

**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, 2017

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

(State or other jurisdiction of
incorporation or organization)

50 Northern Avenue, Boston, Massachusetts

(Address of principal executive offices)

04-3039129

(I.R.S. Employer
Identification No.)

02210

(Zip Code)

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

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

<u>Title of Each Class</u>	<u>Name of Each Exchange on Which Registered</u>
Common Stock, \$0.01 Par Value Per Share	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 and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted 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 and post such files). Yes No

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K (§229.405 of this chapter) is not contained herein, and will not be contained, to the best of the registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K.

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, 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

(Do not check if a smaller reporting 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 (without admitting that any person whose shares are not included in such calculation is an affiliate) based on the last reported sale price of the common stock on June 30, 2017 (the last trading day of the registrant's second fiscal quarter of 2017) was \$31.8 billion. As of January 31, 2018, the registrant had 253,891,984 shares of common stock outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the definitive Proxy Statement for the 2018 Annual Meeting of Shareholders to be held on May 17, 2018 are incorporated by reference into Part III of this Annual Report on Form 10-K.

VERTEX PHARMACEUTICALS INCORPORATED

ANNUAL REPORT ON FORM 10-K

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“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[®]” and “SYMDEKO[™]” 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.

PART I

ITEM 1. BUSINESS

OVERVIEW

We invest in scientific innovation to create transformative medicines for serious diseases. Our business is focused on developing and commercializing therapies for the treatment of cystic fibrosis, or CF, and advancing our research and development programs in other diseases. Our marketed products are ORKAMBI (lumacaftor in combination with ivacaftor), KALYDECO (ivacaftor) and SYMDEKO (tezacaftor in combination with ivacaftor).

Cystic Fibrosis

Our goal is to develop treatment regimens that will provide benefits to all patients with CF and will enhance the benefits that currently are being provided to patients taking our medicines.

Current Medicines

ORKAMBI, KALYDECO and SYMDEKO are collectively approved to treat approximately 45% of the 75,000 CF patients in North America, Europe and Australia. ORKAMBI is approved as a treatment for approximately 28,000 patients who have two copies of the F508del mutation, who we refer to as F508del homozygous patients, in their cystic fibrosis transmembrane conductance regulator, or *CFTR*, gene. KALYDECO is approved for the treatment of approximately 6,000 CF patients who have the G551D mutation or other specified mutations in their *CFTR* gene. SYMDEKO was approved by the United States Food and Drug Administration, or FDA, in February 2018 for the treatment of patients with CF twelve years of age and older who are F508del homozygous or who have at least one mutation that is responsive to tezacaftor/ivacaftor, and provides an additional treatment option to CF patients who were already eligible for either ORKAMBI or KALYDECO. We are currently seeking approval from the European Medicines Agency, or EMA, for tezacaftor in combination with ivacaftor.

Next-generation CFTR Corrector Triple Combination Regimens

In the first quarter of 2018, we selected two next-generation corrector compounds, VX-659 and VX-445, to advance into Phase 3 clinical development as part of separate triple combination regimens. Each of VX-659 and VX-445 have the potential to be combined with both (i) tezacaftor and ivacaftor and (ii) tezacaftor and VX-561, a deuterated version of ivacaftor. We expect to initiate the Phase 3 development program for VX-659 in combination with tezacaftor and ivacaftor in the first half of 2018. In mid-2018, we expect to initiate the Phase 3 development of a once-daily combination of VX-445, tezacaftor and VX-561. Our decision to advance VX-659 and VX-445 was based on available clinical and nonclinical data, including data from an ongoing Phase 2 clinical program, and regulatory discussions are ongoing to finalize the design of the Phase 3 development programs for VX-659 and VX-445.

We believe the triple combination regimens we are evaluating could potentially provide benefits to all CF patients who have at least one F508del mutation in their *CFTR* gene (approximately 90% of all CF patients). This would include (i) the first treatment option that treats the underlying cause of CF for patients who have one copy of the F508del mutation in their *CFTR* gene and a second mutation in their *CFTR* gene that results in minimal *CFTR* function, who we refer to as F508del/Min patients, and (ii) an additional treatment option for patients with CF who are eligible for ORKAMBI, KALYDECO and/or SYMDEKO.

Research and Development Programs

We have a number of ongoing research and development programs in other diseases that we are conducting independently or in collaboration with third parties. We are developing VX-150 and VX-128 as treatments for pain, co-developing CTX001, an investigational gene editing treatment, for the treatment of beta-thalassemia and sickle cell disease, with CRISPR Therapeutics AG, or CRISPR, and developing VX-210 as a treatment for acute spinal cord injury. We plan to continue investing in our research programs and fostering scientific innovation in order to identify and develop transformative medicines. In addition to continuing our research in cystic fibrosis, pain and hemoglobinopathies, our current research programs include programs targeting adrenoleukodystrophy, alpha-1 antitrypsin deficiency and polycystic kidney disease. 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.

CYSTIC FIBROSIS

Background

CF is a rare, 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. There are more than 2,000 known mutations in the *CFTR* gene, some of which result in CF. 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 CRTR 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 open probability of the CFTR protein channels on the cell surface, increasing the flow of salt and water into and out of the cell. CFTR correctors, such as lumacaftor, tezacaftor, VX-659 and VX-445, help CFTR proteins reach the cell surface.

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

KALYDECO (ivacaftor)

KALYDECO (ivacaftor) is an orally-administered CFTR potentiator that is approved in the United States, the European Union, Australia and Canada for the treatment of certain patients with CF who have specific mutations in their *CFTR* gene, including the G551D mutation.

In the fourth quarter of 2017, we obtained results from an open-label Phase 3 clinical trial of KALYDECO in patients with CF one to two years of age with one of 10 mutations in the *CFTR* gene. The clinical trial met its primary endpoint of safety, showing that KALYDECO was generally well tolerated, and safety data were consistent with those seen in previous Phase 3 clinical trials of ivacaftor in children ages two to five years of age and six to eleven years of age. The clinical trial also showed substantial improvements in sweat chloride, a secondary endpoint, as well as in multiple exploratory endpoints evaluating pancreatic function. Based on these results, we expect to submit regulatory approval applications to the FDA and the EMA for ivacaftor for children ages one to two years in the first quarter of 2018. The Phase 3 clinical trial is ongoing in infants younger than one year old.

ORKAMBI (lumacaftor in combination with ivacaftor)

ORKAMBI is an orally-administered combination therapy comprised of lumacaftor, a CFTR corrector, and ivacaftor that is approved in the United States and European Union for the treatment of specified patients with CF who are homozygous for the F508del mutation in their *CFTR* gene. ORKAMBI was originally approved in 2015 for the treatment of F508del homozygous patients twelve years of age and older, and we obtained approval for F508del homozygous patients six to eleven years of age in the United States and European Union in September 2016 and January 2018, respectively.

In the fourth quarter of 2017, we obtained results from a 2-part open-label Phase 3 clinical trial of ORKAMBI in 60 patients with CF two to five years of age who have two copies of the F508del mutation in their *CFTR* gene. The clinical trial met its primary endpoint of safety, showing that ORKAMBI was generally well tolerated and that there were no new safety concerns compared to prior clinical trials of ORKAMBI in patients six through eleven years of age. Secondary endpoints showed decreases in the sweat chloride and improvements in nutritional status as measured by change in weight (weight-for-age z score) and body mass index (BMI-for-age z score). Based on these results, we submitted a New Drug Application, or NDA, to the FDA and expect to submit a Marketing Authorization Application, or MAA, line extension to the EMA in the first quarter of 2018.

SYMDEKO (tezacaftor in combination with ivacaftor)

SYMDEKO is an orally-administered combination therapy comprised of tezacaftor, a CFTR corrector, and ivacaftor that was approved by the FDA in February 2018 for the treatment of patients with CF twelve years of age and older who are F508del homozygous or who have at least one mutation that is responsive to tezacaftor/ivacaftor. The approval was based, in

part, on the results from two Phase 3 clinical trials of tezacaftor in combination with ivacaftor. The clinical trials demonstrated that the tezacaftor/ivacaftor combination provided statistically significant improvements in lung function (percent predicted forced expiratory volume in one second, or ppFEV1) in patients with CF 12 years of age and older who have certain mutations in their *CFTR* gene. The 24-week EVOLVE clinical trial evaluated tezacaftor in combination with ivacaftor in F508del homozygous patients. This clinical trial met its primary endpoint with a mean absolute improvement in ppFEV1 through 24 weeks of 4.0 percentage points from baseline compared to placebo ($p < 0.0001$). The second clinical trial, EXPAND, was an 8-week crossover clinical trial that evaluated the combination treatment in patients with CF who have one mutation that results in residual CFTR function and one F508del mutation. This clinical trial met the primary endpoints of absolute change in ppFEV1 from baseline to the average of the Week 4 and Week 8 measurements, with the tezacaftor/ivacaftor combination treatment demonstrating a mean absolute improvement of 6.8 percentage points compared to placebo ($p < 0.0001$) and the ivacaftor monotherapy group demonstrating a mean absolute improvement of 4.7 percentage points compared to placebo ($p < 0.0001$). Across both clinical trials, the tezacaftor/ivacaftor combination treatment was generally well tolerated.

We submitted an MAA to the EMA for tezacaftor in combination with ivacaftor. The EMA has validated the MAA and we expect the EMA to complete its review in the second half of 2018.

Next-generation CFTR Corrector Compounds

We are investing significant resources in the development of triple combination regimens that include a next-generation CFTR corrector compound. Over the last two years we have been evaluating four next-generation corrector compounds and have obtained positive clinical data from Phase 1 and Phase 2 clinical trials evaluating triple combination regimens including each of these next-generation corrector compounds. In the first quarter of 2018, we selected two next-generation corrector compounds, VX-659 and VX-445, to advance into Phase 3 clinical development as part of separate triple combination regimens. This decision was based on clinical and nonclinical data, including data from an ongoing Phase 2 clinical program. Regulatory discussions are ongoing to finalize the design of the Phase 3 development programs for VX-659 and VX-445, and we expect additional data from these Phase 2 clinical trials in the first half of 2018. We expect to initiate the Phase 3 development program for VX-659 in combination with tezacaftor and ivacaftor in the first half of 2018. In mid-2018, we expect to initiate the Phase 3 development of VX-445 in combination with tezacaftor and VX-561, which is a deuterated version of ivacaftor, as a once-daily regimen. The initiation of this Phase 3 clinical development program for VX-445 in combination with tezacaftor and VX-561 is subject to the receipt of additional data in the first half of 2018 on the combination of VX-445, tezacaftor and VX-561, including data from the ongoing Phase 2 clinical trial, and completion of long-term non-clinical toxicology studies of VX-445.

We believe the triple combination regimens we are evaluating could potentially provide benefits to all CF patients who have at least one F508del mutation in their CFTR gene (approximately 90% of all CF patients). This would include (i) the first treatment option that treats the underlying cause of CF for F508del/Min patients, and (ii) an additional treatment option for patients with CF who are eligible for ORKAMBI, KALYDECO and/or SYMDEKO.

Next-Generation Clinical Data

VX-659

We are evaluating VX-659 (80mg, 240mg and 400mg QD) in a randomized, double-blind Phase 2 clinical trial in combination with tezacaftor and ivacaftor in two different groups of patients 18 years of age and older who have CF: F508del/Min patients (Part 1), and F508del homozygous patients (Part 2). Minimal function mutations are those that result in little-to-no functioning CFTR protein and are not responsive to ivacaftor, tezacaftor or the combination of tezacaftor and ivacaftor. In Part 3 of the clinical trial we are evaluating VX-659 in combination with tezacaftor and VX-561 in F508del/Min patients as a potential once-daily triple combination regimen. The primary objectives for the clinical trial are safety, tolerability and efficacy as assessed by mean absolute change in ppFEV1 from baseline. Secondary endpoints include change in sweat chloride and Cystic Fibrosis Questionnaire-Revised, or CFQR. We have reported data from Part 1 of the clinical trial. Parts 2 and 3 of the clinical trial are ongoing with data expected in the first half of 2018.

Safety Data

In Part 1 of the clinical trial, the triple combination regimen was generally well tolerated. The majority of adverse events were mild or moderate. Serious adverse events were reported in seven patients: three patients in the placebo group (2 with infective pulmonary exacerbations and 1 with decreased pulmonary function test) and four in the triple combination groups (3 with infective pulmonary exacerbations and 1 with influenza). None of these serious adverse events was considered related to treatment and none resulted in treatment discontinuation. The most common adverse events (>10%), regardless of treatment group, were cough, headache, oropharyngeal (throat) pain and sputum increased. There were no discontinuations due to adverse

events. One patient interrupted treatment due to an adverse event in the triple combination treatment groups (rash). The rash resolved following interruption of treatment, and the patient subsequently restarted and completed triple combination treatment without any further incidence.

Efficacy Data

Part 1 of the clinical trial evaluated the triple combination for four weeks in 63 F508del/Min patients (10 in the placebo arm, 11 in the VX-659 80mg arm, 20 in the VX-659 240mg arm and 22 in the VX-659 400mg arm). A summary of the within-group lung function and sweat chloride data is provided below:

VX-659 in F508del/Min Patients		
Mean Absolute Within-Group Change From Baseline Through Day 29*	Mean Absolute Within-Group Change in ppFEV₁ (percentage points)	Mean Absolute Within-Group Change in Sweat Chloride (mmol/L)
Triple placebo	+0.3 (p=0.9053)	+2.9 (p=0.5338)
VX-659 (80mg QD) + tezacaftor (100mg QD) + ivacaftor (150mg q12h)	+10.2 (p=0.0004)	-45.8 (p<0.0001)
VX-659 (240mg QD) + tezacaftor (100mg QD) + ivacaftor (150mg q12h)	+11.6 (p<0.0001)	-43.7 (p<0.0001)
VX-659 (400mg QD) + tezacaftor (100mg QD) + ivacaftor (150mg q12h)	+13.3 (p<0.0001)	-51.4 (p<0.0001)
<i>* all p-values are within group p-values based on mixed effect models; values expressed as 'Through Day 29' are the average of Day 15 and Day 29 measures</i>		

A secondary endpoint in the clinical trial measured mean absolute change in the respiratory domain of CFQ-R, a validated patient-reported outcome measure, at Day 29. CFQ-R results reported are based on a mixed effect model not adjusted for baseline CFQ-R. The mean absolute improvements for patients who received the triple combination were 24.6 points (VX-659 80mg arm), 19.8 points (VX-659 240mg arm) and 21.8 points (VX-659 400mg arm). The improvement for those who received placebo was 4.7 points.

VX-445

We are evaluating VX-445 in an ongoing Phase 2 randomized, double-blind clinical trial. In this clinical trial, we are evaluating the safety and tolerability of single and multiple ascending doses of VX-445 alone and in triple combination with tezacaftor and ivacaftor in healthy volunteers (Parts A, B and C). We also are evaluating the safety, tolerability and efficacy of VX-445 (50mg, 100mg and 200mg QD) in triple combination with tezacaftor and ivacaftor for four weeks in patients with CF 18 years of age and older who are F508del/Min patients (Part D) and F508del homozygous patients (Part E). In Part F of the clinical trial, we are evaluating VX-445 in combination with tezacaftor and VX-561 as a potential once-daily triple combination regimen in F508del/Min patients. The primary objectives of the parts of the clinical trial in CF patients are safety, tolerability and efficacy as assessed by mean absolute change in ppFEV1 from baseline. Secondary endpoints include change in sweat chloride and CFQ-R. We have reported data from Part D of the clinical trial. Parts E and F of the clinical trial are ongoing with data expected in the first half of 2018.

Safety Data

In Part D of the clinical trial, the triple combination regimen was generally well tolerated. The majority of adverse events were mild or moderate. Serious adverse events were reported in five patients: two patients in the placebo group (1 with hemoptysis and 1 with infective pulmonary exacerbation) and three patients in the triple combination groups (1 patient with infective pulmonary exacerbation, jugular vein thrombosis related to a central line and distal intestinal obstruction syndrome; 1 patient with infective pulmonary exacerbation and influenza; and 1 patient with infective pulmonary exacerbation). None of these serious adverse events was considered related to treatment and none resulted in treatment discontinuation. The most common adverse events (>10%), regardless of treatment group, were cough, sputum increased, infective pulmonary exacerbation, hemoptysis, headache, nasal congestion, nausea, oropharyngeal pain and pyrexia. Two patients discontinued treatment due to adverse events in the triple combination treatment groups (1 patient with rash and 1 patient with increased bilirubin without associated elevations in transaminases) and none in the placebo group. Following treatment discontinuation, the rash resolved and the increased bilirubin returned to baseline. Two patients interrupted treatment due to adverse events in the triple combination groups (1 with constipation and 1 with increased bilirubin without associated elevations in transaminases); both events resolved when treatment was interrupted and both patients subsequently restarted and completed triple combination treatment without further incident.

Efficacy Data

Part D of the clinical trial evaluated the triple combination for four weeks in 65 patients who have one *F508del* mutation and one minimal function mutation (12 in the combined placebo arm, 10 in the VX-445 50mg arm, 22 in the VX-445 100mg arm and 21 in the VX-445 200mg arm). A summary of the within-group lung function and sweat chloride data is provided below:

VX-445 in <i>F508del</i> /Min Patients		
Mean Absolute Within-Group Change From Baseline Through Day 29*	Mean Absolute Within-Group Change in ppFEV ₁ (percentage points)	Mean Absolute Within-Group Change in Sweat Chloride (mmol/L)
Triple placebo	0.0 (p=0.9943)	-2.2 (p=0.5804)
VX-445 (50mg QD) + tezacaftor (100mg QD) + ivacaftor (150mg q12h)	+11.1 (p<0.0001)	-38.2 (p<0.0001)
VX-445 (100mg QD) + tezacaftor (100mg QD) + ivacaftor (150mg q12h)	+7.8 (p<0.0001)	-33.2 (p<0.0001)
VX-445 (200mg QD) + tezacaftor (100mg QD) + ivacaftor (150mg q12h)	+13.8 (p<0.0001)	-39.1 (p<0.0001)

* all p-values are within group p-values based on mixed effect models; values expressed as 'Through Day 29' are the average of Day 15 and Day 29 measures

A secondary endpoint in the clinical trial measured mean absolute change in the respiratory domain of CFQ-R at Day 29. CFQ-R results reported are based on a mixed effect model not adjusted for baseline CFQ-R. The mean absolute improvements for patients who received the triple combination were 20.8 points (VX-445 50mg arm), 15.4 points (VX-445 100mg arm) and 25.7 points (VX-445 200mg arm). The improvement for those who received placebo was 4.2 points.

DEVELOPMENT PROGRAMS

Pain

We are developing VX-150 and VX-128, inhibitors of the sodium channel 1.8 (Nav 1.8), as potential treatments for pain. We have obtained positive results from two Phase 2 clinical trials of VX-150:

- In the first quarter of 2017, we announced data from a 14-day Phase 2 randomized, double-blind, placebo-controlled, clinical trial of VX-150 in patients with pain from osteoarthritis of the knee.
- In the first quarter of 2018, we announced data from a Phase 2 randomized, double-blind, placebo-controlled clinical trial evaluating VX-150 as a treatment for patients with acute pain following bunionectomy surgery.

A third Phase 2 clinical trial evaluating VX-150 for the treatment of neuropathic pain caused by small fiber neuropathy is ongoing, and we are planning to initiate a Phase 1 clinical trial of an intravenous formulation of VX-150.

A Phase 1 clinical trial of VX-128, in healthy volunteers is ongoing to evaluate single and multiple ascending doses of VX-128 to support the planned initiation of a Phase 2 clinical trial of VX-128 in acute pain.

Hemoglobinopathies

In conjunction with CRISPR, we are co-developing a treatment aimed at the underlying genetic causes of specified hemoglobinopathies using CRISPR-Cas9 gene editing technology. In the fourth quarter of 2017, CRISPR submitted a clinical trial application for CTX001, an investigational gene editing treatment, in beta-thalassemia, a blood disorder that reduces the production of hemoglobin. The Phase 1/2 trial is designed to assess the safety and efficacy of CTX001 in adult transfusion-dependent beta-thalassemia patients and is expected to begin in Europe in 2018. In 2018, we expect an investigation new drug, or IND, application to be submitted to the FDA for CTX001 as a potential treatment for sickle cell disease.

Influenza

Janssen Pharmaceuticals, Inc., or Janssen, is developing pimodivir (JNJ-63623872), previously referred to as VX-787, as a potential treatment for the influenza A virus. We exclusively licensed pimodivir to Janssen in 2014. During the fourth quarter of 2017, Janssen initiated a Phase 3 clinical trial of pimodivir in combination standard of care treatment in patients who are hospitalized or are outpatients at a higher risk of influenza-related complications.

RESEARCH PROGRAMS

We invest in research and development in order to discover and develop medicines for people with serious diseases. Our research organization seeks to identify new medicines by combining transformative insights into the causal human biology of serious diseases with innovative approaches to therapeutics. Our approach to drug discovery has 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 KALYDECO, ORKAMBI and SYMDEKO for the treatment of cystic fibrosis and INCIVEK (telaprevir) for the treatment of hepatitis C infection. In addition to our approved medicines, we have a number of drug candidates that we are developing independently or that are being developed by collaborators pursuant to collaboration agreements. Over the last several years, we have expanded our research capabilities to include additional innovative therapeutic approaches with a focus on nucleic acid-based therapies. For example, in the fourth quarter of 2017, a clinical trial application was submitted for CTX001, a drug candidate that we are co-developing with CRISPR that utilizes the CRISPR-Cas9 gene editing technology.

We are applying the experience we gained developing medicines for cystic fibrosis to guide our current investments in research and development programs by:

- focusing on validated targets that have been shown in patients to have a causal relationship with respect to serious diseases;
- generating biological assays and identifying clinical biomarkers that we believe will be predictive of clinical responses;
- targeting the discovery and development of medicines that have the potential to offer transformative benefit; and
- identifying 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 cystic fibrosis, pain and hemoglobinopathies, we are focusing our early research efforts on identifying drug candidates for the treatment of serious diseases such as adrenoleukodystrophy, alpha-1 antitrypsin deficiency and polycystic kidney disease.

To augment our internal research programs, we seek 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.

COMMERCIAL ORGANIZATION

Our commercial organization focuses on supporting sales of ORKAMBI, KALYDECO and SYMDEKO 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 whom we believe will be sufficient to support future needs, including support for SYMDEKO which was recently approved by the FDA. 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 a small sales force that promotes KALYDECO and ORKAMBI in jurisdictions where these products are approved.

We market our products through personal interactions with individual physicians, advertising, sending direct mail, public relations activities and other activities. 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.

COLLABORATIONS

We have entered into collaborations with pharmaceutical and other companies and organizations that provide us financial and other resources, including capabilities in research, development, manufacturing and sales and marketing, and licenses to

intellectual property. These collaborations have provided us with drug candidates and/or important financial and non-financial resources that have contributed to our products and a number of the drug candidates in our current development pipeline. We may seek to license or acquire drugs, drug candidates and other technologies that have the potential to add to our pipeline or to provide us with new commercial opportunities. In particular, we are focusing on drug candidates for the treatment of patients with CF and other third-party drug candidates that could be developed for specialty markets. Furthermore, we may seek collaborators to support, develop and/or commercialize some of our current drug candidates and/or additional drug candidates that may emerge from our research activities.

Cystic Fibrosis Foundation Therapeutics Incorporated

We began working with the Cystic Fibrosis Foundation Therapeutics Incorporated, or CFFT, in 1998. We entered into a collaboration agreement with CFFT in 2004 and have amended it several times 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 any approved drugs 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 (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 VX-659 and VX-445. For combination products, such as ORKAMBI and SYMDEKO, sales are allocated equally to each of the active pharmaceutical ingredients in the combination product.

For ivacaftor, lumacaftor and tezacaftor, we will have royalty obligations to CFFT until the expiration of patents covering each compound. We have patents in the United States and European Union covering the composition-of-matter of ivacaftor that expire in 2027 and 2025, respectively, subject to potential patent life extensions. We have patents in the United States and European Union covering the composition-of-matter of lumacaftor that expire in 2030 and 2026, respectively, subject to potential patent life extensions. We have patents in the United States and European Union covering the composition-of-matter of tezacaftor that expire in 2027 and 2028, respectively, subject to potential patent life extensions.

CRISPR Therapeutics AG

In 2015, we entered into a strategic collaboration, option and license agreement with 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. Pursuant to this agreement, we have the exclusive right to license up to six CRISPR-Cas9-based targets and paid CRISPR an upfront payment of \$75.0 million.

We fund all of the discovery activities conducted pursuant to the CRISPR agreement. For potential hemoglobinopathy treatments, including treatments for sickle cell disease and beta-thalassemia, we share equally with CRISPR all research and development costs and worldwide revenues. For other targets that we elect to license, we would lead all development and global commercialization activities. For each target that we elect to license, other than hemoglobinopathy targets, CRISPR has the potential to receive up to \$420.0 million in development, regulatory and commercial milestones and royalties on net sales.

We may terminate the agreement upon 90 days' notice to CRISPR prior to any product receiving marketing approval or upon 270 days' notice after a product has received marketing approval. The agreement also may be terminated by either party for a material breach by the other, subject to notice and cure provisions. Unless earlier terminated, the agreement will continue in effect until the expiration of our payment obligations under the agreement.

In the fourth quarter of 2017, pursuant to the terms of the agreement, we entered a co-development and co-commercialization agreement with CRISPR, under which we and CRISPR will co-develop and co-commercialize CTX001 for the treatment of hemoglobinopathies.

Other Collaborations

Moderna Therapeutics, Inc.

In July 2016, we entered into a strategic collaboration and licensing agreement with Moderna Therapeutics, Inc., or Moderna, pursuant to which the parties are seeking to identify and develop messenger ribonucleic acid, or mRNA, therapeutics for the treatment of CF. In connection with this agreement, we made an upfront payment to Moderna of \$20.0 million. Moderna has the potential to receive future development and regulatory milestones of up to \$275.0 million, including \$220.0 million in approval and reimbursement milestones, as well as tiered royalty payments on net sales. Under the terms of the Moderna agreement, Moderna is leading discovery efforts and we are leading all preclinical, development

and commercialization activities associated with the advancement of mRNA therapeutics that result from this collaboration and we will fund all expenses related to the collaboration.

We may terminate the agreement by providing advance notice to Moderna, with the required length of notice dependent upon whether any product developed under the agreement has received marketing approval. The agreement also may be terminated by either party for a material breach by the other, subject to notice and cure provisions. Unless earlier terminated, the agreement will continue in effect until the expiration of our payment obligations under the agreement.

BioAxone Biosciences, Inc.

In 2014, we entered into a license and collaboration agreement with BioAxone. Pursuant to this agreement, we are collaborating with BioAxone on the research, development and commercialization of VX-210 (formerly referred to as Cethrin), a Rho inhibitor controlled by BioAxone, for the treatment of patients who have spinal cord injuries.

We paid BioAxone an initial payment of \$10.0 million and BioAxone has the potential to receive up to \$90.0 million in milestones and license fees, including development and regulatory milestone payments and a license continuation fee. In addition, BioAxone would receive tiered royalties and commercial milestones based on future net product sales, if any. We hold an option to purchase BioAxone at a predetermined price. The option expires on the earliest of (a) the day the FDA accepts the Biologics License Application submission for VX-210, (b) the day we elect to continue the license instead of exercising the option to purchase BioAxone and (c) March 15, 2018, subject to our option to extend this date by one year. We may terminate our agreement with BioAxone upon 90 days' notice or immediately if we determine that a licensed product is unsafe for administration to humans. The agreement also may be terminated by either party for a material breach by the other or by BioAxone for our inactivity with respect to VX-210, in each case subject to notice and cure provisions. Unless earlier terminated, the agreement will continue until the expiration of our royalty obligations.

Parion Sciences, Inc.

In 2015, we entered into a strategic collaboration and license agreement with Parion Sciences, Inc., or Parion, pursuant to which we are collaborating with Parion to develop ENaC inhibitors, including VX-371 and VX-551, for the potential treatment of CF and other pulmonary diseases.

Parion received an \$80.0 million up-front payment and in 2016, Parion earned a milestone payment of \$5.0 million based upon the achievement of a specified milestone under the agreement. Parion has the potential to receive up to an additional (i) \$485.0 million in development and regulatory milestone payments for development of ENaC inhibitors in CF, including \$360.0 million related to global filing and approval milestones, (ii) \$370.0 million in development and regulatory milestones for VX-371 and VX-551 in non-CF pulmonary indications and (iii) \$230.0 million in development and regulatory milestones if we elect to develop an additional ENaC inhibitor from Parion's research program. Parion will receive tiered royalties on potential sales of licensed products that range from the low double digits to mid-teens as a percentage of net sales.

We may terminate the agreement upon 90 days' notice to Parion prior to any licensed product receiving marketing approval or upon 180 days' notice after a licensed product has received marketing approval. Parion may terminate the agreement upon 30 days' notice if Vertex experiences a change of control prior to the initiation of the first Phase 3 clinical trial for a licensed product, subject to our right to receive specified royalties on any subsequent commercialization of licensed products. The agreement also may be terminated by either party for a material breach by the other, subject to notice and cure provisions. Unless earlier terminated, the agreement will continue in effect until the expiration of our royalty obligations.

Outlicense Arrangements

We have entered into various agreements pursuant to which we have outlicensed rights to certain drug candidates to third-party collaborators. Pursuant to these outlicense arrangements, our 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 arrangements, our collaborators may be required to make upfront payments, milestone payments upon the achievement of certain product research and development objectives and/or pay royalties on future sales, if any, of commercial products resulting from the collaboration.

Merck KGaA

In the first quarter of 2017, we entered into a Strategic Collaboration and License Agreement with Merck KGaA, Darmstadt, Germany, or Merck KGaA. Pursuant to the agreement, we granted Merck KGaA an exclusive worldwide license to research, develop and commercialize four oncology research and development programs. Under the agreement, we granted Merck KGaA exclusive, worldwide rights to our two clinical-stage programs targeting DNA damage repair: our

ataxia telangiectasia and Rad3-related protein inhibitor, or ATR program, including VX-970 and VX-803, and our DNA-dependent protein kinase inhibitor, or DNA-PK program, including VX-984. In addition, we granted Merck KGaA exclusive, worldwide rights to two pre-clinical programs.

Under the agreement, we earned an up-front payment of \$230.0 million. In addition, we will receive tiered royalties on potential sales of licensed products, calculated as a percentage of net sales, that range from (i) mid-single digits to mid-twenties for clinical-stage programs and (ii) mid-single digits to high single digits for the pre-clinical research programs. Merck KGaA will assume full responsibility for development and commercialization costs for all programs.

Merck KGaA may terminate the agreement or any individual program by providing 90 days' notice, or, in the case of termination of a program with a product that has received marketing approval, 180 days' notice. The agreement may also be terminated by either party for a material breach by the other party, subject to notice and cure provisions. Unless earlier terminated, the agreement will continue in effect until the date on which the royalty term and all payment obligations with respect to all products in all countries have expired.

Janssen Pharmaceuticals, Inc.

In 2014, we entered into an agreement with Janssen Inc. Pursuant to this agreement, Janssen Inc. has an exclusive worldwide license to develop and commercialize certain drug candidates for the treatment of influenza, including JNJ-63623872 (formerly VX-787). We received non-refundable payments of \$35.0 million from Janssen Inc. in 2014 and have the potential to receive development, regulatory and commercial milestone payments as well as royalties on future product sales, if any. Janssen Inc. is responsible for costs related to the development and commercialization of the compounds. Janssen Inc. may terminate the agreement, subject to certain exceptions, upon six months' notice. In the fourth quarter of 2017, we earned a \$25.0 million milestone payment from Janssen Inc. related to the initiation of a Phase 3 clinical trial of JNJ-63623872.

INTELLECTUAL PROPERTY

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. We have patents and pending patent applications that relate to potential drug targets, compounds we are developing to modulate those targets, methods of making or using those compounds and proprietary elements of our drug discovery platform.

Much of our technology and many of our processes depend upon the knowledge, experience and skills of key scientific and technical personnel. To protect our rights to our proprietary know-how and technology, we require all employees, as well as our consultants and advisors when feasible, to enter into confidentiality agreements that require disclosure and assignment to us of ideas, developments, discoveries and inventions made by these employees, consultants and advisors in the course of their service to us.

While we have numerous issued patents and pending patent applications in our patent portfolio, we believe that the patents and patent applications in the United States and the European Union that are the most important to our business are those that claim the composition-of-matter of our drugs and drug candidates that have progressed at least into Phase 3 clinical trials. The following table sets forth the status of such primary patents and patent applications in the United States and the European Union covering the composition-of-matter of these drugs and drug candidates:

Drug/Drug Candidate	Status of United States Patent (Anticipated Expiration, Subject to Potential Extensions)	Status of European Union Patent (Anticipated Expiration, Subject to Potential Extensions)
Ivacaftor	Granted (2027)	Granted (2025)
Lumacaftor	Granted (2030)	Granted (2026)
Tezacaftor	Granted (2027)	Granted (2028)

We hold issued patents and pending patent applications in the United States, and in foreign countries we deem appropriate, claiming intellectual property developed as part of our research and development programs. In addition to the composition-of-matter patents and patent applications listed above, we hold or have exclusive licenses to the following intellectual property:

- U.S. and foreign patents and patent applications covering CF potentiators, correctors and ENaC inhibitors, including ivacaftor, lumacaftor, tezacaftor, VX-561, VX-659, VX-445 and VX-371 and many other related compounds, and the use of those potentiators, correctors and ENaC inhibitors to treat CF.

- U.S. and foreign patents and patent applications covering VX-150 and VX-128 and the use of VX-150 and VX-128 to treat pain indications.
- U.S. and foreign patents and patent applications covering VX-210 and the use of VX-210 to treat neurology indications.
- U.S. and foreign patents and patent applications covering the manufacture, pharmaceutical compositions, related solid forms, formulations, dosing regimens and methods of use of most of the above compounds, including ivacaftor, lumacaftor and tezacaftor.

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

We have a U.S. patent that covers the composition-of-matter of ivacaftor that we expect will provide intellectual property protection in the United States through its expiration date in 2027. We have a European patent that covers the composition-of-matter of ivacaftor that we expect will provide intellectual property protection in the European Union through its expiration date in 2025, subject to potential extension.

We have patents in the United States and European Union that cover the composition of matter of lumacaftor that we expect will provide intellectual property protection in these jurisdictions through their expiration dates in 2030 and 2026, respectively, subject to potential extension.

We have patents in the United States and European Union that cover the composition of matter of tezacaftor that we expect will provide intellectual property protection in these jurisdictions through their expiration dates in 2027 and 2028, respectively, subject to potential extension.

MANUFACTURING

Manufacturing Approach and Philosophy

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. Wherever possible, we seek to establish multiple suppliers for each raw material and step in the manufacturing process. However, our supply chain includes a single-source manufacturer for (i) one step in the ivacaftor manufacturing process, (ii) the manufacture of the tablets of ORKAMBI that is used for patients with CF six to eleven years of age and (iii) a pre-formulation step and the manufacture of the tablets for our commercial supply of SYMDEKO.

We expect that we will continue for the foreseeable future to rely on third parties to meet most of our commercial supply needs and a significant portion of our clinical supply needs. 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. 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. 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.

