VERTEX PHARMACEUTICALS INC / MA
Form 10-K
February 11, 2014

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

FORM 10-K

x ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

For the Fiscal Year Ended December 31, 2013

or

o TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

For the transition period from to

Commission file number 000-19319

Vertex Pharmaceuticals Incorporated
(Exact name of registrant as specified in its charter)

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

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

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

Title of Each Class	Name of Each Exchange on Which Registered
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

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

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 o No x

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 x No o

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 during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). Yes x No o

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K 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. x

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer or a smaller reporting company. See definitions of "large accelerated filer," "accelerated filer" and "smaller reporting

company" in Rule 12b-2 of the Exchange Act. (Check one):

Large accelerated filer x	Accelerated filer o	Non-accelerated filer o	Smaller reporting company o
		(Do not check if a smaller reporting company)	

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

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 28, 2013 (the last trading day of the registrant's second fiscal quarter of 2013) was $18.5 billion. As of February 5, 2014, the registrant had 235,771,942 shares of common stock outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the definitive Proxy Statement for the 2014 Annual Meeting of Shareholders to be held on May 7, 2014 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.

PART I

ITEM 1. BUSINESS

OVERVIEW

We are in the business of discovering, developing, manufacturing and commercializing small molecule drugs. We invest in scientific innovation to create transformative medicines for patients with serious diseases in specialty markets. Since mid-2011, we have obtained approval for, and initiated commercial sales of, our first two products: KALYDECO (ivacaftor) and INCIVEK (telaprevir). We market KALYDECO in the United States and international markets for the treatment of patients six years of age and older with cystic fibrosis, or CF, who have a specific genetic mutation in their cystic fibrosis transmembrane conductance regulator, or CFTR, gene, which is referred to as the G551D mutation. INCIVEK is approved in the United States and Canada for the treatment of adults with genotype 1 hepatitis C virus, or HCV, infection. Our collaborators, Janssen Pharmaceutica NV, or Janssen, and Mitsubishi Tanabe Pharma Corporation, or Mitsubishi Tanabe, market telaprevir in other international markets.

Our business is focused on developing and commercializing therapies for the treatment of cystic fibrosis and advancing our other research and early-stage development programs.

Cystic Fibrosis - Our goal is twofold: to develop treatment regimens that will provide benefits to as many patients with CF as possible and to maximize those benefits.

•KALYDECO. KALYDECO was approved in 2012 in the United States and European Union as a treatment for patients with CF six years of age and older who have the G551D mutation in their CFTR gene. We have submitted a supplemental New Drug Application, or sNDA, to the U.S. Food and Drug Administration, or FDA, and a Marketing Authorization Application, or MAA, variation in the European Union seeking approval to market ivacaftor for the treatment of patients with CF six years of age and older who have specified other mutations in their CFTR gene, which were studied in our first label-expansion clinical trial for ivacaftor. We also are seeking to expand the number of patients eligible for treatment with ivacaftor by (i) evaluating ivacaftor as a potential treatment for patients with CF who have residual CFTR function, including patients with CF who have the R117H mutation in their CFTR gene, and (ii) evaluating ivacaftor as a potential treatment for patients with CF two to five years of age who have specific mutations in their CFTR genes.

•Ivacaftor in Combination with CFTR Corrector Compounds. In October 2013, we completed enrollment in an international pivotal Phase 3 development program to evaluate combinations of lumacaftor (VX-809), our most advanced investigational CFTR corrector compound, and ivacaftor. The Phase 3 development program includes two Phase 3 clinical trials, referred to as TRAFFIC and TRANSPORT, that each enrolled patients with CF 12 years of age and older with two copies (homozygous) of the F508del mutation in their CFTR gene. The F508del mutation is the most prevalent genetic mutation that causes CF. We expect data from TRAFFIC and TRANSPORT in mid-2014. If these clinical trials are successful, we plan to submit a New Drug Application, or NDA, to the FDA and an MAA in the European Union, in the second half of 2014. We also are evaluating VX-661, a second investigational CFTR corrector, in combination with ivacaftor, in Phase 2 clinical development.

•CF Research Programs. We are seeking to identify and develop next-generation CFTR corrector compounds that could be evaluated in regimens combining ivacaftor with two CFTR corrector compounds.

