total property and equipment, net	$ 745,080	$ 812,005

The Company recorded depreciation expense of $106.9 million, $72.4 million and $61.4 million in 2019, 2018 and 2017, respectively. The Company's capital lease amortization is included in depreciation expense.

K. Intangible Assets and Goodwill

Intangible Assets

As of December 31, 2019, the Company had $400.0 million of in-process research and development intangible assets classified as 'Other assets" on its consolidated balance sheet. As of December 31, 2018, the Company had no in-process research and development intangible assets recorded on its consolidated balance sheet. In 2019, the Company recorded $387.0 million and $13.0 million of in-process research and development intangible assets related to its acquisitions of Semma and Exonics, respectively. In 2018 and 2017, the Company recorded intangible asset impairment charges of $29.0 million related to VX-210 that was licensed from BioAxone in 2014 and $255.3 million related to Parion's pulmonary ENaC platform, respectively. Please refer to Note B, "Collaborative Arrangements," for further information regarding the events and circumstances associated with these impairment charges.

Goodwill

As of December 31, 2019 and December 31, 2018, goodwill of $1.00 billion and $50.4 million was recorded on the Company's consolidated balance sheet. During 2019, the Company recorded goodwill of $554.6 million and $397.1 million related to its acquisitions of Semma and Exonics, respectively.

Please refer to "Note C, "Acquisitions," for further information on the in-process research and development intangible assets and goodwill that the Company acquired in 2019.

L. Additional Balance Sheet Detail

Accrued expenses consisted of the following:

	As of December 31,	
	2019	2018
	(in thousands)	
Payroll and benefits	$ 159,464	$ 124,753
Research, development and commercial contract costs	105,663	115,300
Product revenue allowances	641,368	550,002
Royalty payable	98,578	101,108
Tax related accruals	72,293	43,281
Other	39,546	24,455
Total	$ 1,116,912	$ 958,899

Other current liabilities consisted of the following:

	As of December 31,	
	2019	2018
	(in thousands)	
Contract liabilities	$ 62,332	$ 24,870
Finance lease liabilities	30,293	5,271
Other	37,680	20,265
Total	$ 130,305	$ 50,406

Other long-term liabilities consisted of the following:

	As of December 31,	
	2019	2018
	(in thousands)	
Advance from collaborator	$ 88,762	$ 82,573
Operating lease liabilities	84,292	—
Other	10,264	26,280
Total	$ 183,318	$ 108,853

M. Leases

Finance Leases

The Company’s finance lease assets and liabilities primarily relate to its corporate headquarters in Boston and research site in San Diego (the “Buildings”). These Buildings are classified as finance leases because the present value of the sum of the lease payments associated with the Buildings exceeds substantially all of the fair value of the Buildings. The Company also has outstanding finance leases for equipment.

Prior to the adoption of ASC 842 on January 1, 2019, the Company was deemed for accounting purposes to be the owner of the Buildings during their construction periods and recorded project construction costs incurred by its landlords. Upon completion of the Buildings, the Company determined that the underlying leases did not meet the criteria for “sale-leaseback” treatment. Accordingly, the Company depreciated the Buildings over 40 years and recorded interest expense associated with the financing obligations for the Buildings. The Company bifurcated the lease payments pursuant to the Buildings into (i) a portion that was allocated to the Buildings and (ii) a portion that is allocated to the land on which the Buildings were constructed. The portion of the lease obligations allocated to the land was treated as an operating lease.

Pursuant to ASC 842, the Company adjusted the amounts recorded on its consolidated balance sheet as of January 1, 2019 for the Buildings to reflect the present value of the lease payments over the remaining lease term related to the Buildings. The finance lease assets associated with the Buildings are amortized to depreciation expense using the straight-line method over the remaining lease term, which is significantly shorter than the Buildings' useful lives. The Company continues to record interest expense associated with the finance lease liabilities for the Buildings.

Corporate Headquarters

In 2011, the Company entered into two lease agreements, pursuant to which the Company leases approximately 1.1 million square feet of office and laboratory space in two buildings in Boston, Massachusetts for a term of 15 years. Base rent payments commenced in December 2013, and will continue through December 2028. The Company utilizes this initial period as its lease term. The Company has an option to extend the lease term for an additional ten years.

San Diego Lease

In 2015, the Company entered into a lease agreement pursuant to which the Company leases approximately 170,000 square feet of office and laboratory space in San Diego, California for a term of 16 years. Base rent payments commenced in the second quarter of 2019, and will continue through May 2034. The Company utilizes this initial period as its lease term. The Company has an option to extend the lease term for up to two additional five-year terms. The Company placed this building into service in the second quarter of 2018.

Operating Leases

The Company's operating leases relate to its real estate leases that are not classified as finance leases.

Aggregate Lease Information Related to the Application of ASC 842

The following information is disclosed in accordance with ASC 842, which became effective January 1, 2019. The components of lease cost recorded in the Company's consolidated statement of operations were as follows:

		2019
Operating lease cost	$	11,972
Finance lease cost		
Amortization of leased assets		49,778
Interest on lease liabilities		52,839
Variable lease cost		27,997
Sublease income		(6,391)
Net lease cost	$	136,195

The Company's variable lease cost during 2019 primarily related to operating expenses, taxes and insurance associated with its finance leases. The Company's sublease income during 2019 primarily related to subleases for an insignificant portion of the Company's corporate headquarters.

The Company’s leases are included on its consolidated balance sheets as follows:

	As of December 31, 2019	As of December 31, 2018 ^
	(in thousands)	
Finance leases		
Property and equipment, net	$ 445,336	$ 640,952
Total finance lease assets	$ 445,336	$ 640,952
Capital lease obligations, current portion	$ —	$ 9,817
Other current liabilities	38,795	5,271
Capital lease obligations, excluding current portion	—	19,658
Construction financing lease obligation, excluding current portion	—	561,892
Long-term finance lease liabilities	538,576	—
Total finance lease liabilities	$ 577,371	$ 596,638
Operating leases		
Other assets	$ 88,202	$ —
Total operating lease assets	$ 88,202	$ —
Other current liabilities	$ 11,504	$ —
Other long-term liabilities	84,292	—
Total operating lease liabilities	$ 95,796	$ —

^ As reported in the Company’s 2018 Annual Report on Form 10-K.

Maturities of the Company’s finance and operating lease liabilities in accordance with ASC 842 as ofDecember 31, 2019 were as follows:

Year	Finance Leases	Operating Leases	Total
		(in thousands)	
2020	$ 84,264	$ 14,598	$ 98,862
2021	89,440	12,907	102,347
2022	87,092	12,610	99,702
2023	85,257	12,451	97,708
2024	90,802	11,488	102,290
Thereafter	425,251	51,251	476,502
Total lease payments	862,106	115,305	977,411
Less: amount representing interest	(284,735)	(19,509)	(304,244)
Present value of lease liabilities	$ 577,371	$ 95,796	$ 673,167

The weighted-average remaining lease terms and discount rates related to the Company’s leases were as follows:

	As of December 31, 2019
Weighted-average remaining lease term (in years)	
Finance leases	9.74
Operating leases	9.70
Weighted-average discount rate	
Finance leases	9.04%
Operating leases	3.75%

Supplemental cash flow information related to the Company's leases was as follows:

		December 31, 2019
		(in thousands)
Cash paid for amounts included in the measurement of lease liabilities:		
Operating cash flows from operating leases	$	10,650
Operating cash flows from finance leases	$	50,527
Financing cash flows from finance leases	$	39,185
Right-of-use assets obtained in exchange for lease obligations		
Operating leases *	$	34,605
Finance leases	$	—

* Includes $33.7 million acquired in 2019 pursuant to the Company's acquisitions of Semma and Exonics.

Additional Lease Information Related to the Application of ASC 840

The following information is disclosed in accordance with ASC 840, Leases (Topic 840) ("ASC 840"), which was applicable until December 31, 2018. As of December 31, 2018, future minimum commitments under the Company's real estate leases with initial terms of more than one year were as follows:

Year		Fan Pier Leases		Other Leases		Total Lease Commitments
				(in thousands)		
2019	$	66,540	$	18,531	$	85,071
2020		72,589		23,397		95,986
2021		72,589		21,656		94,245
2022		72,589		21,172		93,761
2023		72,589		21,482		94,071
Thereafter		389,855		185,336		575,191
Total minimum lease payments	$	746,751	$	291,574	$	1,038,325

As of December 31, 2018, the Company's total sublease income to be received related to its facility leases was $6.2 million. During 2018 and 2017, rental expenses were $17.3 million and $19.2 million, respectively.

The capital leases, which were related to equipment and leasehold improvements, bore interest at rates ranging from less than 1% to 6% per year. The Company's capital lease amortization was included in depreciation expense during 2018 and 2017. The following table set forth the Company's future minimum payments due under capital leases as of December 31, 2018:

Year		(in thousands)
2019	$	10,770
2020		7,282
2021		5,649
2022		3,300
2023		1,974
Thereafter		3,085
Total payments		32,060
Less: amount representing interest		(2,585)
Present value of payments	$	29,475

N. Common Stock, Preferred Stock and Equity Plans

Common Stock and Preferred Stock

The Company is authorized to issue 500,000,000 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 the Company's Board of Directors, and to share ratably in the Company's assets legally available for distribution to the Company's 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.