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 cGMP. 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.

Manufacture of KALYDECO (ivacaftor)

We obtain ivacaftor to meet our commercial and clinical supply needs through a third-party manufacturing network. A disruption in the commercial supply of KALYDECO would have a significant effect on patients, our business and our product revenues.

Manufacture of ORKAMBI (lumacaftor/ivacaftor)

We obtain the bulk materials needed to produce both our commercial and clinical supply of ORKAMBI through a third-party manufacturing network. We have developed several tablet manufacturing processes utilizing various degrees of continuous manufacturing technology as well as a batch manufacturing processes to produce commercial quantities of ORKAMBI. This includes multiple third-party manufacturers that are producing commercial quantities of ORKAMBI using combinations of batch and continuous manufacturing processes, as well as a fully-continuous drug product manufacturing process at our internal facility located in Boston, Massachusetts. 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.

Manufacture of SYMDEKO (tezacaftor/ivacaftor)

We obtain the bulk materials needed to produce both our commercial and clinical supply of SYMDEKO through a third-party manufacturing network. We produce our commercial supply of SYMDEKO using a fully-continuous drug product manufacturing process at our internal facility located in Boston, Massachusetts and are in the process of establishing a second fully-continuous drug product manufacturing location with a third-party.

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. Many of our competitors have substantially greater financial, technical and human resources than we do. We face competition based on the safety and efficacy of our products 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.

Cystic Fibrosis

An increasing number of companies are seeking to identify and develop drug candidates for the treatment of CF, including companies such as Galapagos NV in collaboration with AbbVie, ProQR Therapeutics, Proteostasis Therapeutics, Eloxx Pharmaceuticals and several private companies. Although we are the first company to successfully develop drugs that treat the underlying cause of CF, ORKAMBI, KALYDECO and SYMDEKO are collectively approved to treat only a portion of patients with CF. Our competitors have research and development programs directed at identifying and developing CFTR potentiators, CFTR correctors, ENaC inhibitors 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. Our success in rapidly developing and commercializing KALYDECO, ORKAMBI and SYMDEKO 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 ORKAMBI, KALYDECO, SYMDEKO and/or our other CF drug candidates, if then approved, could face significant competitive pressure.

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 regulation. federal and state statutes and regulations govern the testing, manufacture, safety, efficacy, 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, FDA regulations and guidance often are revised or reinterpreted by the agency in ways that may significantly affect our business and our products. It is impossible to predict whether legislative changes will be enacted, or FDA 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 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 cGMP; 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 cGMP-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, compared to ten months for a standard review.

Manufacturing Quality Control

Among the conditions for NDA or BLA approval is the requirement that the prospective manufacturer’s quality control and manufacturing procedures continually conform with cGMP. In complying with cGMP, 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 the longest existing exclusivity (patent or 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. KALYDECO, ORKAMBI and SYMDEKO have been granted designation as orphan drugs by the FDA.

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.

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.

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. These third-party payors increasingly are reducing reimbursements for 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. Decreases in third-party reimbursement for a product or a decision by a third-party payor 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 will 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. 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 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. The branded prescription drug fee is not tax deductible.

In Europe and many other foreign countries, the success of ORKAMBI and KALYDECO and of any other drug candidates we may develop, depends largely on obtaining and maintaining government reimbursement, because in many foreign countries 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 and France, commercial sales of a new product can occasionally 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 sales 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. 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 profitability of the company placing the drug on the market. Recently, many countries in the European Union have increased the amount of discounts required on pharmaceuticals and these efforts could continue as countries attempt to manage healthcare expenditures, especially in light of the severe fiscal and debt crises experienced by many countries in the European Union. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will provide for reimbursement of our products, or 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.

Other Regulations

Pharmaceutical companies are also subject to various laws pertaining to healthcare “fraud and abuse,” including anti-kickback laws and false claims laws. Anti-kickback laws make it illegal to solicit, offer, receive or pay any remuneration in exchange 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 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 federal “sunshine” provisions. The 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 made to physicians and certain other healthcare practitioners or to teaching hospitals. State laws may also require disclosure of pharmaceutical pricing information and marketing expenditures. Many of these laws and regulations contain ambiguous requirements. 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. The extent of government regulation, which might result from future legislation or administrative action, cannot accurately be predicted.

EMPLOYEES

As of December 31, 2017, we had approximately 2,300 employees, as compared to approximately 2,150 employees as of December 31, 2016. Of these employees, approximately 1,870 were based in the United States and approximately 375 were based in Europe. In February 2017, we decided to consolidate our research activities into our Boston, Milton Park and San Diego locations and closed our research site in Canada. Our scientific staff members have diversified experience and expertise in molecular and cell biology, genetics, biochemistry, synthetic organic chemistry, protein X-ray crystallography, protein nuclear magnetic resonance spectroscopy, microbiology, computational chemistry and computational biology, biophysical chemistry, medicinal chemistry, clinical pharmacology and clinical medicine. Our clinical development personnel have extensive expertise in designing and executing clinical trials. Employees in our commercial organization have extensive experience in selling and marketing pharmaceutical products as well as seeking reimbursement from government and third-party payors for pharmaceutical products. Our employees are not covered by a collective bargaining agreement, except for a small number of employees outside the U.S. We consider our relations with our employees to be good.

OTHER MATTERS

Financial Information and Significant Customers

Financial information about (i) our net product revenues and other revenues generated in the principal geographic regions in which we operate and our significant customers is set forth in Note T, "Segment Information," to our consolidated financial statements included in this Annual Report on Form 10-K, (ii) net income (loss) per share attributable to Vertex common shareholders and our total assets are provided in our consolidated financial statements included in this Annual Report on Form 10-K and (iii) our research and development expenses in each of the last three fiscal years and our deconsolidation of Parion as of September 30, 2017 is provided in Item 7, "Management's Discussion and Analysis of Financial Condition and Results of Operations." A discussion of the risks attendant to our international operations is set forth in the "Risk Factors" section of 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.

DIRECTORS AND EXECUTIVE OFFICERS OF THE REGISTRANT

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

Name	Age	Position
Jeffrey M. Leiden, M.D., Ph.D.	62	Chairman of the Board, Chief Executive Officer and President
David Altshuler, M.D., Ph.D.	53	Executive Vice President, Global Research and Chief Scientific Officer
Stuart A. Arbuckle	52	Executive Vice President and Chief Commercial Officer
Jeffrey A. Chodakewitz, M.D.	62	Executive Vice President, Global Medicines Development and Medical Affairs, and Chief Medical Officer
Michael Parini, J.D.	43	Executive Vice President and Chief Legal and Administrative Officer
Amit K. Sachdev, J.D.	50	Executive Vice President and Chief Regulatory Officer
Ian F. Smith	52	Executive Vice President and Chief Operating Officer
Thomas Graney	53	Senior Vice President and Chief Financial Officer
Paul M. Silva	51	Senior Vice President and Corporate Controller
Sangeeta M. Bhatia, M.D., Ph.D.	49	Director
Alan Garber, M.D., Ph.D.	62	Director
Terrence C. Kearney	63	Director
Yuchun Lee	52	Director
Margaret G. McGlynn	58	Director
Bruce I. Sachs	58	Director
Elaine S. Ullian	70	Director
William Young	73	Director

Dr. Leiden is our Chairman, Chief Executive Officer and President. 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 is a senior advisor to Clarus Ventures. Dr. Leiden serves as a director of Quest Diagnostics Inc., a medical diagnostics company, and 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. Dr. Leiden received his M.D., Ph.D. and B.A. degrees from the University of Chicago.

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, MIT, 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. Mr. Arbuckle holds a BSc in pharmacology and physiology from the University of Leeds.

Dr. Chodakewitz is our Executive Vice President, Global Medicines Development and Medical Affairs and Chief Medical Officer. Dr. Chodakewitz joined Vertex as a Senior Vice President in January 2014 and became an Executive Vice President in October 2014. Prior to joining us, Dr. Chodakewitz spent more than 20 years at Merck & Co., Inc., where he held a variety of roles including Vice President of Clinical Research – Infectious Diseases & Vaccines, Vice President of Clinical Pharmacology/Early Stage Development, Senior Vice President of Late Stage Development, and Senior Vice President of Global Scientific Strategy (Infectious Diseases, Respiratory/Immunology). Prior to his tenure at Merck, he served as the Director of the HIV Outpatient Clinic at the Veterans Administration Medical Center in West Haven, Connecticut and held various academic positions at Yale University and New York University Schools of Medicine. Dr. Chodakewitz serves as a member of the Board of Directors of Tetrphase Pharmaceuticals, Inc., a pharmaceutical company. Dr. Chodakewitz holds B.S. in Biochemistry from Yale University, and an M.D. from the Yale University School of Medicine.

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 Regulatory Officer, a role he assumed in January 2017. He served as our Executive Vice President, Policy, Access and Value, from October 2014 through December 2016. 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. From 2010 through 2013 he established our first international commercial operations in Canada. 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. Mr. Sachdev holds a B.S. from Carnegie Mellon University, and a J.D. from Emory University School of Law.

Mr. Smith is our Executive Vice President and Chief Operating Officer, a role he assumed in September 2017. He was our Executive Vice President, Chief Operating Officer and Chief Financial Officer from January 2017 until September 2017, Executive Vice President and Chief Financial Officer from February 2006 until January 2017, our Senior Vice President and Chief Financial Officer from November 2003 to February 2006, and our Vice President and Chief Financial Officer from October 2001 to November 2003. Prior to joining us, Mr. Smith served as a partner in the Life Science and Technology Practice Group of Ernst & Young LLP, an accounting firm, from 1999 to 2001. Mr. Smith initially joined Ernst & Young's U.K. firm in 1987, and then joined its Boston office in 1995. Mr. Smith has served as a member of the Boards of Directors of Acorda Therapeutics, Inc., a drug development company, since February 2007, and Infinity Pharmaceuticals, Inc., a drug development company, since May 2008. Mr. Smith served on the Board of Directors of Ophthotech Corporation, a biopharmaceutical company, from August 2016 to May 2017. Mr. Smith holds a B.A. in accounting and finance from Manchester Metropolitan University, U.K., is a member of the American Institute of Certified Public Accountants and is a Chartered Accountant of England and Wales.

Mr. Graney is our Senior Vice President and Chief Financial Officer, a position he has held since September 2017. From August 2014 until he joined Vertex, Mr. Graney served as Chief Financial Officer and Senior Vice President of Finance and Corporate Strategy for Ironwood Pharmaceuticals, Inc. From January 2010 to August 2014, Mr. Graney served as Worldwide Vice President of Finance and Chief Financial Officer of Ethicon, Inc., a maker of surgical medical devices and subsidiary of Johnson and Johnson. From 1994 to 2010, Mr. Graney served in various roles of increasing responsibility at Johnson & Johnson, including most recently as Vice President of Finance for J&J Global Supply Chain. Mr. Graney serves on the board of directors of AC Immune SA, a biopharmaceutical company. Mr. Graney holds a Bachelor of Science degree in accounting from the University of Delaware and an M.B.A. in marketing, finance and international business from the Leonard N. Stern School of Business at New York University.

Mr. Silva is our Senior Vice President and Corporate Controller, a position he has held since April 2011. 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 financing 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. Bhatia has been a member of our Board of Directors since June 2015. Dr. Bhatia is a professor at the Massachusetts Institute of Technology, where she currently serves as the John J. and Dorothy Wilson Professor of Health Sciences & Technology/Electrical Engineering & Computer Science. Prior to joining the Massachusetts Institute of Technology in 2005, Dr. Bhatia was a professor of bioengineering and medicine at the University of California at San Diego from 1998 through 2005. Dr. Bhatia also is an investigator for the Howard Hughes Medical Institute, a member of the Department of Medicine at Brigham and Women's Hospital, a member of the Broad Institute and a member of the Koch Institute for Integrative Cancer Research. Dr. Bhatia holds a Sc.B. in biomedical engineering from Brown University, an S.M. and Ph.D. in Mechanical Engineering from the Massachusetts Institute of Technology and an M.D. from Harvard Medical School.

Dr. Garber has been a member of our Board of Directors since June 2017. He is Provost of Harvard University and the Mallinckrodt Professor of Health Care Policy at Harvard Medical School, a Professor of Economics in the Faculty of Arts and Sciences, Professor of Public Policy in the Harvard Kennedy School of Government, and Professor in the Department of Health Policy and Management in the Harvard T.H. Chan School of Public Health. From 1998 until he joined Harvard in 2011, he was the Henry J. Kaiser Jr. Professor, a Professor of Medicine, and a Professor (by courtesy) of Economics, Health Research and Policy, and of Economics in the Graduate School of Business at Stanford University. Dr. Garber is a member of the National Academy of Medicine, the American Society of Clinical Investigation, the Association of American Physicians, the American Academy for Arts and Sciences, and the Board on Science, Technology, and Economic Policy at the National Academies. He is a Fellow of the American Association for the Advancement of Science, the American College of Physicians, and the Royal College of Physicians. Dr. Garber is also a Research Associate with the National Bureau of Economic Research and served as founding Director of its Health Care Program for nineteen years. He has also served as a member of the National Advisory Council on Aging at the National Institutes of Health, as a member of the Board of Health Advisers of the Congressional Budget Office and as Chair of the Medicare Evidence Development and Coverage Advisory Committee at the Centers for Medicare and Medicaid Services. Dr. Garber has been a member of the Board of Directors of Exelixis, Inc., a biopharmaceutical company, since 2005. Dr. Garber holds an A.B. summa cum laude, an A.M. and a Ph.D., all in Economics, from Harvard University, and an M.D. with research honors from Stanford University.

Mr. Kearney has been a member of our Board of Directors since May 2011. Mr. Kearney served as the Chief Operating Officer of Hospira, Inc., a specialty pharmaceutical and medication delivery company, from April 2006 to January 2011. From April 2004 to April 2006, he served as Hospira's Senior Vice President, Finance, and Chief Financial Officer, and he served as Acting Chief Financial Officer through August 2006. Mr. Kearney served as Vice President and Treasurer of Abbott Laboratories from 2001 to April 2004. From 1996 to 2001, Mr. Kearney was Divisional Vice President and Controller for Abbott's International Division. Mr. Kearney serves as a member of the Board of Directors at Acceleron Pharma Inc., a biopharmaceutical company, and AveXis, Inc., a gene therapy company, and served as a member of the Board of Directors at Innoviva, Inc. (formerly known as Theravance, Inc.), a royalty management company, until April 2016. He received his B.S. in biology from the University of Illinois and his M.B.A. from the University of Denver.

Mr. Lee has been a member of our Board of Directors since September 2012. Mr. Lee serves as an Executive in Residence (XIR) and Partner of General Catalyst Partners, a venture capital firm, positions he has held since April of 2013. Mr. Lee also serves as the Chief Executive Officer of Allego, Inc. and is Executive Chairman of Clarabridge, Inc. Mr. Lee was the Vice President of IBM's Enterprise Marketing Management Group from November 2010 through January 2013. Mr. Lee co-founded Unica Corporation, a provider of software and services used to automate marketing processes, in 1992, and was Unica's President and/or Chief Executive Officer from 1992 through November 2010, when Unica was acquired by IBM. From 1989 to 1992, Mr. Lee was a senior consultant at Digital Equipment Corporation, a supplier of general computing technology and consulting services. Mr. Lee holds a B.S. and an M.S. in electrical engineering and computer science from the Massachusetts Institute of Technology and an M.B.A. from Babson College.

Ms. McGlynn has been a member of our Board of Directors since May 2011. Ms. McGlynn served as the President and Chief Executive Officer of the International AIDS Vaccine Initiative, a global not-for-profit organization whose mission is to ensure the development of safe, effective and accessible HIV vaccines for use throughout the world, from July 2011 until September 2015. Ms. McGlynn served as President, Vaccines and Infectious Diseases of Merck & Co., Inc. from 2005 until

2009. Ms. McGlynn joined Merck in 1983 and served in a variety of marketing, sales and managed care roles. Ms. McGlynn serves as a member of the Board of Directors for Air Products and Chemicals, Inc., a company specializing in gases and chemicals for industrial uses, and Amicus Therapeutics, Inc., a biopharmaceutical company. She is also a member of the National Industrial Advisory Committee at the University at Buffalo School of Pharmacy and Pharmaceutical Sciences. Ms. McGlynn holds a B.S. in Pharmacy and an M.B.A. in Marketing from the State University of New York at Buffalo.

Mr. Sachs has been a member of our Board of Directors since 1998. Mr. Sachs is a General Partner at Charles River Ventures, a venture capital firm he joined in 1999. From 1998 to 1999, he served as Executive Vice President and General Manager of Ascend Communications, Inc. From 1997 until 1998, Mr. Sachs served as President and Chief Executive Officer of Stratus Computer, Inc. From 1995 to 1997, he served as Executive Vice President and General Manager of the Internet Telecom Business Group at Bay Networks, Inc. From 1993 to 1995, he served as President and Chief Executive Officer of Xylogics, Inc. Mr. Sachs holds a B.S.E.E. in electrical engineering from Bucknell University, an M.E.E. in electrical engineering from Cornell University, and an M.B.A. from Northeastern University.

Ms. Ullian has been a member of our Board of Directors since 1997. Ms. Ullian served as President and Chief Executive Officer of Boston Medical Center, a private, not-for-profit, 626-bed, academic medical center with a community-based focus, from 1996 through January 2010. From 1994 to 1996, she served as President and Chief Executive Officer of Boston University Medical Center Hospital. From 1987 to 1994, Ms. Ullian served as President and Chief Executive Officer of Faulkner Hospital. She also serves as a director of Thermo Fisher Scientific Inc. and Hologic, Inc. Ms. Ullian holds a B.A. in political science from Tufts University and an M.P.H. from the University of Michigan.

Mr. Young has been a member of our Board of Directors since May 2014. Mr. Young is a Venture Partner at Clarus Ventures, a life sciences venture capital firm, which he joined in 2010. Prior to Clarus Ventures, Mr. Young served from 1999 until June 2009 as the Chairman and Chief Executive Officer of Monogram Biosciences, Inc., a biotechnology company acquired by Laboratory Corporation of America in June 2009. From 1980 to 1999, Mr. Young was employed at Genentech, Inc. in positions of increasing responsibility, including as Chief Operating Officer from 1997 to 1999, where he was responsible for all product development, manufacturing and commercial functions. Prior to joining Genentech, Mr. Young was with Eli Lilly & Co. for 14 years. Mr. Young currently serves as the Chairman of the Board of Directors of NanoString Technologies, Inc., and as a member of the Board of Directors of Theravance BioPharma Inc. Mr. Young retired from BioMarin Pharmaceutical Inc.'s Board of Directors in November 2015 and from Biogen's Board of Directors in June 2014. Mr. Young holds a B.S. in Chemical Engineering from Purdue University, an M.B.A. from Indiana University and an Honorary Doctorate in Engineering from Purdue University. Mr. Young was elected to the National Academy of Engineering in 1993 for his contributions to biotechnology.

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 cystic fibrosis. If we are unable to continue to increase revenues from sales of our cystic fibrosis medicines or if we do not meet the expectations of investors or public equity market analysts, our business would be materially harmed and the market price of our common stock would likely decline.

Substantially all of our net product revenues and the vast majority of our total revenues are derived from the sale of CF medicines. ORKAMBI and KALYDECO net product revenues represented approximately 53% and 34% of our total revenues in the year ended December 31, 2017, respectively. As a result, our future success is dependent on our ability to continue to increase revenues from sales of our CF medicines. In the near term, this will require us to increase CF net product revenues from our current medicines, including SYMDEKO which was approved by the FDA in February 2018. In the longer term, this will require us to successfully develop, obtain approval for and commercialize at least one triple combination therapy that will allow us to treat patients who have one copy of the F508del mutation in their *CFTR* gene and a second mutation in their *CFTR* gene that results in minimal *CFTR* function and to improve the treatment options available to patients with CF who are eligible for our current medicines.

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 we may experience adverse developments with respect to development or commercialization of our CF medicines and/or CF drug candidates; and
- 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.

Additionally, each of our commercial products and our triple combination treatment regimens contain ivacaftor or VX-561, a deuterated version of ivacaftor. As a result, if any of our products or drug candidates were to experience safety issues, ORKAMBI, KALYDECO and SYMDEKO, as well as one or more of our drug candidates, may be adversely affected.

If one or more of the above risks were to materialize or if we are otherwise unable to increase revenues from sales of our CF medicines, our business would be materially harmed and our stock price would likely decline.

We are investing significant resources in the development of our next-generation CFTR corrector compounds in triple combinations and if we are unable to show the safety and efficacy of these compounds, experience delays in doing so or are unable to successfully commercialize at least one of these medicines, our business would be materially harmed.

We are investing significant resources in the development of our next-generation CFTR corrector compounds, and recently selected VX-659 and VX-445 to evaluate in Phase 3 clinical development as part of triple combination treatment regimens for patients with CF. We believe that a significant portion of the long-term value attributed to our company by investors is based on the commercial potential of these triple combination therapies. We are planning to initiate Phase 3 clinical development of VX-659 in the first half of 2018 and VX-445 in mid-2018 based on ongoing Phase 2 clinical trials that enrolled a limited number of patients with CF. We expect to receive additional information regarding these combination regimens, including additional data from these ongoing Phase 2 clinical trials of VX-659 and VX-445 and long-term nonclinical toxicology studies of VX-445, in the first half of 2018, which could adversely affect our planned initiation of Phase 3 clinical trials for these regimens.

In order to ultimately obtain approval for a triple combination regimen, we will need to demonstrate that the compounds are safe and effective in a significantly larger number of patients than were involved in the clinical trials conducted to date. Initial results from ongoing clinical trials may differ materially from final results from such clinical trials. The results from preclinical and early clinical studies do not always accurately predict results in later, large-scale clinical trials. If the data

from our ongoing or planned clinical trials or non-clinical studies of triple combination regimens including our next-generation CFTR compounds are not favorable, the FDA and comparable foreign regulatory authorities may not approve these treatment regimens and/or we may be forced to delay or terminate the development of these treatment regimens, which would have an adverse effect on our business. Even successfully completed large-scale clinical trials may not result in marketable medicines. If a triple combination that includes a next-generation CFTR corrector compounds fails to achieve its primary endpoint in clinical trials, if safety issues arise or if the results from our clinical trials are otherwise inadequate to support regulatory approval of our triple combination therapies, commercialization of that combination regimen could be delayed or halted.

Even if we gain marketing approval for one or more combination therapies containing a next-generation CFTR corrector compound in a timely manner, we cannot be sure that such combination therapy will be commercially successful. In addition, since we expect that a significant portion of the patients for whom a triple combination treatment regimen would be indicated would also be eligible for our then existing medicines, a portion of the revenues from our triple combination regimens will likely displace revenues from our then-marketed products, reducing the overall positive effect of the commercialization of our triple combination regimens on our total revenues.

If the anticipated or actual timing of marketing approvals for these triple combination regimens, or the market acceptance of these triple combination regimens, if approved, including treatment reimbursement levels agreed to by third-party payors, do not meet the expectations of investors or public market analysts, the market price of our common stock would likely decline.

We have experienced challenges commercializing ORKAMBI outside of the United States, and our future revenues will be dependent on our ability to obtain adequate reimbursement for ORKAMBI, tezacaftor in combination with ivacaftor, if approved in ex-U.S. markets, and our future products in ex-U.S. markets.

In most ex-U.S. markets, the pricing and reimbursement of therapeutic and other pharmaceutical products is subject to governmental control. Given recent global economic pressures and geopolitical uncertainty, government authorities particularly in Europe are increasingly attempting to limit or regulate the price of drug products. Reimbursement agencies in Europe are often more conservative than those in the United States and the reimbursement process is often slower since reimbursement decisions are made on a country-by-country basis. Additionally, particular attention is being paid to specialty pharmaceutical products such as KALYDECO and ORKAMBI given the relative higher cost of these products as compared to other types of pharmaceutical products. Due in part to these challenges, we have recognized limited ex-U.S. net product revenues for ORKAMBI as we have yet to complete reimbursement discussions in many ex-U.S. countries, including the United Kingdom and France, which represent significant potential markets for ORKAMBI. In 2017 and 2016, ORKAMBI net product revenues from ex-U.S. markets represented only 13% and 8% respectively, of our total ORKAMBI net product revenues.

Our future product revenues will be dependent on, among other things, our ability to complete reimbursement discussions in ex-U.S. markets for ORKAMBI and to obtain reimbursement in ex-U.S. markets for tezacaftor in combination with ivacaftor, if approved, and any other products that may be approved in the future, including our triple combination regimens. There is no assurance that coverage and reimbursement will be available outside of the United States and, even if it is available, the timing or the level of reimbursement may not be satisfactory. Adverse pricing limitations or a delay in obtaining coverage and reimbursement would decrease our future net product revenues and harm our business.

Our business depends on our ability to obtain marketing authorization and reimbursement for tezacaftor in combination with ivacaftor in ex-U.S. markets. If we are unable to obtain marketing authorization or experience material delays in obtaining marketing authorization for, or reimbursement arrangements relating to, tezacaftor in combination with ivacaftor in ex-U.S. markets, our business could be materially harmed.

In 2017, we submitted an MAA in Europe seeking approval of tezacaftor in combination with ivacaftor in patients with CF 12 years of age and older who have certain mutations in their *CFTR* gene. We expect the EMA to complete its review in the second half of 2018. Obtaining approval of an MAA is a lengthy, expensive and uncertain process, and we may not be successful. Obtaining approval depends on many factors including:

- whether or not the European regulatory authorities determine that the evidence gathered in well-controlled clinical trials, other clinical trials and nonclinical studies demonstrates that the combination regimen is safe and effective; and
- whether or not the European regulatory authorities are satisfied that the manufacturing facilities, processes and controls for the combination are adequate, that the labeling is satisfactory and that plans for post-marketing studies, safety monitoring and risk evaluation and mitigation are sufficient.

Obtaining approval for the combination of tezacaftor and ivacaftor in one country or region does not ensure that we will be able to obtain marketing authorization in any other country or region.

Even if tezacaftor in combination with ivacaftor is approved, the European Commission may limit the indications for which the product may be marketed, require extensive warnings on the product labeling or require expensive and time-consuming clinical trials or reporting as conditions of approval. If we do not obtain approval to market the combination of tezacaftor and ivacaftor in Europe, our business will be materially harmed. Additionally, even if the combination of tezacaftor and ivacaftor receives marketing approval in Europe, coverage and reimbursement may not be available and, even if it is available, the level of reimbursement may not be satisfactory.

We only recently became profitable, and we cannot predict the extent of our future profitability.

We achieved annual profitability on a GAAP basis in 2017 for the first time since 2011. Our ability to sustain profitability depends on the extent to which we can continue to increase our revenue and control our costs in order to, among other things, counter any unforeseen difficulties, complications or other unknown factors that may impair future revenue or require additional expenditures. Our ability to increase our revenues is dependent on our ability to successfully commercialize SYMDEKO and to develop and commercialize additional products, including our triple combination regimens. Our operating expenses may increase due to, among other factors, additional investments to support or accelerate our research and development activities, the expansion of our organization, and/or costs associated with business development activities, including costs to acquire assets or programs, integration costs and the costs to develop drug candidates that are acquired. Because of the numerous risks and uncertainties associated with pharmaceutical product development, we are unable to predict the extent of our future profitability or losses. If we are unable to increase sales of ORKAMBI, sustain sales of KALYDECO, successfully commercialize SYMDEKO and our triple combination regimens, and develop additional products, we may not sustain profitability.

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

Many of our competitors, including major pharmaceutical companies such as Abbvie, Bristol-Myers Squibb, Gilead, Johnson & Johnson, Merck, Merck KGaA, Novartis, Pfizer, Sanofi and Roche, possess substantially greater financial, technical and human resources than we possess. Potential competitors also include other public and private companies, 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. As an example, in 2013 and 2014 we experienced a rapid decline in the number of patients being treated with INCIVEK, a product we previously marketed for the treatment of hepatitis C virus infection.

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.

ORKAMBI, KALYDECO, SYMDEKO 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 indications that we are pursuing. In order to compete successfully in these areas, we must demonstrate improved safety, efficacy and/or tolerability, and ease of manufacturing, and gain and maintain market acceptance over competing drugs.

A number of companies are seeking to identify and develop drug candidates for the treatment of CF, including Galapagos NV in collaboration with AbbVie, ProQR Therapeutics, Proteostasis Therapeutics, Eloxx Pharmaceuticals and several private companies. Our competitors have research and development programs directed at identifying CFTR potentiators, CFTR correctors, ENaC inhibitors and drug candidates with other mechanisms of action or that utilize new therapeutic approaches that seek to address the underlying cause of CF. Our success in rapidly developing and commercializing ORKAMBI, KALYDECO and SYMDEKO may increase the resources that our competitors allocate to the development of these potential treatments for CF. Our competitors are exploring the development of drug candidates both as monotherapies and as part of combination regimens. If one or more competing therapies are successfully developed as a treatment for patients with CF, our revenues from ORKAMBI, KALYDECO, SYMDEKO and/or other compounds, if then approved, could face competitive

pressures. If one or more competing therapies prove to be superior to our existing products and/or drug candidates for the treatment of CF, our business would be materially adversely affected.

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 problems with a product could negatively affect commercial sales of the product, result in restrictions on the product or lead to the withdrawal of the product from the market. Each of our commercial products and our triple combination treatment regimens contain ivacaftor or VX-561, a deuterated version of ivacaftor. As a result, if any of our products or drug candidates were to experience safety issues, ORKAMBI, KALYDECO and SYMDEKO, as well as one or more of our drug candidates, 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.

If we or our collaborators 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. In addition, the manufacturers we engage to make our products and the manufacturing facilities in which our products are made are subject to periodic review and inspection by the FDA and foreign regulatory authorities. If problems are identified during the review or inspection of these manufacturers or manufacturing facilities, it could result in our inability to use the facility to make our product or a determination that inventories are not safe for commercial sale.

If physicians and patients do not accept our drugs, or if patients do not remain on treatment or comply with the 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.

For example, our net product revenues from ORKAMBI have been affected by discontinuations by patients who had previously initiated treatment with ORKAMBI. If the discontinuation rate for ORKAMBI or any of our other drug products increases, or if our drugs otherwise 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 similar governmental control as currently exists in Europe. The Patient Protection and Affordable Care Act, or the ACA, requires discounts under the Medicare drug benefit program and increased the rebates paid by pharmaceutical companies on drugs covered by Medicaid. The ACA also imposes an annual fee, which increases annually, on sales by branded pharmaceutical manufacturers.

In addition, third-party payors attempt to contain health care costs by demanding price discounts or rebates and limiting both the types and variety of drugs that they will cover and the amounts that they will pay for drugs. As a result, they may not cover or provide adequate payment for our products. We might need to conduct post-marketing studies in order to demonstrate the cost-effectiveness of our products or any other future products to such payors' satisfaction. Such studies might require us to commit a significant amount of management's time and our financial and other resources. Our products might not ultimately be considered cost-effective. Adequate third-party reimbursement might not be available to enable us to maintain price levels sufficient to realize an appropriate return on our investment in product development.

Reimbursement rates vary according to the use of the drug and the clinical setting in which it is used, may be based on payments allowed for lower-cost products that already are reimbursed, may be incorporated into existing payments for other products or services and may reflect budgetary constraints and/or imperfections in the data used to calculate these rates. Net prices for products are reduced by mandatory discounts or rebates required by government health care programs and privately-negotiated discounts. While we have implemented policies in an effort to comply with mandated reimbursement rates, the U.S. federal government, state governments and private payors frequently pursue actions against pharmaceutical and biotechnology companies alleging that the companies have overstated prices in order to inflate reimbursement rates. Any such action could adversely affect the pricing of and revenues from our products.

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, the ACA was enacted under the prior U.S. administration, and there is significant uncertainty regarding changes in the laws and regulations applicable to the health care system that may be made under the current administration, and, in particular, 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.

Specialty pharmaceuticals are drugs that are prescribed by specialist physicians to treat rare or life-threatening conditions and typically address smaller patient populations. Each of ORKAMBI, KALYDECO and SYMDEKO is a specialty pharmaceutical product and our research and development programs are primarily focused on developing additional specialty pharmaceutical products. The increasing availability and use of innovative specialty pharmaceuticals, combined with their relative higher cost as compared to other types of pharmaceutical products, is beginning to generate 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 limit the prices that can be charged for our products and may limit our commercial opportunity. The increasing use of health technology 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 also could reduce the net price we receive for our products.

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 the anti-kickback provisions of the federal Social Security Act, laws prohibiting 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 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 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 non-covered 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 ORKAMBI, KALYDECO and SYMDEKO 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 ORKAMBI, KALYDECO and SYMDEKO in these patient populations. These eligible patients represent only a portion of the total 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 Open Payments (commonly known as the Sunshine Act) provisions. Open Payments 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. 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. Failure to comply with the reporting requirements would 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 States 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.

Changes in laws and regulations governing the privacy and protection of data and personal information could adversely affect our business.

We are subject to data privacy and protection laws and regulations that apply to the collection, transmission, storage and use of proprietary information and personally-identifying information, which among other things, imposes certain requirements relating to the privacy, security and transmission of individually identifiable health information. 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.

Various foreign countries also have, or are developing, laws governing the collection, use, disclosure, security, and cross-border transmission of personal information. For example, we are preparing to fulfill our obligations under the new E.U. General Data Protection Regulation, which will be effective in May 2018. The legislative and regulatory landscape for privacy and data protection continues to evolve, and there has been an increasing amount of focus on privacy and data protection issues with the potential to affect our business. For example, privacy requirements in the E.U. govern the transfer of personal information from the European Economic Area to the United States. While we continue to address the implications of changes to E.U. data privacy regulations, the area remains an evolving landscape with new regulations coming into effect and continued legal challenges and our efforts to comply with the evolving data protection rules may be unsuccessful. Failure to comply with laws regarding data protection would expose us to risk of enforcement actions taken by data protection authorities in the E.U. and the potential for significant penalties if we are found to be non-compliant. Similarly, failure to comply with federal and state laws in the United States regarding privacy and security of personal information could expose us to penalties under such laws. 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.

In 2015, the EMA adopted a new policy on publication of clinical data whereby it will publish clinical reports submitted as part of MAAs for drugs. The policy applies to all MAAs, extension of indication or line extension applications submitted in or after 2015. 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, there is a risk of inappropriate disclosure of sensitive information or negative or inaccurate posts or comments about us on any social networking website. 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.

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;
- be proven safe and effective in clinical trials;
- 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

and our ability to develop and commercialize combination treatments for CF, including our next-generation CFTR corrector compounds and develop treatments for 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 of 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 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. Accordingly, 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 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 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 the 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 to obtain and maintain regulatory approval for 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. 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 a 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 Collaborations and other Business Development Activities

Our ability to execute on our long-term strategy depends in part on our ability to acquire rights to additional drugs, drug candidates and other technologies that have the potential to add to our pipeline or provide us with new commercial opportunities.

In order to achieve our long-term business objectives, our strategy is to supplement our internal pipeline by acquiring rights to additional drugs, drug candidates and other technologies that have the potential to provide us with new commercial opportunities, including in the field of treating CF and in therapeutic areas outside of CF. 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 have faced and will continue to face significant competition for these types of drugs, drug candidates and other technologies from a variety of other companies with interests in the specialty pharmaceutical marketplace, 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. Because of these competitive pressures, 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. This competition is most intense for approved drugs and late-stage drug candidates, which have the lowest risk and would have the most immediate effect on our financial performance.