Research and Early-stage Development Programs - We are engaged in a number of other research and early-stage development programs, including programs in the areas of oncology, multiple sclerosis and other serious and rare diseases. Over the last year, we have evaluated in Phase 2 clinical trials: VX-135, an HCV nucleotide analogue, in combination with daclatasvir, an NS5A replication complex inhibitor being developed by Bristol-Myers Squibb, or BMS; VX-509, our JAK3 inhibitor, in patients with rheumatoid arthritis; and VX-787, a drug candidate for the treatment of influenza A. We are in discussions with Alios BioPharma, Inc., or Alios, from whom we exclusively license VX-135, and BMS regarding potential next steps for further clinical evaluation of VX-135 and are seeking collaborators to advance clinical development of VX-509 and VX-787. We plan to continue investing in our research programs and fostering scientific innovation in order to identify and develop transformative medicines. We believe that pursuing research in diverse areas allows us to balance the risks inherent in drug development and may provide drug candidates that will form our pipeline in future years.

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CYSTIC FIBROSIS

Background

Cystic fibrosis is a rare, life-threatening 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. Children must inherit two defective CFTR genes, which are referred to as alleles - one from each parent - to have CF. There are more than 1,900 known mutations in the CFTR gene, some of which result in CF, including two of the most prevalent mutations, the G551D mutation and the F508del mutation.

The G551D mutation results in a defect in the CFTR protein in which the defective CFTR protein reaches the surface of a cell but does not efficiently transport chloride ions across the cell membrane. The F508del mutation results in a defect in the CFTR protein in which the CFTR protein does not reach the surface of cells in sufficient quantities. 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. Ivacaftor, known as a CFTR potentiator, keeps the CFTR protein channels on the cell surface open longer, to increase the flow of salt and water into and out of the cell. CFTR correctors, such as lumacaftor and VX-661, are believed to help CFTR protein reach the cell surface.

We chose to develop KALYDECO (ivacaftor) and our other CF drug candidates because of their potential to improve the function of defective CFTR proteins in patients with CF, which is the underlying cause of CF. We discovered ivacaftor, lumacaftor and VX-661 in our research collaboration with the Cystic Fibrosis Foundation Therapeutics Incorporated, or CFFT. Our research group is continuing to work to identify additional corrector compounds that could be included in future dual- and/or triple-combination treatment regimens with the potential to provide additional benefits to patients with CF. We hold worldwide development and commercialization rights to ivacaftor, lumacaftor and VX-661. We pay royalties to CFFT on net sales of ivacaftor and will pay royalties to CFFT on any net sales of lumacaftor, VX-661 and any other corrector compounds discovered under the CFFT collaboration, if they are approved.

We market KALYDECO in specified approved indications in the United States and international markets. Our ivacaftor development program for additional indications has received a Breakthrough Therapy designation from the FDA. The FDA also has designated the combination regimens of lumacaftor with ivacaftor and VX-661 with ivacaftor for the treatment of patients with CF who have the F508del mutation on both alleles as Breakthrough Therapies. We are expecting data from these clinical programs in 2014.

KALYDECO (ivacaftor)

KALYDECO (ivacaftor) is an orally-administered CFTR potentiator that is approved in the United States, Australia, Canada and the European Union for the treatment of patients six years of age and older with CF who have the G551D mutation in their CFTR gene. KALYDECO has received recognition as a significant innovation in drug development. In the press release announcing KALYDECO's approval, the FDA identified KALYDECO as an excellent example of the promise of personalized medicine and a breakthrough therapy for the CF community, because other existing therapies treat only the symptoms of this genetic disease, while KALYDECO addresses the underlying cause. The Wall Street Journal named KALYDECO as the winner of its 2012 Technology Innovation award in the Medicine and Biotech category. During development, ivacaftor was granted orphan drug designation in the United States and European Union and Fast-track designation in the United States and, due to its promise, was advanced rapidly through development. In 2008, we evaluated ivacaftor in a small Phase 2a clinical trial that enrolled 39 patients with CF who had the G551D mutation on at least one allele. Based on the safety and efficacy data from this clinical trial, we moved directly into a Phase 3 clinical program, which we initiated in May 2009 and completed in mid-2011. We filed for approval to market ivacaftor in the United States in November 2011 and obtained approval from the FDA in January 2012, which was more than two months ahead of the original target date established by the FDA. We also obtained rapid approval for ivacaftor in the European Union and Canada later in 2012. We use the brand name KALYDECO only 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 the compound by its scientific (or generic) name ivacaftor.