The Company is authorized to issue 1,000,000 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 the Company's shareholders. As of December 31, 2019 and 2018, the Company had no shares of preferred stock issued or outstanding.

Share Repurchase Program

During 2018, the Company's Board of Directors approved a share repurchase program (the "2018 Share Repurchase Program"), pursuant to which the Company was authorized to repurchase up to $500.0 million of its common stock between February 1, 2018 and December 31, 2019.

During the years ended December 31, 2019 and 2018, the Company repurchased 832,186 and 2,093,891 shares, respectively, of its common stock under the 2018 Share Repurchase Program for an aggregate of $150.0 million and $350.0 million, respectively, including commissions and fees. As of June 30, 2019, the Company had repurchased the entire $500.0 million it was authorized to repurchase of its common stock under the 2018 Share Repurchase Program.

In July 2019, the Company's Board of Directors approved a new share repurchase program (the "2019 Share Repurchase Program"), pursuant to which the Company is authorized to repurchase up to $500.0 million of its common stock between August 1, 2019 and December 31, 2020. The Company expects to fund further repurchases of its common stock through a combination of cash on hand and cash generated by operations. During the year ended December 31, 2019, the Company repurchased 213,548 shares of its common stock under the 2019 Share Repurchase Program for an aggregate of$36.0 million including commissions and fees. As of December 31, 2019, there is a total of $464.0 million remaining for repurchases under the 2019 Share Repurchase Program.

Under the 2018 and 2019 Share Repurchase Programs, the Company is authorized to purchase shares from time to time through open market or privately negotiated transactions. Such purchases are made pursuant to Rule 10b5-1 plans or other means as determined by the Company's management and in accordance with the requirements of the SEC.

Stock and Option Plans

The purpose of each of the Company's stock and option plans is to attract, retain and motivate its employees, consultants and directors. Awards granted under these plans can be nonstatutory stock options ("NSOs"), incentive stock options ("ISOs"), restricted stock units ("RSUs") including performance-based RSUs ("PSUs"), restricted stock ("RSs"), or other equity-based awards, as specified in the individual plans.

Shares issued under all of the Company's plans are funded through the issuance of new shares. The following table contains information about the Company's equity plans:

			As of December 31, 2019	
Title of Plan	**Group Eligible**	**Type of Award Granted**	**Awards Outstanding**	**Additional Awards Authorized for Grant**
2013 Stock and Option Plan	Employees, Non-employee Directors and Consultants	NSO, RS, RSU and PSU	9,577,268	15,778,703
2006 Stock and Option Plan	Employees, Non-employee Directors and Consultants	NSO, RS and RSU	651,842	—
		Total	10,229,110	15,778,703

All options granted under the Company's 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, 2019, the stock and option plan under which the Company is authorized to make new equity awards is the Company's 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. In the three years ended December 31, 2019, the Company's shareholders approved increases in the number of shares authorized for issuance pursuant to the 2013 Stock and Option Plan of (i) 5,000,000 shares in 2019, (ii) 8,000,000 shares in 2018 and (iii) 6,750,000 shares in 2017.

During the three years ended December 31, 2019, grants to current employees and directors primarily had a grant date that was the same as the date the award was approved by the Company's Board of Directors. During the three years ended December 31, 2019, for grants to new employees and directors, the date of grant for awards was the employee's first day of employment or the date the director was elected to the Company's Board of Directors. All options awarded under the Company's stock and option plans expire not more than 10 years from the grant date.

Stock Options

The following table summarizes information related to the outstanding and exercisable options during the year ended December 31, 2019:

	Stock Options	**Weighted-average Exercise Price**	**Weighted-average Remaining Contractual Life**	**Aggregate Intrinsic Value**
	(in thousands)	**(per share)**	**(in years)**	**(in thousands)**
Outstanding at December 31, 2018	8,551	$ 111.46		
Granted	1,521	$ 184.50		
Exercised	(3,327)	$ 95.57		
Forfeited	(467)	$ 146.59		
Expired	(6)	$ 182.96		
Outstanding at December 31, 2019	6,272	$ 134.92	7.12	$ 522,740
Exercisable at December 31, 2019	3,333	$ 114.15	6.06	$ 346,943

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 2019, which was $218.26 based on the average of the high and low price of the Company's 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 2019, 2018 and 2017 was $325.9 million, $258.2 million and $302.8 million, respectively. The total cash received by the Company as a result of employee stock option exercises during 2019, 2018 and 2017 was $317.8 million, $263.4 million and $323.3 million, respectively.

The following table summarizes information about stock options outstanding and exercisable at December 31, 2019:

	Options Outstanding				Options Exercisable	
Range of Exercise Prices	Number Outstanding	Weighted-average Remaining Contractual Life	Weighted-average Exercise Price		Number Exercisable	Weighted-average Exercise Price
	(in thousands)	(in years)	(per share)		(in thousands)	(per share)
$29.07–$40.00	108	1.58	$	37.62	108	$ 37.62
$40.01–$60.00	277	2.55	$	49.69	277	$ 49.69
$60.01–$80.00	140	4.31	$	74.55	136	$ 74.53
$80.01–$100.00	1,670	6.25	$	89.42	1144	$ 90.10
$100.01–$120.00	243	5.11	$	109.23	241	$ 109.17
$120.01–$140.00	454	5.67	$	129.77	447	$ 129.85
$140.01–$160.00	1,036	8.10	$	155.50	383	$ 155.39
$160.01–$180.00	720	8.46	$	168.04	233	$ 164.48
$180.01–$189.38	1,624	8.90	$	185.41	364	$ 184.85
Total	6,272	7.12	$	134.92	3,333	$ 114.15

Restricted Stock and Restricted Stock Units (excluding PSUs)

The following table summarizes the restricted stock unit and restricted stock activity of the Company during the year ended December 31, 2019:

	Restricted Stock Units (excluding PSUs)		Restricted Stock	
	Number of Shares	Weighted-average Grant-date Fair Value	Number of Units	Weighted-average Grant-date Fair Value
	(in thousands)	(per share)	(in thousands)	(per share)
Unvested at December 31, 2018	2,717	$ 140.10	480	$ 104.91
Granted	1,717	$ 181.87	—	$ —
Vested	(974)	$ 133.15	(375)	$ 108.23
Cancelled	(329)	$ 149.83	(13)	$ 100.79
Unvested at December 31, 2019	3,131	$ 163.61	92	$ 91.97

The total fair value of restricted stock units that vested during 2019, 2018 and 2017 (measured on the date of vesting) was $178.2 million, $104.8 million and $33.2 million, respectively. The total fair value of restricted stock that vested during 2019, 2018 and 2017 (measured on the date of vesting) was $70.7 million, $114.5 million and $157.0 million, respectively.

Performance-based RSUs (PSUs)

The potential range of shares issuable pursuant to the Company's PSU awards range from 0% to 200% of the target shares based on financial and non-financial measures. Fifty percent of PSUs that could be earned have a one-year performance period with the amount actually earned dependent upon the Company's financial performance and with vesting of the earned shares in three equal installments over a three-year period. The remaining 50% of PSUs that could be earned have a three-year performance period with the amount actually earned dependent upon the achievement of multiple clinical development milestones and with the earned shares cliff vesting at the end of the three-year performance period.

The following table summarizes the PSU activity of the Company during the year ended December 31, 2019:

	Performance-Based RSU		
	Number of Units		**Weighted-average Grant-date Fair Value**
	(in thousands)		**(per share)**
Unvested at December 31, 2018 (1)	759	$	110.50
Granted (2)	449	$	183.48
Vested	(403)	$	109.23
Cancelled	(71)	$	104.61
Unvested at December 31, 2019	734	$	143.21

(1) "Unvested" represents the Company's 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 2019 and (ii) any change in the number of shares issuable pursuant to outstanding PSUs based on performance certification during 2019.

The total fair value of PSUs that vested during 2019, 2018 and 2017 (measured on the date of vesting) was $73.3 million $23.2 million and $1.3 million, respectively.

Employee Stock Purchase Plan

The Company has 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 the Company's 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. During 2019, the Company's shareholders approved an increase in the number of shares authorized for issuance pursuant to the ESPP of 2,000,000 shares. As of December 31, 2019, there were 2,199,376 shares of common stock authorized for issuance pursuant to the ESPP.

In 2019, the following shares were issued to employees under the ESPP:

		Year Ended December 31, 2019
		(in thousands, except per share amount)
Number of shares		202,693
Average price paid per share	$	138.18

Employee Benefits

The Company has a 401(k) retirement plan (the "Vertex 401(k) Plan") in which substantially all of its 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. The Company may declare discretionary matching contributions to the Vertex 401(k) Plan. The Company pays matching contributions in the form of cash. For the years ended December 31, 2019, 2018 and 2017, the Company contributed approximately $15.8 million, $13.9 million and $12.3 million to the plan, respectively.

O. Stock-based Compensation Expense

The Company recognizes share-based payments to employees as compensation expense using the fair value method. The fair value of stock options and shares purchased pursuant to the ESPP is calculated using the Black-Scholes option pricing model. The fair value of restricted stock and restricted stock units, including PSUs, is based on the intrinsic value on the date of grant. Stock-based compensation, measured at the grant date based on the fair value of the award, is typically recognized as expense ratably over the requisite service period.