We may not realize the anticipated benefits of potential acquisitions or licenses to businesses, drugs, drug candidates and other technologies, and the integration following any such acquisition or license may disrupt our business and management.

We may acquire a business or the rights to drugs, drug candidates or other technologies. In recent years we have entered into both acquisition and collaboration arrangements, including our acquisition of VX-561 from Concert, our agreement with 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 and our agreement with Moderna pursuant to which we are seeking to identify and develop mRNA therapeutics for the treatment of CF. With respect to each of these transactions and any additional acquisition of a business or rights to drugs, drug candidates or other technologies, we may not realize the anticipated benefits of such transaction, each of which involves numerous risks. These risks include:

- failure to successfully further develop the acquired or licensed drugs or technology or to achieve strategic objectives, including successfully developing and commercializing the drugs, drug candidates or technologies that we acquire or license;
- inadequate or unfavorable data from clinical trials evaluating the acquired or licensed drug or drug candidates;
- entry into markets in which we have no or limited direct prior experience or where competitors in such markets have stronger market positions;
- disruption of our ongoing business and distraction of our management and employees from other opportunities and challenges;
- potential failure of the due diligence processes to identify significant problems, liabilities or other shortcomings or challenges of an acquired company, or acquired or licensed product or technology, including but not limited to, problems, liabilities or other shortcomings or challenges with respect to intellectual property, product quality, safety, accounting practices, employee, customer 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;
- difficulty in integrating the drugs, drug candidates, technologies, business operations and personnel of an acquired asset or company, including the integration of VX-561 into our development programs for VX-445 and VX-659; 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 and licensing arrangements are inherently risky, and ultimately, if we do not complete an announced acquisition or license transaction or integrate an acquired business, or an acquired or licensed drug, drug candidate or other technology successfully and in a timely manner, we may not realize the benefits of the acquisition or license to the extent anticipated and the perception of the effectiveness of our management team and our company may suffer in the marketplace. 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 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 strategic transactions, our expenses and short-term costs may increase materially and adversely affect our liquidity and short-term net income (loss). Future licenses or acquisitions could result in potentially dilutive issuances of equity securities, the incurrence of debt, the creation of contingent liabilities, impairment expenses related to goodwill, and impairment or amortization expenses related to other intangible assets, 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 with CRISPR, Janssen, Merck KGaA, Moderna and Parion, 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.
- Any future 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, 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, in January 2017, we granted Merck KGaA an exclusive worldwide license to research, develop and commercialize four of our oncology research and development programs. 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 or similar regulatory authorities outside the United States, 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. 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 of ivacaftor, lumacaftor and tezacaftor for commercial sale (as KALYDECO, ORKAMBI and/or SYMDEKO). We also require 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. Our supply chain includes a single-source manufacturer for (i) one step in the ivacaftor manufacturing process, (ii) the manufacture of the tablets of ORKAMBI that is used for patients with CF six to eleven years of age and (iii) a pre-formulation step and the manufacture of the tablets for our commercial supply of SYMDEKO. As a result, if we or our third-party manufacturers become unable or unwilling to continue manufacturing product on our behalf 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 certain pre-clinical work and clinical trials, 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 CFFT, to assist in the design and review of, and to conduct our clinical trials, including enrolling qualified patients. 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 these activities, it may result in a delay of the affected clinical trial or drug development program. 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.

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 Leahy-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 force for only a short period following commercialization of such drug candidate resulting in a minimal, if any, period of patent exclusivity. To the extent our drug candidates are not commercialized significantly ahead of the expiration date of any applicable patent, or to the extent 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 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 ORKAMBI and KALYDECO 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. New laws in the E.U., also 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. Risks associated with conducting operations in foreign countries 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 a timely manner;
- differing patient treatment infrastructures, particularly since our business is focused on the treatment of rare diseases that 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;
- import and export licensing requirements, tariffs, and other trade and travel restrictions;
- 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 Foreign Corrupt Practices Act 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 Foreign Corrupt Practices Act. 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;
- transition from a U.S.-centric company into an organization capable of developing and commercializing multiple drug candidates in international markets; and
- enhance our compliance and legal resources.

Risk Relating to the Referendum of the United Kingdom's Membership of the European Union.

Our European headquarters and European research facility are located in the United Kingdom, and a significant portion of our ex-U.S. net product revenues are derived from sales in the United Kingdom. In June 2016, the United Kingdom, or the U.K., held a referendum in which voters approved an exit from the E.U., commonly referred to as "Brexit." The U.K. government provided official notice of withdrawal from the E.U. in the first half of 2017, and is currently negotiating the terms of the U.K.'s withdrawal. The withdrawal could, among other outcomes, disrupt the free movement of goods, services and people between the U.K. and the E.U., undermine bilateral cooperation in key policy areas and significantly disrupt trade between the U.K. and the E.U. In addition, 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. The announcement of Brexit caused significant volatility in global stock markets and currency exchange rate fluctuations that resulted in the strengthening of the U.S. dollar against foreign currencies in which we conduct business. The withdrawal of the U.K. from the E.U. may also create global economic uncertainty, which may cause third-party payors, including governmental organizations, to closely monitor their costs and reduce their spending budgets. 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 class action lawsuits and claims related to product liability, intellectual property and breach of contract. Such proceedings may involve claims for, or the possibility of, 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 or 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, there can be no assurance that our efforts will prevent breakdowns or breaches in our systems that could adversely affect our business.

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

Because our drug discovery and development activities are highly technical in nature, 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 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 have increased competition for the available pool of skilled employees, especially in technical fields, and the high cost of living in Massachusetts makes it difficult to attract employees from other parts of the country to Massachusetts. 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 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.

The loss of the services of key employees or the failure to effectively integrate key employees could negatively affect our business.

Our future success will depend in large part on our ability to retain the services of our key scientific and management personnel and to integrate new scientific and management personnel into our business. A loss of key personnel or a failure to properly integrate new personnel could be disruptive. We have entered into employment agreements with some executives and provide compensation-related 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 options, restricted stock and restricted stock units—is 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. A failure to retain, as well as hire, train and effectively integrate into our organization a sufficient number of qualified scientists, professionals, sales personnel and senior management would negatively affect 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 four 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 disaster recovery 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, the loss or critical data and/or large expenses to repair or replace the facility, which would 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, 2017 to December 31, 2017, our common stock traded between \$73.34 and \$167.86 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;
- prescription data and other information disclosed by third parties regarding our business or products;
- 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;
- developments in domestic and international governmental policy or regulation, for example, relating to intellectual property rights;
- 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 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 October 2016, we entered into a credit agreement providing for a \$500 million revolving facility, \$300 million of which was drawn at closing and subsequently paid off in February 2017. 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 \$300.0 million. All outstanding borrowings under the credit agreement mature on October 13, 2021. Our 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 EBITDA 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. All obligations under the credit agreement, and the guarantees of those obligations, are secured by substantially all of our assets and the assets of all guarantors (excluding intellectual property, owned and leased real property and certain other excluded property), including the pledge of all or a portion of the equity interests of certain of our subsidiaries. If we fail to satisfy our obligations under the credit agreement or are unable to obtain sufficient funds to make payments, the lenders could foreclose on our pledged collateral.

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, 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.

A change in tax laws, treaties or regulations, or their interpretation, of any country in which we operate could materially affect us if we generate taxable income in a future period. For example, on December 22, 2017, the United States enacted H.R.1., known as the Tax Cuts and Jobs Act. We currently do not expect H.R.1. to have a material impact on our financial statements as long as we maintain a valuation allowance on the majority of our net operating losses and other deferred tax assets, however we are still in the process of evaluating the new law and do not know the full effect it will have on our business, including our financial statements.

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.

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. Additionally, our pledge of specified assets as collateral to secure our obligations under our credit agreement may limit our ability to obtain additional debt financing. 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.

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

As of December 31, 2017, we had 253.3 million shares of common stock issued and outstanding. As of December 31, 2017, we also had outstanding options to purchase 9.8 million shares of common stock with a weighted-average exercise price of \$91.57 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, restricted stock 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. Although we recently amended our charter to eliminate staggered terms for our Board of Directors, our shareholders will not have the ability to vote for all members of the Board of Directors on an annual basis until 2020. 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 CF net product revenues;
- our expectations regarding clinical trials, development timelines and regulatory authority filings and submissions for ivacaftor, lumacaftor, tezacaftor, VX-659, VX-445, VX-150, VX-128 and VX-210 and the MAA for tezacaftor in combination with ivacaftor;
- our ability to obtain reimbursement for ORKAMBI in ex-U.S. markets and our ability to otherwise successfully market ORKAMBI, KALYDECO, SYMDEKO or any of our other drug candidates for which we obtain regulatory approval;
- our expectations regarding the timing and structure of clinical trials of our drugs and drug candidates, including ivacaftor, lumacaftor, tezacaftor, VX-659, VX-445, VX-150, VX-128 and VX-210, and the expected timing of our receipt of data from our ongoing and planned clinical trials;
- 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, 2017 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. The 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. In addition, in connection with our relocation to Boston, we entered into a lease in June 2012 for approximately 100,000 square feet of space in the Boston Marine Industrial Park, in close proximity to our corporate headquarters. We are using this additional space for certain logistical and laboratory operations and manufacturing equipment that complement the office and laboratory facilities at our corporate headquarters.

Additional United States and Worldwide Locations

In addition to our facilities in Massachusetts, we lease an aggregate of approximately 300,000 square feet of space. This includes laboratory and office space to support our research and development organizations in San Diego, California and Milton Park, Abingdon, England, and office space in many of the countries in which we sell our products. In addition, in December 2015, we entered into a lease for approximately 170,000 square feet of office and laboratory space under construction in San Diego, California, which will replace our existing facility in San Diego. We will commence lease payments in the second quarter of 2019 and the lease has a term of 16 years.

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

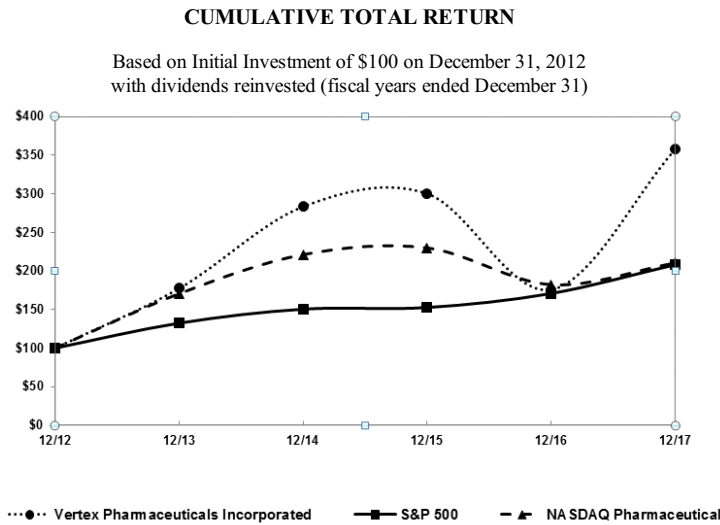
Our common stock is traded on The NASDAQ Global Select Market under the symbol “VRTX.” The following table sets forth for the periods indicated the high and low sale prices per share of our common stock as reported by NASDAQ Stock Market LLC:

Year Ended December 31, 2017:		High	Low
First quarter	\$	111.88	\$ 73.34
Second quarter		137.26	107.24
Third quarter		167.86	125.50
Fourth quarter		158.04	136.50
Year Ended December 31, 2016:		High	Low
First quarter	\$	124.96	\$ 75.90
Second quarter		96.49	75.92
Third quarter		103.73	83.50
Fourth quarter		97.93	71.46

Shareholders

As of January 31, 2018, there were 1,455 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 have never declared or paid any cash dividends on our common stock, and 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

The table set forth below shows all repurchases of securities by us during the three months ended December 31, 2017:

Period	Total Number of Shares Purchased	Average Price Paid per Share	Total Number of Shares Purchased as Part of Publicly Announced Plans or Programs	Maximum Number of Shares that May Yet be Purchased Under the Plans or Programs
Oct. 1, 2017 to Oct. 31, 2017	6,163	\$ 0.01	—	—
Nov. 1, 2017 to Nov. 30, 2017	8,450	\$ 0.01	—	—
Dec. 1, 2017 to Dec. 31, 2017	2,121	\$ 0.01	—	—

The repurchases were made under the terms of our Amended and Restated 2006 Stock and Option Plan and Amended and Restated 2013 Stock and Option Plan. Under these plans, we award shares of restricted stock to our employees that typically are subject to a lapsing right of repurchase by us. We may exercise this right of repurchase if a restricted stock recipient's service to us is terminated. If we exercise this right, we are required to repay the purchase price paid by or on behalf of the recipient for the repurchased restricted shares, which typically is the par value per share of \$0.01. Repurchased shares are returned and are available for future awards under the terms of our Amended and Restated 2013 Stock and Option Plan.

On January 31, 2018, we announced that our Board of Directors had authorized a share repurchase program, or Share Repurchase Program, pursuant to which up to \$500.0 million of common stock can be repurchased through December 31, 2019. The primary objective of the Share Repurchase Program is to reduce the impact of dilution from employee equity programs. Purchases under the Share Repurchase Program may be made through the open public market or through privately negotiated transactions, and may be made pursuant to Rule 10b5-1 plans or other means as determined by our management and in accordance with the requirements of the Securities and Exchange Commission.

ITEM 6. SELECTED FINANCIAL DATA

The following unaudited selected consolidated financial data are derived from our audited consolidated financial statements and have been revised to reflect discontinued operations. 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,				
	2017	2016	2015	2014	2013
Consolidated Statements of Operations Data:					
(in thousands, except per share amounts)					
Product revenues, net					
ORKAMBI product revenues, net	\$ 1,320,850	\$ 979,590	\$ 350,663	\$ —	\$ —
KALYDECO product revenues, net	844,630	703,432	631,674	463,750	371,285
INCIVEK product revenues, net	—	610	17,987	24,071	466,360
Total product revenues, net	2,165,480	1,683,632	1,000,324	487,821	837,645
Royalty revenues	7,988	16,600	23,959	40,919	156,592
Collaborative revenues (1)	315,184	1,945	8,053	51,675	217,738
Total revenues	2,488,652	1,702,177	1,032,336	580,415	1,211,975
Total costs and expenses (2)	2,365,409	1,692,241	1,499,215	1,272,827	1,821,983
(Benefit from) provision for income taxes (3)	(107,324)	16,665	30,381	6,958	(122,422)
Income (loss) from continuing operations attributable to Vertex	263,484	(112,052)	(556,334)	(737,643)	(503,622)
(Loss) income from discontinued operations attributable to Vertex(4)	—	—	—	(912)	58,594
Net income (loss) attributable to Vertex	\$ 263,484	\$ (112,052)	\$ (556,334)	\$ (738,555)	\$ (445,028)
Diluted income (loss) from continuing operations per share attributable to Vertex common shareholders	\$ 1.04	\$ (0.46)	\$ (2.31)	\$ (3.14)	\$ (2.24)
Shares used in per diluted share calculations	253,225	244,685	241,312	235,307	224,906
As of December 31,					
(in thousands)					
Consolidated Balance Sheet Data:					
Cash, cash equivalents and marketable securities	\$ 2,088,666	\$ 1,434,557	\$ 1,042,462	\$ 1,387,106	\$ 1,465,076
Total assets	3,546,014	2,896,787	2,498,587	2,334,679	2,319,041
Total current liabilities (5)	807,260	792,537	506,167	368,254	397,829
Long-term debt obligations, excluding current portion	—	—	223,863	280,569	—
Construction financing lease obligation, excluding current portion(6)	563,406	486,359	472,611	473,073	440,937
Other long-term obligations	133,042	279,700	202,318	116,600	123,870

- (1) In 2017, we recorded \$246.6 million of collaborative revenues, which consisted of \$230.0 million related to an upfront payment and \$16.6 million related to research and development and transition activities, from Merck KGaA, which were primarily attributable to the upfront payment made by Merck KGaA to us pursuant to a collaboration agreement. See Note B, “Collaborative Arrangements and Acquisitions.”
- (2) Total costs and expenses included (i) in 2017 and 2013, intangible asset impairment charges, (ii) in 2017, \$160.0 million for an asset acquisition and (iii) in 2017, 2014 and 2013, \$14.2 million, \$50.9 million and \$40.5 million, respectively, of restructuring charges related to our closure of our research site in Canada in 2017, the relocation of our corporate headquarters in 2014 and workforce reduction primarily related to the commercial support of INCIVEK in 2013. See Note J, “Intangible Assets and Goodwill”, Note B, “Collaborative Arrangements and Acquisitions” and Note Q, “Restructuring Expenses.”
- (3) In 2017 and 2013, we recorded benefits from income taxes related to the impairment of intangible assets. See Note P, “Income Taxes.” and Note B, “Collaborative Arrangements and Acquisitions.”
- (4) (Loss) income from discontinued operations attributable to Vertex relates to our collaboration with Alios BioPharma, Inc., in 2012 through 2013, which we deconsolidated as of December 31, 2013.
- (5) As of December 31, 2017, we have \$232.4 million recorded as current liabilities related to cash received by us for sales of ORKAMBI in France for which the price has not been established. See Note A, “Nature of Business and Accounting Policies.”
- (6) In 2011 and 2015, we entered into leases in which we are deemed to be the owner for accounting purposes. See Note L, “Long Term Obligations.”

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 serious diseases. Our business is focused on developing and commercializing therapies for the treatment of cystic fibrosis, or CF, and advancing our research and development programs in other diseases. Our marketed products are ORKAMBI (lumacaftor in combination with ivacaftor), KALYDECO (ivacaftor) and SYMDEKO (tezacaftor in combination with ivacaftor). Our total net product revenues were \$2.2 billion in 2017, an increase of 29% over net product revenues of \$1.7 billion in 2016, due to increased ORKAMBI and KALYDECO net product revenues.

Cystic Fibrosis

Current Medicines

ORKAMBI, KALYDECO and SYMDEKO are collectively approved to treat approximately 45% of the 75,000 CF patients in North America, Europe and Australia. ORKAMBI is approved as a treatment for approximately 28,000 patients who have two copies of the F508del mutation, or F508del homozygous, in their cystic fibrosis transmembrane conductance regulator, or *CFTR*, gene. KALYDECO is approved for the treatment of approximately 6,000 CF patients who have the G551D mutation or other specified mutations in their *CFTR* gene. SYMDEKO was approved by the United States Food and Drug Administration, or FDA, in February 2018 for the treatment of patients with CF twelve years of age and older who are F508del homozygous or who have at least one mutation that is responsive to tezacaftor/ivacaftor, and provides an additional treatment option to CF patients who were already eligible for either ORKAMBI or KALYDECO. We are currently seeking approval from the European Medicines Agency for tezacaftor in combination with ivacaftor.

Next-generation CFTR Corrector Compounds

In the first quarter of 2018, we selected two next-generation corrector compounds, VX-659 and VX-445, to advance into Phase 3 clinical development as part of separate triple combination regimens. Each of VX-659 and VX-445 have the potential to be combined with both (i) tezacaftor and ivacaftor and (ii) tezacaftor and VX-561, a deuterated version of ivacaftor. We expect to initiate the Phase 3 development program for VX-659 in combination with tezacaftor and ivacaftor in the first half of 2018. In mid-2018, we expect to initiate the Phase 3 development of a once-daily combination of VX-445, tezacaftor and VX-561. Our decision to advance VX-659 and VX-445 was based on available clinical and nonclinical data, including data from an ongoing Phase 2 clinical program, and regulatory discussions are ongoing to finalize the design of the Phase 3 development programs for VX-659 and VX-445.

We believe the triple combination regimens we are evaluating could potentially provide benefits to all CF patients who have at least one F508del mutation in their *CFTR* gene (approximately 90% of all CF patients). This would include (i) the first treatment option that treats the underlying cause of CF for patients who have one copy of the F508del mutation in their *CFTR* gene and a second mutation in their *CFTR* gene that results in minimal *CFTR* function, who we refer to as F508del/Min patients, and (ii) an additional treatment option for patients with CF who are eligible for ORKAMBI, KALYDECO and/or SYMDEKO.

Research and Development

We have a number of ongoing research and development programs in other diseases that we are conducting independently or in collaboration with third parties. We are developing VX-150 and VX-128 as treatments for pain, co-developing CTX001, an investigational gene editing treatment, for the treatment of beta-thalassemia and sickle cell disease, with CRISPR Therapeutics AG, or CRISPR, and developing VX-210 as a treatment for acute spinal cord injury. We plan to continue investing in our research programs and fostering scientific innovation in order to identify and develop transformative medicines for people with serious diseases. In addition to continuing our research in cystic fibrosis, pain and hemoglobinopathies, our current internal research programs include programs targeting adrenoleukodystrophy, alpha-1 antitrypsin deficiency and polycystic kidney disease. To supplement our internal research programs, we seek 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 and to access technologies needed to execute on our strategy. 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.

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 and can take 10 to 15 years or more. 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 foreign jurisdictions. 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 foreign 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 foreign laws, 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 make it illegal for a prescription drug manufacturer to solicit, offer, receive or pay any remuneration to induce the referral of business, including the purchase or prescription of a particular drug that is reimbursed by a state or federal 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 that govern our international business practices with respect to payments to government officials. 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 covered 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 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. In Europe and other ex-U.S. markets, we work to obtain government reimbursement for ORKAMBI on a country-by-country basis, because in many foreign countries patients are unable to access prescription pharmaceutical products that are not reimbursed by their governments.

In the United States, we worked successfully with third party payors in order to promptly obtain appropriate levels of reimbursement for KALYDECO and ORKAMBI and are beginning that process for SYMDEKO. We also successfully obtained reimbursement for KALYDECO in each significant ex-U.S. market within two years of approval. Since we obtained approval for ORKAMBI in 2015, we have experienced significant challenges in obtaining reimbursement for ORKAMBI in ex-U.S. markets, to date, having reached a pricing and reimbursement agreement for ORKAMBI in several European countries, including Germany, Ireland and Italy, but remaining in negotiations with a number of other European countries,

including the United Kingdom and France, which represent significant potential markets for ORKAMBI. While we have innovative reimbursement arrangements in place in certain ex-U.S. jurisdiction such as Ireland that will allow rapid access to tezacaftor in combination with ivacaftor, if approved, and ORKAMBI for younger patients, in most significant markets we will need to obtain country-by-country reimbursement for each new medicine and each label expansions for a current medicine.

Collaboration Arrangements

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:

- CRISPR, pursuant to which we are collaborating on the discovery and development of potential new treatments aimed at the underlying genetic causes of human diseases using CRISPR-Cas9 gene editing technology;
- Moderna Therapeutics, Inc., or Moderna, pursuant to which we are seeking to identify and develop messenger ribonucleic acid, or mRNA, therapeutics for the treatment of CF;
- BioAxone Biosciences, Inc., or BioAxone, pursuant to which we are evaluating VX-210 as a potential treatment for patients who have spinal cord injuries; and
- Parion Sciences, Inc., or Parion, pursuant to which we are developing epithelial sodium channel, or ENaC, inhibitors for the treatment of pulmonary diseases.

Generally, when we in-license a technology or drug candidate, we make upfront payments to the collaborator, assume the costs of the program and agree to make contingent payments, which could consist of milestone, royalty and option payments. 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. For example, the upfront payments and expenses incurred in connection with our CRISPR and Moderna collaborations are being expensed as research expenses because the collaboration represents a small portion of these collaborators overall business. CRISPR and Moderna's activities unrelated to our collaborations have no effect on our consolidated financial statements. Parion and BioAxone have historically been accounted for as variable interest entities, or VIEs, and historically have been included in our consolidated financial statements due to (i) the significance of the respective licensed programs to Parion and BioAxone as a whole, (ii) our power to control the significant activities under each collaboration and (iii) our obligation to absorb losses and right to receive benefits that potentially could be significant. As of September 30, 2017, we determined that the above conditions were no longer satisfied with respect to Parion following the results of a Phase 2 clinical trial of VX-371 that did not meet its primary efficacy endpoint. As a result, we no longer account for Parion as a VIE and have deconsolidated Parion from our consolidated financial statements as of September 30, 2017. BioAxone continues to be accounted for as a VIE and remains included in our consolidated financial statements as of December 31, 2017.

Collaborators 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, prior to its deconsolidation as of September 30, 2017, and BioAxone, the activities unrelated to our collaborations with these entities have represented approximately 2% or less of our total revenues and total expenses on an annual basis. As a result of the deconsolidation of Parion, we expect these amounts to decrease in future periods. For any consolidated VIEs, we evaluate the fair value of the contingent payments payable by us on a quarterly basis. Changes in the fair value of these contingent future payments affect net income attributable to Vertex on a dollar-for-dollar basis, with increases in the fair value of contingent payments payable by us to a VIE resulting in a decrease in net income attributable to Vertex (or an increase in net loss attributable to Vertex) and decreases in the fair value of contingent payments payable by us to a VIE resulting in an increase in net income attributable to Vertex (or decrease in net loss attributable to Vertex). For additional information regarding our VIEs see Note B "Collaborative Arrangements and Acquisitions" and our critical accounting policies "Collaborations; Variable Interest Entities."

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

- Merck KGaA, Darmstadt, Germany, or Merck KGaA, pursuant to which Merck KGaA obtained rights to four oncology research and development programs; and

- Janssen Pharmaceuticals, Inc., or Janssen, Inc., which is evaluating JNJ-63623872 (formerly VX-787) for the treatment of influenza in a Phase 3 clinical development program.

Pursuant to these outlicensing 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/or royalty revenues resulting from these programs.

RESULTS OF OPERATIONS

				2017/2016 Comparison		2016/2015 Comparison	
	2017	2016	2015	Increase/(Decrease)		Increase/(Decrease)	
				\$	%	\$	%
	(in thousands)			(in thousands, except percentages)			
Revenues	\$ 2,488,652	\$ 1,702,177	\$ 1,032,336	\$ 786,475	46%	\$ 669,841	65 %
Operating costs and expenses	2,365,409	1,692,241	1,499,215	673,168	40%	193,026	13 %
Other items, net	140,241	(121,988)	(89,455)	262,229	n/a	(32,533)	(36)%
Net income (loss) attributable to Vertex	<u>\$ 263,484</u>	<u>\$ (112,052)</u>	<u>\$ (556,334)</u>	\$ 375,536	n/a	\$ 444,282	80 %
Net income (loss) per diluted share attributable to Vertex common shareholders	\$ 1.04	\$ (0.46)	\$ (2.31)				
Diluted shares used in per share calculations	253,225	244,685	241,312				

Net Income (Loss) Attributable to Vertex

Comparison of Net Income (Loss) Attributable to Vertex 2017 vs. 2016

Net income attributable to Vertex was \$263.5 million in 2017 as compared to a net loss attributable to Vertex of \$(112.1) million in 2016. Our revenues increased significantly in 2017 as compared to 2016 primarily due to increased ORKAMBI and KALYDECO net product revenues and \$230.0 million in one-time collaborative revenues related to the strategic collaboration and license agreement we established with Merck KGaA in the first quarter of 2017. Our operating costs and expenses increased in 2017 as compared to 2016 primarily due to increases in our cost of product revenues related to our increased net product revenues, increases in our research and development expenses, which included \$160.0 million in development expenses incurred in connection with the acquisition of VX-561 from Concert, increases in our sales and administrative expenses and a \$255.3 million intangible asset impairment charge related to Parion's pulmonary ENaC platform.

Other items, net in 2017 primarily reflect a benefit from income taxes and certain other benefits associated with the impairment of Parion's pulmonary ENaC platform, for which there were no comparable benefits in 2016, and a decrease in interest expense, net to \$57.6 million. Other items, net in 2016 primarily reflects interest expense, net of \$81.4 million, a provision for income taxes of \$16.7 million and net income attributable to noncontrolling interest of \$28.0 million.

Comparison of Net Loss Attributable to Vertex 2016 vs. 2015

Net loss attributable to Vertex was \$(112.1) million in 2016 as compared to a net loss attributable to Vertex of \$(556.3) million in 2015. Our revenues increased significantly in 2016 as compared to 2015 primarily due to an increase in ORKAMBI net product revenues, which we began recognizing in mid-2015, and an increase in KALYDECO net product revenues, partially offset by decreases in our royalty revenues and collaborative revenues. Our operating costs and expenses increased in 2016 as compared to 2015 primarily due to increases in cost of product revenues, research and development expenses, sales, general and administrative expenses.

The change in our other items, net between 2016 and 2015 was primarily due to a \$54.9 million increase in the fair value of contingent payments related to our consolidated VIEs in 2016, which resulted in an increase in net loss attributable to Vertex.

Earnings Per Share

In 2017, 2016 and 2015, net income (loss) attributable to Vertex was \$1.04, \$(0.46) and \$(2.31), respectively, per diluted share. In 2017, 2016 and 2015, the number of diluted shares used to calculate net income (loss) per common share was 253.2 million, 244.7 million and 241.3 million, respectively. The increase in diluted shares was primarily due to our issuance of shares of common stock pursuant to our employee equity programs.

Revenues

				2017/2016 Comparison		2016/2015 Comparison	
	2017	2016	2015	Increase/(Decrease)		Increase/(Decrease)	
				\$	%	\$	%
	(in thousands)			(in thousands, except percentages)			
Product revenues, net	\$ 2,165,480	\$ 1,683,632	\$ 1,000,324	\$ 481,848	29 %	\$ 683,308	68 %
Royalty revenues	7,988	16,600	23,959	(8,612)	(52)%	(7,359)	(31)%
Collaborative revenues	315,184	1,945	8,053	313,239	n/a	(6,108)	(76)%
Total revenues	\$ 2,488,652	\$ 1,702,177	\$ 1,032,336	\$ 786,475	46 %	\$ 669,841	65 %

Product Revenues, Net

	2017	2016	2015
	(in thousands)		
ORKAMBI	\$ 1,320,850	\$ 979,590	\$ 350,663
KALYDECO	844,630	703,432	631,674
Total CF product revenues, net	\$ 2,165,480	\$ 1,683,022	\$ 982,337

In 2017, ORKAMBI net product revenues were \$1.32 billion, including \$167.6 million of net product revenues from ex-U.S. markets, compared to ORKAMBI net product revenues of \$979.6 million in 2016, including \$76.4 million of net product revenues from ex-U.S. markets. ORKAMBI sales commenced in mid-2015 and net product revenues were \$350.7 million during 2015, including \$1.6 million of net product revenues from ex-U.S. markets. SYMDEKO was approved by the FDA in February 2018 and we expect that a portion of the patients currently receiving ORKAMBI will switch to SYMDEKO following its approval. Our consolidated balance sheet includes \$232.4 million collected as of December 31, 2017 in France related to ORKAMBI supplied under early access programs at the invoiced price. Pursuant to the revenue recognition guidance applicable through December 31, 2017, we have not recognized any net product revenues to date on sales of ORKAMBI in France because the price was not fixed or determinable. Please refer to Critical Accounting Policies - Revenue Recognition below for a discussion of our early access program for ORKAMBI in France and the application of the new revenue recognition guidance that becomes effective on January 1, 2018.

In 2017, KALYDECO net product revenues were \$844.6 million, including \$334.2 million of net product revenues from ex-U.S. markets, compared to KALYDECO net product revenues of \$703.4 million in 2016, including \$303.9 million of net product revenues from ex-U.S. markets. In 2015, KALYDECO net product revenues were \$631.7 million, including \$266.1 million of net product revenues from ex-U.S. markets. The increases year-over-year were primarily due to additional patients being treated with KALYDECO as we completed reimbursement discussions in various ex-U.S. jurisdictions and to the increased number of patients eligible to receive KALYDECO through label expansions.

In 2018, we believe that our total CF net product revenues will increase as compared to 2017 and will be dependent on our ability to successfully commercialize SYMDEKO in the United States and on our ability to continue to expand the number of patients eligible for our medicines and to obtain approval and reimbursement for our medicines, including tezacaftor in combination with ivacaftor, in ex-U.S. markets.

Royalty Revenues

Our royalty revenues were \$8.0 million, \$16.6 million and \$24.0 million in 2017, 2016 and 2015, respectively. Our royalty revenues primarily consist of revenues related to a cash payment we received in 2008 when we sold our rights to certain HIV royalties. Pursuant to the new revenue recognition guidance that became applicable on January 1, 2018, we do not expect to recognize royalty revenues in future periods related to the 2008 cash payment because the remaining \$6.9 million that was deferred as of December 31, 2017 will be recorded as a cumulative effect adjustment to our accumulated deficit, net of deferred costs, in the first quarter of 2018. Our future royalty revenues will be dependent on if, and when, our collaborators, including Janssen, Inc. and Merck KGaA, are able to successfully develop drug candidates that we have outlicensed to them.

Collaborative Revenues

Our collaborative revenues were \$315.2 million, \$1.9 million and \$8.1 million in 2017, 2016 and 2015, respectively. In 2017, our collaborative revenues included (i) \$230.0 million in revenues related to the one-time upfront payment earned in the first quarter of 2017 from Merck KGaA and (ii) a \$25.0 million milestone related to our license agreement with Janssen, Inc. for the treatment of influenza. Our 2017 collaborative revenues also included \$40.0 million in revenues related to upfront and milestone payments earned by Parion in the second and third quarter of 2017 pursuant to a license agreement Parion entered into with a third party. We are not a party to the Parion license agreement and have no economic interest in either the license or these milestone payments. These revenues were included in our consolidated financial statements because during these periods we were consolidating Parion as a VIE. Parion was deconsolidated as a VIE as of September 30, 2017 and any future payments received by Parion pursuant to this license agreement will no longer be recognized by us as collaborative revenue. Our collaborative revenues have historically fluctuated significantly from one period to another and may continue to fluctuate in the future.

Operating Costs and Expenses

	2017	2016	2015	2017/2016 Comparison		2016/2015 Comparison	
				Increase/(Decrease)		Increase/(Decrease)	
				\$	%	\$	%
	(in thousands)			(in thousands, except percentages)			
Cost of product revenues	\$ 272,675	\$ 206,811	\$ 117,151	\$ 65,864	32 %	\$ 89,660	77 %
Royalty expenses	2,444	3,649	7,361	(1,205)	(33)%	(3,712)	(50)%
Research and development expenses	1,324,625	1,047,690	995,922	276,935	26 %	51,768	5 %
Sales, general and administrative expenses	496,079	432,829	376,575	63,250	15 %	56,254	15 %
Restructuring expenses	14,246	1,262	2,206	12,984	n/a	(944)	(43)%
Intangible asset impairment charge	255,340	—	—	255,340	n/a	—	n/a
Total costs and expenses	\$ 2,365,409	\$ 1,692,241	\$ 1,499,215	\$ 673,168	40 %	\$ 193,026	13 %

Cost of Product Revenues

Our cost of product revenues includes 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 Cystic Fibrosis Foundation Therapeutics Incorporated, or CFFT, our tiered third-party royalties on sales of KALYDECO, ORKAMBI and SYMDEKO, 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 product revenues as a percentage of CF product revenues is lower at the beginning of each calendar year.