KALYDECO is approved for the treatment of patients with CF six years of age and older who have at least one copy of the G551D mutation in their CFTR gene. We believe there are approximately 2,000 patients with CF six years of age and

older in North America, Europe and Australia who have the G551D mutation in the CFTR gene. Since KALYDECO's approval in 2012, most of these patients have started treatment with KALYDECO. KALYDECO currently is available to eligible patients in the United States, England, Scotland, Northern Ireland, Wales, the Republic of Ireland, France, Germany, Austria, Denmark, Greece, Italy, the Netherlands, Norway and Sweden. In many international markets, including Australia and Canada, patients generally are not able to obtain access to drugs until the relevant agencies authorize public reimbursement for the cost of the drug. We are in discussions with regulatory agencies in Australia and Canada regarding public reimbursement of KALYDECO costs in these countries.

We submitted an sNDA to the FDA and an MAA variation in the European Union in September 2013 and October 2013, respectively, seeking approval to market ivacaftor for the treatment of patients with CF six years of age and older who have specified other mutations in their CFTR gene. These submissions incorporated clinical data from our first ivacaftor label-expansion Phase 3 clinical trial. The FDA has set a target date of March 27, 2014 to complete its review of this sNDA under the Prescription Drug User Fee Act (PDUFA). We estimate that in North America, Europe and Australia approximately 400 patients with CF six years of age and older have at least one of the mutations evaluated in this clinical trial, including approximately 150 patients in the United States.

CF Drug Development Programs

We are continuing our work in CF to develop treatment regimens that will provide benefits to as many patients with CF as possible and to maximize those benefits. We are seeking to increase the number of patients with CF who could benefit from our medicines both by evaluating ivacaftor in additional patient groups who may benefit, and by evaluating combinations of ivacaftor with our investigational corrector compounds, lumacaftor and VX-661, in patients with the most prevalent form of CF, those with two copies of the F508del mutation.

Ivacaftor

We have completed a Phase 3 clinical trial to evaluate ivacaftor in patients with the R117H mutation in their CFTR gene. We are conducting a fully-enrolled proof-of-concept Phase 2 clinical trial in which we are evaluating ivacaftor in patients with CF who have clinical evidence of residual CFTR function. We also are conducting a fully-enrolled Phase 3 clinical trial in which we are evaluating ivacaftor, in the form of minitablets or granules, as a treatment for children with CF two to five years of age with particular mutations in their CFTR gene, including the G551D mutation.

R117H Mutation

In December 2013, we reported data from a Phase 3 clinical trial that evaluated ivacaftor in patients six years of age and older with CF who have the R117H mutation on at least one allele of their CFTR gene. Patients diagnosed with CF who have the R117H mutation exhibit a range of severity and signs and symptoms of the disease.

The 24-week doubled-blinded Phase 3 clinical trial enrolled 69 patients. Patients 12 years of age and older had lung function at screening of 40 to 90 percent predicted FEV_1, and children six to eleven years of age had FEV_1 at screening of 40 to 105 percent predicted FEV_1. FEV_1 is a measure of the amount of air that an individual can exhale in one second. The primary endpoint of the clinical trial was the absolute change from baseline in FEV_1 throughout the treatment period for ivacaftor compared to placebo across all patients (intent-to-treat). The clinical trial did not meet its primary endpoint of a statistically significant absolute change from baseline in FEV_1. However, a pre-specified subgroup analysis demonstrated a clinical benefit in patients with CF 18 years of age and older who have the R117H mutation on at least one allele. We plan to meet with the FDA in early 2014 to discuss these results and the potential submission of an sNDA for patients with the R117H mutation. We estimate that in North America, Europe and Australia approximately 1,100 patients with CF six years of age and older have at least one copy of the R117H mutation in their CFTR gene. In the United States, approximately 300 patients with CF 18 years of age and older have the R117H mutation in their CFTR gene.

Results from R117H Clinical Trial

Lung Function (FEV_1) Results In the Total Clinical Trial Population. The primary endpoint of the clinical trial was the absolute change from baseline in FEV_1 throughout the treatment period for ivacaftor compared to placebo across all patients (intent-to-treat). In the clinical trial, the mean absolute improvement in percent predicted FEV_1 between those treated with ivacaftor and placebo was 2.1 percentage points ($p=0.20$). The result of statistical testing is often defined in terms of a "p-value," with $p<0.05$ generally considered to represent a statistically significant difference. The

treatment difference for this endpoint was not statistically significant, thus the clinical trial did not meet its

primary endpoint. The mean absolute percent predicted FEV_1 improvement during ivacaftor treatment (within-group) was 2.6 percentage points (p = 0.03).