The effect of stock-based compensation expense during the three years ended December 31, 2019 was as follows:

	2019	2018	2017
	(in thousands)		
Stock-based compensation expense by line item:			
Cost of sales	$ 5,575	$ 4,543	$ 2,500
Research and development expenses	224,558	203,112	181,900
Sales, general and administrative expenses	130,356	117,392	108,836
Total stock-based compensation expense included in costs and expenses	360,489	325,047	293,236
Income tax effect	(124,225)	—	—
Total stock-based compensation included in costs and expenses, net of tax	$ 236,264	$ 325,047	$ 293,236

The Company maintained a valuation allowance on the majority of its NOLs and other deferred tax assets until December 31, 2018. Therefore, there was no "Income tax effect" of stock-based compensation expense for the years ended December 31, 2018 and 2017.

The stock-based compensation expense by type of award during the three years ended December 31, 2019 was as follows:

	2019	2018	2017
	(in thousands)		
Stock-based compensation expense by type of award:			
Restricted stock and restricted stock units (including PSUs)	$ 254,276	$ 207,845	$ 181,258
Stock options	96,737	107,854	105,367
ESPP share issuances	11,196	9,933	9,017
Stock-based compensation expense related to inventories	(1,720)	(585)	(2,406)
Total stock-based compensation expense included in costs and expenses	$ 360,489	$ 325,047	$ 293,236

The Company capitalizes stock-based compensation expense to inventories, all of which is attributable to employees who support the Company's manufacturing operations for the Company's products.

The following table sets forth the Company's unrecognized stock-based compensation expense as of December 31, 2019, by type of award and the weighted-average period over which that expense is expected to be recognized:

	As of December 31, 2019	
	Unrecognized Expense	Weighted-average Recognition Period
	(in thousands)	(in years)
Type of award:		
Restricted stock and restricted stock units (including PSUs)	$ 374,185	2.05
Stock options	$ 130,153	2.50
ESPP share issuances	$ 4,724	0.55

Stock Options

The Company issues stock options with service conditions, which are generally the vesting periods of the awards. The Company uses the Black-Scholes option pricing model to estimate the fair value of stock options at the grant date. The Black-Scholes option pricing model uses the option exercise price as well as estimates and assumptions related to the expected price volatility of the Company's stock, the rate of return on risk-free investments, the expected period during which the options will be outstanding, and the expected dividend yield for the Company's stock to estimate the fair value of a stock option on the grant date. The options granted during 2019, 2018 and 2017 had a weighted-average grant-date fair value per share of $61.32, $60.83 and $43.27, respectively.

The fair value of each option granted during 2019, 2018 and 2017 was estimated on the date of grant using the Black-Scholes option pricing model with the following weighted-average assumptions:

	2019	2018	2017
Expected stock price volatility	36.99%	40.50%	45.31%
Risk-free interest rate	2.32%	2.61%	1.94%
Expected term of options (in years)	4.27	4.55	4.68
Expected annual dividends	—	—	—

The weighted-average valuation assumptions were determined as follows:

- *Expected stock price volatility:* Expected stock price volatility is calculated using the trailing one month average of daily implied volatilities prior to the grant date. Implied volatility is based on options to purchase the Company's stock with remaining terms of greater than one year that are regularly traded in the market.
- *Risk-free interest rate:* The Company bases the risk-free interest rate on the interest rate payable on U.S. Treasury securities in effect at the time of grant for a period that is commensurate with the assumed expected option term.
- *Expected term of options:* The expected term of options represents the period of time options are expected to be outstanding. The Company uses historical data to estimate employee exercise and post-vest termination behavior. The Company believes that all groups of employees exhibit similar exercise and post-vest termination behavior and therefore does not stratify employees into multiple groups in determining the expected term of options.
- *Expected annual dividends:* The estimate for annual dividends is $0.00 because the Company has not historically paid, and does not intend for the foreseeable future to pay, a dividend.

Restricted Stock, Restricted Stock Units and Performance-based Restricted Stock Units

The Company awards restricted stock and restricted stock units with service conditions, which are generally the vesting periods of the awards.

The Company grants PSUs to certain members of senior management. Half of the PSUs contain financial goals as the performance metric and the other half contain non-financial goals. A target number of shares is established for each award, however the actual number of shares that are issued when an award vests may range from zero to 200% of the target amount depending upon the level of achievement of the applicable performance metric. The financial-based PSUs 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. The non-financial based PSUs cliff vest at the end of the 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.

Prior to 2017, the Company also awarded, to certain members of senior management, on an annual basis, restricted stock and restricted stock units that vested upon the earlier of the satisfaction of (i) a performance condition or (ii) a service condition.

Employee Stock Purchase Plan

The weighted-average fair value of each purchase right granted during 2019, 2018 and 2017 was $47.79, $44.04 and $35.90, respectively. The following table reflects the weighted-average assumptions used in the Black-Scholes option pricing model for 2019, 2018 and 2017:

	2019	2018	2017
Expected stock price volatility	33.43%	36.51%	39.09%
Risk-free interest rate	2.08%	2.36%	1.24%
Expected term (in years)	0.74	0.75	0.75
Expected annual dividends	—	—	—

The expected stock price volatility for ESPP offerings is based on implied volatility. The Company bases the risk-free interest rate on the interest rate payable on U.S. Treasury securities in effect at the time of grant for a period that is commensurate with the assumed expected term. The expected term represents purchases and purchase periods that take place within the offering period. The expected annual dividends estimate is $0.00 because the Company has not historically paid, and does not for the foreseeable future intend to pay, a dividend.

P. Income Taxes

The components of income (loss) before provision for (benefit from) income taxes during the three years ended December 31, 2019 consisted of the following:

	2019	2018	2017
		(in thousands)	
United States	$ 1,263,379	$ 812,086	$ 330,340
Foreign	131,540	(211,845)	(346,029)
Income (loss) before provision for (benefit from) income taxes	$ 1,394,919	$ 600,241	$ (15,689)

The components of the provision for (benefit from) income taxes during the three years ended December 31, 2019 consisted of the following:

	2019	2018	2017
		(in thousands)	
Current taxes:			
Federal	$ —	$ 772	$ 11,559
Foreign	37,194	15,600	3,576
State	13,528	9,018	5,025
Total current taxes	50,722	25,390	20,160
Deferred taxes:			
Federal	184,312	(1,105,053)	(113,805)
Foreign	(24,797)	(364,919)	(3,222)
State	7,872	(42,280)	(10,457)
Total deferred taxes	167,387	(1,512,252)	(127,484)
Provision for (benefit from) income taxes	$ 218,109	$ (1,486,862)	$ (107,324)

A reconciliation of the provision for (benefit from) income taxes as computed by applying the U.S. federal statutory rate of 21% for the years ended December 31, 2019 and 2018 and 35% for the year ended December 31, 2017 to the provision for (benefit from) income taxes is as follows:

	2019	2018	2017
		(in thousands)	
Income (loss) before provision for (benefit from) income taxes	$ 1,394,919	$ 600,241	$ (15,689)
Expected provision for (benefit from) income taxes	292,933	126,051	(5,491)
State taxes, net of federal benefit	8,478	8,680	4,742
Foreign income tax rate differential	6,178	23,427	77,801
Tax credits	(59,459)	(52,629)	(58,204)
Benefit from income taxes attributable to valuation allowances	(2,672)	(1,563,169)	(575,801)
Permanent items	4,822	1,421	15,324
Tax rate change	—	—	575,192
Stock compensation (benefit) shortfalls and cancellations	(56,324)	(49,044)	(21,453)
Officer’s compensation	10,666	8,310	6,501
Deconsolidation of VIE	—	(9,390)	(126,183)
Uncertain tax positions	14,070	15,431	—
Other	(583)	4,050	248
Provision for (benefit from) income taxes	$ 218,109	$ (1,486,862)	$ (107,324)

The Company is subject to U.S. federal, state, and foreign income taxes. The Company’s provision for income taxes in 2019 has increased compared to historical amounts due to the release of the Company’s valuation allowance on the majority of its NOLs and other deferred tax assets as of December 31, 2018. Starting in 2019, the Company began recording a provision for income taxes approximating statutory rates on its pre-tax income The Company’s effective tax rate for 2019 is lower than the U.S. statutory rate primarily due to excess tax benefits related to stock-based compensation and research and development tax credits partially offset by a change in the Company’s valuation allowance as well as the tax impact of officer compensation. Due to the Company's ability to offset its pre-tax income against previously benefited NOLs, the majority of its tax provision represents a non-cash expense until its NOLs have been fully utilized.

In 2019, the “Benefit from income taxes attributable to valuation allowances” in the tax rate reconciliation table above related to a release of a valuation allowance in the United Kingdom of $30.5 million related to the execution of a reimbursement agreement in France in November 2019, partially offset by an increase in the valuation allowance in the United States on state credits and NOLs. In 2018, the change in the “Benefit from income taxes attributable to valuation allowances” was primarily related to the release of the Company’s valuation allowances on the majority of its NOLs and other deferred tax assets related to the United States and the United Kingdom. In 2017, the “Benefit from income taxes attributable to valuation allowances” was primarily due to the utilization of NOLs in the United States and a decrease in the U.S. federal corporate tax rate from 35% to 21% partially offset by the adoption of ASU 2016-09.

In 2018 and 2017, “Deconsolidation of VIE” in the Company’s tax rate reconciliation above related to the impairments of VX-210 and Parion’s pulmonary ENaC platform, respectively, and the decreases in the Company’s fair value of the contingent payments to BioAxone and Parion associated with these deconsolidations, respectively. Please refer to Note K, “Intangible Assets and Goodwill,” for further information regarding these impairments.