Our cost of product revenues have been increasing due primarily to increased net product revenues. In each of 2016 and 2015, our cost of product revenues included a \$13.9 million commercial milestone that was earned by CFFT and was related to sales of ORKAMBI. There are no further commercial milestones payable to CFFT. In 2018, we expect our cost of product revenues as a percentage of total CF product revenues to be similar to the cost of product revenues as a percentage of total CF product revenues in 2017.

Royalty Expenses

Royalty expenses primarily consist of expenses related to a subroyalty payable to a third party on net sales of an HIV protease inhibitor sold by GlaxoSmithKline. Royalty expenses do not include royalties we pay to CFFT on sales of KALYDECO and ORKAMBI, which instead are included in cost of product revenues.

Research and Development Expenses

				2017/2016 Comparison		2016/2015 Comparison	
	2017	2016	2015	Increase/(Decrease)		Increase/(Decrease)	
				\$	%	\$	%
	(in thousands)			(in thousands, except percentages)			
Research expenses	\$ 311,206	\$ 314,602	\$ 337,797	\$ (3,396)	(1)%	\$ (23,195)	(7)%
Development expenses	1,013,419	733,088	658,125	280,331	38 %	74,963	11 %
Total research and development expenses	\$ 1,324,625	\$ 1,047,690	\$ 995,922	\$ 276,935	26 %	\$ 51,768	5 %

Our research and development expenses include internal and external costs incurred for research and development of our drugs and drug candidates. We do not assign our internal costs, such as salary and benefits, stock-based compensation expense, laboratory supplies and other direct expenses and infrastructure costs, to individual 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 \$3.4 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 2015, 2016 and 2017, 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. We expect the EMA to complete its review of our MAA for tezacaftor in combination with ivacaftor in the second half of 2018. We cannot make a meaningful estimate when, if ever, our other clinical development programs will generate revenues and cash flows.

Research Expenses

				2017/2016 Comparison		2016/2015 Comparison	
	2017	2016	2015	Increase/(Decrease)		Increase/(Decrease)	
				\$	%	\$	%
	(in thousands)			(in thousands, except percentages)			
Research Expenses:							
Salary and benefits	\$ 81,229	\$ 80,845	\$ 81,752	\$ 384	<1%	\$ (907)	(1)%
Stock-based compensation expense	60,122	51,034	49,744	9,088	18 %	1,290	3 %
Laboratory supplies and other direct expenses	45,822	43,151	37,058	2,671	6 %	6,093	16 %
Outsourced services	39,497	33,682	24,210	5,815	17 %	9,472	39 %
Collaboration and asset acquisition payments	8,425	33,000	75,000	(24,575)	(74)%	(42,000)	(56)%
Infrastructure costs	76,111	72,890	70,033	3,221	4 %	2,857	4 %
Total research expenses	\$ 311,206	\$ 314,602	\$ 337,797	\$ (3,396)	(1)%	\$ (23,195)	(7)%

Over the past three years we have maintained a substantial and consistent investment in our internal research activities. Our total research expenses have been affected by research expenses associated with our business development activities, which are reflected in collaboration and asset acquisition payments. Collaboration and asset acquisition payments in 2016 included a \$20.0 million upfront payment to Moderna and approximately \$10.0 million in expenses related to the acquisition of early-stage research assets. Collaboration and asset acquisition payments in 2015 consisted of a \$75.0 million upfront payment we made to CRISPR. We expect to continue to invest in our research programs with a focus on identifying drug candidates with the goal of creating transformative medicines.

Development Expenses

				2017/2016 Comparison		2016/2015 Comparison	
	2017	2016	2015	Increase/(Decrease)		Increase/(Decrease)	
	(in thousands)			\$	%	\$	%
				(in thousands, except percentages)			
Development Expenses:							
Salary and benefits	\$ 208,769	\$ 177,399	\$ 164,466	\$ 31,370	18%	\$ 12,933	8%
Stock-based compensation expense	121,778	102,417	103,211	19,361	19%	(794)	(1)%
Laboratory supplies and other direct expenses	45,594	42,861	30,611	2,733	6%	12,250	40%
Outsourced services	337,901	282,137	248,506	55,764	20%	33,631	14%
Collaboration and asset acquisition payments	160,250	—	—	160,250	n/a	—	n/a
Drug supply costs	13,660	12,510	9,799	1,150	9%	2,711	28%
Infrastructure costs	125,467	115,764	101,532	9,703	8%	14,232	14%
Total development expenses	\$ 1,013,419	\$ 733,088	\$ 658,125	\$ 280,331	38%	\$ 74,963	11%

Our development expenses increased by \$280.3 million, or 38%, in 2017 as compared to 2016 and increased by \$75.0 million, or 11%, in 2016 as compared to 2015. The increase in 2017 as compared to 2016 was primarily due to the \$160.0 million payment to Concert in connection with the acquisition of VX-561 in the third quarter of 2017 and to increased outsourced services expenses related to ongoing clinical trials, including trials involving our next-generation CFTR corrector compounds that we are evaluating as part of triple combination treatment regimens. We expect our development expenses, excluding collaboration and asset acquisition payments, to increase in 2018 as compared to 2017 due to expenses related to the advancement of our triple combination regimens into Phase 3 development.

The increased development expenses in 2016 as compared to 2015 were primarily due to an increase in outsourced services related to clinical trials, including our Phase 3 development program for tezacaftor in combination with ivacaftor and increases in salary and benefits, laboratory supplies and other direct expenses and infrastructure costs.

Sales, General and Administrative Expenses

				2017/2016 Comparison		2016/2015 Comparison	
	2017	2016	2015	Increase/(Decrease)		Increase/(Decrease)	
	(in thousands)			\$	%	\$	%
				(in thousands, except percentages)			
Sales, general and administrative expenses	\$ 496,079	\$ 432,829	\$ 376,575	\$ 63,250	15%	\$ 56,254	15%

Sales, general and administrative expenses increased by 15% in 2017 as compared to 2016, and by 15% in 2016 as compared to 2015. These increases were primarily due to increased global support for KALYDECO and ORKAMBI and costs incurred to prepare for the launch of SYMDEKO in the United States.

Restructuring Expenses

In 2017, 2016 and 2015, we recorded restructuring expenses of \$14.2 million, \$1.3 million and \$2.2 million, respectively. Our restructuring expenses in 2017 were 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 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 attributable to Parion. There were no corresponding intangible asset impairment charges in 2016 or 2015.

Other Items, Net

Interest Expense, Net

Our interest expense, net relates primarily to interest expenses associated with our real estate leases and interest on our outstanding debt. In 2017, 2016 and 2015, interest expense, net was \$57.6 million, \$81.4 million and \$84.2 million, respectively. The decrease in interest expense, net in 2017 as compared to 2016 was primarily due to the repayment of the \$300.0 million outstanding under our revolving credit facility in February 2017. In 2018, we expect that we will incur approximately \$66 million in interest expenses related to our real estate leases and that our interest expense related to outstanding debt will be dependent on whether, and to what extent, we reborrow amounts under our credit facility.

Other (Expense) Income, Net

In 2017, other (expense) income, net was an expense of \$81.4 million primarily related to the deconsolidation of Parion. In 2016, we recorded net other income of \$4.1 million primarily related to foreign exchange gains. In 2015, we recorded net other expense of \$6.7 million primarily related to foreign exchange losses.

Income Taxes

In 2017, we recorded a benefit from income taxes of \$107.3 million, related to a benefit from income taxes of \$114.1 million attributable to noncontrolling interest primarily as a result of our impairment of Parion's pulmonary ENaC platform and decrease in the fair value of the contingent payments payable by us to Parion in the third quarter of 2017, partially offset by a provision for income taxes of \$6.8 million related primarily to U.S. state and foreign taxes. As discussed below in Critical Accounting Policies - Income Taxes, we continue to maintain a valuation allowance on the majority of our net operating losses and other deferred tax assets and are in the process of determining the impact that H.R.1., known as the Tax Cuts and Jobs Act of 2017, will have on our provision for (benefit from) income taxes in the future.

In 2016, we recorded a provision for income taxes of \$16.7 million, principally due to income taxes payable by our VIEs. In 2015, we recorded a provision for income taxes of \$30.4 million, principally due to the consolidation of Parion as a VIE into our consolidated financial statements.

Noncontrolling Interest (VIEs)

The net (income) loss attributable to noncontrolling interest (VIEs) recorded on our consolidated statements of operations reflects Parion (through September 30, 2017) and BioAxone's net (income) 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 (income) loss attributable to noncontrolling interest related to our VIEs for the three years ended December 31, 2017 is as follows:

	2017	2016	2015
	(in thousands)		
Loss attributable to noncontrolling interest before (benefit from) provision for income taxes and changes in fair value of contingent payments	\$ 223,379	\$ 10,086	\$ 6,646
(Benefit from) provision for income taxes	(114,090)	16,743	29,731
Decrease (increase) in fair value of contingent payments	62,560	(54,850)	(4,530)
Net loss (income) attributable to noncontrolling interest	<u>\$ 171,849</u>	<u>\$ (28,021)</u>	<u>\$ 31,847</u>

The net loss attributable to noncontrolling interest in the year ended December 31, 2017 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 and benefit from income taxes of \$126.2 million related to these charges. The net income attributable to noncontrolling interest in 2016 and the net loss attributable to noncontrolling interest in 2015 were primarily related to an increase in the fair value of contingent payments based on a Phase 2 clinical trial of VX-371

achieving its primary safety endpoint and a provision for income taxes related to our \$80.0 million upfront payment to Parion, respectively. As of September 30, 2017, we have deconsolidated Parion.

LIQUIDITY AND CAPITAL RESOURCES

The following table summarizes the components of our financial condition as of December 31, 2017 and 2016:

			Increase/(Decrease)	
			\$	%
	2017	2016	(in thousands, except percentages)	
Cash, cash equivalents and marketable securities	\$ 2,088,666	\$ 1,434,557	\$ 654,109	46%
Working Capital				
Total current assets	\$ 2,648,963	\$ 1,831,540	\$ 817,423	45%
Total current liabilities	(807,260)	(792,537)	(14,723)	2%
Total working capital	\$ 1,841,703	\$ 1,039,003	\$ 802,700	77%

As of December 31, 2017, we had cash, cash equivalents and marketable securities of \$2.1 billion, which represented an increase of \$654.1 million from approximately \$1.4 billion as of December 31, 2016. The increase in our cash, cash equivalents and marketable securities balance in 2017 was primarily due to increased cash receipts from product sales, cash received from issuances of common stock under our employee benefit plans and \$193.6 million of the \$230.0 million upfront payment received from our collaboration with Merck KGaA, partially offset by cash expenditures in 2017, related to among other things research and development expenses and sales, general and administrative expenses, the \$300.0 million repayment of our revolving credit facility and the \$160.0 million payment to Concert in connection with the acquisition of VX-561. We expect that our future cash flows will be substantially dependent on our CF product sales.

As of December 31, 2017, total working capital was \$1.8 billion, which represented an increase of \$802.7 million from approximately \$1.0 billion as of December 31, 2016. The most significant items that increased total working capital in 2017 were \$844.9 million cash provided by operations and \$344.8 million cash received from issuances of common stock under our employee benefit plans, partially offset by the \$300.0 million repayment of our revolving credit facility.

Sources of Liquidity

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 are receiving cash flows from sales of ORKAMBI and KALYDECO from the United States and ex-U.S. markets and will begin receiving cash flows from sales of SYMDEKO in the United States in 2018. We submitted an MAA to the EMA for tezacaftor in combination with ivacaftor and expect the EMA to complete its review in the second half of 2018. Future net product revenues for ORKAMBI and, if approved, tezacaftor in combination with ivacaftor, from ex-U.S. markets will be dependent on, among other things, the timing of and ability to complete reimbursement discussions in European countries.

In February 2017, we repaid the \$300.0 million we had borrowed under our \$500.0 million revolving credit facility. 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 \$300.0 million.

In 2015 and 2017, we also received significant proceeds from the issuance of common stock under our employee benefit plans and more limited proceeds from employee benefit plans in 2016. The amount and timing of future proceeds from employee benefits plans is uncertain. Other possible sources of liquidity include strategic collaborative agreements that include research and/or development funding, commercial debt, public and private offerings of our equity and debt securities, development milestones and royalties on sales of products, software and equipment leases, 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 incur substantial operating expenses to conduct research and development activities and to operate our organization. Under the terms of our credit agreement entered into in October 2016, we are required to repay all outstanding principal amounts in 2021. We also have substantial facility and capital lease obligations, including leases for two buildings in Boston,

Massachusetts that continue through 2028 and capital expenditures for our building under construction in San Diego, California. As of December 31, 2017, we have collected approximately \$232.4 million from ORKAMBI early access programs in France for which the price is not fixed or determinable. We expect we will be required to repay a portion of the collected amounts to the French government based on the difference between the invoiced price of ORKAMBI and the final price for ORKAMBI in France once we conclude our ongoing pricing discussions with the French government.

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 that require additional capital. Our board of directors has also authorized a share repurchase program pursuant to which we may use up to \$500.0 million to repurchase shares of our common stock through December 31, 2019.

We expect that cash flows from ORKAMBI, KALYDECO and SYMDEKO, 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 ORKAMBI, KALYDECO and SYMDEKO, 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 have a \$500.0 million revolving credit facility that we entered into in October 2016. We may repay and reborrow amounts under the revolving credit agreement without penalty. In addition, subject to certain conditions, we may request that the borrowing capacity under this credit agreement be increased by an additional \$300.0 million. We may raise additional capital 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, 2017:

	Payments Due by Period				
	2018	2019-2020	2021-2022	2023 and later	Total
	(in thousands)				
Fan Pier Leases	\$ 61,606	\$ 145,178	\$ 145,178	\$ 462,442	\$ 814,404
Facility leases, excluding Fan Pier Leases	22,845	43,409	41,959	187,343	295,556
Capital lease obligations	24,004	15,686	5,382	387	45,459
Research, development and drug supply costs	34,878	—	—	—	34,878
Other	4,653	4,004	308	7,572	16,537
Total contractual commitments and obligations	<u>\$ 147,986</u>	<u>\$ 208,277</u>	<u>\$ 192,827</u>	<u>\$ 657,744</u>	<u>\$ 1,206,834</u>

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.

In December 2015, we entered into a lease agreement, pursuant to which we agreed to lease approximately 170,000 square feet of office and laboratory space in a building under construction in San Diego, California. We expect to commence base rent payments in the second quarter of 2019 and the lease has a term of 16 years. The future minimum rental payments that we are obligated to pay after taking occupancy are included in "Facility leases, excluding Fan Pier Leases."

The table also reflects leases of equipment and leasehold improvements that are accounted for as capital leases.

Research, Development and Drug Supply Costs

The amounts reflected in “Research, development and drug supply costs”, do not include certain payments we are obligated to make 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, 2017, we had accrued \$35.8 million related to these contracts for costs incurred for services provided through December 31, 2017, and we have approximately \$148.5 million in cancelable future commitments based on existing contracts as of December 31, 2017. 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. Our payment obligations under these collaboration agreements include the following:

- *CFFT*: CFFT has the right to tiered royalties ranging from single digits to sub-teens on any approved drugs first synthesized and/or tested during a research term on or before February 28, 2014, including KALYDECO, ORKAMBI, lumacaftor, ivacaftor and tezacaftor and 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 VX-659 and VX-445. For combination products, such as ORKAMBI and SYMDEKO, sales are allocated equally to each of the active pharmaceutical ingredients in the combination product.
- *CRISPR*: CRISPR has the potential to receive milestone and royalty payments, including up to \$420.0 million in development, regulatory and commercial milestone payments for each of up to six targets pursuant to the collaboration.
- *Moderna*: Moderna has the potential to receive milestone and royalty payments, including up to \$275.0 million in development and regulatory milestones.
- *BioAxone*: BioAxone has the potential to receive milestone and royalty payments, including up to \$90.0 million in development and regulatory milestone payments (including a license continuation fee).
- *Parion*: Parion has the potential to receive milestone and royalty payments, including up to \$485.0 million in development and regulatory milestone payments for the development of VX-371 and/or VX-551 to treat CF.

In addition to the above collaborations, in 2017 we acquired certain CF assets including VX-561 from Concert pursuant to an asset purchase agreement. Under the asset purchase agreement, Concert has the potential to receive milestone payments, including up to \$90.0 million in milestones based on regulatory approval in the U.S. and reimbursement in the U.K., Germany or France.

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, 2017, we did not have any liabilities associated with uncertain tax positions. As of December 31, 2017, we cannot reasonably estimate the amount we expect to pay within the next twelve months in connection with any such settlements.

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 provide information regarding these obligations annually in our proxy statement for our annual meeting of shareholders.

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;
- intangible assets;
- collaborations; variable interest entities;
- research and development accruals;
- commercial supplies and inventories;
- income taxes;
- leases; and
- stock-based compensation expense.

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 providers in North America as well as government-owned and supported customers in international markets, collectively, our customers. Our customers in North America 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 upon delivery to our customers as long as:

- there is persuasive evidence that an arrangement exists between us and our customer;
- collectability is reasonably assured; and
- the price is fixed or determinable.

In order to conclude that the price is fixed or determinable, we must be able to calculate our gross product revenues from our customers and reasonably estimate our net product revenues upon delivery to our customers' locations. Our gross product revenues are based on the fixed price for our products that we charge our customers. We estimate our net product revenues by deducting from our gross product revenues (i) trade allowances, such as invoice discounts for prompt payment and customer fees, (ii) estimated government and private payor rebates, chargebacks and discounts, (iii) estimated reserves for expected product returns and (iv) estimated costs of co-pay assistance programs for patients, as well as other incentives for certain indirect customers. We make significant estimates and judgments that 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.

The value of the rebates, chargebacks and discounts 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, chargebacks and discounts, 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, chargebacks and discounts based on new information, including information regarding actual rebates, chargebacks and discounts for our products, as it becomes available. Claims by third-party payors for rebates, chargebacks and discounts are submitted to us significantly after the related sales, potentially resulting in adjustments in the period in which the new information becomes known.

Our customers generally have the right to return unopened unprescribed packages subject to contractual limitations. To date, returns have been minimal and, based on inventory levels held by our customers and our distribution model, we believe that returns of products will continue to be minimal. We track actual returns by individual production lots and will continue to monitor inventory levels in the distribution channel. If necessary, we will adjust our estimated product returns based on new information as it becomes available.

In certain instances, we may be unable to reasonably conclude that the price is fixed or determinable at the time of delivery, in which case we defer the recognition of revenues. Once we are able to determine that the price is fixed or determinable, we recognize the revenues associated with the units in which revenue recognition was deferred. For example, we began distributing ORKAMBI in France in 2015 through early access programs but have not recognized any revenues from product sales through December 31, 2017 because the price is not fixed or determinable due to the ongoing pricing discussions regarding the reimbursement rate for ORKAMBI in France. Our consolidated balance sheets included \$232.4 million and \$73.4 million collected as of December 31, 2017 and 2016, respectively, in France related to ORKAMBI that are classified as "Customer deposits". We expect that the difference between the amounts collected based on the invoiced price and the final price for ORKAMBI in France will be returned to the French government.

Because we concluded that the price is not fixed or determinable as of December 31, 2017, the amounts classified as customer deposits related to shipments of ORKAMBI under early access programs will be subject to the new guidance applicable to revenue recognition that became effective January 1, 2018. Pursuant to the new guidance, we will record a cumulative effect adjustment to our accumulated deficit in the first quarter of 2018. The amount of the adjustment to accumulated deficit will be determined based upon (i) the status of pricing discussions in France upon adoption and (ii) our estimate of the amount of consideration we expect to retain related to the French ORKAMBI sales that occurred on or prior to December 31, 2017 that will not be subject to a significant reversal in amounts recognized. For ORKAMBI sales in France that occur after December 31, 2017 under the early access programs, we will recognize product revenues based on our estimate of consideration we expect to retain that will not be subject to a significant reversal in amounts recognized. In periods after the first quarter of 2018, if our estimates regarding the amounts we will receive for ORKAMBI supplied pursuant to these programs change, the effect of the change in estimates, which may be significant, would be reflected in net product revenues in the period in which the change in estimate occurred. For more information regarding the new guidance please see Note A, "Nature of Business and Accounting Policies."

Collaborative Revenues

We recognize revenues generated through collaborative research, development and/or commercialization agreements. The terms of these agreements typically include payment to us of one or more of the following: nonrefundable, up-front license fees; development and commercial milestone payments; funding of research and/or development activities; and royalties on net sales of licensed products. Each of these types of payments that result in collaborative revenues, except for revenues from royalties on net sales of licensed products, which are classified as royalty revenues.

For each collaborative research, development and/or commercialization agreement that results in revenues, we determine (i) whether multiple deliverables exist, (ii) whether the undelivered elements have value to the customer on a stand-alone basis, (iii) how the deliverables should be separated and (iv) how the consideration should be allocated to the deliverables. We allocate consideration in an arrangement using the relative selling price method based on our best estimate of selling price of deliverables if we do not have vendor-specific objective evidence or third-party evidence. As part of the accounting for these agreements, we must develop assumptions that require judgment to determine the best estimate of selling price. We utilize key assumptions to determine the best estimate of selling price, which may include patient enrollment requirements from regulatory authorities, development timelines, reimbursement rates for personnel costs, discount rates, and estimated third-party development costs.

Intangible Assets

We maintain an indefinite-lived in-process research and development asset on our consolidated balance sheet until either the research and development 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 take an impairment charge in the period in which the impairment occurs.

We assess the fair value of assets, including intangible assets such as in-process research and development assets, using a variety of methods, including present-value models that are based upon multiple probability-weighted scenarios involving the development and potential commercialization of the underlying drug candidates. The present-value models require us to make significant assumptions regarding the estimates that market participants would make in evaluating a drug candidate, including the probability of successfully completing clinical trials and obtaining regulatory approval to market the drug candidate, the timing of and the expected costs to complete in-process research and development projects, future net cash flows from potential drug sales, which are based on estimates of the sales price of the drug, the number of patients who will be diagnosed and treated and our competitive position in the marketplace, and appropriate discount and tax rates.

We test our intangible assets for impairment on an annual basis as of October 1, and more frequently if indicators are present or changes in circumstance suggest that impairment may exist. Events that could result in an impairment, or trigger an interim impairment assessment, include the receipt of additional clinical or nonclinical data regarding our drug candidate or a potentially competitive drug candidate, changes in the clinical development program for a drug candidate or new information regarding potential sales for the drug. In connection with each annual impairment assessment and any interim impairment assessment, we compare the fair value of the asset as of the date of the assessment with the carrying value of the asset on our consolidated balance sheet.

As of December 31, 2017, we had \$29.0 million as an indefinite-lived intangible asset recorded on our consolidated balance sheet related to BioAxone, our variable interest entity (VIE) that we consolidated as of December 31, 2017. In the third quarter of 2017, a full intangible asset impairment charge of \$255.3 million related to Parion's pulmonary ENaC platform was recorded. We had recorded the indefinite-lived intangible asset for Parion on our consolidated balance sheet based on our estimate of the fair value of Parion's pulmonary ENaC platform in June 2015 and made significant estimates regarding: (i) the probability of obtaining regulatory approval for an ENaC drug candidate; (ii) the timing and expected costs to develop and commercialize an ENaC drug candidate; (iii) future cash flows from potential product sales with respect to an ENaC drug candidate and (iv) appropriate discount and tax rates. The timing of this impairment charge was based on changes in our estimates regarding the potential to develop this asset, which were reflected in our reported results in the period in which they became known.

Collaborations; Variable Interest Entities

Our collaborations require us to apply accounting policies that involve significant judgments and that have a material effect on our consolidated financial statements. We review each collaboration agreement pursuant to which we license assets owned by a collaborator in order to determine whether we have 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 connection with this assessment, we consider and make judgments regarding the following, among other factors: (1) whether the collaborator is a business; (2) the purpose and design of the collaborator; (3) the value of the licensed asset(s) as compared to the value of the collaborator as a whole; and (4) which party has the power to direct the activities that most significantly affect the collaborator's economic performance. For example, in connection with the Parion collaboration, we consolidated Parion's financial statements into our financial statements from June 2015 through September 2017. To reach this conclusion we determined that (a) Parion was a business; (b) the purpose and redesign of Parion was to advance the development and commercialization of the licensed assets with a company that is able to effectively develop and commercialize products for the treatment of cystic fibrosis and other pulmonary diseases; (c) the licensed assets represented significantly more than half the value of Parion; and (d) through the joint steering committee, we had the power to direct the development and commercialization of Parion's ENaC inhibitors, which were the activities that most significantly affected the economic performance of Parion during this period of time. Similarly, we have determined that BioAxone is a VIE that we have consolidated into our financial statements since 2014.

We evaluate on a quarterly basis if we continue to have a variable interest in each VIE and are the primary beneficiary of the VIE, and if we later determine that we no longer have a variable interest or are no longer the primary beneficiary, we deconsolidate the applicable VIE. This evaluation involves an assessment of the activities being conducted pursuant to our collaboration agreement with the collaborator, the collaborator's financial statements, discussions with the collaborator's management regarding its other activities, including any new collaborations, financing activities, clinical data and the collaborator's other programs.

After evaluating the results from a Phase 2 clinical trial of VX-371 that did not meet its primary efficacy endpoint, we determined, based on among other things, the significance of the ENaC development activities and the decrease in the fair value of Parion's pulmonary ENaC platform relative to Parion's other activities, that we were no longer the primary beneficiary of Parion as we no longer had the power to direct the significant activities of Parion. Accordingly, we deconsolidated Parion as of September 30, 2017.

We believe that the following effects of the consolidation and deconsolidation of VIEs on our consolidated financial statements are the most significant:

- In each period, we record net income (loss) attributable to our VIEs noncontrolling interest. This net income (loss) reflects our VIEs net income (loss) for the period as adjusted for gains and losses in the fair value of the contingent payments, which consist of milestone, royalty and option payments, payable by us to our VIEs. Determining the fair value of the contingent payments payable by us to our VIEs requires us to make significant estimates regarding the probability and potential timing of achieving each of the milestones pursuant to the agreement, future potential net sales of licensed products and appropriate discount rates. We expect that the net income (loss) attributed to noncontrolling interest will continue to be affected by changes in the fair value of the contingent payments. In 2017, the fair value of contingent payments payable by us decreased by \$62.6 million primarily due to the Phase 2 clinical trial of VX-371 not meeting its primary efficacy endpoint. In 2016 and 2015, the fair value of contingent payments payable by us increased by \$54.9 million and \$4.5 million, respectively. The increase in fair value of the contingent payments in 2016 primarily related to a separate Phase 2 clinical trial of VX-371 achieving its primary safety endpoint. The changes in the fair value of contingent payments decrease or increase our net loss attributable to Vertex on a dollar-for-dollar basis.
- We recorded \$255.3 million and \$29.0 million, respectively, of intangible assets on our consolidated balance sheet based on our estimate of the fair value of Parion's and BioAxone's in-process research and development assets as of the applicable transaction date and made significant estimates regarding: (i) the probability of obtaining regulatory approval for the applicable licensed drug candidate(s); (ii) the timing and expected costs to develop and commercialize the applicable licensed drug candidate(s); (iii) future cash flows from potential product sales with respect to the applicable licensed drug candidate(s) and (iv) appropriate discount and tax rates. If we are successful in developing a drug candidate, we will amortize the carrying value of the relevant intangible asset. We test these in-process research and development assets for impairment on an annual basis as of October 1, and more frequently if indicators are present or changes in circumstances suggest that impairment may exist. In September 2017, we determined that the intangible assets associated with Parion's ENaC program has been impaired primarily due to the Phase 2 clinical trial of VX-371 not meeting its primary efficacy endpoint. If the fair value of any other licensed program becomes impaired as the result of safety or efficacy data from any ongoing or future clinical trial conducted by us or our competitors or because of any other information regarding the prospects of successfully developing or commercializing the applicable licensed drug candidate(s), we could incur significant charges in the period in which the impairment occurs.
- The revenues, research and development expenses and sales, general and administrative expenses of our VIEs that are unrelated to the programs that we in-license from our VIEs and that are consolidated into our financial statements are set forth in the table below and represent approximately 2% or less of our revenues, research and development expenses and sales, general and administrative expenses in each period:

	2017	2016	2015
	(in thousands)		
Revenues	\$ 43,376	\$ 944	\$ 2,888
Research and development expenses	(7,729)	(6,762)	(3,642)
Sales, general and administrative expenses	(3,826)	(4,160)	(5,836)
Other (expenses) income, net	(255,200)	(108)	(56)
Loss attributable to noncontrolling interest before provision for income taxes and changes in fair value of contingent payments	\$ (223,379)	\$ (10,086)	\$ (6,646)

To the extent that BioAxone pursues other programs, expenses related to those activities would be reflected in our research and development expenses and our sales, general and administrative expenses as a result of the financial statement consolidation. We would not be entitled to any benefits from those activities. In future periods, BioAxone could increase their operating expenses related to other activities and any such increases would affect our operating expenses as presented in our consolidated financial statements.

- We reflect all of our VIEs' cash and cash equivalents under the heading "Restricted cash and cash equivalents (VIE)" on our consolidated balance sheets. We do not have any rights to our VIEs cash or cash equivalents, these resources are not available to fund research and development programs pursuant to the collaborations and these amounts do not provide us with any additional liquidity. Our VIEs have control over the restricted cash and cash equivalents (VIE), including the ability to distribute the restricted cash and cash equivalents to their equity holders, and as a result, these assets, although carried on our consolidated balance sheets, are not included in the discussion of our liquidity and should be disregarded when evaluating our financial condition.

In order to account for the fair value of the intangible assets and contingent payments related to collaborations with our VIEs under GAAP, we use present-value models based on assumptions regarding the probability of achieving the relevant milestones, estimates regarding the timing of achieving the milestones, estimates of future product sales and the appropriate discount rates. We base our estimates of the probability of achieving the relevant milestones on industry data for similar assets and our own experience. The discount rates used in the valuation model 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 during each reporting period. Changes in these assumptions could have a material effect on the fair value of the contingent payments and affect the analysis of whether or not an intangible asset is impaired.

Research and Development Accruals

Research and development expenses, including amounts funded through research and development collaborations, are expensed as incurred. When third-party service providers' billing terms do not coincide with our period-end, we are required to make estimates of our obligations to those third parties, including clinical trial and pharmaceutical development costs, contractual services costs, costs for drug supply, marketing expenses and infrastructure expenses incurred in a given accounting period and record accruals at the end of the period. We base our estimates on our knowledge of the research and development programs, services performed for the period, experience with related activities and the expected duration of the third-party service contract, where applicable.

Commercial Supplies and Inventories

We began capitalizing the costs of our tezacaftor inventories in the first quarter of 2017. Tezacaftor in combination with ivacaftor, or SYMDEKO, is a combination therapy that was approved by the FDA in February 2018. We capitalize 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 sale of the inventories. In determining whether or not to capitalize such inventories, we evaluate, 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 timing and availability of reimbursement. In addition, we evaluate risks associated with manufacturing the drug candidate and the remaining shelf life of the inventories.

After we begin capitalizing inventories, we perform an assessment of the recoverability of capitalized inventory during each reporting period, and write down any excess and obsolete inventories to their net realizable value in the period in which the impairment is first identified. Periodic assessments of the recoverability of capitalized costs involve significant estimates and judgments on the part of management, including the outlook for commercial sales, which can be effected by the existence of current or anticipated competitive medicines, including additional medicines that we develop that are alternative treatments to our previously approved medicines and the timing and availability of reimbursement. As of December 31, 2017, all of our inventories are related to CF products. Our inventory write offs for 2017 were \$15.3 million and we had no write offs in 2016 and 2015. The write offs in 2017 were primarily due to delays in securing reimbursement in certain markets.

Income Taxes

We utilize the asset and liability method of accounting for income taxes. Under this method, deferred tax assets and liabilities are determined based on the difference between the financial statement carrying amounts and tax basis of assets and liabilities using enacted tax rates in effect for years in which the temporary differences are expected to reverse. If our estimate of the tax effect of reversing temporary differences is (i) not reflective of actual outcomes, (ii) modified to reflect new developments or interpretations of the tax law, or (iii) revised to incorporate new accounting principles, or changes in the expected timing or manner of the reversal, our results of operations could be materially impacted. We provide a valuation allowance when it is more likely than not that deferred tax assets will not be realized. We recognize the benefit of an uncertain tax position that has been taken or we expect to take on income tax returns if such tax position is more likely than not to be sustained.

We maintain a valuation allowance on the majority of our net operating losses and other deferred tax assets. Accordingly, we have not reported any tax benefit relating to the remaining net operating loss carryforwards and income tax credit carryforwards that are available for utilization in future periods. Our U.S. federal net operating loss carryforwards totaled approximately \$3.6 billion as of December 31, 2017. On a periodic basis, we reassess the valuation allowance on our deferred income tax assets, weighing positive and negative evidence to assess the recoverability of the deferred tax assets. In 2017, we reassessed the valuation allowance and considered negative evidence, including our cumulative losses over the three years ended December 31, 2017, and positive evidence, including our income during the year ended December 31, 2017 and our projections of future income. After assessing both the negative evidence and the positive evidence, we concluded that we should continue to maintain the valuation allowance on the majority of our net operating losses and other deferred tax assets as of December 31, 2017 given the significance of the weight of the negative evidence. Based on our recent financial performance and our future projections, we could record a reversal of all, or a portion of the valuation allowance associated with U.S. deferred tax assets in future periods. However, any such change is subject to actual performance and other considerations that may present positive or negative evidence at the time of the assessment. Our total deferred tax asset balance subject to the valuation allowance was approximately \$1.6 billion at December 31, 2017.

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. If we determine that these deferred tax assets are not realizable in a future period, we would record material changes to income tax expense in that period.

On December 22, 2017, H.R.1, known as the Tax Cuts and Jobs Act, was signed into law. The new law did not have a significant impact on our consolidated financial statements for the year ended December 31, 2017 because we maintain a valuation allowance on the majority of our net operating losses and other deferred tax assets. We are in the process of determining the impact that the new law will have on our consolidated financial statements in 2018 and beyond; however, we do not expect it to have a material impact as long as we maintain a valuation allowance on the majority of our net operating losses and other deferred tax assets.

Leases

In 2011, we entered into two leases for our corporate headquarters. Our corporate headquarters were built during the period from 2011 through December 2013. We lease our corporate headquarters pursuant to leases that expire in 2028, subject to our right to extend the leases for an additional 10 years. Because we were involved in the construction project, we were deemed for accounting purposes to be the owner of the buildings during the construction period. Accordingly, we recorded project construction costs incurred by the landlord as an asset and a related financing obligation in “Property and equipment, net” and “Construction financing lease obligation,” respectively, on our consolidated balance sheets.

Upon completion of the construction of the corporate headquarters buildings, we evaluated the leases and determined that the leases did not meet the criteria for “sale-leaseback” treatment. Accordingly, we depreciate the asset and incur interest expense related to the financing obligation recorded on our consolidated balance sheet. We bifurcate our lease payments pursuant to the leases into (i) a portion that is allocated to the buildings and (ii) a portion that is allocated to the land on which the buildings were constructed. We incurred \$60.1 million in interest expense, \$13.3 million in depreciation expense and \$6.5 million in operating expense in 2017 related to these leases. In 2018, we expect interest expense, depreciation expense and operating expenses related to the leases for our corporate headquarters to be approximately consistent with that from 2017.