Secondary Endpoints. In the clinical trial, the mean relative treatment difference in percent predicted FEV_1 was 5.0 percent (p = 0.06) through the 24-week treatment period. The mean relative percent predicted FEV_1 improvement during ivacaftor treatment (within-group) was 4.8 percent (p=0.01). Treatment with ivacaftor, regardless of age, resulted in statistically significant decreases in sweat chloride and improvement in patient-reported outcomes as measured by the respiratory domain of the Cystic Fibrosis Questionnaire Revised (CFQ-R). No significant differences in the frequency of pulmonary exacerbations or changes in body mass index were noted.

Safety and Tolerability. The safety and tolerability results observed in this clinical trial were consistent with those observed in prior Phase 3 clinical trials of ivacaftor in patients with CF who have the G551D mutation. The most commonly observed adverse events in those who received ivacaftor were infective pulmonary exacerbation, cough and headache, which occurred with similar frequency compared to those who received placebo. Serious adverse events occurred in 17 percent of patients who received placebo versus 12 percent for patients who received ivacaftor.

Subgroup Analyses. A pre-specified subgroup analysis was conducted to evaluate the effect of ivacaftor on patients 18 years of age and older, in patients 12 to 17 years of age and in patients six to eleven years of age. Data from these subgroup analyses are provided below:

- Patients 18 years of age and older: 50 patients 18 years of age and older were enrolled in this clinical trial and had a mean baseline percent predicted FEV_1 of 65 percent. A pre-specified subset analysis in these patients showed statistically significant improvements in lung function and other key secondary endpoints. In these patients, the mean absolute improvement in percent predicted FEV_1 between treatment with ivacaftor and placebo was 5.0 percentage points (p=0.01) and the mean relative improvement in percent predicted FEV_1 was 9.1 percent (p=0.008) in each case through the 24-week treatment period. An additional analysis was conducted on percent predicted FEV_1 four weeks following the completion of treatment with ivacaftor. Mean lung function returned toward baseline in the patients who received ivacaftor, who showed a -3.1 percentage point (p=0.001) mean absolute within-group change from Week 24 to Week 28 (four weeks after the end of treatment). Data from these subgroup analyses of patients 18 years of age and older are provided below:

	Ivacaftor (n=24)	Placebo (n=26)	Treatment Difference
Mean Absolute Change in FEV_1*	4.5 (p=0.002)	-0.5 (p=0.728)	5.0 (p=0.01)
Mean Relative Change in FEV_1	7.7 (p=0.002)	-1.5 (p=0.526)	9.1 (p=0.008)
Proportion of Patients with Mean Absolute Improvement in FEV_1 of 5 percentage points or more	54.2%	15.4%	38.8% (p=0.007)
CFQ-R Score (respiratory domain)*	12.2 (p=<0.0001)	-0.5 (p=0.861)	12.6 (p=0.002)

*Pre-specified analyses

- Patients 12 to 17 years of age: Two patients 12 to 17 years of age enrolled in this clinical trial; one received placebo and one received ivacaftor. There were too few patients to make a statistical comparison of patients in this age range.
- Patients six to eleven years of age: Seventeen patients six to eleven years of age enrolled in this clinical trial and had a mean baseline percent predicted FEV_1 of 96 percent. In these patients, there was a mean absolute decline from baseline in percent predicted FEV_1 of -2.8 percentage points (p=0.132) in patients who received ivacaftor (n=9) compared to a mean absolute increase from baseline in percent predicted FEV_1 of 3.5 percentage points (p=0.084) for patients who received placebo (n=8). The mean absolute treatment difference was -6.3 percentage points (p=0.03).

Pediatric Formulation

We are conducting a fully-enrolled Phase 3 clinical trial to evaluate ivacaftor, in the form of minitablets or granules, as a treatment for children with CF two to five years of age with specific mutations in their CFTR gene, including the G551D

mutation. We expect data from this clinical trial in the second quarter of 2014. If this clinical trial is successful, we plan to submit an NDA in the second half of 2014. We estimate that in North America, Europe and Australia approximately 300 patients with CF two to five years of age have one of the CFTR mutations in their CFTR gene that is being evaluated in this clinical trial.