The Company operates in foreign tax jurisdictions, which impose income taxes at different rates than the United States. The impact of these rate differences, which are primarily related to the Company’s operations in the United Kingdom, is included in the “Foreign income tax rate differential” in the Company’s tax rate reconciliation above. Other items that affected the Company’s tax rate reconciliation table were related to equity and executive compensation, research and development credits and Orphan Drug Credits during the three years ended December 31, 2019.

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,	
	2019	**2018**
	(in thousands)	
Deferred tax assets:		
Net operating loss	$ 512,256	$ 882,014
Tax credit carryforwards	549,543	487,635
Intangible assets	275,290	241,775
Deferred revenues	18,833	19,311
Stock-based compensation	85,199	93,915
Accrued expenses	44,367	17,795
Finance lease liabilities	119,160	130,849
Operating lease assets	13,114	—
Other	8,596	6,831
Gross deferred tax assets	1,626,358	1,880,125
Valuation allowance	(205,192)	(168,491)
Total deferred tax assets	1,421,166	1,711,634
Deferred tax liabilities:		
Property and equipment	(101,235)	(128,407)
Acquired intangibles	(87,160)	—
Deferred revenue	—	(73,357)
Unrealized gain	(28,838)	(10,198)
Operating lease liabilities	(13,118)	—
Net deferred tax assets	$ 1,190,815	$ 1,499,672

In 2019, the Company completed acquisitions of Semma and Exonics, resulting in the inclusion of these entities deferred tax bases into the Company's consolidated deferred tax assets and deferred tax liabilities. As of the acquisition date, Semma's deferred tax liabilities were $54.2 million. Exonics' deferred tax assets were not material to the Company's financial statements.

On a periodic basis, the Company reassesses the valuation allowance on its deferred income tax assets weighing positive and negative evidence to assess the recoverability of the deferred tax assets. In the fourth quarter of 2018, the Company assessed the valuation allowance and considered positive evidence, including significant cumulative consolidated and U.S. income over the three years ended December 31, 2018, revenue growth, clinical trial data from the Company's triple combination regimens, competitor clinical progress and expectations regarding future profitability, and negative evidence, including the potential impact of competition on the Company's projections and cumulative losses in one of the jurisdictions. After assessing both the positive evidence and the negative evidence, the Company determined it was more likely than not that its deferred tax assets would be realized in the future and released the valuation allowance on the majority of its NOLs and other deferred tax assets as of December 31, 2018, resulting in a benefit from income taxes of $1.56 billion. As of December 31, 2019, the Company maintained a valuation allowance of $205.2 million related primarily to U.S. state and foreign tax attributes.

As of December 31, 2019, the Company had NOL carryforwards of $1.5 billion, of which $1.3 billion were subject to expiration and $181.1 million had an indefinite carryforward period, and tax credits of $399.0 million for U.S. federal income tax purposes. As of December 31, 2019, the Company had NOL carryforwards of $903.7 million and tax credits of $161.7 million for U.S. state income tax purposes. These U.S. federal and state NOL carryforwards and tax credits expire at various dates through 2039 and may be used to offset future federal and state income tax liabilities, respectively. As of December 31, 2019, the Company had foreign net operating loss carryforwards of $896.9 million, including $16.0 million that were subject to expiration at various dates through 2039 and $880.9 million that had an indefinite carryforward period.

Unrecognized tax benefits during the three years ended December 31, 2019 were as follows:

	2019	2018	2017
	(in thousands)		
Balance at beginning of the period	$ 19,549	$ 3,814	$ —
Increases related to current period tax positions	14,407	9,704	3,814
Increases related to prior period tax positions	598	6,031	—
Decreases related to prior period tax positions	(156)	—	—
Settlement with Tax Authorities	(478)	—	—
Balance at end of period	$ 33,920	$ 19,549	$ 3,814

As of December 31, 2019, the Company has classified $13.4 million and $20.5 million of its unrecognized tax benefits as credits to "Deferred tax assets" and "Accrued expenses," respectively, on its consolidated balance sheet.

The Company has reviewed the tax positions taken, or to be taken, in its tax returns for all tax years currently open to examination by a taxing authority. Unrecognized tax benefits represent the aggregate tax effect of differences between tax return positions and the benefits recognized in the financial statements. As of December 31, 2019 and 2018, the Company had $33.9 million and $19.5 million, respectively, of gross unrecognized tax benefits, which would affect the Company's tax rate if recognized. As of December 31, 2017, the Company had $3.8 million of gross unrecognized tax benefits, which would not affect the Company's tax rate if recognized. The Company does not expect that its unrecognized tax benefits will materially change within the next twelve months. The Company accrues interest and penalties related to unrecognized tax benefits as a component of its "Provision for (benefit from) income taxes." As of December 31, 2019, no significant interest or penalties were accrued. The Company did not recognize any material interest or penalties related to uncertain tax positions during the three years ended December 31, 2019.

As of December 31, 2019, foreign earnings, which were not significant, have been retained indefinitely by the Company's foreign subsidiaries for indefinite reinvestment. Upon repatriation of those earnings, in the form of dividends or otherwise, the Company could be subject to withholding taxes payable to the various foreign countries.

The Company files U.S. federal income tax returns and income tax returns in various state, local and foreign jurisdictions. The Company is no longer subject to any tax assessment from an income tax examination in the United States or any other major taxing jurisdiction for years before 2011, except where the Company has NOLs or tax credit carryforwards that originate before 2011. The Company has various income tax examinations ongoing at any time throughout the world. During the year ended December 31, 2019, the Company concluded tax examinations with Austria, Canada, Germany and Italy, with no material adjustments.

Q. Commitments and Contingencies

Revolving Credit Facility

In September 2019, the Company and certain of its subsidiaries entered into a Credit Agreement (the "2019 Credit Agreement") with Bank of America, N.A., as administrative agent and the lenders referred to therein. The 2019 Credit Agreement provides for a $500.0 million unsecured revolving facility, which was not drawn upon at closing. Amounts drawn pursuant to the 2019 Credit Agreement, if any, may be used to finance the Company's working capital needs, and for general corporate or other lawful purposes. The Company had no borrowings outstanding under the 2019 Credit Agreement as of December 31, 2019. The 2019 Credit Agreement also provides that, subject to satisfaction of certain conditions, the Company may request that the borrowing capacity under the 2019 Credit Agreement be increased by an additional $500.0 million. The 2019 Credit Agreement, which matures on September 17, 2024, supersedes the Company's credit agreement entered into in 2016 with Bank of America, N.A serving in the same capacity. Additionally, the 2019 Credit Agreement provides a sublimit of $50.0 million for letters of credit.

Direct costs related to the 2019 Credit Agreement, which were not material to the Company's financial statements, were deferred and will be recorded over the term of the 2019 Credit Agreement.

Any amounts borrowed under the 2019 Credit Agreement will bear interest, at the Company's option, at either a base rate or a Eurocurrency rate, in each case plus an applicable margin. Under the 2019 Credit Agreement, the applicable margins on base rate loans range from 0.125% to 0.50% and the applicable margins on Eurocurrency loans range from 1.125% to 1.50%, in each case based on the Company's consolidated leverage ratio (the ratio of the Company's total consolidated funded indebtedness to the Company's consolidated EBITDA for the most recently completed four fiscal quarter period).

Any amounts borrowed pursuant to the 2019 Credit Agreement are guaranteed by certain of the Company's existing and future domestic subsidiaries, subject to certain exceptions.

The 2019 Credit Agreement contains customary representations and warranties and affirmative and negative covenants, including financial covenants to maintain (i) 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 and (ii) a consolidated interest coverage ratio (the ratio of the Company's consolidated EBITDA to its consolidated interest expenses for the most recently completed four fiscal quarter period) of 2.50 to 1.00, in each case measured on a quarterly basis. The 2019 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.

Guaranties and Indemnifications

As permitted under Massachusetts law, the Company's Articles of Organization and By-laws provide that the Company will indemnify certain of its 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 the Company could be required to make under these indemnification provisions is unlimited. However, the Company has purchased directors' and officers' liability insurance policies that could reduce its monetary exposure and enable it to recover a portion of any future amounts paid. No indemnification claims currently are outstanding, and the Company believes the estimated fair value of these indemnification arrangements is minimal.

The Company customarily agrees in the ordinary course of its business to indemnification provisions in agreements with clinical trial investigators and sites in its drug development programs, sponsored research agreements with academic and not-for-profit institutions, various comparable agreements involving parties performing services for the Company, and its real estate leases. The Company also customarily agrees to certain indemnification provisions in its drug discovery, development and commercialization collaboration agreements. With respect to the Company's 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 the Company's contractual obligations arising out of the research or clinical testing of the Company's compounds or drug 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 the Company, to violations of law by the Company or to certain breaches of the Company's contractual obligations. The indemnification provisions appearing in the Company's collaboration agreements are similar to those for the other agreements discussed above, but in addition provide some limited indemnification for its 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 the Company believes 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 the Company could be required to make under these provisions is generally unlimited. The Company has purchased insurance policies covering personal injury, property damage and general liability that reduce its exposure for indemnification and would enable it in many cases to recover all or a portion of any future amounts paid. The Company has never paid any material amounts to defend lawsuits or settle claims related to these indemnification provisions. Accordingly, the Company believes the estimated fair value of these indemnification arrangements is minimal.