In 2015, we entered into a lease agreement for a research and development facility under construction in San Diego. Because we are involved in the construction project, we are deemed for accounting purposes to be the owner of the building during the construction period and are recording project construction costs incurred by the landlord. As of December 31, 2017, we have recorded \$94.6 million and \$87.4 million in “Property and equipment, net” and “Construction financing lease obligation”, respectively, on our consolidated balance sheet. We will need to evaluate this lease based on “sale-leaseback” criteria upon completion of the construction, which is anticipated to be in the first half of 2018. We currently expect this lease will not meet the criteria and will be accounted for in the same manner as we have accounted for the leases for our corporate headquarters.

Stock-based Compensation Expense

Stock-based compensation expense is determined based on the fair value of the equity 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 that accelerate vesting of the award, we estimate the likelihood of satisfaction of the performance conditions, which affects the period over which the expense is recognized, and recognize the expense using the accelerated

attribution model. For awards with performance conditions in which the award does not vest unless the performance condition is met, we recognize expense only if we estimate that achievement of the performance condition is probable. If we conclude that vesting is probable, we recognize expense from the date that we reach this conclusion through the estimated vesting date. Starting in 2016, we also granted awards with a variable number of shares issuable pursuant to such awards. Half of the PSUs contain financial goals 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 will be issued when an award vests may range from zero to 200% of the target amount depending on the level of achievement of the applicable performance metric. We also provide to employees who have rendered a certain number of years of service and meet certain age requirements, partial or full acceleration of vesting of their equity awards, subject to certain conditions including a notification period, upon a termination of employment other than for cause. If our estimates regarding the employees who will be eligible for partial or full acceleration of their equity awards, if the likelihood of achievement of a performance conditions changes or if any of our other assumptions or estimates prove incorrect, our stock-based compensation expense, or the period over which our stock-based compensation is recognized, could be materially affected.

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 2017.

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 is 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 October 2016, we entered into a credit agreement. Loans under the credit agreement bear interest, at our option, at either a base rate or a Eurodollar rate, in each case plus an applicable margin. The applicable margin on base rate loans ranges from 0.75% to 1.50% and the applicable margin on Eurodollar loans ranges from 1.75% to 2.50%, in each case, based on our consolidated leverage ratio (as defined in the credit agreement). 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, 2017, we had no principal or interest outstanding. A portion of our interest expense, net in 2018 will be dependent on whether, and to what extent, we reborrow 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, Swiss Franc, British Pound, Australian Dollar and Canadian Dollar 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 affects to our net revenues from international product sales from movements in foreign currency exchange rates are partially mitigated by the natural, opposite affect that foreign currency 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 and Australian Dollar related to forecasted product revenues that qualify for hedge accounting treatment under U.S. GAAP. We do not seek hedge accounting treatment for our forward contracts related to monetary assets and liabilities that impact our operating results. As of December 31, 2017, we held foreign exchange forward contracts with notional amounts totaling \$488.1 million. As of December 31, 2017, our outstanding foreign exchange forward contracts had a net fair value of \$(15.2) million.

Based on our foreign currency exchange rate exposures at December 31, 2017, a hypothetical 10% adverse fluctuation in exchange rates would decrease the fair value of our foreign exchange forward contracts that are designated as cash flow hedges by approximately \$36.5 million at December 31, 2017. The resulting loss on these forward contracts would be offset by the gain on the underlying transactions and therefore would have minimal impact on future anticipated earnings and cash flows. Similarly, adverse fluctuations in exchange rates that would decrease the fair value of our foreign exchange forward contracts that are not designated as hedge instruments would be offset by a positive impact of the underlying monetary assets and liabilities.

ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA

The information required by this Item 8 is contained on pages F-1 through F-50 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 of December 31, 2017. In making this assessment, it used the criteria set forth in the Internal Control—Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework)(COSO). Based on its assessment, the Company's management has concluded that, as of December 31, 2017, the Company's internal control over financial reporting is effective based on those criteria.

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. During the quarter ended December 31, 2017, there were no 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, 2017, 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, 2017, based on the COSO criteria.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) ("PCAOB"), the consolidated balance sheets of Vertex Pharmaceuticals Incorporated as of December 31, 2017 and 2016, 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, 2017, and the related notes and our report dated February 14, 2018 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 14, 2018

ITEM 9B. OTHER INFORMATION

Not applicable.

PART III

Portions of our definitive Proxy Statement for the 2018 Annual Meeting of Shareholders, or 2018 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 2018 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 2018 Annual Meeting and Nominations for Director,” “Section 16(a) Beneficial Ownership Reporting Compliance” and “Code of Conduct.” The information regarding executive officers required by this Item 10 as well as certain information regarding our directors 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 2018 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 2018 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 2018 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 2018 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:

	Page Number in this Form 10-K
Report of Independent Registered Public Accounting Firm	F-1
Consolidated Statements of Operations for the years ended December 31, 2017, 2016 and 2015	F-2
Consolidated Statements of Comprehensive Income (Loss) for the years ended December 31, 2017, 2016 and 2015	F-3
Consolidated Balance Sheets as of December 31, 2017 and 2016	F-4
Consolidated Statements of Shareholders' Equity and Noncontrolling Interest for the years ended December 31, 2017, 2016 and 2015	F-5
Consolidated Statements of Cash Flows for the years ended December 31, 2017, 2016 and 2015	F-6
Notes to Consolidated Financial Statements	F-7

(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
3.1	Restated Articles of Organization of Vertex Pharmaceuticals Incorporated, as amended.		10-Q (Exhibit 3.1)	July 28, 2017	000-19319
3.2	Amended and Restated By-Laws of Vertex Pharmaceuticals Incorporated.		10-Q (Exhibit 3.2)	July 28, 2017	000-19319
4.1	Specimen stock certificate.	X			
Collaboration and Asset Purchase Agreements					
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
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
10.6	Strategic Collaboration, Option and License Agreement, dated October 26, 2015, by and among CRISPR Therapeutics AG, CRISPR Therapeutics Limited, CRISPR Therapeutics, Inc., Tracr Hematology Ltd., Vertex Pharmaceuticals Incorporated and Vertex Pharmaceuticals (Europe) Limited.†		10-K (Exhibit 10.6)	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
10.7	Amendment #1 to Strategic Collaboration, Option and License Agreement, dated December 12, 2017, by and among CRISPR Therapeutics AG, CRISPR Therapeutics Limited, CRISPR Therapeutics, Inc., Tracr Hematology Ltd., Vertex Pharmaceuticals Incorporated and Vertex Pharmaceuticals (Europe) Limited.†	X			
10.8	Strategic Collaboration and License Agreement, dated January 10, 2017, between Vertex Pharmaceuticals Incorporated and Merck KGaA, Darmstadt, Germany.†		10-Q (Exhibit 10.1)	April 28, 2017	000-19319
10.9	Asset Purchase Agreement, dated March 3, 2017, by and among Vertex Pharmaceuticals (Europe) Ltd., as Buyer, Vertex Pharmaceuticals, Inc., as Guarantor, and Concert Pharmaceuticals, Inc.		10-Q (Exhibit 10.2)	April 28, 2017	000-19319
Leases					
10.10	Lease, dated May 5, 2011, between Fifty Northern Avenue LLC and Vertex Pharmaceuticals Incorporated.†		10-Q (Exhibit 10.4)	August 9, 2011	000-19319
10.11	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
10.12	Lease, dated December 2, 2015, between ARE-SD Region No. 23, LLC and Vertex Pharmaceuticals Incorporated.		10-K (Exhibit 10.10)	February 16, 2016	000-19319
10.13	First Amendment to Lease, dated as of March 1, 2017, between ARE-SD Region No. 23 and Vertex Pharmaceuticals Incorporated.		10-Q (Exhibit 10.3)	April 28, 2017	000-19319
Financing Agreements					
10.14	Credit Agreement, dated as of October 13, 2016, among Vertex Pharmaceuticals Incorporated, Bank of America, N.A. and the other lenders party thereto.		10-K (Exhibit 10.12)	February 23, 2017	000-19319
10.15	First Amendment to Credit Agreement, dated as of February 9, 2017, among Vertex Pharmaceuticals Incorporated, Bank of America, N.A. and the other lenders party thereto.		10-K (Exhibit 10.13)	February 23, 2017	000-19319
Equity Plans					
10.16	Amended and Restated 2006 Stock and Option Plan.*		10-Q (Exhibit 10.3)	August 8, 2012	000-19319
10.17	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
10.18	Form of Restricted Stock Agreement under Amended and Restated 2006 Stock and Option Plan (granted prior to July 30, 2013).*		8-K (Exhibit 10.3)	May 15, 2006	000-19319
10.19	Form of Restricted Stock Agreement (Performance Accelerated Restricted Stock) under Amended and Restated 2006 Stock and Option Plan (granted prior to July 30, 2013).*		8-K (Exhibit 10.4)	May 15, 2006	000-19319
10.20	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
10.21	Form of Restricted Stock Agreement under Amended and Restated 2006 Stock and Option Plan (granted on or after July 30, 2013).*		10-K (Exhibit 10.21)	February 13, 2015	000-19319
10.22	Form of Restricted Stock Unit Agreement under Amended and Restated 2006 Stock and Option Plan (granted on or after July 30, 2013).*		10-K (Exhibit 10.22)	February 13, 2015	000-19319
10.23	Amended and Restated 2013 Stock and Option Plan.*		DEF 14A (Appendix C)	April 28, 2017	000-19319
10.24	Form of Non-Qualified Stock Option Agreement under 2013 Stock and Option Plan.*		10-K (Exhibit 10.17)	February 13, 2015	000-19319
10.25	Form of Restricted Stock Agreement under 2013 Stock and Option Plan.*		10-K (Exhibit 10.18)	February 13, 2015	000-19319
10.26	Form of Restricted Stock Unit Agreement under 2013 Stock and Option Plan (U.S.).*		10-K (Exhibit 10.25)	February 16, 2016	000-19319
10.27	Form of Restricted Stock Unit Agreement under 2013 Stock and Option Plan (International).*		10-K (Exhibit 10.19)	February 13, 2015	000-19319
10.28	Non-Employee Director Deferred Compensation Plan.*		10-K (Exhibit 10.27)	February 16, 2016	000-19319
10.29	Vertex Pharmaceuticals Incorporated Employee Stock Purchase Plan, as amended and restated as of July 12, 2016.*		10-Q (Exhibit 10.1)	August 1, 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
Agreements with Executive Officers and Directors					
10.30	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
10.31	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
10.32	Employment Agreement, dated as of August 27, 2012, between Vertex Pharmaceuticals Incorporated and Stuart Arbuckle.*		10-Q (Exhibit 10.1)	November 6, 2012	000-19319
10.33	Change of Control Agreement, dated as of August 27, 2012, between Vertex Pharmaceuticals Incorporated and Stuart Arbuckle.*		10-Q (Exhibit 10.2)	November 6, 2012	000-19319
10.34	Employment Agreement, dated as of December 12, 2014, between Vertex Pharmaceuticals Incorporated and David Altshuler.*		10-K (Exhibit 10.34)	February 16, 2016	000-19319
10.35	Change of Control Agreement, dated as of December 12, 2014, between Vertex Pharmaceuticals Incorporated and David Altshuler.*		10-K (Exhibit 10.35)	February 16, 2016	000-19319
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	Employment Agreement, dated as of December 2, 2013, between Vertex Pharmaceuticals Incorporated and Jeffrey Chodakewicz.*		10-Q (Exhibit 10.1)	May 4, 2015	000-19319
10.39	Change of Control Agreement, dated as of December 2, 2013, between Vertex Pharmaceuticals Incorporated and Jeffrey Chodakewicz.*		10-Q (Exhibit 10.2)	May 4, 2015	000-19319
10.40	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
10.41	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
10.42	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
10.43	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
10.44	Employment Agreement, dated as of September 6, 2017, between Vertex Pharmaceuticals Incorporated and Tom Graney.*		10-Q (Exhibit 10.1)	October 30, 2017	000-19319
10.45	Change of Control Agreement, dated as of September 6, 2017, between Vertex Pharmaceuticals Incorporated and Tom Graney.*		10-Q (Exhibit 10.2)	October 30, 2017	000-19319
10.46	Vertex Employee Compensation Plan.*	X			
10.47	Vertex Pharmaceuticals Non-Employee Board Compensation.*	X			
Subsidiaries					
21.1	Subsidiaries of Vertex Pharmaceuticals Incorporated.	X			
Consent					
23.1	Consent of Independent Registered Public Accounting Firm, Ernst & Young LLP.	X			
Certifications					
31.1	Certification of the Chief Executive Officer under Section 302 of the Sarbanes-Oxley Act of 2002.	X			
31.2	Certification of the Chief Financial Officer under Section 302 of the Sarbanes-Oxley Act of 2002.	X			
32.1	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			

Exhibit Number	Exhibit Description	Filed with this report	Incorporated by Reference herein from—Form or Schedule	Filing Date/ Period Covered	SEC File/ Reg. Number
101.DEF	XBRL Taxonomy Extension Definition	X			

* Management contract, compensatory plan or agreement.

†Confidential portions of this document have been filed separately with the Securities and Exchange Commission pursuant to a request for confidential treatment.

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, 2017 and 2016, 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, 2017, 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, 2017 and 2016, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2017, 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, 2017, 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 14, 2018 expressed an unqualified opinion thereon.

Basis for Opinion

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

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedure 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.

/s/ Ernst & Young LLP

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

Boston, Massachusetts

February 14, 2018

VERTEX PHARMACEUTICALS INCORPORATED

Consolidated Statements of Operations

(in thousands, except per share amounts)

	Year Ended December 31,		
	2017	2016	2015
Revenues:			
Product revenues, net	\$ 2,165,480	\$ 1,683,632	\$ 1,000,324
Royalty revenues	7,988	16,600	23,959
Collaborative revenues	315,184	1,945	8,053
Total revenues	<u>2,488,652</u>	<u>1,702,177</u>	<u>1,032,336</u>
Costs and expenses:			
Cost of product revenues	272,675	206,811	117,151
Royalty expenses	2,444	3,649	7,361
Research and development expenses	1,324,625	1,047,690	995,922
Sales, general and administrative expenses	496,079	432,829	376,575
Restructuring expenses	14,246	1,262	2,206
Intangible asset impairment charge	255,340	—	—
Total costs and expenses	<u>2,365,409</u>	<u>1,692,241</u>	<u>1,499,215</u>
Income (loss) from operations	123,243	9,936	(466,879)
Interest expense, net	(57,550)	(81,432)	(84,206)
Other (expense) income, net	(81,382)	4,130	(6,715)
Loss before (benefit from) provision for income taxes	(15,689)	(67,366)	(557,800)
(Benefit from) provision for income taxes	(107,324)	16,665	30,381
Net income (loss)	91,635	(84,031)	(588,181)
Loss (income) attributable to noncontrolling interest	171,849	(28,021)	31,847
Net income (loss) attributable to Vertex	<u>\$ 263,484</u>	<u>\$ (112,052)</u>	<u>\$ (556,334)</u>
Amounts per share attributable to Vertex common shareholders:			
Net income (loss):			
Basic	\$ 1.06	\$ (0.46)	\$ (2.31)
Diluted	\$ 1.04	\$ (0.46)	\$ (2.31)
Shares used in per share calculations:			
Basic	248,858	244,685	241,312
Diluted	253,225	244,685	241,312

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,		
	2017	2016	2015
Net income (loss)	\$ 91,635	\$ (84,031)	\$ (588,181)
Changes in other comprehensive income (loss):			
Unrealized holding gains on marketable securities, net of tax of \$(2.7) million, \$(3.8) million and zero, respectively	6,954	17,395	249
Unrealized (losses) gains on foreign currency forward contracts, net of tax of \$3.4 million, \$(3.9) million and zero, respectively	(26,530)	7,736	1,767
Foreign currency translation adjustment	(13,169)	(5,782)	(1,109)
Total changes in other comprehensive (loss) income	(32,745)	19,349	907
Comprehensive income (loss)	58,890	(64,682)	(587,274)
Comprehensive loss (income) attributable to noncontrolling interest	171,849	(28,021)	31,847
Comprehensive income (loss) attributable to Vertex	<u>\$ 230,739</u>	<u>\$ (92,703)</u>	<u>\$ (555,427)</u>

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,	
	2017	2016
Assets		
Current assets:		
Cash and cash equivalents	\$ 1,665,412	\$ 1,183,945
Marketable securities, available-for-sale	423,254	250,612
Restricted cash and cash equivalents (VIE)	1,489	47,762
Accounts receivable, net	281,343	200,364
Inventories	111,830	77,604
Prepaid expenses and other current assets	165,635	71,253
Total current assets	<u>2,648,963</u>	<u>1,831,540</u>
Property and equipment, net	789,437	698,362
Intangible assets	29,000	284,340
Goodwill	50,384	50,384
Cost method investments	20,447	20,276
Other assets	7,783	11,885
Total assets	<u>\$ 3,546,014</u>	<u>\$ 2,896,787</u>
Liabilities and Shareholders' Equity		
Current liabilities:		
Accounts payable	\$ 73,994	\$ 61,451
Accrued expenses	443,961	315,249
Deferred revenues, current portion	5,169	6,005
Accrued restructuring expense, current portion	2,175	6,047
Capital lease obligations, current portion	22,531	19,426
Customer deposits	232,401	73,416
Credit facility	—	300,000
Other liabilities, current portion	27,029	10,943
Total current liabilities	<u>807,260</u>	<u>792,537</u>
Deferred revenues, excluding current portion	1,726	6,632
Accrued restructuring expense, excluding current portion	—	1,907
Capital lease obligations, excluding current portion	20,496	34,976
Deferred tax liability	6,341	134,063
Construction financing lease obligation, excluding current portion	563,406	486,359
Advance from collaborator, excluding current portion	78,431	73,423
Other liabilities, excluding current portion	26,048	28,699
Total liabilities	<u>1,503,708</u>	<u>1,558,596</u>
Commitments and contingencies		
Shareholders' equity:		
Preferred stock, \$0.01 par value; 1,000,000 shares authorized; none issued and outstanding at December 31, 2017 and 2016	—	—
Common stock, \$0.01 par value; 500,000,000 shares authorized, 253,253,362 and 248,300,517 shares issued and outstanding at December 31, 2017 and 2016, respectively	2,512	2,450
Additional paid-in capital	7,157,362	6,506,795
Accumulated other comprehensive (loss) income	(11,572)	21,173
Accumulated deficit	(5,119,723)	(5,373,836)
Total Vertex shareholders' equity	<u>2,028,579</u>	<u>1,156,582</u>
Noncontrolling interest	13,727	181,609
Total shareholders' equity	<u>2,042,306</u>	<u>1,338,191</u>
Total liabilities and shareholders' equity	<u>\$ 3,546,014</u>	<u>\$ 2,896,787</u>

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		Additional Paid-in Capital	Accumulated Other Comprehensive Income (Loss)	Accumulated Deficit	Total Vertex Shareholders' Equity	Noncontrolling Interest	Total Shareholders' Equity
	Shares	Amount						
Balance, December 31, 2014	241,764	\$ 2,385	\$ 5,777,154	\$ 917	\$ (4,705,450)	\$ 1,075,006	\$ 21,177	\$ 1,096,183
Other comprehensive income, net of tax	—	—	—	907	—	907	—	907
Net loss	—	—	—	—	(556,334)	(556,334)	(31,847)	(588,181)
Issuance of common stock under benefit plans	4,543	42	185,234	—	—	185,276	14	185,290
Stock-based compensation expense	—	—	235,112	—	—	235,112	—	235,112
Noncontrolling interest upon consolidation	—	—	—	—	—	—	164,317	164,317
Balance, December 31, 2015	246,307	\$ 2,427	\$ 6,197,500	\$ 1,824	\$ (5,261,784)	\$ 939,967	\$ 153,661	\$ 1,093,628
Other comprehensive income, net of tax	—	—	—	19,349	—	19,349	—	19,349
Net (loss) income	—	—	—	—	(112,052)	(112,052)	28,021	(84,031)
Issuance of common stock under benefit plans	1,994	23	67,983	—	—	68,006	—	68,006
Stock-based compensation expense	—	—	241,312	—	—	241,312	(73)	241,239
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 income, 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

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,		
	2017	2016	2015
Cash flows from operating activities:			
Net income (loss)	\$ 91,635	\$ (84,031)	\$ (588,181)
Adjustments to reconcile net income (loss) to net cash provided by (used in) operating activities:			
Stock-based compensation expense	290,736	237,705	231,025
Depreciation expense	61,397	61,398	62,343
Write-downs of inventories to net realizable value	15,292	—	—
Deferred income taxes	(120,513)	16,961	3,283
Impairment of property and equipment	1,951	—	2,516
Intangible asset impairment charge	255,340	—	—
Acquired in-process research and development	160,000	—	—
Deconsolidation of VIE	76,644	—	—
Other non-cash items, net	(2,804)	6,140	9,532
Changes in operating assets and liabilities:			
Accounts receivable, net	(71,759)	(39,095)	(110,098)
Inventories	(44,984)	(16,450)	(23,146)
Prepaid expenses and other assets	(111,063)	(2,631)	(4,009)
Accounts payable	8,753	(11,745)	(1,709)
Accrued expenses and other liabilities	246,217	88,649	102,746
Accrued restructuring expense	(5,987)	(7,426)	(30,492)
Deferred revenues	(5,913)	(13,372)	(19,242)
Net cash provided by (used in) operating activities	<u>844,942</u>	<u>236,103</u>	<u>(365,432)</u>
Cash flows from investing activities:			
Maturities of marketable securities	369,214	757,562	1,067,443
Purchases of marketable securities	(532,581)	(616,625)	(633,041)
Expenditures for property and equipment	(99,421)	(56,563)	(45,302)
Purchase of in-process research and development	(160,000)	—	—
Investment in note receivable	—	(20,000)	(30,000)
Investment in equity securities	—	(13,075)	—
(Decrease) increase in restricted cash and cash equivalents (VIE)	(15,329)	31,148	11,685
Increase (decrease) in restricted cash and cash equivalents and other assets	436	22,022	(21,929)
Payment for acquisition of variable interest entity	—	—	(80,000)
Net cash (used in) provided by investing activities	<u>(437,681)</u>	<u>104,469</u>	<u>268,856</u>
Cash flows from financing activities:			
Issuances of common stock under benefit plans	344,840	68,230	185,592
Payments on revolving credit facility	(300,000)	—	—
Advance from collaborator	12,500	75,000	—
Payments on construction financing lease obligation	(541)	(432)	(381)
Proceeds related to construction financing lease obligation	27,182	—	—
Proceeds from capital lease financing	7,484	11,208	23,662
Payments on capital lease obligations	(18,795)	(17,597)	(19,954)
Repayments of advanced funding	(4,266)	—	—
Payments on senior secured term loan	—	(75,000)	—
Proceeds from revolving credit facility	—	74,965	—
Payments of debt issuance costs	—	(3,103)	—
Net cash provided by financing activities	<u>68,404</u>	<u>133,271</u>	<u>188,919</u>
Effect of changes in exchange rates on cash	5,802	(4,666)	(2,834)
Net increase in cash and cash equivalents	<u>481,467</u>	<u>469,177</u>	<u>89,509</u>
Cash and cash equivalents—beginning of period	1,183,945	714,768	625,259
Cash and cash equivalents—end of period	<u>\$ 1,665,412</u>	<u>\$ 1,183,945</u>	<u>\$ 714,768</u>

Supplemental disclosure of cash flow information:

Cash paid for interest	\$	68,696	\$	83,656	\$	85,613
Cash paid for (received from) income taxes	\$	6,414	\$	(2,579)	\$	1,806
Non-cash investing and financing activities:						
Capitalization of costs related to construction financing lease obligation	\$	40,855	\$	14,238	\$	—
Issuances of common stock from employee benefit plans receivable	\$	844	\$	68	\$	361
Proceeds from revolving credit facility directly paid to settle all outstanding obligations under the term loan	\$	—	\$	225,000	\$	—

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 our research and development programs in other indications. The Company’s marketed products are ORKAMBI (lumacaftor in combination with ivacaftor), KALYDECO (ivacaftor) and SYMDEKO (tezacaftor in combination with 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, 2017, the Company had cash, cash equivalents and marketable securities of \$2.1 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.

Vertex 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 consolidated financial statements reflect the operations of (i) the Company, (ii) its wholly-owned subsidiaries and (iii) consolidated variable interest entities (“VIEs”). On September 30, 2017, the Company deconsolidated Parion Sciences, Inc. (“Parion”), a VIE the Company had consolidated since June 4, 2015. The Company’s consolidated balance sheet as of December 31, 2017 excludes Parion. All material intercompany balances and transactions have been eliminated. The Company operates in one segment, pharmaceuticals. Please refer to Note T, “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 amounts in the consolidated balance sheets for the period ended December 31, 2016 between “Accounts receivable, net” and “Prepaid expenses and other current assets” to conform with the current year presentation.

Use of Estimates

The preparation of consolidated financial statements in accordance with accounting principles generally accepted in the United States of America (“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 the calculation of revenues, inventories, research and development expenses, stock-based compensation expense, the fair value of intangible assets, goodwill, noncontrolling interest, the consolidation and deconsolidation of VIEs, leases, the fair value of cash flow hedges, deferred tax asset valuation allowances and the provision for or benefit from 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

Product Revenues, Net

The Company sells its products principally to a limited number of specialty pharmacy providers in North America as well as government-owned and supported customers in international markets (collectively, its “Customers”). The Company’s Customers in North America subsequently resell the products to patients and health care providers. The Company recognizes

VERTEX PHARMACEUTICALS INCORPORATED

Notes to Consolidated Financial Statements (Continued)

net revenues from product sales upon delivery as long as (i) there is persuasive evidence that an arrangement exists between the Company and the Customer, (ii) collectibility is reasonably assured and (iii) the price is fixed or determinable.

In order to conclude that the price is fixed or determinable, the Company must be able to (i) calculate its gross product revenues from sales to Customers and (ii) reasonably estimate its net product revenues upon delivery to its Customer's locations. The Company calculates gross product revenues based on the price that the Company charges its Customers. The Company estimates its net product revenues by deducting from its gross product revenues (a) trade allowances, such as invoice discounts for prompt payment and Customer fees, (b) estimated government and private payor rebates, chargebacks and discounts, (c) estimated reserves for expected product returns and (d) estimated costs of co-pay assistance programs for patients, as well as other incentives for certain indirect customers.

Trade Allowances: 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 payment terms for sales to Customers in the United States ("U.S.") generally include a discount for payment within 30 days. The Company expects 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 and Discounts: The Company contracts primarily 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 and discounts 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 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.

Product Returns: The Company estimates the amount of each product that will be returned and deducts these estimated amounts from its gross revenues at the time the revenues are recognized. The Company's Customers have the right to return unopened unprescribed packages, subject to contractual limitations. To date, product returns have been minimal and, based on inventory levels held by its Customers and its distribution model, the Company believes that returns of its products will continue to be minimal.

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. The Company's co-pay mitigation programs are intended to reduce each participating patient's portion of the financial responsibility for a product's purchase price to a specified dollar amount. 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 its accruals for co-pay mitigation rebates and deducts these estimated amounts from its gross product revenues at the later of the date (i) the revenues are recognized or (ii) the incentive is offered. The Company's co-pay mitigation rebates are subject to expiration.

VERTEX PHARMACEUTICALS INCORPORATED
Notes to Consolidated Financial Statements (Continued)

The following table summarizes activity in each of the product revenue allowance and reserve categories for the three years ended December 31, 2017:

	Trade Allowances	Rebates, Chargebacks and Discounts	Product Returns	Other Incentives	Total
(in thousands)					
2017					
Beginning Balance	\$ 2,568	\$ 81,927	\$ 3,492	\$ 1,214	\$ 89,201
Provision related to current period sales	25,892	176,996	4,038	15,595	222,521
Adjustments related to prior period sales	(189)	(8,943)	(13)	(493)	(9,638)
Credits/payments made	(25,507)	(137,765)	(4,496)	(11,633)	(179,401)
Ending Balance	<u>\$ 2,764</u>	<u>\$ 112,215</u>	<u>\$ 3,021</u>	<u>\$ 4,683</u>	<u>\$ 122,683</u>
2016					
Beginning Balance	\$ 2,089	\$ 44,669	\$ 1,228	\$ 1,310	\$ 49,296
Provision related to current period sales	20,075	134,198	3,047	6,602	163,922
Adjustments related to prior period sales	(90)	154	(17)	(151)	(104)
Credits/payments made	(19,506)	(97,094)	(766)	(6,547)	(123,913)
Ending Balance	<u>\$ 2,568</u>	<u>\$ 81,927</u>	<u>\$ 3,492</u>	<u>\$ 1,214</u>	<u>\$ 89,201</u>
2015					
Beginning Balance	\$ 1,463	\$ 29,102	\$ 4,713	\$ 745	\$ 36,023
Provision related to current period sales	10,890	65,781	779	3,755	81,205
Adjustments related to prior period sales	(214)	(19,410)	(993)	(235)	(20,852)
Credits/payments made	(10,050)	(30,804)	(3,271)	(2,955)	(47,080)
Ending Balance	<u>\$ 2,089</u>	<u>\$ 44,669</u>	<u>\$ 1,228</u>	<u>\$ 1,310</u>	<u>\$ 49,296</u>

The Company makes significant estimates and judgments that materially affect the Company's 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. In 2017, the Company's adjustments relating to prior period sales were less than 0.5% of total net product revenues and primarily related to U.S. rebates, chargebacks and discounts. In 2016, the Company's adjustments relating to prior period sales were insignificant. In 2015, the Company's adjustments relating to prior period sales principally related to the Company's estimates for INCIVEK following the Company's withdrawal of INCIVEK from the market in the U.S. in the fourth quarter of 2014.

In certain instances, the Company may be unable to reasonably conclude that the price is fixed or determinable at the time of delivery, in which case it defers the recognition of revenues. Once the Company is able to determine that the price is fixed or determinable, it recognizes the net product revenues associated with the units in which revenue recognition was deferred.

French Early Access Programs

The Company began distributing ORKAMBI through early access programs in France during the fourth quarter of 2015. The Company's ORKAMBI net product revenues for the three years ended December 31, 2017 do not include any net product revenues from sales of ORKAMBI in France because the price was not fixed or determinable. As of December 31, 2017, the Company's consolidated balance sheet includes \$232.4 million collected in France related to shipments of ORKAMBI under the early access programs that is classified as "Customer deposits." The Company expects that the difference between the amounts collected based on the invoiced price and the final price for ORKAMBI in France will be returned to the French government.

VERTEX PHARMACEUTICALS INCORPORATED

Notes to Consolidated Financial Statements (Continued)

Because the Company concluded that the price was not fixed or determinable as of December 31, 2017, the amounts classified as “Customer deposits” related to shipments of ORKAMBI under early access programs will be subject to the new guidance applicable to revenue recognition that became effective January 1, 2018. Pursuant to the new guidance, the Company will record a cumulative effect adjustment to the Company’s accumulated deficit in the first quarter of 2018. The amount of the adjustment to accumulated deficit will be determined based upon (i) the status of pricing discussions in France upon adoption and (ii) the Company’s estimate of the amount of consideration the Company expects to retain related to ORKAMBI sales in France that occurred on or prior to December 31, 2017 that will not be subject to a significant reversal in amounts recognized. For ORKAMBI sales in France that occur after December 31, 2017 under the early access programs, the Company will recognize net product revenues based on the Company’s estimate of consideration the Company expects to retain that will not be subject to a significant reversal in amounts recognized. In periods after the first quarter of 2018, if the Company’s estimate regarding the amounts it will receive for ORKAMBI supplied pursuant to these programs changes, the effect of the change in estimate would be reflected in net product revenues in the period in which the change in estimate occurred. Please refer to *Recent Accounting Pronouncements* included in this Note A “Nature of Business and Accounting Policies” below for more information regarding the new revenue recognition guidance.

Royalty Revenues

The Company has sold its rights to receive certain royalties on sales of an HIV protease inhibitor (fosamprenavir) and recognizes the revenues related to this sale as royalty revenues. Pursuant to the revenue recognition guidance that was in effect until December 31, 2017, in the circumstance where the Company sold its rights to future royalties under a license agreement and also maintained continuing involvement in the royalty arrangement (but not significant continuing involvement in the generation of the cash flows payable to the purchaser of the future royalty rights), the Company deferred recognition of the proceeds it received for the royalty stream. It recognized these deferred revenues over the life of the license agreement utilizing the units-of-revenue method pursuant to this revenue recognition guidance. In the first quarter of 2018, the Company will record a \$6.5 million cumulative effect adjustment to its accumulated deficit equal to the net deferred revenues and costs recorded as of December 31, 2017. This adjustment will be recorded utilizing the modified retrospective approach upon adoption of the new revenue recognition guidance described in *Recent Accounting Pronouncements* included in this Note A “Nature of Business and Accounting Policies” below that became effective January 1, 2018. The adjustment will be made because there are no material performance obligations remaining related to the royalty arrangement. The Company does not expect to record any royalty revenues in future periods based on sales of the HIV protease inhibitor. Please refer to Note O, “Other Arrangements” for further information related to this transaction.

Collaborative 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 of one or more of the following: nonrefundable, up-front license fees; development and commercial milestone payments; funding of research and/or development activities; and royalties on net sales of licensed products. Each of these types of payments results in collaborative revenues except for revenues from royalties on net sales of licensed products, which are classified as royalty revenues.

For each collaborative research, development and/or commercialization agreement that result in revenues, the Company determines (i) whether multiple deliverables exist, (ii) whether the undelivered elements have value to the customer on a stand-alone basis, (iii) how the deliverables should be separated and (iv) how the consideration should be allocated to the deliverables. For arrangements entered into or materially modified after January 1, 2011, the Company allocates consideration in an arrangement using the relative selling price method based on management’s best estimate of selling price of deliverables if it does not have vendor-specific objective evidence or third-party evidence. As part of the accounting for these agreements, the Company must develop assumptions that require judgment to determine the best estimate of selling price. Key assumptions utilized by the Company to determine the best estimate of selling price may include forecasted revenues, patient enrollment requirements from regulatory authorities, development timelines, reimbursement rates for personnel costs, discount rates, and estimated third-party development costs.

The Company evaluates amendments to its existing arrangements to determine whether they have been materially modified. In making its determination that an arrangement has been materially modified, the Company considers whether

VERTEX PHARMACEUTICALS INCORPORATED

Notes to Consolidated Financial Statements (Continued)

there have been significant changes to the consideration under the arrangement, the deliverables under the arrangement, the timing of deliverables and the period of the arrangement. If the arrangement is determined to have been materially modified, the Company allocates fixed consideration under the arrangement using its best estimate of selling price to the remaining undelivered elements at the date of material modification. Any consideration remaining after the allocation is recognized as revenue.

Up-front License Fees: If the license to the Company's intellectual property is determined to have stand-alone value from the other deliverables identified in the arrangement, the Company recognizes revenues from nonrefundable, up-front license fees upon delivery. If these licenses do not have stand-alone value, the Company recognizes revenues from nonrefundable, up-front license fees on a straight-line basis over the contracted or estimated period of performance. The Company evaluates the period of performance each reporting period and adjusts the period of performance on a prospective basis if there are changes to be made.

Milestone Payments: At the inception of each agreement that includes research and development milestone payments, the Company evaluates whether each milestone is substantive. The Company recognizes revenues related to substantive milestones in full in the period in which the substantive milestone is achieved if payment is reasonably assured. If a milestone is not considered substantive, the Company recognizes the applicable milestone payment over the period of performance.

Research and Development Activities: If the Company is entitled to reimbursement from its collaborators for specified research and development expenses, the Company determines whether the research and development funding would result in collaborative revenues or an offset to research and development expenses in accordance with the provisions of gross or net revenue presentation.

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's receivables from Greece, Italy, Portugal and Spain were not material as of December 31, 2017. The Company believes that its allowance for doubtful accounts was adequate at December 31, 2017. Please refer to Note T, "Segment Information," for further information.

Cash and Cash Equivalents

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

Marketable Securities

The Company's marketable securities consist of investments in government-sponsored enterprise securities, corporate equity securities, corporate debt securities and commercial paper that are classified as available-for-sale as of December 31, 2017. 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 with their unrealized gains and losses included as a component of accumulated

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Notes to Consolidated Financial Statements (Continued)

other comprehensive income (loss), which is a separate component of shareholders' equity, until such gains and losses are realized. The fair value of these securities is based on quoted prices for identical or similar assets.

The Company reviews investments in marketable 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 trade allowances 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. For awards with performance conditions that accelerate vesting of the award, the Company estimates the likelihood of satisfaction of the performance conditions, which affects the period over which the expense is recognized, and recognizes the expense using the accelerated attribution model.

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. Less than 5% of the Company's employees were eligible for partial or full acceleration of any of their equity awards as of December 31, 2017. 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; laboratory supplies and other direct expenses; outsourced services, including clinical trial and pharmaceutical development costs; collaboration and asset

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acquisition payments; expenses associated with drug supplies that are not being capitalized; and infrastructure costs, including facilities costs and depreciation expense.

Advertising Expenses

The Company expenses the costs of advertising, including promotional expenses, as incurred. Advertising expenses, recorded in sales, general and administrative expenses, were \$35.2 million, \$31.4 million and \$24.5 million in 2017, 2016 and 2015, respectively.

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 product revenues in the consolidated statements of operations. Shipping and handling costs incurred for product shipments are recorded as incurred in cost of product revenues 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, 40 years for buildings and for leasehold improvements, the shorter of the useful life of the improvements or the estimated remaining life of the associated lease. Amortization expense of assets acquired under capital leases is included in depreciation expense. 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. The Company expenses costs related to the planning and post-implementation phases of development of software for internal use as these costs are incurred. Maintenance and enhancement costs (including costs in the post-implementation stages) are expensed as incurred, unless such costs relate to substantial upgrades and enhancements to the software resulting in added functionality, in which case the costs are capitalized. Amortization of capitalized internally developed software costs is recorded in depreciation expense over the useful life of the related asset.

The Company records certain construction costs incurred by a landlord as an asset and a corresponding financing obligation on the Company's consolidated balance sheets when the Company is determined to be the owner of a building during construction for accounting purposes. Upon completion of the project, the Company performs a sale-leaseback analysis to determine if the Company can remove the assets and corresponding liability from its consolidated balance sheet.

Capital Leases

The assets and liabilities associated with capital lease agreements are recorded at the present value of the minimum lease payments at the inception of the lease agreement. The assets are depreciated using the straight-line method over the shorter

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Notes to Consolidated Financial Statements (Continued)

of the useful life of the related asset or the remaining life of the associated lease. Amortization of assets that the Company leases pursuant to a capital lease is included in depreciation expense. 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. Assets recorded under capital leases are recorded within "Property and equipment, net" and liabilities related to those assets are recorded within "Capital lease obligations, current portion" and "Capital lease obligations, excluding current portion" on the Company's consolidated balance sheets.

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 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. The Company evaluates whether it continues to be the primary beneficiary of any consolidated VIEs on a quarterly basis. 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.

Assets recorded as a result of consolidating VIEs' financial results into the Company's consolidated balance sheet do not represent additional assets that could be used to satisfy claims against the Company's general assets. With respect to the Company's VIEs, the VIEs' assets are not significant, except for the VIEs' cash and cash equivalents. The Company records the cash and cash equivalents of consolidated VIEs as "Restricted cash and cash equivalents (VIE)" because the Company does not have control over the VIEs' cash and cash equivalents. The VIEs' cash and cash equivalents were \$1.5 million and \$47.8 million as of December 31, 2017 and 2016, respectively. The Company also has recorded the liabilities of its consolidated VIEs for which creditors do not have recourse to the Company's general assets outside of the VIE.

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

The present-value models used to estimate the fair values of research and development assets and contingent payments pursuant to collaborations incorporate significant assumptions, including: assumptions regarding the probability of obtaining marketing approval and/or achieving relevant development milestones for a drug candidate; estimates regarding the timing of and the expected costs to develop a drug candidate; estimates of future cash flows from potential product sales and/or the potential to achieve certain commercial milestones with respect to a drug candidate; and the appropriate discount and tax rates.

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Notes to Consolidated Financial Statements (Continued)

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 product revenues 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 assets that are acquired in a transaction that does not qualify as a business combination under GAAP and that do not have an alternative future use are expensed in the period in which the assets are 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.

Noncontrolling Interest

The Company records noncontrolling interest, which has historically related to consolidated VIEs, on its consolidated balance sheets. The Company records net loss (income) attributable to noncontrolling interest on its consolidated statements of operations, reflecting the VIEs' net loss (income) for the reporting period, adjusted for changes in the noncontrolling interest holders' claim to net assets, including contingent milestone, royalty and option payments, each of which is evaluated each reporting period.

Deconsolidation and Discontinued Operations

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.

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.

Derivative Instruments, Embedded Derivatives and Hedging Activities

The Company has entered into financial transactions involving free-standing derivative instruments and embedded derivatives in the past. Embedded derivatives are required to be bifurcated from the host instruments if the derivatives are not clearly and closely related to the host instruments. The Company determines the fair value of each derivative instrument or embedded derivative that is identified on the date of issuance and at the end of each quarterly period. The estimates of the fair value of the derivatives include significant assumptions regarding the estimates market participants would make in order to evaluate these derivatives.

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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", which is a separate component of shareholders' equity, as unrealized gains and losses until the forecasted underlying transaction occurs. Unrealized gains and losses on these foreign currency forward contracts are included in (i) "Prepaid expenses and other current assets," (ii) "Other assets," (iii) "Other liabilities, current portion" and (iv) "Other liabilities, excluding current portion," respectively, on the Company's consolidated balance sheets. Realized gains and losses for the effective portion of such contracts are recognized in "Product revenues, net" in the consolidated statement of operations when the contract is settled with the counterparty. 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 assesses, both at inception and on an ongoing basis, whether the foreign currency forward contracts used in hedging transactions are highly effective in offsetting the changes in cash flows of the hedged items. The Company also assesses hedge ineffectiveness quarterly and, if determined to be ineffective, records the gain or loss related to the ineffective portion to earnings in "Other (expense) income, net" in its consolidated statements of operations. The Company did not record any ineffectiveness related to these hedging transactions in the three years ended December 31, 2017.

The Company also enters into foreign currency forward contracts with contractual maturities of less than one month designed to mitigate the effect of changes in foreign exchange rates on monetary assets and liabilities including intercompany balances. These contracts are not designated as hedging instruments pursuant to GAAP. Realized gains and losses for such contracts are recognized in "Other (expense) income, net" in the consolidated statement of operations when the contract is settled with the counterparty.

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. In estimating the expenses and liabilities related to these facilities, the Company utilizes the probability-weighted discounted cash-flows of the Company's ongoing lease obligations. In estimating the expense and liability under its lease obligations, the Company estimates (i) the costs to be incurred to satisfy rental and build-out commitments under the lease (including operating costs), (ii) the lead-time necessary to sublease the space, (iii) the projected sublease rental rates and (iv) the anticipated durations of subleases. The Company uses a credit-adjusted risk-free rate to discount the estimated cash flows.

In periods subsequent to the initial measurement, the Company measures changes to the liability using the credit-adjusted risk-free discount rate applied in the initial period. The Company evaluates and adjusts these liabilities as appropriate for changes in circumstances on a quarterly basis. Changes to the Company's estimate of these liabilities are recorded as additional restructuring expenses (credits). In addition, because the Company's estimate of these liabilities includes the application of a discount rate to reflect the time-value of money, the Company records imputed interest costs related to these liabilities each quarter. These costs are included in "Restructuring expenses" on the Company's consolidated statements of operations.

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.

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Foreign Currency Translation and Transactions

The Company primarily operates with entities that have the U.S. dollar denominated as their functional currency. Non-U.S. dollar denominated functional currency subsidiaries have assets and liabilities translated into U.S. dollars at rates of exchange in effect at the end of the year. Revenue and expense amounts 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", which is a separate component of shareholders' equity. Included in "Accumulated other comprehensive (loss) income" are net unrealized losses related to foreign currency translation of \$21.0 million, \$7.9 million and \$2.1 million at December 31, 2017, 2016 and 2015, respectively. Net foreign currency exchange transaction gains or losses are included in net income (loss) on the Company's consolidated statement of operations. Net transaction losses were \$5.5 million and \$6.8 million for 2017 and 2015, respectively, and net transaction gains were \$4.0 million for 2016.

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.

Recent Accounting Pronouncements

In 2014, the Financial Accounting Standards Board ("FASB") issued new guidance applicable to revenue recognition that became effective January 1, 2018. The new guidance applies a more principles based approach to recognizing revenue. Under the new guidance, revenue is recognized when a customer obtains control of promised goods or services and is recognized 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 new guidance must be adopted using either a modified retrospective approach or a full retrospective approach for all periods presented. Under the modified retrospective method, the cumulative effect of applying the standard would be recognized at the date of initial application within accumulated deficit. Under the full retrospective approach, the standard would be applied to each prior reporting period presented. Upon adoption, the Company will use the modified retrospective method. The Company has evaluated the new guidance and the effect the adoption will have on the consolidated financial statements. The Company's project team has finalized its review of existing customer contracts and current accounting policies and has concluded that the following will be impacted by applying the requirements of the new standard beginning in the first quarter of 2018:

- The Company will be required to estimate the amount of consideration it expects to retain on shipments of ORKAMBI under early access programs in France whereby the associated product has received regulatory approval but the price is not fixed or determinable based on the status of ongoing pricing discussions as of December 31, 2017. Please refer to "Product Revenues, Net" above for further information related to the impact of the new revenue recognition on these sales.
- The Company expects to recognize \$6.5 million that was received with the sale of its HIV protease inhibitor royalty stream in 2008 net of deferred costs associated with this sale as a cumulative effect adjustment to its accumulated deficit due to the new revenue recognition guidance. Please refer to "Royalty Revenues" above and Note O, "Other Arrangements" for further information related to this transaction.

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The Company has implemented appropriate changes to its internal controls to support revenue recognition and additional revenue-related disclosures under the new standard.

In 2016, the FASB issued amended guidance applicable to share-based compensation to employees that 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. The amended guidance became effective for the Company January 1, 2017. The amended guidance eliminates the requirement that excess tax benefits be realized as a reduction in current taxes payable before the associated tax benefit can be recognized as an increase in additional paid-in capital. This created approximately \$410.8 million of deferred tax asset (“DTA”) relating to federal and state net operating losses (“NOLs”) that are fully reserved by an equal increase in valuation allowance. The Company recorded DTAs of approximately \$404.7 million relating to federal NOLs and approximately \$6.1 million relating to state NOLs, both of which are 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 the Company’s accumulated deficit of \$9.4 million, which increased the accumulated deficit as of January 1, 2017. This change also resulted in an increase to the DTA of \$3.4 million, which is 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 income statement and classification in the statement of cash flows were adopted prospectively, and as such, the prior periods were not retrospectively adjusted.

In 2016, the FASB issued amended guidance related to the recording of financial assets and financial liabilities. Under the amended guidance, equity investments (except those accounted for under the equity method of accounting or those that result in consolidation of the investee) are to be measured at fair value with changes in fair value recognized in net income (loss). However, an entity has the option to either measure equity investments without readily determinable fair values either (i) at fair value or (ii) at cost adjusted for changes in observable prices minus impairment. Changes in measurement under either alternative will be recognized in net income (loss). The amended guidance became effective January 1, 2018. The Company held publicly traded equity investments as well as equity investments accounted for under the cost method as of December 31, 2017. In the first quarter of 2018, the Company will record a cumulative effect adjustment to its accumulated deficit equal to the \$25.1 million unrealized gain, net of tax, recorded in accumulated other comprehensive income (loss) as of December 31, 2017 related to its publicly traded equity investments. This adjustment will decrease the Company’s accumulated deficit as of January 1, 2018. Adoption of the amended guidance will have no effect on the Company’s equity investments accounted for under the cost method because there have been no changes in observable prices or impairments identified that would adjust the cost of the investment as of December 31, 2017 compared to the original cost basis of these investments. The implementation of this amended guidance is expected to increase volatility in net income as the volatility currently recorded in other comprehensive income (loss) related to changes in the fair market value of equity investments will be reflected in net income (loss) after adoption.

In 2016, the FASB issued amended guidance applicable to leases that will be effective for the year ending December 31, 2019. Early adoption is permitted. This guidance requires entities to recognize assets and liabilities for leases with lease terms of more than 12 months on the balance sheet and requires a modified retrospective adoption approach. The Company is in the process of evaluating this guidance and determining the expected effect on its consolidated financial statements; however, it anticipates that the amended guidance will result in the Company recording additional assets and corresponding liabilities on its consolidated balance sheets. The Company expects the implementation of the new standard will have an impact on its internal controls, systems, and processes.

In 2016, the FASB issued amended guidance related to intra-entity transfers other than inventory. This guidance removes the current exception in GAAP prohibiting entities from recognizing current and deferred income tax expenses or benefits related to transfer of assets, other than inventory, within the consolidated entity. The current 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. The amended guidance became effective for the Company on January 1, 2018. In the first quarter of 2018, the Company will record a deferred tax asset and corresponding full valuation allowance upon adoption of this new guidance equal to the unamortized cost of intellectual property transferred to the United Kingdom (“U.K.”) in 2014 multiplied by appropriate statutory rates. As a result, there will be no cumulative effect adjustment to accumulated deficit.

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In 2017, the FASB issued amended guidance related to business combinations. The amended guidance clarifies the definition of a business with the objective of adding guidance to assist entities with evaluating whether transactions should be accounted for as acquisitions (or disposals) of assets or businesses. The new accounting guidance is effective for annual periods beginning after December 15, 2017, including interim periods within those periods. The Company early adopted this new guidance as of January 1, 2017 and has applied this new guidance to acquisitions completed subsequent to adoption.

In 2017, the FASB issued amended guidance related to measurements of goodwill. The amended guidance eliminates a step from the goodwill impairment test. Under the amended guidance, an entity should perform its annual or interim goodwill impairment test by comparing the fair value of a reporting unit with its carrying amount. 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 that reporting unit. The amended guidance is effective for the year-ending December 31, 2020. Early adoption is permitted. The Company does not expect a significant effect on its consolidated financial statements upon adoption of this new guidance.

In 2017, the FASB issued amended guidance related to the scope of stock option modification accounting, to reduce diversity in practice and provide clarity regarding existing guidance. The new accounting guidance became effective January 1, 2018. The Company does not expect the adoption of this guidance to have a material effect on its consolidated financial statements and related disclosures.

In 2017, the FASB issued amended guidance applicable to hedge accounting. The new accounting guidance is effective for annual periods beginning after December 15, 2018, including interim periods within those periods. Early adoption is permitted. The amended guidance helps simplify certain aspects of hedge accounting and enables entities to more accurately present their risk management activities in their financial statements. The Company is in the process of evaluating this guidance and determining the expected effect on its consolidated financial statements.

B. Collaborative Arrangements and Acquisitions

Cystic Fibrosis Foundation Therapeutics Incorporated

The Company has a research, development and commercialization agreement with Cystic Fibrosis Foundation Therapeutics Incorporated ("CFFT") that was originally entered into in May 2004, and was most recently amended in October 2016 (the "2016 Amendment"). Pursuant to the agreement, as amended, the Company has 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 VX-659 and VX-445, and tiered royalties ranging from single digits to sub-teens on any approved drugs 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 (tezacaftor in combination with ivacaftor). For combination products, such as ORKAMBI, sales will be allocated equally to each of the active pharmaceutical ingredients in the combination product.

In each of the fourth quarter of 2015 and the first quarter of 2016, CFFT earned a commercial milestone payment of \$13.9 million from the Company upon achievement of certain sales levels of lumacaftor. There were no commercial milestone payments in the year ended December 31, 2017, and there are no additional commercial milestone payments payable by the Company to CFFT pursuant to the agreement. Pursuant to the 2016 Amendment, the CFFT provided the Company an upfront payment of \$75.0 million and agreed to provide development funding to the Company of up to \$6.0 million annually. The upfront payment plus any future development funding represent a form of financing pursuant to Accounting Standards Codification ("ASC") 730, *Research and Development*, and thus the amounts are recorded as a liability on the consolidated balance sheet, primarily reflected in "Advance from collaborator, excluding current portion". The liability is reduced over the estimated royalty term of the agreement. Reductions in the liability are reflected as an offset to cost of product revenues and as interest expense.

The Company began marketing KALYDECO in 2012 and began marketing ORKAMBI in 2015. The Company received approval for SYMDEKO in the United States in February 2018 and has submitted an MAA to the EMA seeking approval for tezacaftor in combination with ivacaftor in the E.U. The Company expects the EMA to complete its review of the MAA in the second half of 2018. The Company has royalty obligations to CFFT for ivacaftor, lumacaftor and tezacaftor until the expiration of patents covering those compounds. The Company has patents in the U.S. and E.U. covering the composition-

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of-matter of ivacaftor that expire in 2027 and 2025, respectively, subject to potential patent extensions. The Company has patents in the U.S. and E.U. covering the composition-of-matter of lumacaftor that expire in 2030 and 2026, respectively, subject to potential extension. The Company has patents in the U.S. and E.U. covering the composition-of-matter of tezacaftor that expire in 2027 and 2028, respectively, subject to potential extension.

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 has the exclusive right to license up to six CRISPR-Cas9-based targets. In connection with the CRISPR Agreement, the Company made an upfront payment to CRISPR of \$75.0 million and a \$30.0 million investment in CRISPR pursuant to a convertible loan agreement that converted into preferred stock in January 2016. The Company expensed \$75.0 million to research and development, and the \$30.0 million investment was recorded at cost on the Company’s consolidated balance sheet. In the second quarter of 2016, the Company made an additional preferred stock investment in CRISPR of approximately \$3.1 million. In connection with CRISPR’s initial public offering in October 2016, the Company purchased \$10.0 million of common shares at the public offering price and the Company’s preferred stock investments in CRISPR converted into common shares. As of December 31, 2017, the Company recorded the fair value of its investment in CRISPR common shares of \$74.8 million in marketable securities and a \$31.6 million unrealized gain related to these common shares in accumulated other comprehensive income (loss) on the consolidated balance sheet. In January 2018, the Company purchased an additional \$21.5 million of CRISPR’s common shares.

The Company funds all of the discovery activities conducted pursuant to the CRISPR Agreement. For targets that the Company elects to license, other than hemoglobinopathy treatments, the Company would lead all development and global commercialization activities. For each target that the Company elects to license, other than hemoglobinopathy targets, CRISPR has the potential to receive up to \$420.0 million in development, regulatory and commercial milestones and royalties on net product sales. 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 of beta-thalassemia and sickle cell disease.

The Company may terminate the CRISPR Agreement upon 90 days’ notice to CRISPR prior to any product receiving marketing approval or upon 270 days’ notice after a product has received marketing approval. The CRISPR Agreement also may be terminated by either party for a material breach by the other, subject to notice and cure provisions. Unless earlier terminated, the CRISPR Agreement will continue in effect until the expiration of the Company’s payment obligations under the CRISPR Agreement.

In the fourth quarter of 2017, the Company entered a co-development and co-commercialization agreement with CRISPR pursuant to the terms of the CRISPR Agreement, under which the Company and CRISPR will co-develop and co-commercialize CTX001 for the treatment of hemoglobinopathy treatments, including treatments for sickle cell disease and beta-thalassemia.

Merck KGaA

On January 10, 2017, the Company entered into a strategic collaboration and license agreement (the “Merck KGaA Agreement”) with Merck KGaA, Darmstadt, Germany (“Merck KGaA”). Pursuant to the Merck KGaA Agreement, the Company granted Merck KGaA an exclusive worldwide license to research, develop and commercialize four oncology research and development programs. Under the Merck KGaA Agreement, the Company granted Merck KGaA exclusive, worldwide rights to two clinical-stage programs targeting DNA damage repair: its ataxia telangiectasia and Rad3-related protein inhibitor program, including VX-970 and VX-803, and its DNA-dependent protein kinase inhibitor program, including VX-984. In addition, the Company granted Merck KGaA exclusive, worldwide rights to two pre-clinical programs.

The Merck KGaA Agreement provided for an upfront payment from Merck KGaA to the Company of \$230.0 million. During the first quarter of 2017, the Company received \$193.6 million of the upfront payment and the remaining \$36.4 million was remitted to the German tax authorities. Pursuant to a tax treaty between the U.S. and Germany, the Company filed a refund application for the tax withholding. The income tax receivable is included in “Prepaid expenses and other

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current assets” as of December 31, 2017. In addition to the upfront payment, the Company will receive tiered royalties on potential sales of licensed products, calculated as a percentage of net sales, that range from (i) mid-single digits to mid-twenties for clinical-stage programs and (ii) mid-single digits to high single digits for the pre-clinical research programs. Merck KGaA has assumed full responsibility for development and commercialization costs for all programs.

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 Merck KGaA, pursuant to the Merck KGaA Agreement, under the multiple element arrangement accounting guidance. The Company concluded that the license has stand-alone value from the research and development and transition activities based on the resources and know-how possessed by Merck KGaA, 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 approximately \$246.6 million in collaborative revenues related to the \$230.0 million upfront payment upon delivery of the license and \$16.6 million for research and development and transition activities during the year ended December 31, 2017. The Company recorded the reimbursement for the research and development and transition activities in its consolidated statements of operations as a collaborative revenue primarily due to the fact that it is the primary obligor in the arrangement.

Merck KGaA may terminate the Merck KGaA Agreement or any individual program by providing 90 days’ notice, or, in the case of termination of a program with a product that has received marketing approval, 180 days’ notice. The Merck KGaA Agreement also may be terminated by either party for a material breach by the other party, subject to notice and cure provisions. Unless earlier terminated, the Merck KGaA Agreement will continue in effect until the date on which the royalty term and all payment obligations with respect to all products in all countries have expired.

Variable Interest Entities (VIE)

The Company has entered into several agreements pursuant to which it has licensed rights to certain drug candidates from third-party collaborators, resulting in the consolidation of the third parties’ financial statements into the Company’s consolidated financial statements as VIEs. In order to account for the fair value of the contingent payments, which consist of milestone, royalty and option payments, related to these collaborations under GAAP, the Company uses present-value models based on assumptions regarding the probability of achieving the relevant milestones, estimates regarding the timing of achieving the milestones, estimates of future product sales and the appropriate discount rates. The Company bases its estimates of the probability of achieving the relevant milestones on industry data for similar assets and its own experience. The discount rates used in the valuation model 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. Changes in these assumptions could have a material effect on the fair value of the contingent payments. The following collaborations have been reflected in the Company’s financial statements as consolidated VIEs for portions or all of the periods presented:

Parion Sciences, Inc.

In June 2015, the Company entered into a strategic collaboration and license agreement (the “Parion Agreement”) with Parion Sciences, Inc. (“Parion”) to collaborate with Parion to develop investigational epithelial sodium channel (“ENaC”) inhibitors, including VX-371 (formerly P-1037) and VX-551 (formerly P-1055), for the potential treatment of CF and all other pulmonary diseases. The Company is responsible for all costs, subject to certain exceptions, related to development and commercialization of the compounds.

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Pursuant to the Parion Agreement, the Company has worldwide development and commercial rights to Parion's lead investigational ENaC inhibitors, VX-371 and VX-551, for the potential treatment of CF and all other pulmonary diseases and has the option to select additional compounds discovered in Parion's research program. In 2015, Parion received an \$80.0 million up-front payment, and in 2016, Parion earned a milestone payment of \$5.0 million based upon the achievement of a specified milestone under the Parion Agreement. Parion has the potential to receive up to an additional (i) \$485.0 million in development and regulatory milestone payments for development of ENaC inhibitors in CF, including \$360.0 million related to global filing and approval milestones, (ii) \$370.0 million in development and regulatory milestones for VX-371 and VX-551 in non-CF pulmonary indications and (iii) \$230.0 million in development and regulatory milestones should the Company elect to develop an additional ENaC inhibitor from Parion's research program. The Company agreed to pay Parion tiered royalties that range from the low double digits to mid-teens as a percentage of potential sales of licensed products.

The Company may terminate the Parion Agreement upon 90 days' notice to Parion prior to any licensed product receiving marketing approval or upon 180 days' notice after a licensed product has received marketing approval. If the Company experiences a change of control prior to the initiation of the first Phase 3 clinical trial for a licensed product, Parion may terminate the Parion Agreement upon 30 days' notice, subject to the Company's right to receive specified royalties on any subsequent commercialization of licensed products. The Parion Agreement also may be terminated by either party for a material breach by the other, subject to notice and cure provisions. Unless earlier terminated, the Parion Agreement will continue in effect until the expiration of the Company's royalty obligations, which expire on a country-by-country basis on the later of (i) the date the last-to-expire patent covering a licensed product expires or (ii) ten years after the first commercial sale in the country.

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 from June 4, 2015 until the Company deconsolidated Parion effective September 30, 2017. Notwithstanding the applicable accounting treatment, the Company's interests in Parion have been and continue to be limited to those accorded to the Company in the Parion Agreement.

The effect of consolidating Parion's financial statements included \$255.3 million of intangible assets on the Company's consolidated balance sheet for Parion's in-process research and development assets. These in-process research and development assets relate to Parion's pulmonary ENaC platform, including the intellectual property related to VX-371 and VX-551, that are licensed by Parion to the Company. The Company also recorded the fair value of the net assets attributable to noncontrolling interest of \$164.3 million, deferred tax liability of \$91.0 million resulting primarily from a basis difference in the intangible assets and certain other net liabilities held by Parion of \$10.5 million. The difference between the fair values of the consideration and noncontrolling interest and the fair value of Parion's net assets was recorded as goodwill. When determining the valuation of goodwill, the fair value of consideration for the license was zero since there was no consideration transferred outside the consolidated financial statements. While there was a transfer of \$80.0 million for the upfront payment to Parion, the cash remained within the Company's consolidated balance sheet since Parion was part of the consolidated entity. The cash received, net of any cash spent by Parion, was recorded as restricted cash and cash equivalents (VIE) within the consolidated balance sheet as it was attributed to the noncontrolling interest holders of Parion.

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. The Company evaluated the license agreement entered into by Parion as a reconsideration event to determine whether it should continue to consolidate Parion as a variable interest entity into its consolidated financial statements. The Company determined that there was no substantive change in the design of Parion subsequent to Parion's agreement with Shire. Additionally, the Company concluded that at the time it was appropriate to continue to consolidate the financial results of Parion. 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. The Company has no interest in Parion's license agreement with Shire, including the economic benefits and/or obligations derived therefrom.

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As of September 30, 2017, the Company determined that the 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. The Company recorded an impairment charge of \$255.3 million, which represented the entire value of the intangible asset 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 of \$255.3 million, 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 were recorded in the third quarter of 2017 and 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. The loss of \$7.1 million was approximately the difference between (i) the aggregate of \$85.0 million in upfront and milestone payments that the Company has made to Parion to date pursuant to the Parion Agreement and (ii) losses the Company recorded in 2015, 2016, and the first half of 2017 based on increases in the fair value of contingent payments payable by the Company to Parion.

Please refer to Note J, "Intangible Assets and Goodwill," for further information regarding the impairment of Parion's pulmonary ENaC platform.

In connection with the deconsolidation of Parion, the Company evaluated whether the results of Parion should be presented as discontinued operations for the year ending December 31, 2017. The Company concluded that the deconsolidation of Parion based on data from the Phase 2 clinical trial of VX-371 is not a development that significantly impacts the Company's overall operations and financial results or plans to treat patients with CF. Research and development expenses incurred related to this program accounted for a minor portion of the Company's overall annual research and development expenses and the Company remains focused on developing medicines to treat CF. Therefore, the Company has not presented the results related to Parion as discontinued operations in its consolidated statements of operations for the year ending December 31, 2017.

BioAxone Biosciences, Inc.

In October 2014, the Company entered into a license and collaboration agreement (the "BioAxone Agreement") with BioAxone Biosciences, Inc. ("BioAxone"), which resulted in the consolidation of BioAxone as a VIE beginning on October 1, 2014. The Company paid BioAxone initial payments of \$10.0 million in the fourth quarter of 2014.

BioAxone has the potential to receive up to \$90.0 million in milestones and fees, including development and regulatory milestone payments and a license continuation fee. The Company recorded an in-process research and development intangible asset of \$29.0 million for VX-210 and a corresponding deferred tax liability of \$11.3 million attributable to BioAxone. The Company holds an option to purchase BioAxone at a predetermined price. The option expires on the earliest of (a) the day the FDA accepts the Biologics License Application submission for VX-210, (b) the day the Company elects to continue the license instead of exercising the option to purchase BioAxone and (c) March 15, 2018, subject to the Company's option to extend this date by one year.

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Aggregate VIE Financial Information

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

	2017	2016	2015
	(in thousands)		
Loss attributable to noncontrolling interest before (benefit from) provision for income taxes and changes in fair value of contingent payments	\$ 223,379	\$ 10,086	\$ 6,646
(Benefit from) provision for income taxes	(114,090)	16,743	29,731
Decrease (increase) in fair value of contingent payments	62,560	(54,850)	(4,530)
Net loss (income) attributable to noncontrolling interest	\$ 171,849	\$ (28,021)	\$ 31,847

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. The increase in the fair value of the contingent payments for the year ended December 31, 2016 was primarily due to a separate Phase 2 clinical trial of VX-371 achieving its primary safety endpoint in the second quarter of 2016. The increase in the fair value of the contingent payments for the year ended December 31, 2015 was primarily due to changes in market interest rates and the time value of money. During three years ended December 31, 2017, the (increases) decreases in the fair value of the contingent payments related to the Company's VIEs were as follows:

	2017	2016	2015
	(in thousands)		
Parion	\$ 63,460	\$ (64,800)	\$ (3,660)
BioAxone	(900)	9,950	(870)

The fair value of the contingent payments related to the Parion Agreement and the BioAxone Agreement as of the dates set forth in the table were as follows:

	December 31, 2017	December 31, 2016
	(in thousands)	
Parion	\$ —	\$ 238,800
BioAxone	18,900	18,000

The following table summarizes items related to the Company's VIEs included in the Company's consolidated balance sheets as of the dates set forth in the table. Amounts as of December 31, 2017 related to BioAxone while amounts as of December 31, 2016 related to Parion and BioAxone.

	December 31, 2017	December 31, 2016
	(in thousands)	
Restricted cash and cash equivalents (VIE)	\$ 1,489	\$ 47,762
Prepaid expenses and other current assets	22	6,812
Intangible assets	29,000	284,340
Other assets	256	399
Accounts payable	1,021	415
Taxes payable	2,171	1,330
Other current liabilities	—	2,137
Deferred tax liability, net	4,756	131,446
Other liabilities	—	300
Noncontrolling interest	13,727	181,609

The Company has recorded the VIEs' cash and cash equivalents as "Restricted cash and cash equivalents (VIE)" because (i) the Company does not have any interest in or control over the VIEs' cash and cash equivalents and (ii) the Company's

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agreements with each VIE do not provide for the VIEs' cash and cash equivalents to be used for the development of the assets that the Company licensed from the applicable VIE. Assets recorded as a result of consolidating the Company's VIEs' financial condition into the Company's balance sheets do not represent additional assets that could be used to satisfy claims against the Company's general assets.

Other Collaborations

The Company has entered into various agreements pursuant to which it collaborates with third parties, including inlicensing and outlicensing arrangements. Although the Company does not consider any of these arrangements to be material, the most notable of these arrangements are described below.

Moderna Therapeutics, Inc.

In July 2016, the Company entered into a strategic collaboration and licensing agreement (the "Moderna Agreement") with Moderna Therapeutics, Inc. ("Moderna"), pursuant to which the parties are seeking to identify and develop messenger Ribonucleic Acid ("mRNA") therapeutics for the treatment of CF. In connection with the Moderna Agreement, in the third quarter of 2016, the Company made an upfront payment to Moderna of \$20.0 million and a \$20.0 million cost-method investment in Moderna pursuant to a convertible promissory note that converted into preferred stock in August 2016. Moderna has the potential to receive future development and regulatory milestones of up to \$275.0 million, including \$220.0 million in approval and reimbursement milestones, as well as tiered royalty payments on future sales.

Under the terms of the Moderna Agreement, Moderna will lead discovery efforts and the Company will lead all preclinical, development and commercialization activities associated with the advancement of mRNA Therapeutics that result from this collaboration and will fund all expenses related to the collaboration.

The Company may terminate the Moderna Agreement by providing advance notice to Moderna, with the required length of notice dependent on whether any product developed under the Moderna Agreement has received marketing approval. The Moderna Agreement also may be terminated by either party for a material breach by the other, subject to notice and cure provisions. Unless earlier terminated, the Moderna Agreement will continue in effect until the expiration of the Company's payment obligations under the Moderna Agreement.

The Company evaluates the carrying value of its \$20.0 million cost-method investment in Moderna, which is not a publicly traded company, for impairment on a quarterly basis and has not recorded any adjustments to the carrying value of its investment to date.

Janssen Pharmaceuticals, Inc.

In 2014, the Company entered into an agreement (the "Janssen Influenza Agreement") with Janssen Pharmaceuticals, Inc. ("Janssen Inc."). Pursuant to the agreement, Janssen Inc. has an exclusive worldwide license to develop and commercialize certain drug candidates for the treatment of influenza, including JNJ-63623872 (formerly VX-787). The Company received non-refundable payments of \$35.0 million from Janssen Inc. in 2014, which were recorded as collaborative revenues. In the fourth quarter of 2017, the Company recognized \$25.0 million in collaborative revenues due to a milestone that was achieved based on the Phase 3 clinical trial Janssen initiated in the fourth quarter of 2017. The Company has the potential to receive additional regulatory and commercial milestone payments as well as royalties on future product sales, if any.

Janssen Inc. is responsible for costs related to the development and commercialization of the compounds. The Company recorded reimbursement for development activities conducted by the Company on behalf of Janssen of \$2.0 million, \$14.7 million and \$22.8 million in 2017, 2016 and 2015, respectively. The reimbursements are recorded as a reduction to development expense in the Company's consolidated statements of operations primarily due to the fact that Janssen Inc. directs the activities and selects the suppliers associated with these activities. Janssen Inc. may terminate the Janssen Influenza Agreement, subject to certain exceptions, upon six months' notice.