Other Contingencies

The Company has certain contingent liabilities that arise in the ordinary course of its business activities. The Company accrues a reserve for contingent liabilities when it is probable that future expenditures will be made and such expenditures can be reasonably estimated. There were no material contingent liabilities accrued as of December 31, 2019 or 2018.

R. Segment Information

Segment reporting is prepared on the same basis that the Company's chief executive officer, who is the Company's chief operating decision maker, manages the business, makes operating decisions and assesses performance. The Company operates in one segment, pharmaceuticals. Enterprise-wide disclosures about revenues, significant customers, and property and equipment, net by location are presented below.

Revenues by Product

Product revenues, net consisted of the following:

	2019 (as reported under ASC 606)	2018 (as reported under ASC 606)	2017 (as reported under ASC 605)
		(in thousands)	
TRIKAFTA	$ 420,105	$ —	$ —
SYMDEKO/SYMKEVI	1,417,668	768,657	—
ORKAMBI	1,331,891	1,262,166	1,320,850
KALYDECO	991,062	1,007,502	844,630
Total product revenues, net	$ 4,160,726	$ 3,038,325	$ 2,165,480

Revenues by Geographic Location

Net product revenues are attributed to countries based on the location of the customer. Collaborative and royalty revenues are attributed to countries based on the location of the Company's subsidiary associated with the collaborative arrangement related to such revenues. Total revenues from external customers and collaborators by geographic region consisted of the following:

	2019 (as reported under ASC 606)	2018 (as reported under ASC 606)	2017 (as reported under ASC 605)
		(in thousands)	
United States	$ 3,062,555	$ 2,365,079	$ 1,986,786
Outside of the United States			
Europe	885,762	543,179	420,317
Other	214,504	139,339	81,549
Total revenues outside of the United States	1,100,266	682,518	501,866
Total revenues	$ 4,162,821	$ 3,047,597	$ 2,488,652

Significant Customers

Gross revenues and accounts receivable from each of the Company's customers who individually accounted for10% or more of total gross revenues and/or 10% or more of total gross accounts receivable consisted of the following:

	Percent of Total Gross Revenues			Percent of Gross Accounts Receivable	
	Year Ended December 31,			As of December 31,	
	2019 (as reported under ASC 606)	2018 (as reported under ASC 606)	2017 (as reported under ASC 605)	2019	2018
McKesson Corporation	17%	14%	<10%	22%	16%
Walgreen Co.	15%	20%	17%	14%	16%
Accredo/Curascript	14%	14%	14%	15%	10%

Long-lived Assets by Location

Long-lived assets by location consisted of the following:

	As of December 31,	
	2019	2018
	(in thousands)	
United States	$ 768,572	$ 778,157
Outside of the United States		
United Kingdom	57,383	30,496
Other	7,327	3,352
Total long-lived assets outside of the United States	64,710	33,848
Total long-lived assets	$ 833,282	$ 812,005

S. Quarterly Financial Data (unaudited)

The following tables set forth the Company's quarterly financial data for the two years ended December 31, 2019:

	Three Months Ended			
	March 31, 2019	June 30, 2019	September 30, 2019	December 31, 2019
	(in thousands, except per share amounts)			
Revenues:				
Product revenues, net (1)	$ 857,253	$ 940,380	$ 949,828	$ 1,413,265
Collaborative and royalty revenues	1,182	913	—	—
Total revenues	858,435	941,293	949,828	1,413,265
Costs and expenses:				
Cost of sales	95,092	135,740	131,914	185,012
Research and development expenses (2)	339,490	379,091	555,948	480,011
Sales, general and administrative expenses	147,045	156,502	159,674	195,277
Change in fair value of contingent consideration	—	—	2,959	1,500
Total costs and expenses	581,627	671,333	850,495	861,800
Income from operations	276,808	269,960	99,333	551,465
Interest income	15,615	18,076	17,628	12,359
Interest expense	(14,868)	(14,837)	(14,548)	(14,249)
Other income (expense), net (3)	42,610	53,939	(31,747)	127,375
Income before provision for income taxes	320,165	327,138	70,666	676,950
Provision for income taxes (4)	51,534	59,711	13,148	93,716
Net income attributable to Vertex	$ 268,631	$ 267,427	$ 57,518	$ 583,234
Amounts per share attributable to Vertex common shareholders:				
Net income:				
Basic	$ 1.05	$ 1.04	$ 0.22	$ 2.26
Diluted	$ 1.03	$ 1.03	$ 0.22	$ 2.23
Shares used in per share calculations:				
Basic	255,695	256,154	256,946	258,003
Diluted	260,175	259,822	260,473	262,108

	Three Months Ended			
	March 31, 2018	June 30, 2018	September 30, 2018	December 31, 2018
	(in thousands, except per share amounts)			
Revenues:				
Product revenues, net	$ 637,729	$ 749,912	$ 782,511	$ 868,173
Collaborative and royalty revenues	3,070	2,245	2,024	1,933
Total revenues	640,799	752,157	784,535	870,106
Costs and expenses:				
Cost of sales	71,613	104,382	111,255	122,289
Research and development expenses (2)	310,553	337,532	330,510	437,881
Sales, general and administrative expenses	129,808	137,303	137,295	153,210
Restructuring (income) expenses	(76)	62	(174)	4
Intangible asset impairment charge	—	—	—	29,000
Total costs and expenses	511,898	579,279	578,886	742,384
Income from operations	128,901	172,878	205,649	127,722
Interest income	5,789	8,049	10,543	13,971
Interest expense	(16,886)	(18,155)	(18,686)	(18,744)
Other income (expense), net (3)	96,838	53,819	(60,995)	(90,452)
Income before (benefit from) provision for income taxes	214,642	216,591	136,511	32,497
(Benefit from) provision for income taxes (4)	(12,659)	10,341	8,055	(1,492,599)
Net income	227,301	206,250	128,456	1,525,096
(Income) loss attributable to noncontrolling interest (5)	(17,038)	1,110	290	25,431
Net income attributable to Vertex	$ 210,263	$ 207,360	$ 128,746	$ 1,550,527
Amounts per share attributable to Vertex common shareholders:				
Net income:				
Basic	$ 0.83	$ 0.82	$ 0.51	$ 6.08
Diluted	$ 0.81	$ 0.80	$ 0.50	$ 5.97
Shares used in per share calculations:				
Basic	253,231	254,135	254,905	254,868
Diluted	258,526	258,584	259,788	259,812

1. In the fourth quarter of 2019, the Company updated its transaction price and recognized net product revenues of $155.8 million related to prior period ORKAMBI sales upon reaching a reimbursement agreement with the French government for ORKAMBI, including ORKAMBI distributed through early access programs. See Note A, "Nature of Business and Accounting Policies."

2. In the third quarter of 2019, the Company incurred research and development expenses of $175.0 million related to its CRISPR DMD/DM1 Agreement. In the fourth quarter of 2018, the Company incurred research and development expenses of $95.0 million to related license agreements with Merck KGaA, Darmstadt, Germany, and Arbor. See Note B, "Collaborative Arrangements."

3. In 2019 and 2018, "Other income (expense), net" was primarily related to changes in the fair value of the Company's equity investment in CRISPR. See Note F, "Marketable Securities and Equity Investments."

4. In the fourth quarter of 2018, the Company released the valuation allowance on the majority of its NOLs and other deferred tax assets as of December 31, 2018 resulting in a benefit from income taxes of $1.56 billion. Starting in 2019, the Company began recording a provision for income taxes approximating statutory rates on its pre-tax income. See Note P, "Income Taxes."

5. In 2018, the Company had a noncontrolling interest in BioAxone, which it consolidated as a VIE until December 31, 2018. Following the deconsolidation of BioAxone as of December 31, 2018, the Company did not have a noncontrolling interest in any entities in 2019. See Note B, "Collaborative Arrangements."

DESCRIPTION OF SECURITIES
REGISTERED PURSUANT TO SECTION 12 OF
THE SECURITIES EXCHANGE ACT OF 1934

Vertex Pharmaceuticals Incorporated (the "Company" or "Vertex") has one class of securities registered under Section 12 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"): our common stock, par value $0.01 per share ("Common Stock").

DESCRIPTION OF CAPITAL STOCK

The following summary of our capital stock is based on the provisions of the Massachusetts Business Corporation Act (the "MBCA"), our Restated Articles of Organization, as amended, (the "Articles") and our Amended and Restated By-laws, as amended (the "By-laws"). This description does not purport to be complete and is subject to, and qualified in its entirety by reference to the full text of our Articles and our By-laws, each of which is filed and incorporated by reference as an exhibit to our Annual Report on Form 10-K, of which this Exhibit is a part, and the MBCA. You should read our Articles and Bylaws and the applicable provisions of the MBCA for a complete statement of provisions described under this caption "Description of Capital Stock" and for other provisions that may be important to you**.**

Authorized Capital Shares

Our authorized capital stock consists of 500,000,000 shares of Common Stock and 1,000,000 shares of preferred stock, par value $0.01 per share ("Preferred Stock"). The number of authorized shares of any class may be increased or decreased by an amendment to our Articles proposed by our board of directors and approved by a majority of voting shares voted on the issue at a meeting at which a quorum exists.