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Asset Acquisition

Concert Pharmaceuticals

In July 2017, the Company acquired certain CF assets including VX-561 (formerly CTP-656) (the “Concert Assets”) from Concert Pharmaceuticals Inc. (“Concert”) pursuant to an asset purchase agreement that was entered into in March 2017 (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, Vertex 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 would receive up to an additional \$90.0 million in milestones based on regulatory approval in the U.S. and reimbursement in the UK, 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 as a research and development expense in 2017. The total cost of the transaction was \$165.1 million including \$5.1 million of transaction costs that were recorded as sales, general and administrative expenses. If the Company achieves regulatory approval and reimbursement milestones, the Company will record the value of the milestone as an intangible asset and will begin amortizing the asset in cost of product revenues in the period that the relevant milestone is achieved.

C. Earnings Per Share

Basic net income (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, restricted stock units and performance-based restricted stock units, or PSUs, that have been issued but are not yet vested. Diluted net income (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.

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The following table sets forth the computation of basic and diluted net income (loss) per share for three years ended December 31, 2017:

	2017	2016	2015
	(in thousands, except per share amounts)		
<i>Basic net income (loss) attributable to Vertex per common share calculation:</i>			
Net income (loss) attributable to Vertex common shareholders	\$ 263,484	\$ (112,052)	\$ (556,334)
Less: Undistributed earnings allocated to participating securities	(293)	—	—
Net income (loss) attributable to Vertex common shareholders—basic	\$ 263,191	\$ (112,052)	\$ (556,334)
Basic weighted-average common shares outstanding	248,858	244,685	241,312
Basic net income (loss) attributable to Vertex per common share	\$ 1.06	\$ (0.46)	\$ (2.31)
<i>Diluted net income (loss) attributable to Vertex per common share calculation:</i>			
Net income (loss) attributable to Vertex common shareholders	\$ 263,484	\$ (112,052)	\$ (556,334)
Less: Undistributed earnings allocated to participating securities	(288)	—	—
Net income (loss) attributable to Vertex common shareholders—diluted	\$ 263,196	\$ (112,052)	\$ (556,334)
Weighted-average shares used to compute basic net income (loss) per common share	248,858	244,685	241,312
Effect of potentially dilutive securities:			
Stock options	2,797	—	—
Restricted stock and restricted stock units (including PSUs)	1,542	—	—
Employee stock purchase plan	28	—	—
Weighted-average shares used to compute diluted net income (loss) per common share	253,225	244,685	241,312
Diluted net income (loss) attributable to Vertex per common share	\$ 1.04	\$ (0.46)	\$ (2.31)

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

	2017	2016	2015
	(in thousands)		
Stock options	3,554	12,642	11,145
Unvested restricted stock and restricted stock units (including PSUs)	411	3,546	3,024

D. 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:

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- 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. As of December 31, 2017, the Company's investments were primarily in money market funds, government-sponsored enterprise securities, corporate equity securities, corporate debt securities and commercial paper. 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, 2017, all of the Company's financial assets and liabilities that were subject to fair value measurements were valued using observable 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 corporate debt securities and commercial paper, which consisted of investments in highly-rated investment-grade corporations and foreign currency forward contracts with highly reputable and creditworthy counterparties. During 2017, 2016 and 2015, the Company did not record an other-than-temporary impairment charge related to its financial assets.

The following table sets forth the Company's financial assets and liabilities (excluding VIE cash and cash equivalents) subject to fair value measurements:

	Fair Value Measurements as of December 31, 2017			
	Total	Fair Value Hierarchy		
		Level 1	Level 2	Level 3
(in thousands)				
Financial instruments carried at fair value (asset position):				
Cash equivalents:				
Money market funds	\$ 614,951	\$ 614,951	\$ —	\$ —
Government-sponsored enterprise securities	12,678	12,678	—	—
Commercial paper	57,357	—	57,357	—
Marketable securities:				
Corporate equity securities	74,821	74,821	—	—
Government-sponsored enterprise securities	2,303	2,303	—	—
Corporate debt securities	265,867	—	265,867	—
Commercial paper	80,263	—	80,263	—
Prepaid and other current assets:				
Foreign currency forward contracts	13	—	13	—
Total financial assets	\$ 1,108,253	\$ 704,753	\$ 403,500	\$ —
Financial instruments carried at fair value (liability position):				
Other liabilities, current portion:				
Foreign currency forward contracts	\$ (13,642)	\$ —	\$ (13,642)	\$ —
Other liabilities, excluding current portion:				
Foreign currency forward contracts	(866)	—	(866)	—
Total financial liabilities	\$ (14,508)	\$ —	\$ (14,508)	\$ —

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	Fair Value Measurements as of December 31, 2016			
	Total	Fair Value Hierarchy		
		Level 1	Level 2	Level 3
	(in thousands)			
Financial instruments carried at fair value (asset position):				
Cash equivalents:				
Money market funds	\$ 280,560	\$ 280,560	\$ —	\$ —
Marketable securities:				
Corporate equity securities	64,560	64,560	—	—
Government-sponsored enterprise securities	15,508	15,508	—	—
Corporate debt securities	111,140	—	111,140	—
Commercial paper	59,404	—	59,404	—
Prepaid and other current assets:				
Foreign currency forward contracts	14,407	—	14,407	—
Other assets:				
Foreign currency forward contracts	1,186	—	1,186	—
Total financial assets	\$ 546,765	\$ 360,628	\$ 186,137	\$ —
Financial instruments carried at fair value (liability position):				
Other liabilities, current portion:				
Foreign currency forward contracts	\$ (144)	\$ —	\$ (144)	\$ —
Total financial liabilities	\$ (144)	\$ —	\$ (144)	\$ —

The Company's VIE invested in cash equivalents consisting of money market funds of \$1.5 million as of December 31, 2017, which are valued based on Level 1 inputs. These cash equivalents are not included in the table above. The Company's noncontrolling interest related to the Company's VIE includes the fair value of the contingent payments, which consist of milestone, royalty and option payments, which are valued based on Level 3 inputs. Please refer to Note B, "Collaborative Arrangements and Acquisitions," for further information.

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Notes to Consolidated Financial Statements (Continued)

E. Marketable Securities

A summary of the Company's cash, cash equivalents and marketable securities is shown below:

	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
(in thousands)				
December 31, 2017				
Cash and cash equivalents:				
Cash and money market funds	\$ 1,595,377	\$ —	\$ —	\$ 1,595,377
Government-sponsored enterprise securities	12,679	—	(1)	12,678
Commercial paper	57,371	—	(14)	57,357
Total cash and cash equivalents	<u>\$ 1,665,427</u>	<u>\$ —</u>	<u>\$ (15)</u>	<u>\$ 1,665,412</u>
Marketable securities:				
Corporate equity securities	\$ 43,213	\$ 31,608	\$ —	\$ 74,821
Government-sponsored enterprise securities	2,304	—	(1)	2,303
Corporate debt securities (matures within 1 year)	215,639	—	(363)	215,276
Corporate debt securities (matures after 1 year through 5 years)	50,697	—	(106)	50,591
Commercial paper (matures within 1 year)	80,372	—	(109)	80,263
Total marketable securities	<u>392,225</u>	<u>31,608</u>	<u>(579)</u>	<u>423,254</u>
Total cash, cash equivalents and marketable securities	<u>\$ 2,057,652</u>	<u>\$ 31,608</u>	<u>\$ (594)</u>	<u>\$ 2,088,666</u>
December 31, 2016				
Cash and cash equivalents:				
Cash and money market funds	\$ 1,183,945	\$ —	\$ —	\$ 1,183,945
Total cash and cash equivalents	<u>\$ 1,183,945</u>	<u>\$ —</u>	<u>\$ —</u>	<u>\$ 1,183,945</u>
Marketable securities:				
Corporate equity securities	\$ 43,213	\$ 21,347	\$ —	\$ 64,560
Government-sponsored enterprise securities (matures within 1 year)	15,506	2	—	15,508
Corporate debt securities (matures within 1 year)	111,225	—	(85)	111,140
Commercial paper (matures within 1 year)	59,331	73	—	59,404
Total marketable securities	<u>229,275</u>	<u>21,422</u>	<u>(85)</u>	<u>250,612</u>
Total cash, cash equivalents and marketable securities	<u>\$ 1,413,220</u>	<u>\$ 21,422</u>	<u>\$ (85)</u>	<u>\$ 1,434,557</u>

The Company has a limited number of marketable securities in insignificant loss positions as of December 31, 2017, which the Company 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. There were no charges recorded for other-than-temporary declines in fair value of marketable securities nor gross realized gains or losses recognized in 2017, 2016 or 2015.

VERTEX PHARMACEUTICALS INCORPORATED
Notes to Consolidated Financial Statements (Continued)

F. 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) on marketable securities, net of tax	Unrealized (losses) gains on foreign currency forward contracts, net of tax	Total
	(in thousands)			
Balance at December 31, 2014	\$ (971)	\$ (123)	\$ 2,011	\$ 917
Other comprehensive (loss) income before reclassifications	(1,109)	249	6,493	5,633
Amounts reclassified from accumulated other comprehensive income (loss)	—	—	(4,726)	(4,726)
Net current period other comprehensive (loss) income	(1,109)	249	1,767	907
Balance at December 31, 2015	<u>\$ (2,080)</u>	<u>\$ 126</u>	<u>\$ 3,778</u>	<u>\$ 1,824</u>
Other comprehensive (loss) income before reclassifications	(5,782)	17,395	17,383	28,996
Amounts reclassified from accumulated other comprehensive income (loss)	—	—	(9,647)	(9,647)
Net current period other comprehensive (loss) income	(5,782)	17,395	7,736	19,349
Balance at December 31, 2016	<u>\$ (7,862)</u>	<u>\$ 17,521</u>	<u>\$ 11,514</u>	<u>\$ 21,173</u>
Other comprehensive (loss) income before reclassifications	(13,169)	6,954	(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)	6,954	(26,530)	(32,745)
Balance at December 31, 2017	<u>\$ (21,031)</u>	<u>\$ 24,475</u>	<u>\$ (15,016)</u>	<u>\$ (11,572)</u>

G. Hedging

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 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 determines 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, 2017, all hedges were determined to be highly effective and the Company had not recorded any ineffectiveness related to the hedging program.

VERTEX PHARMACEUTICALS INCORPORATED
Notes to Consolidated Financial Statements (Continued)

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

	As of December 31,	
	2017	2016
Foreign Currency	(in thousands)	
Euro	\$ 257,230	\$ 164,368
British pound sterling	77,481	65,237
Australian dollar	30,501	23,776
Total foreign currency forward contracts	\$ 365,212	\$ 253,381

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 the Company's consolidated balance sheets:

As of December 31, 2017			
Assets		Liabilities	
Classification	Fair Value	Classification	Fair Value
(in thousands)			
Prepaid and other current assets	\$ 13	Other liabilities, current portion	\$ (13,642)
Other assets	—	Other liabilities, excluding current portion	(866)
Total assets	\$ 13	Total liabilities	\$ (14,508)

As of December 31, 2016			
Assets		Liabilities	
Classification	Fair Value	Classification	Fair Value
(in thousands)			
Prepaid and other current assets	\$ 14,407	Other liabilities, current portion	\$ (144)
Other assets	1,186	Other liabilities, excluding current portion	—
Total assets	\$ 15,593	Total liabilities	\$ (144)

The following table summarizes the potential effect of offsetting derivatives by type of financial instrument on the Company's consolidated balance sheets:

	As of December 31, 2017				
	Gross Amounts Recognized	Gross Amounts Offset	Gross Amount Presented	Gross Amount Not Offset	Legal Offset
Foreign currency forward contracts	(in thousands)				
Total assets	\$ 13	\$ —	\$ 13	\$ (13)	\$ —
Total liabilities	(14,508)	—	(14,508)	13	(14,495)

	As of December 31, 2016				
	Gross Amounts Recognized	Gross Amounts Offset	Gross Amount Presented	Gross Amount Not Offset	Legal Offset
Foreign currency forward contracts	(in thousands)				
Total assets	\$ 15,593	\$ —	\$ 15,593	\$ (144)	\$ 15,449
Total liabilities	(144)	—	(144)	144	—

In 2016, Company began entering into foreign exchange forward contracts with contractual maturities of less than one month designed to mitigate the effect of changes in foreign exchange rates on monetary assets and liabilities including intercompany balances. The Company recognized a loss of \$14.1 million and a gain of \$6.9 million, recorded in other

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Notes to Consolidated Financial Statements (Continued)

income (expense), net, during 2017 and 2016, respectively, related to foreign exchange contracts, which are not designated as hedging instruments under GAAP.

As of December 31, 2017, the notional amount of foreign exchange contracts where hedge accounting under GAAP is not applied was \$122.8 million. The following table summarizes the fair value of the Company's outstanding foreign currency forward contracts not designated for hedge accounting under GAAP included on the Company's consolidated balance sheets:

		As of December 31,	
		2017	2016
		(in thousands)	
Prepaid expenses and other current assets	\$	—	\$ 660
Other liabilities, current portion		684	—

H. Inventories

Inventories consisted of the following:

		As of December 31,	
		2017	2016
		(in thousands)	
Raw materials	\$	20,924	\$ 6,348
Work-in-process		74,237	56,672
Finished goods		16,669	14,584
Total	\$	111,830	\$ 77,604

I. Property and Equipment

Property and equipment, net consisted of the following:

		As of December 31,	
		2017	2016
		(in thousands)	
Buildings	\$	634,061	\$ 548,232
Furniture and equipment		256,509	236,634
Software		151,890	134,321
Leasehold improvements		117,806	108,702
Computers		61,294	58,271
Total property and equipment, gross		1,221,560	1,086,160
Less: accumulated depreciation		(432,123)	(387,798)
Total property and equipment, net	\$	789,437	\$ 698,362

Total property and equipment, gross, as of December 31, 2017 and 2016, included \$100.9 million and \$101.3 million, respectively, for property and equipment recorded under capital leases. Accumulated depreciation, as of December 31, 2017 and 2016, included \$43.4 million and \$37.9 million, respectively, for property and equipment recorded under capital leases.

Total property and equipment, gross, as of December 31, 2017 and 2016, included \$21.1 million and \$17.8 million, respectively, for capitalized internally developed software. Accumulated depreciation, as of December 31, 2017 and 2016, included \$13.0 million and \$9.2 million, respectively, for capitalized internally developed software.

The Company recorded depreciation expense of \$61.4 million, \$60.8 million and \$60.0 million in 2017, 2016 and 2015, respectively.

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Notes to Consolidated Financial Statements (Continued)

J. Intangible Assets and Goodwill

Intangible Assets

As of December 31, 2017 and December 31, 2016, in-process research and development intangible assets of \$29.0 million and \$284.3 million, respectively, were recorded on the Company's consolidated balance sheet. In 2015, the Company recorded an in-process research development intangible asset of \$255.3 million related to Parion's pulmonary ENaC platform, including the intellectual property related to VX-371 and VX-551, that are licensed by Parion to the Company. In 2014, the Company recorded an in-process research and development intangible asset of \$29.0 million related to VX-210 that is licensed by BioAxone to the Company.

In connection with its preparation of its financial statements for September 30, 2017, the Company determined that there were indicators that the value of the pulmonary ENaC platform intangible asset had become impaired. The Company determined that the fair value of the intangible asset had decreased 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 discounted cash flow model pertaining to the impairment of the pulmonary ENaC platform includes (i) assumptions regarding 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. The Company recorded a \$255.3 million impairment charge and a benefit from income taxes of \$97.7 million in 2017 attributable to noncontrolling interest.

Goodwill

As of each of December 31, 2017 and December 31, 2016, goodwill of \$50.4 million was recorded on the Company's consolidated balance sheet.

K. Additional Balance Sheet Detail

Prepaid and other current assets consisted of the following:

	As of December 31,	
	2017	2016
	(in thousands)	
Prepaid expenses	\$ 62,475	\$ 36,134
Collaborative accounts receivable	28,907	719
Other receivables and assets	74,253	34,400
Total	\$ 165,635	\$ 71,253

Accrued expenses consisted of the following:

	As of December 31,	
	2017	2016
	(in thousands)	
Payroll and benefits	\$ 113,026	\$ 86,387
Research, development and commercial contract costs	98,411	62,756
Product revenue allowances	119,919	86,533
Royalty payable	73,044	52,845
Other	39,561	26,728
Total	\$ 443,961	\$ 315,249

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Notes to Consolidated Financial Statements (Continued)

L. Long Term Obligations

Fan Pier Leases

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 (the “Buildings”) at Fan Pier in Boston, Massachusetts (the “Fan Pier Leases”). The Company commenced lease payments in December 2013, and will make lease payments pursuant to the Fan Pier Leases through December 2028. The Company has an option to extend the term of the Fan Pier Leases for an additional 10 years.

Because the Company was involved in the construction project, the Company was deemed for accounting purposes to be the owner of the Buildings during the construction period and recorded project construction costs incurred by the landlord. Upon completion of the Buildings, the Company evaluated the Fan Pier Leases and determined that the Fan Pier Leases did not meet the criteria for “sale-leaseback” treatment. Accordingly, the Company began depreciating the asset and incurring interest expense related to the financing obligation in 2013. The Company bifurcates its lease payments pursuant to the Fan Pier Leases into (i) a portion that is 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 is treated as an operating lease that commenced in 2011. The Company recorded interest expense of \$60.1 million in 2017 and \$60.2 million in each of 2016 and 2015. The Company recorded depreciation expense of \$13.3 million in each of 2017, 2016 and 2015. In each of 2017, 2016 and 2015, the Company recorded rent expense of \$6.5 million.

Property and equipment, net, included \$475.7 million and \$489.0 million as of December 31, 2017 and 2016, respectively, related to construction costs for the Buildings. The carrying value of the construction financing lease obligation related to the Buildings, which excludes interest that will be imputed over the course of the Company’s lease agreement for the Buildings, was \$472.1 million and \$472.6 million, as of December 31, 2017 and 2016, respectively.

San Diego Lease

On December 2, 2015, the Company entered into a lease agreement for 3215 Merryfield Row, San Diego, California with ARE-SD Region No. 23, LLC. Pursuant to this agreement, the Company agreed to lease approximately 170,000 square feet of office and laboratory space in a building under construction in San Diego, California (“San Diego Lease”) for a term of 16 years. The Company expects base rent payments will commence in the second quarter of 2019. Pursuant to the San Diego Lease, during the initial 16-year term, the Company will pay an average of approximately \$10.2 million per year in aggregate rent, exclusive of operating expenses. The Company has the option to extend the lease term for up to two additional five-year terms.

Because the Company is involved in the construction project, the Company is deemed for accounting purposes to be the owner of the San Diego building during the construction period and recorded project construction costs incurred by the landlord. The Company bifurcates its lease payments pursuant to the San Diego Lease into (i) a portion that is allocated to the San Diego building and (ii) a portion that is allocated to the land on which the San Diego building was constructed. Although the Company will not begin making lease payments pursuant to the San Diego Lease until the commencement date, the portion of the lease obligation allocated to the land is treated for accounting purposes as an operating lease that commenced in the fourth quarter of 2016. Upon completion of the San Diego building, the Company will evaluate the San Diego Lease and determine if the San Diego Lease meets the criteria for “sale-leaseback” treatment. If the San Diego Lease meets the “sale-leaseback” criteria, the Company will remove the asset and the related liability from its consolidated balance sheet and treat the San Diego Lease as either an operating or a capital lease based on the Company’s assessment of the accounting guidance. The Company expects that upon completion of construction of the San Diego building the San Diego Lease will not meet the “sale-leaseback” criteria. If the San Diego Lease does not meet “sale-leaseback” criteria, the Company will treat the San Diego Lease as a financing obligation and will depreciate the asset over its estimated useful life.

Property and equipment, net, included \$94.6 million and \$15.0 million as of December 31, 2017 and 2016, respectively, related to construction costs for the San Diego building. The carrying value of the construction financing lease obligation for the San Diego building was \$87.4 million and \$12.6 million as of December 31, 2017 and 2016, respectively.

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Notes to Consolidated Financial Statements (Continued)

Revolving Credit Facility

In October 2016, the Company entered into a Credit Agreement (the "Credit Agreement") with Bank of America, N.A., as administrative agent and the lenders referred to therein. The Credit Agreement provides for a \$500.0 million revolving facility, \$300.0 million of which was drawn at closing (the "Loans") and was repaid in February 2017. The Credit Agreement also provides that, subject to satisfaction of certain conditions, the Company may request that the borrowing capacity under the Credit Agreement be increased by an additional \$300.0 million. The Credit Agreement matures on October 13, 2021.

The proceeds of the borrowing under the Credit Agreement were used primarily to repay the Company's existing indebtedness under the Macquarie Loan. The Loans will bear interest, at the Company's option, at either a base rate or a Eurodollar rate, in each case plus an applicable margin. Under the Credit Agreement, the applicable margins on base rate loans range from 0.75% to 1.50% and the applicable margins on Eurodollar loans range from 1.75% to 2.50%, in each case based on the Company's consolidated leverage ratio (the ratio of the Company's total consolidated debt to the Company's trailing twelve-month EBITDA).

The Loans are guaranteed by certain of the Company's domestic subsidiaries and secured by substantially all of the Company's assets and the assets of the Company's domestic subsidiaries (excluding intellectual property, owned and leased real property and certain other excluded property) and by the equity interests of the Company's subsidiaries, subject to certain exceptions. Under the terms of the Credit Agreement, the Company must maintain, subject to certain limited exceptions, a consolidated leverage ratio of 3.00 to 1.00 and consolidated EBITDA of at least \$200.0 million, in each case to be measured on a quarterly basis.

The Credit Agreement contains customary representations and warranties and usual and customary affirmative and negative covenants. The Credit Agreement also contains customary events of default. In the case of a continuing event of default, the administrative agent would be entitled to exercise various remedies, including the acceleration of amounts due under outstanding loans.

Term Loan

In 2014, the Company entered into a credit agreement with the lenders party thereto, and Macquarie US Trading LLC ("Macquarie"), as administrative agent. The credit agreement provided for a \$300.0 million senior secured term loan ("Macquarie Loan"). On October 13, 2016, the Company terminated and repaid all outstanding obligations under the Macquarie Loan. The Company incurred a charge of \$2.2 million in the fourth quarter of 2016 related to a loss on extinguishment attributable to the Macquarie Loan that was recorded as "Interest expense, net" in the Company's consolidated statements of operations.

The Macquarie Loan initially bore interest at a rate of 7.2% per annum, which was reduced to 6.2% per annum based on the FDA's approval of ORKAMBI and was reduced to a rate of LIBOR plus 5.0% per annum during the third year of the term. The Company incurred \$5.3 million in fees paid to Macquarie that were recorded as a discount on the term loan and that were recorded as additional interest expense using the effective interest method over the term of the loan in the Company's consolidated statements of operations.

M. Common Stock, Preferred Stock and Equity Plans

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, 2017 and 2016, the Company had no shares of preferred stock issued or outstanding.

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Notes to Consolidated Financial Statements (Continued)

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 incentive stock options ("ISOs"), nonstatutory stock options ("NSOs"), restricted stock ("RSs"), restricted stock units ("RSUs") including performance-based RSUs ("PSUs") 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:

Title of Plan	Group Eligible	Type of Award Granted	As of December 31, 2017	
			Awards Outstanding	Additional Awards Authorized for Grant
2013 Stock and Option Plan	Employees, Non-employee Directors and Consultants	NSO, RS, RSU and PSU	10,388,723	11,427,114
2006 Stock and Option Plan	Employees, Non-employee Directors and Consultants	NSO, RS and RSU	3,102,768	—
Total			13,491,491	11,427,114

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, 2017, 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, 2017, the Company's shareholders approved increases in the number of shares authorized for issuance pursuant to the 2013 Stock and Option Plan of (i) 6,750,000 shares in 2017, and (ii) 7,800,000 shares in 2015, plus the number of shares that remained available for issuance under the Company's 2006 Stock and Option Plan, which rolled-over into the 2013 Stock and Option Plan in 2015.

During the three years ended December 31, 2017, 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, 2017, 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, 2017:

	Stock Options (in thousands)	Weighted-average Exercise Price (per share)	Weighted-average Remaining Contractual Life (in years)	Aggregate Intrinsic Value (in thousands)
Outstanding at December 31, 2016	12,642	\$ 81.41		
Granted	2,359	\$ 108.43		
Exercised	(4,561)	\$ 70.90		
Forfeited	(611)	\$ 99.53		
Expired	(62)	\$ 105.24		
Outstanding at December 31, 2017	9,767	\$ 91.57	6.95	\$ 585,293
Exercisable at December 31, 2017	5,313	\$ 80.14	5.75	\$ 375,472

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

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Notes to Consolidated Financial Statements (Continued)

price on the last business day of 2017, which was \$150.71 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 2017, 2016 and 2015 was \$302.8 million, \$48.6 million and \$252.9 million, respectively. The total cash received by the Company as a result of employee stock option exercises during 2017, 2016 and 2015 was \$323.3 million, \$48.5 million and \$165.6 million, respectively.

The following table summarizes information about stock options outstanding and exercisable at December 31, 2017:

Range of Exercise Prices	Options Outstanding			Options Exercisable		
	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)	
\$18.93–\$20.00	128	0.10	\$ 18.93	128	\$ 18.93	
\$20.01–\$40.00	810	1.88	\$ 34.43	810	\$ 34.43	
\$40.01–\$60.00	798	4.49	\$ 49.15	798	\$ 49.15	
\$60.01–\$80.00	746	6.19	\$ 75.49	653	\$ 75.40	
\$80.01–\$100.00	4,350	8.07	\$ 89.31	1,514	\$ 89.51	
\$100.01–\$120.00	1,087	7.11	\$ 109.34	633	\$ 109.24	
\$120.01–\$140.00	1,223	7.63	\$ 130.20	734	\$ 129.89	
\$140.01–\$160.00	—	—	\$ —	—	\$ —	
\$160.01–\$163.74	625	9.54	\$ 162.94	43	\$ 162.94	
Total	9,767	6.95	\$ 91.57	5,313	\$ 80.14	

Restricted Stock and Restricted Stock Units (excluding PSUs)

The following table summarizes the restricted stock and restricted stock unit activity of the Company during the year ended December 31, 2017:

	Restricted Stock		Restricted Stock Units (excluding PSUs)	
	Number of Units	Weighted-average Grant-date Fair Value	Number of Shares	Weighted-average Grant-date Fair Value
	(in thousands)	(per share)	(in thousands)	(per share)
Unvested at December 31, 2016	2,613	\$ 102.54	798	\$ 92.62
Granted	—	\$ —	1,719	\$ 113.13
Vested	(1,206)	\$ 102.99	(278)	\$ 94.72
Cancelled	(178)	\$ 102.45	(228)	\$ 97.86
Unvested at December 31, 2017	1,229	\$ 102.12	2,011	\$ 109.27

The total fair value of restricted stock that vested during 2017, 2016 and 2015 (measured on the date of vesting) was \$157.0 million, \$74.1 million and \$124.0 million, respectively. The total fair value of restricted stock units that vested during 2017, 2016 and 2015 (measured on the date of vesting) was \$33.2 million, \$5.3 million and \$8.0 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 product revenue 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.

VERTEX PHARMACEUTICALS INCORPORATED
Notes to Consolidated Financial Statements (Continued)

The following table summarizes the PSU activity of the Company during the year ended December 31, 2017:

	Performance-Based RSU	
	Number of Units	Weighted-average Grant-date Fair Value
	(in thousands)	(per share)
Unvested at December 31, 2016 (1)	135	\$ 91.05
Granted (2)	392	\$ 86.71
Vested	(15)	\$ 91.05
Cancelled	(28)	\$ 86.52
Unvested at December 31, 2017	484	\$ 87.59

(1) Represents the Company's 2016 PSUs based on the target number of shares issuable at the end of each of the financial and non-financial performance periods.

(2) Represents (i) the target number of shares issuable for the Company's 2017 PSUs at the end of each of the financial and non-financial performance periods and (ii) a decrease in shares issuable under 2016 PSUs based on 2016 financial performance.

The total fair value of PSUs that vested during 2017 (measured on the date of vesting) was \$1.3 million. There were no PSUs that vested during 2016, which was the first year that the Company granted PSUs.

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. As of December 31, 2017, there were 616,256 shares of common stock authorized for issuance pursuant to the ESPP.

In 2017, the following shares were issued to employees under the ESPP:

	Year Ended December 31, 2017	
	(in thousands, except per share amount)	
Number of shares		275
Average price paid per share	\$	80.71

N. 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 expense recognized over the requisite service period is recorded net of the impact for actual awards that were forfeited prior to vesting in the year ended December 31, 2017 in accordance with new accounting guidance that became effective in 2017. Prior to adoption, the expense recognized included an estimate of awards that would be forfeited prior to vesting for the years ended December 31, 2016 and 2015.

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Notes to Consolidated Financial Statements (Continued)

The effect of stock-based compensation expense during the three years ended December 31, 2017 was as follows:

	2017	2016	2015
	(in thousands)		
Stock-based compensation expense by line item:			
Research and development expenses	\$ 181,900	\$ 153,451	\$ 152,955
Sales, general and administrative expenses	108,836	84,254	78,070
Total stock-based compensation expense included in costs and expenses	<u>\$ 290,736</u>	<u>\$ 237,705</u>	<u>\$ 231,025</u>

The stock-based compensation expense by type of award during the three years ended December 31, 2017 was as follows:

	2017	2016	2015
	(in thousands)		
Stock-based compensation expense by type of award:			
Stock options	\$ 105,367	\$ 114,768	\$ 129,276
Restricted stock and restricted stock units (including PSUs)	181,258	118,709	98,811
ESPP share issuances	9,017	7,835	7,025
Less: stock-based compensation expense capitalized to inventories	(4,906)	(3,607)	(4,087)
Total stock-based compensation expense included in costs and expenses	<u>\$ 290,736</u>	<u>\$ 237,705</u>	<u>\$ 231,025</u>

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, 2017, by type of award and the weighted-average period over which that expense is expected to be recognized:

Type of award:	As of December 31, 2017	
	Unrecognized Expense	Weighted-average Recognition Period
	(in thousands)	(in years)
Stock options	\$ 147,402	2.45
Restricted stock and restricted stock units (including PSUs)	\$ 254,302	2.47
ESPP share issuances	\$ 4,245	0.59

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 2017, 2016 and 2015 had a weighted-average grant-date fair value per share of \$43.27, \$37.93 and \$52.16, respectively.

The fair value of each option granted during 2017, 2016 and 2015 was estimated on the date of grant using the Black-Scholes option pricing model with the following weighted-average assumptions:

	2017	2016	2015
Expected stock price volatility	45.31%	46.77%	47.29%
Risk-free interest rate	1.94%	1.32%	1.61%
Expected term of options (in years)	4.68	4.91	5.28
Expected annual dividends	—	—	—

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Notes to Consolidated Financial Statements (Continued)

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

In February 2016, the Company began granting PSUs to certain members of senior management. Half of the PSUs contained financial goals as the performance metric and the other half contained non-financial goals. A target number of shares was established for each award, however the actual number of shares that will be 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.

In addition, in 2015 and 2014, the Company issued, pursuant to a retention program, restricted stock awards to certain members of senior management that vested on various dates in the fourth quarter of 2017 and in January 2018 upon the satisfaction of both (i) a performance condition and (ii) a service condition.

Employee Stock Purchase Plan

The weighted-average fair value of each purchase right granted during 2017, 2016 and 2015 was \$35.90, \$26.86 and \$37.84, respectively. The following table reflects the weighted-average assumptions used in the Black-Scholes option pricing model for 2017, 2016 and 2015:

	2017	2016	2015
Expected stock price volatility	39.09%	48.22%	47.20%
Risk-free interest rate	1.24%	0.56%	0.40%
Expected term (in years)	0.75	0.75	0.72
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

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Notes to Consolidated Financial Statements (Continued)

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.

O. Other Arrangements

Sale of HIV Protease Inhibitor Royalty Stream

In 2008, the Company sold to a third party its rights to receive royalty payments from GlaxoSmithKline plc, net of royalty amounts to be earned by and due to a third party, for a one-time cash payment of \$160.0 million. These royalty payments relate to net sales of HIV protease inhibitors, which had been developed pursuant to a collaboration agreement between the Company and GlaxoSmithKline plc. The Company has been recognizing the payment received over the expected life of the collaboration agreement with GlaxoSmithKline plc based on the units-of-revenue method. As of December 31, 2017, the Company had \$6.9 million in deferred revenues related to the one-time cash payment. In the first quarter of 2018, the Company will record a cumulative effect adjustment to its accumulated deficit equal to the amount the Company deferred as of December 31, 2017, net of deferred costs, as there are no material performance obligations remaining related to the Company's sales of HIV protease inhibitors. This adjustment will be pursuant to the new guidance applicable to revenue recognition that became effective January 1, 2018 that is described in Note A, "Nature of Business and Accounting Policies."

P. Income Taxes

The components of loss before provision for (benefit from) income taxes during the three years ended December 31, 2017 consisted of the following:

	2017	2016	2015
	(in thousands)		
United States	\$ 330,340	\$ (147,860)	\$ (272,326)
Foreign	(346,029)	80,494	(285,474)
Loss before (benefit from) provision for income taxes	<u>\$ (15,689)</u>	<u>\$ (67,366)</u>	<u>\$ (557,800)</u>

The components of the provision for (benefit from) income taxes during the three years ended December 31, 2017 consisted of the following:

	2017	2016	2015
	(in thousands)		
Current taxes:			
United States	\$ 11,559	\$ (3,821)	\$ 25,623
Foreign	3,576	1,794	831
State	5,025	1,836	3,629
Total current taxes	<u>\$ 20,160</u>	<u>\$ (191)</u>	<u>\$ 30,083</u>
Deferred taxes:			
United States	\$ (113,805)	\$ 18,659	\$ 497
Foreign	(3,222)	(3,359)	(355)
State	(10,457)	1,556	156
Total deferred taxes	<u>\$ (127,484)</u>	<u>\$ 16,856</u>	<u>\$ 298</u>
(Benefit from) provision for income taxes	<u>\$ (107,324)</u>	<u>\$ 16,665</u>	<u>\$ 30,381</u>

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Notes to Consolidated Financial Statements (Continued)

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

	2017	2016	2015
	(in thousands)		
Loss before (benefit from) provision for income taxes	\$ (15,689)	\$ (67,366)	\$ (557,800)
Expected benefit from income taxes	(5,491)	(23,578)	(195,230)
State taxes, net of federal benefit	4,742	3,621	3,800
Foreign income tax rate differential	77,801	21,346	47,402
Tax credits	(49,088)	(47,773)	(55,696)
Provision for (benefit from) income taxes attributable to valuation allowances	(584,917)	14,837	226,169
Permanent items	21,825	24,749	5,817
Rate change	575,192	12,836	(1,224)
Stock compensation (benefit) shortfalls and cancellations	(21,453)	4,162	951
Tax attribute expiration	—	9,947	—
Deconsolidation of VIE	(126,183)	—	—
Other	248	(3,482)	(1,608)
(Benefit from) provision for income taxes	<u>\$ (107,324)</u>	<u>\$ 16,665</u>	<u>\$ 30,381</u>

The Company operates in many foreign tax jurisdictions, which impose income taxes at different rates than the U.S. The impact of these rate differences, which is primarily related to the Company's operations in the U.K., is included in the "Foreign income tax rate differential" in the Company's tax rate reconciliation above, which reconciles the U.S. federal statutory tax rate to the Company's effective tax rate. In 2017, the effect of "Permanent items" was related to equity compensation, Research and Development Credits, Orphan Drug Credits, and foreign amortization.

The change in the "Provision for (benefit from) income taxes attributable to valuation allowances" on deferred tax assets in the tax rate reconciliation table above is primarily related to the U.S., U.K. and Canada. In 2017, the valuation allowance decreased by \$178.2 million primarily due to the utilization of net operating losses ("NOLs") in the U.S. and a decrease in the U.S. corporate tax rate from 35% to 21% partially offset by the adoption of ASU 2016-09. In 2016, the valuation allowance increased by \$14.8 million primarily due to an increase in tax credits in the U.S. and an increase in the net operating loss in the U.K., both due to the uncertainty in the Company's ability to use them in future periods. In 2015, the valuation allowance increased by \$306.4 million primarily related to an increase in net operating losses that were incurred with no corresponding benefit due to the uncertainty in the Company's ability to use them in future periods.

On December 22, 2017, H.R.1., known as the Tax Cuts and Jobs Act, was signed into law. The new law did not have a significant impact on the Company's consolidated financial statements for the year ended December 31, 2017 because it maintains a valuation allowance on the majority of its net operating losses and other deferred tax assets. However, the reduction of the U.S. federal corporate tax rate from 35% to 21% resulted in increases to the amounts reflected in "Provision for (benefit from) income taxes attributable to valuation allowances" and "Rate change" in the Company's tax reconciliation table above for the year ended December 31, 2017 compared to the years ended December 31, 2016 and 2015. The change in the U.S. federal corporate tax rate, which is effective January 1, 2018, is also reflected in the Company's deferred tax table below. Lastly, the Company has discussed Staff Accounting Bulletin No. 118's ("SAB 118") possible impact on the Company's consolidated financial statements below.

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Notes to Consolidated Financial Statements (Continued)

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,	
	2017	2016
	(in thousands)	
Deferred tax assets:		
Net operating loss	\$ 1,004,404	\$ 1,232,399
Tax credit carryforwards	440,429	367,402
Intangible assets	54,091	34,938
Deferred revenues	19,593	31,205
Stock-based compensation	83,196	110,446
Inventories	4,250	4,705
Accrued expenses	17,808	23,078
Construction financing lease obligation	109,354	177,735
Other	1,417	27
Gross deferred tax assets	1,734,542	1,981,935
Valuation allowance	(1,552,942)	(1,731,186)
Total deferred tax assets	181,600	250,749
Deferred tax liabilities:		
Property and equipment	(101,019)	(169,089)
Acquired intangibles	(6,341)	(134,063)
Deferred revenue	(73,357)	(73,357)
Unrealized gain	(6,401)	(7,967)
Net deferred tax liabilities	\$ (5,518)	\$ (133,727)

The Company presents its deferred tax assets and deferred tax liabilities gross on its consolidated balance sheets. As of December 31, 2017, \$4.8 million of the deferred tax liabilities were attributable to the Company's collaboration with BioAxone. As of December 31, 2016, \$131.4 million of the deferred tax liabilities were attributable to the Company's collaborations with BioAxone and Parion. Please refer to Note B, "Collaborative Arrangements and Acquisitions," and Note J, "Intangible Assets and Goodwill," for further information regarding the decrease in the deferred tax liability in 2017, which was primarily related to the Company's collaboration with Parion.

For U.S. federal income tax purposes, as of December 31, 2017, the Company had net operating loss carryforwards of approximately \$3.6 billion and tax credits of \$312.5 million, which may be used to offset future federal income and tax liability, respectively. For U.S. state income tax purposes, as of December 31, 2017, the Company had net operating loss carryforwards of approximately \$880.7 million and tax credits of \$115.7 million, which may be used to offset future state income and tax liability, respectively. These U.S. federal and state net operating loss carryforwards and tax credits expire at various dates through 2037.

The Company maintains a valuation allowance on the majority of its net operating losses and other deferred tax assets. Accordingly, the Company has not reported any benefits from income taxes relating to the remaining NOLs and income tax credit carryforwards that will be utilized in future periods in these jurisdictions. 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 2017, the Company reassessed the valuation allowance and considered negative evidence, including its cumulative losses over the three years ended December 31, 2017, and positive evidence, including its income during the year ended December 31, 2017. After assessing both the negative evidence and the positive evidence, the Company concluded that it should continue to maintain the valuation allowance on its net operating losses and the majority of its other deferred tax assets as of December 31, 2017. Based on the Company's recent financial performance and its future projections, it could record a reversal of all, or a portion of the valuation allowance associated with U.S. deferred tax assets in future periods. However, any such change is subject to actual performance and other considerations that may present positive

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Notes to Consolidated Financial Statements (Continued)

or negative evidence at the time of the assessment. The Company's total deferred tax asset balance subject to the valuation allowance was approximately \$1.6 billion at December 31, 2017.

Unrecognized tax benefits during the three years ended December 31, 2017 were not material to the Company's consolidated financial statements. 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. The total amount of unrecognized tax benefits, that is the aggregate tax effect of differences between tax return positions and the benefits recognized in the financial statements, as of December 31, 2017, 2016 and 2015 were \$3.8 million, zero and \$0.4 million, respectively. The Company recognizes interest and penalties related to income taxes as a component of provision for (benefit from) income taxes. As of December 31, 2017, no interest and penalties have been accrued.

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 U.S. or any other major taxing jurisdiction for years before 2011, except where the Company has net operating losses or tax credit carryforwards that originate before 2011. The Company currently is under examination in Canada for 2011 through 2013, Germany for 2012 through 2015 and Italy for 2015 and 2016. No adjustments have been reported. The Company is not under examination by any other jurisdictions for any tax year. The Company concluded audits with Internal Revenue Service, Delaware, Pennsylvania, Texas and Revenue Quebec during 2016, and Massachusetts and New York during 2015, with no material adjustments.

On December 22, 2017, the SEC staff issued SAB 118 to address the application of GAAP in situations when a registrant does not have the necessary information available, prepared, or analyzed (including computations) in reasonable detail to complete the accounting for certain income tax effects of H.R.1. The Company has recognized the provisional tax impacts related to deemed repatriated earnings and the revaluation of deferred tax assets and liabilities and included these amounts in its consolidated financial statements for the year ended December 31, 2017. The Company has an accumulated deficit from its foreign operations and does not have an associated liability from the repatriation tax on accumulated earnings in H.R.1. The ultimate impact may differ from these provisional amounts, possibly materially, due to, among other things, additional analysis, changes in interpretations and assumptions the Company has made, additional regulatory guidance that may be issued, and actions the Company may take as a result of H.R.1. The Company's accounting treatment is expected to be complete when the 2017 U.S. corporate income tax return is filed in 2018. As of December 31, 2017, foreign earnings, which were not significant, have been retained indefinitely by the Company's foreign subsidiaries for 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.

Q. Restructuring Expenses

The Company has adopted several plans to restructure its facilities and operations for which it has incurred restructuring expenses in the three years ended December 31, 2017. The most significant restructuring event during the three years ended December 31, 2017 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. As of December 31, 2017, the restructuring liability associated with this restructuring event relates to the lease for the research site in Canada that terminates in October 2018. The Company does not anticipate any significant additional charges related to this restructuring event in the future. The restructuring charge and other activities related to this restructuring event recorded during the year ended December 31, 2017 were as follows:

		2017
		(in thousands)
Liability, beginning of the period	\$	—
Restructuring expense		12,503
Cash payments		(8,602)
Asset impairments and other non-cash items		(1,812)
Liability, end of the period	\$	2,089

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Notes to Consolidated Financial Statements (Continued)

R. 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. Beginning in mid-2013, the Company began paying matching contributions in the form of cash. For the years ended December 31, 2017, 2016 and 2015, the Company contributed approximately \$12.3 million, \$11.8 million and \$12.8 million to the plan, respectively. As of December 31, 2017, 754,744 shares of common stock remained available for grant under the Vertex 401(k) Plan.

S. Commitments and Contingencies

Lease Obligations

The Company moved into its corporate headquarters to Boston, Massachusetts in January 2014. In December 2015, the Company entered into a lease agreement for 3215 Merryfield Row, San Diego, California. Please refer to Note L, "Long Term Obligations," for additional information regarding both of these commitments.

As of December 31, 2017, future minimum commitments under the facility leases with initial terms of more than one year were as follows:

Year	Fan Pier Leases	San Diego Leases	Other Leases	Total Lease Commitments
(in thousands)				
2018	\$ 61,606	\$ 2,979	\$ 19,866	\$ 84,451
2019	72,589	5,324	15,002	92,915
2020	72,589	9,127	13,956	95,672
2021	72,589	9,127	12,163	93,879
2022	72,589	9,127	11,542	93,258
Thereafter	462,442	129,394	57,949	649,785
Total minimum lease payments	<u>\$ 814,404</u>	<u>\$ 165,078</u>	<u>\$ 130,478</u>	<u>\$ 1,109,960</u>

As of December 31, 2017, the Company's total sublease income to be received related to its facility leases was \$6.0 million, all of which relates to subleases expiring in 2018.

During 2017, 2016 and 2015, rental expense was \$19.2 million, \$19.1 million and \$18.1 million, respectively. The majority of the Company's lease payments related to the Fan Pier Leases are recorded as interest expense because the Company is deemed for accounting purposes to be the owner of the Buildings. Please refer to Note L, "Long Term Obligations," for further information.

The Company has outstanding leases, which are accounted for as capital leases, for equipment and leasehold improvements. The capital leases bear interest at rates ranging from less than 1% to 9% per year. The following table sets forth the Company's future minimum payments due under capital leases as of December 31, 2017:

Year	(in thousands)
2018	\$ 24,004
2019	10,252
2020	5,434
2021	3,676
2022	1,706
Thereafter	387
Total payments	45,459
Less: amount representing interest	(2,432)
Present value of payments	<u>\$ 43,027</u>

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Notes to Consolidated Financial Statements (Continued)

In addition, the Company has committed to make potential future milestone and royalty payments pursuant to certain collaboration agreements. Payments generally become due and payable upon the achievement of certain developmental, regulatory and/or commercial milestones. Please refer to Note B, "Collaborative Arrangements and Acquisitions," for further information.

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, 2017 or 2016.

T. 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.

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Notes to Consolidated Financial Statements (Continued)

Revenues by Product

Product revenues, net consisted of the following:

	2017	2016	2015
	(in thousands)		
ORKAMBI	\$ 1,320,850	\$ 979,590	\$ 350,663
KALYDECO	844,630	703,432	631,674
INCIVEK	—	610	17,987
Total product revenues, net	<u>\$ 2,165,480</u>	<u>\$ 1,683,632</u>	<u>\$ 1,000,324</u>

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:

	2017	2016	2015
	(in thousands)		
United States	\$ 1,986,786	\$ 1,321,807	\$ 763,316
Outside of the United States			
Europe	420,317	320,456	219,596
Other	81,549	59,914	49,424
Total revenues outside of the United States	<u>501,866</u>	<u>380,370</u>	<u>269,020</u>
Total revenues	<u>\$ 2,488,652</u>	<u>\$ 1,702,177</u>	<u>\$ 1,032,336</u>

In 2017, 2016 and 2015, revenues attributable to the U.K. were the largest contributor to the Company's European revenues.

Significant Customers

Gross revenues and accounts receivable from each of the Company's customers who individually accounted for 10% 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,		
	2017	2016	2015	2017	2016	2015
Walgreen Co.	17%	19%	20%	20%	15%	15%
Accredo/Curascript	14%	15%	15%	12%	10%	10%
CVS/Caremark	<10%	19%	17%	n/a	17%	17%

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Notes to Consolidated Financial Statements (Continued)

Property and Equipment, Net by Location

Property and equipment, net by location consisted of the following:

	As of December 31,	
	2017	2016
(in thousands)		
United States	\$ 753,128	\$ 665,552
Outside of the United States		
United Kingdom	31,279	26,921
Other	5,030	5,889
Total property and equipment, net outside of the United States	36,309	32,810
Total property and equipment, net	\$ 789,437	\$ 698,362

U. Quarterly Financial Data (unaudited)

The following table sets forth the Company's quarterly financial data for the two years ended December 31, 2017.

	Three Months Ended			
	March 31, 2017	June 30, 2017	September 30, 2017	December 31, 2017
(in thousands, except per share amounts)				
Revenues:				
Product revenues, net	\$ 480,622	\$ 513,988	\$ 549,642	\$ 621,228
Royalty revenues	1,551	2,861	2,231	1,345
Collaborative revenues (1)	232,545	27,286	26,292	29,061
Total revenues	714,718	544,135	578,165	651,634
Costs and expenses:				
Cost of product revenues	46,242	70,535	72,186	83,712
Royalty expenses	746	670	688	340
Research and development expenses (2)	273,563	289,451	454,947	306,664
Sales, general and administrative expenses	113,326	127,249	120,710	134,794
Restructuring expenses	9,999	3,523	337	387
Intangible asset impairment charge (3)	—	—	255,340	—
Total costs and expenses	443,876	491,428	904,208	525,897
Income (loss) from operations	270,842	52,707	(326,043)	125,737
Interest expense, net	(16,765)	(14,664)	(13,574)	(12,547)
Other expense, net (3)	(544)	(2,537)	(77,553)	(748)
Income (loss) before provision for (benefit from) income taxes	253,533	35,506	(417,170)	112,442
Provision for (benefit from) income taxes (3)	3,985	4,337	(125,903)	10,257
Net income (loss)	249,548	31,169	(291,267)	102,185
(Income) loss attributable to noncontrolling interest (3)	(1,792)	(13,173)	188,315	(1,501)
Net income (loss) attributable to Vertex	\$ 247,756	\$ 17,996	\$ (102,952)	\$ 100,684
Amounts per share attributable to Vertex common shareholders:				
Net income (loss):				
Basic	\$ 1.01	\$ 0.07	\$ (0.41)	\$ 0.40
Diluted	\$ 0.99	\$ 0.07	\$ (0.41)	\$ 0.39
Shares used in per share calculations:				
Basic	246,024	247,521	250,268	251,557
Diluted	248,700	251,635	250,268	256,804

VERTEX PHARMACEUTICALS INCORPORATED

Notes to Consolidated Financial Statements (Continued)

	Three Months Ended			
	March 31, 2016	June 30, 2016	September 30, 2016	December 31, 2016
(in thousands, except per share amounts)				
Revenues:				
Product revenues, net	\$ 394,410	\$ 425,651	\$ 409,689	\$ 453,882
Royalty revenues	3,596	5,282	3,835	3,887
Collaborative revenues	74	675	259	937
Total revenues	398,080	431,608	413,783	458,706
Costs and expenses:				
Cost of product revenues	49,789	44,154	53,222	59,646
Royalty expenses	860	1,098	855	836
Research and development expenses (4)	255,860	271,008	272,370	248,452
Sales, general and administrative expenses	105,214	111,652	106,055	109,908
Restructuring expenses	687	343	8	224
Total costs and expenses	412,410	428,255	432,510	419,066
(Loss) income from operations	(14,330)	3,353	(18,727)	39,640
Interest expense, net	(20,698)	(20,155)	(20,140)	(20,439)
Other income (expense), net	4,411	(1,219)	(167)	1,105
(Loss) income before provision for (benefit from) income taxes	(30,617)	(18,021)	(39,034)	20,306
Provision for (benefit from) income taxes	5,485	18,130	503	(7,453)
Net (loss) income	(36,102)	(36,151)	(39,537)	27,759
(Income) loss attributable to noncontrolling interest	(5,529)	(28,374)	696	5,186
Net (loss) income attributable to Vertex	\$ (41,631)	\$ (64,525)	\$ (38,841)	\$ 32,945
Amounts per share attributable to Vertex common shareholders:				
Net (loss) income:				
Basic	\$ (0.17)	\$ (0.26)	\$ (0.16)	\$ 0.13
Diluted	\$ (0.17)	\$ (0.26)	\$ (0.16)	\$ 0.13
Shares used in per share calculations:				
Basic	243,831	244,482	244,920	245,454
Diluted	243,831	244,482	244,920	247,757

- In the first quarter of 2017, the Company recognized \$230.0 million of collaborative revenues related to an upfront payment from Merck KGaA pursuant to the Company's collaboration with Merck KGaA. In each of the second and third quarters of 2017, the Company recognized \$20.0 million of collaborative revenues related to payments that Parion, which was a variable interest entity during these periods, received from Shire pursuant to a license agreement. In the fourth quarter of 2017, the Company recognized \$25.0 million of collaborative revenues related to a milestone achieved pursuant to its license agreement with Janssen Inc. pursuant to which Janssen is developing JNJ-63623872 for the treatment of influenza. See Note B, "Collaborative Arrangements and Acquisitions," for further information.
- In the third quarter of 2017, the Company incurred research and development expenses of approximately \$160.0 million to acquire certain CF assets including VX-561 from Concert. See Note B, "Collaborative Arrangements and Acquisitions," for further information.
- In the third quarter of 2017, the Company recorded a \$255.3 million intangible asset impairment charge related to Parion's pulmonary ENaC platform indefinite-lived in-process research and development asset, a decrease in the fair value of the contingent payments payable by the Company to Parion of \$69.6 million and benefit from income taxes of \$126.2 million resulting from these charges. These charges and benefit from income taxes were attributable to noncontrolling interest. See Note B, "Collaborative Arrangements and Acquisitions," and Note J, "Intangible Assets and Goodwill," for further information.
- In the second quarter of 2016, the Company incurred research and development expenses of approximately \$10.0 million to acquire certain early-stage research assets. In the third quarter of 2016, the Company incurred research and development expenses related to a \$20.0 million upfront payment to Moderna Therapeutics, Inc. See Note B, "Collaborative Arrangements and Acquisitions," for further information.

VERTEX PHARMACEUTICALS INCORPORATED

THE COMPANY WILL FURNISH TO THE HOLDER UPON REQUEST WITHOUT CHARGE THE DESIGNATIONS, PREFERENCES AND RELATIVE, PARTICIPATING, OPTIONAL OR OTHER SPECIAL RIGHTS OF EACH CLASS OF STOCK OR SERIES THEREOF AND THE QUALIFICATIONS, LIMITATIONS OR RESTRICTIONS OF SUCH PREFERENCES AND/OR RIGHTS.

The following abbreviations, when used in the inscription on the face of this certificate, shall be construed as though they were written out in full according to applicable laws or regulations:

TEN COM - as tenants in common	UNIF GIFT MIN ACT -Custodian..... <small>(Cust)</small> <small>(Minor)</small>
TEN ENT - as tenants by the entireties	under Uniform Gifts to Minors Act..... <small>(State)</small>
JT TEN - as joint tenants with right of survivorship and not as tenants in common	UNIF TRF MIN ACT -Custodian (until age) <small>(Cust)</small> <small>(Minor)</small> <small>(State)</small>
under Uniform Transfers to Minors Act..... <small>(Minor)</small> <small>(State)</small>

Additional abbreviations may also be used though not in the above list.

For value received, _____ hereby sell, assign and transfer unto _____

(PLEASE PRINT OR TYPEWRITE NAME AND ADDRESS, INCLUDING POSTAL ZIP CODE, OF ASSIGNEE)

_____ Shares
of the common stock represented by the within Certificate, and do hereby irrevocably constitute and appoint _____ Attorney
to transfer the said stock on the books of the within-named Company with full power of substitution in the premises.

Dated: _____ 20 _____

Signature: _____

Signature: _____

Notice: The signature to this assignment must correspond with the name as written upon the face of the certificate, in every particular, without alteration or enlargement, or any change whatever.

Signature(s) Guaranteed- Medallion Guarantee Stamp
THE SIGNATURE(S) SHOULD BE GUARANTEED BY AN ELIGIBLE GUARANTOR INSTITUTION (Banks, Stockbrokers, Savings and Loan Associations and Credit Unions) WITH MEMBERSHIP IN AN APPROVED SIGNATURE GUARANTEE MEDALLION PROGRAM, PURSUANT TO S.E.C. RULE 17A-15.

SECURITY INSTRUCTIONS
THIS IS WATERMARKED PAPER. DO NOT ACCEPT WITHOUT NOTING WATERMARK. HOLD TO LIGHT TO VERIFY WATERMARK.



The IRS requires that the named transfer agent ("we") report the cost basis of certain shares or units acquired after January 1, 2011. If your shares or units are covered by the legislation, and you requested to sell or transfer the shares or units using a specific cost basis calculation method, then we have processed as you requested. If you did not specify a cost basis calculation method, then we have defaulted to the first in, first out (FIFO) method. Please consult your tax advisor if you need additional information about cost basis.
If you do not keep in contact with the issuer or do not have any activity in your account for the time period specified by state law, your property may become subject to state unclaimed property laws and transferred to the appropriate state.

1534291

Confidential Materials omitted and filed separately with the Securities and Exchange Commission. Triple asterisks denote omissions.

**AMENDMENT NO. 1
TO THE
STRATEGIC COLLABORATION, OPTION AND LICENSE AGREEMENT**

This Amendment No. 1 to the Strategic Collaboration, Option and License Agreement, dated October 26, 2015, between Vertex Pharmaceuticals Incorporated (“**Vertex Parent**”) and Vertex Pharmaceuticals (Europe) Limited (“**Vertex UK**” and together with Vertex Parent, “**Vertex**”), on the one hand, and CRISPR Therapeutics AG (“**CRISPR AG**”), CRISPR Therapeutics, Inc. (“**CRISPR Inc.**”), CRISPR Therapeutics Limited (“**CRISPR UK**”) and TRACR Hematology Ltd (“**Tracr**” and together with CRISPR AG, CRISPR Inc. and CRISPR UK “**CRISPR**”), on the other hand (this “**Amendment**”) is entered into as of this 12th day of December, 2017 (the “**Amendment Effective Date**”) by and between Vertex and CRISPR. Capitalized terms used and not defined herein have their respective meanings set forth in the Agreement (as defined below).

RECITALS

WHEREAS, Vertex and CRISPR entered into that certain Strategic Collaboration, Option and License Agreement, dated October 26, 2015 (the “**Agreement**”);

WHEREAS, pursuant to Section 6.1.2(c) of the Agreement, Vertex and CRISPR are entering into a Joint Development and Commercialization Agreement (the “**JDCA**”) with respect to certain Shared Products; and

WHEREAS, in connection with the execution of the JDCA, Vertex and CRISPR now wish to amend and update certain portions of the Agreement as set forth herein;

NOW, THEREFORE, in consideration of the respective covenants, representations, warranties and agreements set forth herein, the Parties hereto agree as follows:

**ARTICLE 1
AMENDMENTS**

1.1 Amendment to Section 1.27. Section 1.27 of the Agreement is hereby deleted in its entirety and replaced with the following:

“1.27. “**Collaboration Target**” means a Vertex Target that Vertex has selected as the subject of a Research Plan in accordance with Section 2.3.3. For clarity, if Vertex exercises an Option with respect to any such Vertex Target, such Vertex Target shall continue to constitute a “Collaboration Target” under this Agreement during the Agreement Term.”

1.2 Amendment to Section 1.117. The final sentence of the third paragraph of Section 1.117 of the Agreement is hereby deleted in its entirety and replaced with the following: “For clarity, [***].”

1.3 Amendment to Section 2.13.2. The final sentence of Section 2.13.2 of the Agreement is hereby deleted in its entirety and replaced with the following: “For the avoidance of doubt, each Party’s obligations under this Section 2.13.2 will terminate (a) with respect to a [***] and (b) with respect to a [***].”

1.4 Amendment to Section 3.1.2 . Clause (h) of Section 3.1.2 of the Agreement is hereby deleted in its entirety and replaced with the following:

(h) perform such other duties as are specifically assigned to the JRC under this Agreement or any Joint Development & Commercialization Agreement.

1.5 Amendment to Section 4.1.1 .

(a) The first sentence of Section 4.1.1 of the Agreement is hereby deleted in its entirety and replaced with the following: “CRISPR hereby grants to Vertex and its Affiliates an exclusive option to obtain the Exclusive License with respect a maximum of six Collaboration Targets (each, an “ **Option** ,” and such six Collaboration Target maximum, the “ **Option Cap** ”), [***].”

(b) The second sentence of Section 4.1.1 of the Agreement is hereby deleted in its entirety and replaced with the following: “On a Collaboration Program-by-Collaboration Program basis, at any time starting on the Effective Date, but no later than [***] days after Vertex’s receipt of an Option Exercise Data Package for the applicable Collaboration Program (the “ **Option Deadline** ”), Vertex will notify CRISPR as to whether or not Vertex is exercising the Option for such Collaboration Program; *provided* , that if, following receipt of the applicable Option Exercise Data Package, Vertex delivers a Continuation Notice to the JRC, the Option Deadline will be extended until the date that is [***] days after Vertex’s receipt of a revised Option Exercise Data Package reflecting the results of the Continuation Research as provided in Section 2.6.”

1.6 Amendment to Section 7.2 . Section 7.2 of the Agreement is hereby deleted in its entirety and replaced with the following:

“7.2. **Reserved** .”

1.7 Amendment to Section 11.1 . Section 11.1 of the Agreement is hereby deleted in its entirety and replaced with the following:

“11.1. **Agreement Term; Expiration** . This Agreement is effective as of the Effective Date and, unless earlier terminated pursuant to the other provisions of this ARTICLE 11, will continue in full force and effect until this Agreement expires as follows:

- 11.1.1. on a country-by-country and Product-by-Product basis, on the date of expiration of (a) all payment obligations under this Agreement or any Joint Development & Commercialization Agreement and (b) any payment obligations of either Party with respect to Opt-Out Royalties (as defined in the applicable Joint Development & Commercialization Agreement), in each case ((a) and (b)), with respect to such Product in such country;
- 11.1.2. in its entirety upon the expiration of (a) all payment obligations under this Agreement or any Joint Development & Commercialization Agreement and (b) any payment obligations of either Party with respect to Opt-Out Royalties (as defined in the applicable Joint Development & Commercialization Agreement), in each case ((a) and (b)), with respect to all Products in all countries pursuant to Section 11.1.1; and
- 11.1.3. in its entirety upon expiration of all Options if Vertex has not exercised any Option as provided in Section 4.1.1.”

1.8 Amendment to Section 13.5 . Section 13.5 of the Agreement is hereby deleted in its entirety and replaced with the following:

“13.5. **Notices** . All notices which are required or permitted hereunder will be in writing and sufficient if delivered personally, sent by nationally-recognized overnight courier or sent by electronic mail, confirmation of receipt requested, addressed as follows:

If to Vertex:

Vertex Pharmaceuticals Incorporated
Attn: Business Development
50 Northern Avenue
Boston, Massachusetts 02110
E-mail: phil_tinmouth@vrtx.com

with a copy to:

Vertex Pharmaceuticals Incorporated
Attn: Corporate Legal
50 Northern Avenue
Boston, Massachusetts 02110
E-mail: paige_goodwin@vrtx.com

and:

Ropes & Gray LLP
Attn: Marc A. Rubenstein
Prudential Tower
800 Boylston Street
Boston, Massachusetts 02199-3600
E-mail: marc.rubenstein@ropesgray.com

If to CRISPR:

CRISPR Therapeutics AG
Attn: Chief Executive Officer
Baarerstrasse 14
6300 Zug
Switzerland
E-mail: samarth.kulkarni@crisprtx.com

with a copy to:

Goodwin Proctor LLP
Attn: Christopher Denn
53 State Street
Boston, Massachusetts 02109
E-mail: cdenn@goodwinlaw.com

or to such other address as the Party to whom notice is to be given may have furnished to the other Party in writing in accordance herewith. In addition, each Party will deliver a courtesy copy to the other Party's Alliance Manager concurrently with such notice. Any such notice will be deemed to have been given: (a) when delivered if personally delivered on a Business Day (or, if delivered on a non-business day, then on the next Business Day); (b) on receipt if sent by overnight courier; or (c) when confirmation of receipt is sent, if sent by electronic mail. Any notices required or permitted under this Agreement that are delivered by Vertex to CRISPR AG pursuant to this Section 13.5 shall be deemed properly delivered hereunder to each of CRISPR UK, CRISPR AG, CRISPR Inc. and Tracr.”

1.9 Amendment of Certain Cross-References .

- (a) The reference to “this Section 8.1.3” in Section 8.1.2(d) is hereby deleted and replaced with a reference to “this Section 8.1.2”.
- (b) The reference to “Section 11.2.5 (Public Announcements; Publications)” in Section 11.4.1(c) is hereby deleted.
- (c) The reference to “Schedule 2.2” in Section 2.2 of Schedule G is hereby deleted and replaced with a reference to “Schedule I”.
- (d) The reference to “Schedule F” in Schedule I is hereby deleted and replaced with a reference to “Schedule G”.
- (e) The reference to “Schedule I” in Schedule L is hereby deleted and replaced with a reference to “this Schedule L”.

ARTICLE 2 DESIGNATION OF [*] AS COLLABORATION TARGET**

The Parties hereby agree that the [***] (“ [***] ”) is a Collaboration Target under the Agreement, effective as of the Amendment Effective Date.

ARTICLE 3 DEEMED OPTION EXERCISE BY VERTEX

Notwithstanding anything to the contrary in the Agreement, the execution of the JDCA by the Parties shall be deemed to constitute an exercise by Vertex of the Option with respect to [***]. In accordance with Section 4.1.1 of the Agreement, as amended by this Amendment, such Option exercise with respect to [***]

ARTICLE 4 REFERENCE TO AND EFFECT ON THE AGREEMENT

4.1 Reference to Agreement . Upon and after the effectiveness of this Amendment, each reference in the Agreement to “this Agreement”, “hereunder”, “hereof” or words of like import referring to the Agreement shall mean and be a reference to the Agreement as modified and amended hereby.

4.2 Effectiveness of Amendment . Upon execution and delivery of this Amendment by both Parties, the amendments set forth above shall be effective as of the Amendment Effective Date. Except as specifically amended above, the Agreement is and shall continue to be in full force and effect and is hereby in all respects ratified and confirmed and shall constitute the legal, valid, binding and enforceable obligations of the Parties.

ARTICLE 5 MISCELLANEOUS

5.1 Governing Law. This Amendment, and all claims arising under or in connection therewith, will be governed by and interpreted in accordance with the substantive laws of The Commonwealth of Massachusetts, without regard to conflict of law principles thereof.

5.2 Descriptive Headings . The descriptive headings of this Amendment are for convenience only and will be of no force or effect in construing or interpreting any of the provisions of this Amendment.

5.3 Counterparts . This Amendment may be executed in two counterparts, each of which will be an original and both of which will constitute together the same document. Counterparts may be signed and delivered by facsimile or digital transmission (.pdf), each of which will be binding when received by the applicable Party.

[*Signature Page Follows*]

IN WITNESS WHEREOF , the Parties have caused this Amendment to be executed by their representatives thereunto duly authorized as of the Amendment Effective Date.

**VERTEX PHARMACEUTICALS
INCORPORATED**

By: /s/ Ian Smith
Name: Ian Smith
Title: Executive Vice President, Chief Operating Officer

VERTEX PHARMACEUTICALS (EUROPE) LIMITED

By: /s/ Ian Smith
Name: Ian Smith
Title: Director

CRISPR THERAPEUTICS AG

By: /s/ Rodger Novak
Name: Rodger Novak
Title: President

CRISPR THERAPEUTICS LIMITED

By: /s/ Tyler Dylan-Hyde
Name: Tyler Dylan-Hyde
Title: Director and Chief Legal Officer

CRISPR THERAPEUTICS, INC.

By: /s/ Rodger Novak
Name: Rodger Novak
Title: President

TRACR HEMATOLOGY LTD.

By: /s/ Tyler Dylan-Hyde
Name: Tyler Dylan-Hyde
Title: Director

Vertex Employee Compensation Plan

On an annual basis in the first quarter of the fiscal year the Management Development and Compensation Committee of our Board of Directors adopts an employee compensation plan for our officers and other employees, including our named executive officers, together with performance goals for that fiscal year. The plan addresses three components of employee compensation—base salary, performance bonuses which serve as short-term incentives and equity grants which serve as long-term incentives—that are designed to motivate, reward and retain employees by aligning compensation with the achievement of strategic corporate goals.

Upon completion of each performance period (usually a calendar year), our Board of Directors assigns a performance rating on the basis of achievement of goals for the company set by the Board, in consultation with our chief executive officer, early in the performance period. The amount available for payment of performance bonuses is established on the basis of this performance rating, and is allocated to employees on the basis of salary tier and individual performance rating. The base salaries of the executive officers are set based on market and other competitive factors. Merit increases to base salaries for other employees are made on the basis of individual performance rating. Annual equity grants, made in the form of stock options, restricted stock grants or units, or a combination of both are made on the basis of salary tier and individual performance.

The Board of Directors retains broad discretion to determine the appropriate form and level of compensation, particularly for our executives, on the basis of its assessment of our executives, the demand for talent, our performance and other factors. Key corporate performance factors generally include, among other things, achievement of regulatory and commercialization goals, research and development productivity, enhancements of organizational capabilities, financial goals and other aspects of our performance. We reserve the right to modify the plan, and the key corporate performance factors and criteria under the plan, at any time.

Vertex Pharmaceuticals Annual Non-Employee Board Compensation

<u>Annual Retainer</u>	\$100,000
<u>Committee Chair Compensation</u>	
Audit & Finance Committee Chair	\$30,000 annual retainer
Management Development & Compensation Committee Chair	\$25,000 annual retainer
Corporate Governance & Nominating Committee Chair	\$20,000 annual retainer
Science & Technology Committee Chair	\$20,000 annual retainer
<u>Committee Membership Fee (Non Chairs)</u>	
Audit & Finance Committee Member	\$15,000 annual retainer
Management Development & Compensation Committee Member	\$12,500 annual retainer
Corporate Governance & Nominating Committee Member	\$10,000 annual retainer
Science & Technology Committee Member	\$10,000 annual retainer
<u>Lead Independent Director Compensation</u>	\$40,000 annual retainer
<u>Annual Equity Grants</u>	
On June 1 on each year of service, a \$475,000 value-based award, comprised of restricted stock units (\$275,000) and options (\$200,000)	
<ul style="list-style-type: none"> • Options are fully vested upon grant • Restricted shares cliff vest on the 1 year anniversary of the grant date 	

Each of our non-employee directors is eligible to defer the cash and restricted stock portion of his/her compensation set forth above and elect to receive deferred stock units that convert to common stock in specified circumstances.

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 Pharmaceuticals Technology (Shanghai) Co., Ltd. (2)

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

-
- (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

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. 333-211096) of Vertex Pharmaceuticals Incorporated,
- (2) Registration Statement (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 No. 333-184784) pertaining to the Vertex Pharmaceuticals Incorporated Employee Stock Purchase Plan, and
- (4) Registration Statement (Form S-8 Nos. 333-219559, 333-188737, 333-197466 and 333-206075) 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 14, 2018, 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, 2017.

/s/ Ernst & Young LLP

Boston, Massachusetts
February 14, 2018

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 14, 2018

/s/ Jeffrey M. Leiden

Jeffrey M. Leiden
Chief Executive Officer and President

CERTIFICATION

I, Thomas Graney, 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 14, 2018

/s/ Thomas Graney

Thomas Graney
Senior Vice President and Chief Financial Officer

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, 2017 (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 14, 2018

/s/ Jeffrey M. Leiden

Jeffrey M. Leiden
Chief Executive Officer and President

Date: February 14, 2018

/s/ Thomas Graney

Thomas Graney
Senior 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.