Description of Common Stock

Dividend Rights

After satisfaction of any dividend rights of holders of Preferred Stock, holders of Common Stock are entitled ratably to any dividend declared by our board of directors out of funds legally available for this purpose.

Voting Rights

Each stockholder of record of our Common Stock is entitled to one vote for each share held on every matter properly submitted to the stockholders for their vote. Generally, a matter submitted for stockholder action shall be approved with a majority of the votes properly cast, except when a larger vote is required by law, our Articles or our By-laws. Other than in a contested election where directors are elected by a plurality vote, a director nominee shall be elected to the board of directors if the votes properly cast in favor of election of a director exceed the votes properly withheld in such election.

Holders of our Common Stock do not have cumulative voting rights.

Liquidation Rights

Upon our liquidation, dissolution or winding up, the holders of our Common Stock are entitled to receive ratably our net assets available, if any, after the payment of all debts and other liabilities and subject to the prior rights of any outstanding preferred stock.

Other Rights and Preferences

Holders of our Common Stock have no preemptive, subscription, redemption, conversion or exchange rights and no sinking fund provisions. There are no restrictions on alienability of our Common Stock or liabilities to further calls or assessments by the Company.

The rights, preferences and privileges of holders of Common Stock are subject to, and may be adversely affected by, the rights of the holders of shares of any series of preferred stock that we may designate and issue in the future.

Anti-Takeover Effects of Provisions of Massachusetts Law

We are subject to Chapter 110F of the Massachusetts General Laws, an anti-takeover law. In general, this statute prohibits a publicly-held Massachusetts corporation from engaging in a "business combination" with an "interested stockholder" for a period of three years after the date of the transaction in which the person becomes an interested stockholder, unless (i) prior to the date such stockholder became an interested stockholder, the board of directors approved the business combination or transaction which resulted in the stockholder becoming interested, (ii) the interested stockholder acquires 90% of the outstanding voting stock of the corporation (excluding shares held by certain affiliates of the corporation) at the time it becomes an interested stockholder, or (iii) the business combination is approved by both the board of directors and at least two-thirds of the outstanding voting stock of the corporation (excluding shares held by the interested stockholder). Generally, an "interested stockholder" is a person who, together with affiliates and associates, owns (or at any time within the prior three years did own) 5% or more of the outstanding voting stock of the corporation. A "business combination" includes a merger, a stock or asset sale, and certain other transactions resulting in a financial benefit to the interested stockholders.

We are subject to Chapter 110D of the Massachusetts General Laws, entitled "Regulation of Control Share Acquisitions." In general, this statute provides that any stockholder of a corporation subject to this statute who acquires 20% or more of the outstanding voting stock of a corporation may not vote such stock unless the stockholders of the corporation so authorize. The board of directors may amend our by-laws to exclude us from this statute prospectively.

NASDAQ Listing

Our Common Stock is listed on the NASDAQ Global Select Market under the symbol "VRTX."

VERTEX PHARMACEUTICALS INCORPORATED
2013 STOCK AND OPTION PLAN

Form of Restricted Stock Unit Award

This Agreement sets forth the terms and conditions of a Restricted Stock Unit Award granted pursuant to the provisions of the 2013 Stock and Option Plan (as it may be amended or restated, the "Plan") of Vertex Pharmaceuticals Incorporated (the "Company") to the Participant whose name appears below, of a contingent entitlement of the Participant to receive the number of Shares of Common Stock of the Company set forth below, pursuant to the provisions of the Plan and on the following express terms and conditions. Capitalized terms not otherwise defined herein shall have the same meanings as set forth in the Plan, and any Restricted Stock Units evidenced hereby are granted subject to the terms of the Plan.

1. Name of Participant to whom the Restricted Stock Unit Award is granted:

Participant Name: #ParticipantName#
Employee ID: #EmployeeID#

2. Number of Shares of Common Stock in the Restricted Stock Unit Award (the "Shares"):

#QuantityGranted# Shares

3. Date of grant of the Restricted Stock Unit Award:

#GrantDate# ("MM/DD/YYYY")

4. Vesting.

4.1 Vesting Schedule. Except as otherwise provided in this Section 4, the Restricted Stock Unit Award shall vest according to the Appendix: Vesting Schedule.

On each vesting date, the Participant shall be entitled to receive the applicable number of shares of Common Stock that shall thereafter be delivered by the Company to the Participant in accordance with this Agreement and the Plan within two business days of the applicable vesting date. Except as provided in Section 4.2 or 4.3 of this Agreement, upon any Termination of Service of the Participant for any reason, vesting of the Shares shall immediately cease, and the unvested portion of the Restricted Stock Unit Award shall immediately be forfeited.

4.2 Termination for Cause.

(a) If the Participant's employment with the Company is terminated due to Cause, any portion of the Restricted Stock Unit Award that has not vested prior to the date written notice of such termination is provided to the Participant shall be immediately forfeited. If the Participant is notified that the Company is investigating or evaluating whether the Company will terminate Participant's employment or other service to the Company for Cause, the Company may, at its election, suspend the vesting of this Restricted Stock Unit Award by written notice to the Participant. If after such notification it is determined or otherwise agreed that Participant's service to the Company will not be terminated for Cause, vesting of the Shares shall resume pursuant to the original schedule and any Shares that would have vested during such suspension immediately shall vest.

(b) "<u>Cause</u>" shall mean (i) the Participant's dishonesty or fraud, or (ii) the willful misconduct by the Participant or willful failure by the Participant to perform his or her responsibilities to the Company (including, without limitation, any material breach by the Participant of any provision of any Company policy or any employment, consulting, advisory, nondisclosure, non-competition or other similar agreement between the Participant and the Company), in each case as determined in good faith by the Company, which determination shall be conclusive.

4.3 Career Employment Provision. If a Participant experiences a Termination of Service other than for Cause, and the Participant is a Qualified Participant (as defined below), then (a) an additional number of Shares equal to (i) the sum of 50% plus 10% for each full year of service as an Employee and/or a Non-Employee Director to the Company or an Affiliate in excess of five (5) full years of service multiplied by (ii) the number of unvested Shares subject to this Restricted Stock Unit Award immediately prior to the Participant's Termination of Service, shall vest on the date of the Termination of Service and (b) any remaining unvested Shares shall be forfeited. A "<u>Qualified Participant</u>" shall mean a Participant (i) who is at least fifty-five (55) years old, (ii) who has completed at least five (5) full years of service as an Employee and/or a Non-Employee Director to the Company or an Affiliate, (iii) whose age plus full years of service as an Employee and/or a Non-Employee Director to the Company or an Affiliate is 65 or greater and (iv) who has completed a mandatory transitional period of employment with the Company following notice of the Termination of Service, the duration of which will be no fewer than twelve (12) months, except as may be determined by the Company in its sole discretion or as may be required by applicable law.

5. Agreement with respect to Tax Payments, Withholding and Sale of a Portion of Shares. The Participant acknowledges and agrees that any income or other taxes, fees or social security or comparable contributions due from the Participant with respect to the vesting of the Restricted Stock Unit Award or the issuance of Shares pursuant to this Agreement shall be the Participant's responsibility. In connection with the foregoing, the Participant agrees that the Company shall be entitled to hold back Shares based on the Fair Market Value of the Shares on the Vesting Date in satisfaction of tax withholding requirements. The Participant agrees to pay to the Company as soon as practicable, including through payroll, the amount of any tax withholding, that is for whatever reason, not satisfied through such hold back. The Participant further acknowledges that the Restricted Stock Unit Award made hereunder is subject to Participant's acceptance of the terms of this Section 5, and other terms and provisions of this Agreement.

6. Restrictions on Transfer. Except as provided in Section 10 of the Plan, this Restricted Stock Unit Award may not be sold, transferred, assigned, hypothecated, pledged, encumbered or otherwise disposed of, whether voluntarily or by operation of law, at any time before the Participant receives Shares. Any such purported transfer shall be null and void, and shall not be recognized by the Company or recorded on its books.

7. No Rights as a Shareholder. The Participant shall have no rights as a shareholder, including voting and dividend rights, with respect to the Restricted Stock Unit Award subject to this Agreement.

8. No Obligation to Maintain Relationship. The Participant acknowledges that: (i) the Company is not obligated by the Plan or this Restricted Stock Unit Award to continue the Participant as an Employee, Non-Employee Director, consultant or advisor of the Company or an Affiliate; (ii) the Plan is discretionary in nature and may be modified, suspended or terminated by the Company at any time; (iii) the grant of this Restricted Stock Unit Award is a one-time benefit that does not create any contractual or other right to receive future grants of equity, or benefits in lieu thereof; (iv) all determinations with respect to any such future grants, including, but not limited to, the times when restricted stock unit awards shall be granted, the number of shares subject to each restricted stock unit award, and the time or times when each restricted stock unit award shall vest, will be at the sole discretion of the Company; (v) the Participant's participation in the Plan is voluntary; (vi) the value of this Restricted Stock Unit Award is an extraordinary item of compensation which is outside the scope of the Participant's employment or consulting contract, if any; and (vii) this Restricted Stock Unit Award is not part of normal or expected compensation for purposes of calculating any severance, resignation, redundancy, end of service payments, bonuses, long-service awards, pension or retirement benefits or similar payments.

9. Code Section 409A. Pursuant to Section 25 of the Plan, if and to the extent (i) any portion of any payment, compensation or other benefit provided to a Participant pursuant to this Restricted Stock Unit Award in connection with his or her employment termination constitutes "nonqualified deferred compensation" within the meaning of Section 409A of the Code and (ii) the Participant is a specified employee as defined in Section 409A(a)(2)(B)(i) of the Code, in each case as determined by the Company in accordance with its procedures, by which determinations the Participant (through accepting this Restricted Stock Unit Award) agrees that he or she is bound, such portion of the payment, compensation or other benefit shall not be paid before the day that is six months plus one day after the date of "separation from service" (as determined under Section 409A of the Code), except as Section 409A of the Code may then permit.

10. Plan. The Participant hereby acknowledges receipt of a copy of the Plan as presently in effect and the Prospectus with respect thereto. All of the terms and provisions of the Plan, and any additional terms and conditions provided to Participants located outside of the United States, are incorporated herein by reference, and this Restricted Stock Unit Award is subject to those terms and provisions in all respects.

VERTEX PHARMACEUTICALS INCORPORATED

By: ________________________________

Exhibit 10.35

May 18, 2012

Paul M. Silva
23 Tammer Lane
Hopkinton, MA 01748

RE: Amended and Restated Change of Control Agreement

Dear Paul:

You are a key member of the senior management team of Vertex Pharmaceuticals Incorporated (the "Company"). As a result, the Company would like to provide you with the following "change of control" benefits to help ensure that if the Company becomes involved in a "change of control" transaction, there will be no distraction from your attention to the needs of the Company.

I. *Definitions*. For the purposes of this Amended and Restated Change of Control Agreement (this "Agreement"), capitalized terms shall have the following meanings:

1. "Cause" shall mean:

(a) your conviction of a crime involving moral turpitude;

(b) your willful refusal or failure to follow a lawful directive or instruction of the Company's Board of Directors or the individual(s) to whom you report, provided that you receive prior written notice of the directive(s) or instruction(s) that you failed to follow, and provided further that the Company, in good faith, gives you 30 days to correct such failure and further provided that if you correct the failure(s), any termination of your employment on account of such failure shall not be treated for purposes of this Agreement as a termination of employment for "Cause";

(c) in carrying out your duties you commit (i) willful gross negligence, or (ii) willful gross misconduct, resulting in either case in material harm to the Company, unless such act, or failure to act, was believed by you, in good faith, to be in the best interests of the Company; or

(d) your violation of the Company's policies made known to you regarding confidentiality, securities trading or inside information.

2. "Change of Control" shall mean that:

(a) any "person" or "group" as such terms are used in Sections 13(d) and 14(d)(2) of the Securities Exchange Act of 1934 (the "Act"), becomes a beneficial owner, as such term is used in Rule 13d-3 promulgated under the Act, of securities of the Company representing more than 50% of the combined voting power of the outstanding securities of the Company having the right to vote in the election of directors; or

(b) all or substantially all the business or assets of the Company are sold or disposed of, or the Company or a subsidiary of the Company combines with another company pursuant to a merger, consolidation, or other similar transaction, other than (i) a transaction solely for the purpose of reincorporating the Company or one of its subsidiaries in a different jurisdiction or recapitalizing or reclassifying the Company's stock; or (ii) a merger or consolidation in which the shareholders of the Company immediately prior to such merger or consolidation continue to own at least a majority of the outstanding voting securities of the Company or the surviving entity immediately after the merger or consolidation.

3. "Code" shall mean the Internal Revenue Code of 1986, as amended.

4. "Disability" shall mean a disability as determined under the Company's long-term disability plan or program in effect at the time the disability first occurs, or if no such plan or program exists at the time of disability, then a "disability" as defined Section 22(e)(3) of the Code.

5. "Good Reason" shall mean one of the following events has occurred without your consent:

(a) your annual base salary is decreased;

(b) the office to which you are assigned is relocated to a place 35 or more miles away; or

(c) following a Change of Control, the Company's successor fails to assume the Company's rights and obligations under this Agreement;

provided that Good Reason shall not exist unless and until within 30 days after the event giving rise to Good Reason under (a), (b) or (c) above has occurred, you deliver a written termination notice to the Company stating that an event giving rise to Good Reason has occurred and identifying with reasonable detail the event that you assert constitutes Good Reason under (a), (b) or (c) above and the Company fails or refuses to cure or eliminate the event giving rise to Good Reason on or within 30 days after receiving your notice. To avoid doubt, the termination of your employment would become effective at the close of business on the thirtieth day after the Company receives your termination notice, unless the Company cures or eliminates the event giving rise to Good Reason prior to such time.

6. "Termination Date" shall mean the last day of your employment with the Company.

II. *Severance Benefits upon Change of Control* . If:

(A) your employment is terminated by the Company (except for termination for Cause or due to a Disability) and the Termination Date is within 90 days prior to a Change of Control or within 12 months after a Change of Control; or

(B) you, of your own initiative, (i) terminate your employment for Good Reason (in accordance with the notice and cure provisions set forth in Section I.5 above) and (ii) the event giving rise to Good Reason occurs within 90 days prior to a Change of Control or within 12 months after a Change of Control;

then, you shall receive the following benefits:

1. *Severance Payment*. In exchange for your execution within 60 days of the Termination Date of a general release, in a form satisfactory to the Company, of all claims against the Company, its subsidiaries, and its and their officers, directors and representatives, that becomes enforceable and irrevocable within such 60-day period, the Company shall make a cash payment (the "Severance Payment") to you in an amount equal to:

(a) (i) your annual base salary (provided, however, that if you terminate your employment for Good Reason based on a reduction in your annual base salary, then the annual base salary to be used in calculating the Severance Payment shall be your annual base salary in effect immediately prior to such reduction in annual base salary) plus your target bonus under any bonus program applicable to you for the year in which the Termination Date occurs, multiplied by (ii) 50% plus 3.846% for each year of continuous service with the Company (up to a maximum of 100%); plus

(b) all cash incentive compensation awards earned by you but not paid prior to the Termination Date; provided that, if a fiscal year has been completed and the incentive award for such fiscal year has not been determined, the incentive compensation for such completed fiscal year shall equal the target bonus for such fiscal year.

Except with respect to any portion of the Severance Payment that is delayed as set forth in this paragraph, the Severance Payment shall be made in cash within ten days after the execution by you of the general release referred to above and expiration without revocation of any applicable revocation periods under such general release (or, if the Change of Control resulting in your becoming entitled to such benefits occurs after such execution and expiration, within ten days after the Change of Control), provided that, if the 60-day period during which the general release is required to become effective and irrevocable begins in one calendar year and ends in another calendar year, the Severance Payment shall not be made before the first day of the second calendar year. The Severance Payment shall be divided into two portions, consisting of a portion that does not constitute "nonqualified deferred compensation" within the meaning of Section 409A of the Code and a portion, if any, that does constitute nonqualified deferred compensation. If you are a "specified employee" as defined in Section 409A(a)(2)(B)(i) of the Code, the commencement of the delivery of any such payments that constitute nonqualified deferred compensation payable upon a "separation from service" under Section 409A(a)(2)(A)(i) of the Code will be delayed until the first business day that is more than six months after your Termination Date. The determination of whether, and the extent to which, any of the payments to be made to you hereunder are nonqualified deferred compensation shall be made after the application of all applicable exclusions, including those set forth under Treasury Reg. § 1.409A-1(b)(9). Any payments that are intended to qualify for the exclusion for separation pay due to involuntary separation from service set forth in Reg. §1.409A-1(b)(9)(iii) must be paid no later than the last day of the second taxable year following the taxable year in which the Termination Date occurs. To the extent that the termination of your employment does not constitute a separation of service under Section 409A(a)(2)(A)(i) of the Code (as the result of further services that are reasonably anticipated to be provided by you to the Company at the time your employment is terminated), the payment of any non-qualified deferred compensation will be further delayed until the first business day that is more than six months after the date of a subsequent event constituting a separation of service under Section 409A(a)(2)(A)(i) of the Code.

2. *Accelerated Vesting.*

(a) On the Termination Date, stock options for the purchase of the Company's securities held by you as of the Termination Date and not then exercisable shall immediately become exercisable in full. The options to which this accelerated vesting applies shall remain exercisable until the earlier of (a) the end of the 90-day period immediately following the later of (i) the Termination Date or (ii) the date of the Change of Control and (b) the date the stock option(s) would otherwise expire; and

(b) On the Termination Date, the Company's lapsing repurchase right with respect to shares of restricted stock held by you shall lapse in full (subject to your making satisfactory arrangements with the Company providing for the payment to the Company of all required withholding taxes).

Notwithstanding anything to the contrary in this Agreement, the terms of any option agreement or restricted stock agreement shall govern the acceleration, if any, of vesting or lapsing of the Company's repurchase rights and period of exercisability of such awards, as applicable, except to the extent that the terms of this Agreement are more favorable to you.

3. *Continued Insurance Coverage*. If COBRA coverage is elected by you, the Company shall pay the cost of insurance continuation premiums on your behalf (whether or not covered by COBRA) to continue

standard medical, dental and life insurance coverage for you (or the cash equivalent of same if you are ineligible for continued coverage) until the earlier of (i) the date 12 months after the Termination Date or (ii) the date you begin receiving substantially equivalent coverage and benefits through a subsequent employer.

4. *No Mitigation.* You shall not be required to mitigate the amount of the Severance Payment or any other benefit provided under this Agreement by seeking other employment or otherwise, nor shall the amount of any payment or benefit provided for in this Agreement be reduced (except as provided in Article II Section 3(ii)) by any compensation earned by you as the result of other employment, by retirement benefits, or be offset against any amount claimed to be owed by you to the Company or otherwise (except for any required withholding taxes); provided, that if the Company makes any other severance payments to you under any other program or agreement, such amounts shall be offset against the payments the Company is obligated to make pursuant to this Agreement.

III. *Miscellaneous*.

1. *Employee's Obligations*. Upon the termination of employment, you shall promptly deliver to the Company all property of the Company and all material documents, statistics, account records, programs and other similar tangible items which may by in your possession or under your control and which relate in a material way to the business or affairs of the Company or its subsidiaries, and no copies of any such documents or any part thereof shall be retained by you.

2. *Entire Agreement*. This Agreement and the "*Employee Non-Disclosure, Non-Competition & Inventions Agreement*" previously executed by you covers the entire understanding of the parties as to the subject matter hereof, superseding all prior understandings and agreements related hereto, including the previous Change of Control Agreement between you and the Company. No modification or amendment of the terms and conditions of this Agreement shall be effective unless in writing and signed by the parties or their respective duly authorized agents, provided, however, that the Company may, without your consent, unilaterally adopt amendments that may be required so that this Agreement continues to comply with applicable law or regulation, including without limitation Section 409A of the Code, provided such amendments do not adversely affect the benefits to be provided to you under Section II of this Agreement.

3. *Governing Law*. This Agreement shall be governed by the laws of The Commonwealth of Massachusetts, as applied to contracts entered into and performed entirely in Massachusetts by Massachusetts residents.

4. *Successors and Assigns*. This Agreement may be assigned by the Company upon a sale, transfer or reorganization of the Company. Upon a Change of Control, the Company shall require the successor to assume the Company's rights and obligations under this Agreement. The Company's failure to do so shall constitute a material breach of this Agreement. This Agreement shall be binding upon and inure to the benefit of the parties hereto and their successors, permitted assigns, legal representatives and heirs.

Kindly indicate your acceptance of the foregoing by signing and dating this Agreement as noted below, and returning one fully executed original to my attention.

Very truly yours,

Vertex Pharmaceuticals Incorporated

By: /s/ Jeffrey M. Leiden, M.D., Ph.D.
Jeffrey M. Leiden, M.D., Ph.D.

President, Chairman and
Chief Executive Officer

ACCEPTED AND AGREED:

/s/ Paul M. Silva
Paul M. Silva
Sr. Vice President

Date: May 18, 2012

Exhibit 21.1

Subsidiaries of Vertex Pharmaceuticals Incorporated

Vertex Pharmaceuticals (San Diego) LLC, a Delaware limited liability company

Vertex Securities Corporation, a Massachusetts corporation

Vertex Pharmaceuticals (Distribution) Incorporated, a Delaware corporation

Vertex Pharmaceuticals (Cayman) Limited, a Cayman Islands company (3)

Vertex Pharmaceuticals (Cayman II) Limited, a Cayman Islands company

Vertex Pharmaceuticals (Cayman III) Limited, a Cayman Islands company (5)

Vertex Pharmaceuticals (Cayman 509) Limited, a Cayman Islands company

Vertex Pharmaceuticals (Cayman 765) Limited, a Cayman Islands company

Vertex Pharmaceuticals (Cayman 787) Limited, a Cayman Islands company

Vertex Pharmaceuticals (Delaware) LLC, a Delaware limited liability company

Vertex Pharmaceuticals (Puerto Rico) LLC, a Delaware limited liability company

Vertex Pharmaceuticals (Canada) Incorporated, a Canadian company (1)

Vertex Pharmaceuticals (Singapore) Pte. Ltd., a Singapore company

Vertex Holdings, Inc., a Delaware corporation

Vertex Pharmaceuticals (Europe) Limited, a United Kingdom company (5)

Vertex Pharmaceuticals (Switzerland) Sàrl, a Swiss company

Vertex Pharmaceuticals (Ireland) Limited, an Irish company (6)

Vertex Pharmaceuticals (U.K.) Limited, a United Kingdom company (6)

Vertex Pharmaceuticals (France) SAS, a French company

Vertex Pharmaceuticals (Germany) GmbH, a German company

Vertex Pharmaceuticals (Australia) Pty. Ltd., an Australian company

Vertex Pharmaceuticals (Spain), S.L., a Spanish company

Vertex Pharmaceuticals (Netherlands) B.V., a Dutch company

Vertex Pharmaceuticals (Italy) S.r.L., an Italian company

Vertex Farmaceutica do Brasil LTDA, a Brazilian company (4)

Vertex Pharmaceuticals GmbH, an Austrian company (6)

Vertex Pharmaceuticals (Portugal), Unipessoal Lda., a Portuguese company (6)

Vertex Pharmaceuticals (CH) GmbH, a Swiss company (6)

Vertex Pharmaceuticals (Sweden) AB, a Sweden company (6)

Vertex Pharmaceuticals Single Member Societe Anonyme, a Greek company (6)

Vertex Pharmaceuticals (Poland) sp. z.o.o (5) (6)

The Vertex Foundation, Inc., a Delaware corporation

Torreyana Insurance Company, Inc., a Vermont corporation

Vertex Pharmaceuticals (Czech Republic) s.r.o (6)

Exonics Therapeutics, Inc., a Delaware corporation

Semma Therapeutics, Inc., a Delaware corporation

CytoSolv, Inc., a Rhode Island corporation (7)

----

(1) a subsidiary of Vertex Pharmaceuticals (Delaware) LLC
(2) a subsidiary of Vertex Pharmaceuticals (Singapore) Pte. Ltd.
(3) a subsidiary of Vertex Holdings, Inc.
(4) a subsidiary of Vertex Pharmaceuticals (UK) Limited
(5) a subsidiary of Vertex Pharmaceuticals (Cayman) Limited
(6) a subsidiary of Vertex Pharmaceuticals (Europe) Limited
(7) a subsidiary of Semma Therapeutics, Inc.

Exhibit 23.1

Consent of Independent Registered Public Accounting Firm

We consent to the incorporation by reference in the following Registration Statements:

(1) Registration Statement (Form S-3 No. 333-229656) of Vertex Pharmaceuticals Incorporated,

(2) Registration Statements (Form S-8 Nos. 333-134482, 333-150946, 333-160442, 333-166803 and 333-184787) pertaining to the Vertex Pharmaceuticals Incorporated Amended and Restated 2006 Stock and Option Plan (formerly known as the Vertex Pharmaceuticals Incorporated 2006 Stock and Option Plan),

(3) Registration Statement (Form S-8 Nos. 333-184784 and 333-232945) pertaining to the Vertex Pharmaceuticals Incorporated Employee Stock Purchase Plan, and

(4) Registration Statements (Form S-8 Nos. 333-226363, 333-219559, 333-188737, 333-197466, 333-206075 and 333-232948) pertaining to the Amended and Restated Vertex Pharmaceuticals Incorporated 2013 Stock and Option Plan (formerly known as the Vertex Pharmaceuticals Incorporated 2013 Stock and Option Plan);

of our reports dated February 13, 2020, with respect to the consolidated financial statements of Vertex Pharmaceuticals Incorporated and the effectiveness of internal control over financial reporting of Vertex Pharmaceuticals Incorporated, included in this Annual Report (Form 10-K) of Vertex Pharmaceuticals Incorporated for the year ended December 31, 2019.

/s/ Ernst & Young LLP

Boston, Massachusetts
February 13, 2020

Exhibit 31.1

CERTIFICATION

I, Jeffrey M. Leiden, certify that:

1. I have reviewed this Annual Report on Form 10-K of Vertex Pharmaceuticals Incorporated;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   a) designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   b) designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, 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;

   c) evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   d) disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date:	February 13, 2020	/s/ Jeffrey M. Leiden
		Jeffrey M. Leiden Chief Executive Officer and President

Exhibit 31.2

CERTIFICATION

I, Charles F. Wagner, Jr., certify that:

1. I have reviewed this Annual Report on Form 10-K of Vertex Pharmaceuticals Incorporated;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   a) designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   b) designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, 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;

   c) evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   d) disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: February 13, 2020	/s/ Charles F. Wagner, Jr.
	Charles F. Wagner, Jr. Executive Vice President and Chief Financial Officer

Exhibit 32.1

SECTION 906 CEO/CFO CERTIFICATION

Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002 (Subsections (a) and (b) of Section 1350, Chapter 63 of Title 18, United States Code) each of the undersigned officers of Vertex Pharmaceuticals Incorporated, a Massachusetts corporation (the "Company"), does hereby certify, to such officer's knowledge, that:

The Annual Report on Form 10-K for the year ended December 31, 2019 (the "Form 10-K") of the Company fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934, and the information contained in the Form 10-K fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: February 13, 2020

/s/ Jeffrey M. Leiden

Jeffrey M. Leiden
Chief Executive Officer and President

Date: February 13, 2020

/s/ Charles F. Wagner, Jr.

Charles F. Wagner, Jr.

Executive Vice President and Chief Financial Officer

A signed original of this written statement required by Section 906 has been provided to the Company and will be retained by the Company and furnished to the Securities and Exchange Commission or its staff upon request.