Residual CFTR Function

We are conducting a fully-enrolled proof-of-concept Phase 2 clinical trial in which we are evaluating ivacaftor in patients with CF who have clinical evidence of residual CFTR function. We expect data from this clinical trial in the second quarter of 2014. We estimate that in North America, Europe and Australia more than 3,000 patients with CF six years of age and older have non-R117H CFTR mutations that result in residual function.

Lumacaftor in Combination with Ivacaftor

Phase 3 Program in Patients with CF Who Have Two Copies (homozygous) of the F508del Mutation

We have completed enrollment of patients in an international pivotal Phase 3 clinical program to evaluate combinations of lumacaftor and ivacaftor in patients with CF who have two copies (homozygous) of the F508del mutation in their CFTR gene. We are conducting two 24-week Phase 3 clinical trials, which are referred to as TRAFFIC and TRANSPORT, that are designed to support approval of the combination of lumacaftor and ivacaftor for patients 12 years of age and older. Each Phase 3 clinical trial enrolled approximately 550 patients with CF who are homozygous for the F508del mutation, for a total of approximately 1,100 patients. TRAFFIC and TRANSPORT are identical in design and together are being conducted at approximately 200 clinical trial sites in North America, Europe and Australia. Two treatment regimens of lumacaftor (600mg once-daily (QD) and 400mg every twelve hours (q12h)) in combination with ivacaftor (250mg every twelve hours (q12h)) are being evaluated. Fixed-dose tablets that contain both lumacaftor and ivacaftor or placebo are being used in both clinical trials. In TRAFFIC and TRANSPORT, we will evaluate absolute and relative improvement in percent predicted FEV_1, as well as change in body mass index (BMI) or weight gain, number of pulmonary exacerbations and improvements in patient-reported outcomes as measured by the CFQ-R. Following recent discussions with regulatory agencies, we have agreed that for both TRAFFIC and TRANSPORT the primary endpoint will be absolute change in percent predicted FEV_1 through 24 weeks compared to placebo. The initial 24-week treatment period in TRAFFIC and TRANSPORT is being followed by a separate rollover double-blind extension clinical trial where all eligible patients, including those who received placebo, will receive one of the combination treatment regimens for up to an additional 96 weeks.

We expect data from TRAFFIC and TRANSPORT in mid-2014. If these clinical trials are successful, we plan to submit an NDA to the FDA and an MAA in the European Union in the second half of 2014. We believe that in North America, Europe and Australia more than 28,000 patients with CF six years of age and older have two copies of the F508del mutation in their CFTR gene, including approximately 22,000 patients 12 years of age and older.

We also are conducting a clinical trial to evaluate lumacaftor in combination with ivacaftor in children with CF six to eleven years of age who have two copies of the F508del mutation. We have completed part 1 of this clinical trial and expect to begin part 2 of this clinical trial in the second half of 2014. If this clinical trial is successful, we plan to use the data from this clinical trial, along with data from TRAFFIC and TRANSPORT, for registration of this combination in patients six to eleven years of age, which we expect would occur subsequent to approval in patients 12 years of age and older, if achieved.

The two combination dosing regimens we selected for evaluation in TRAFFIC and TRANSPORT were evaluated in separate parts of a Phase 2 clinical trial of lumacaftor and ivacaftor referred to as Cohort 2 and Cohort 3. Safety results from Cohort 2 and Cohort 3 were similar to one another. In both dose groups, lumacaftor was generally well-tolerated alone and in combination with ivacaftor. The most common adverse events in both groups were respiratory in nature. In Cohort 3, one patient in the treatment group discontinued treatment because of a pulmonary adverse event.

- Cohort 2 - We evaluated the 600mg once-daily (QD) dose of lumacaftor in combination with ivacaftor (250mg q12h) in Cohort 2 in 21 patients with CF who are homozygous for the F508del mutation. This regimen resulted in statistically significant improvements in lung function (within group and versus placebo) during the combination dosing period, as set forth in the following table:

		Mean Absolute and Relative Changes in Percent Predicted FEV_1		
		Day 0 - 28; lumacaftor alone	Day 28 - 56; lumacaftor + ivacaftor	Day 0 - 56
lumacaftor (600mg QD) + ivacaftor (250mg q12h)	Within Group			
	Absolute	-2.9 (p=0.07)	+6.1 (p<0.001)	+3.4 (p=0.03)
	Relative	-3.5 (p=0.13)	+9.7 (p<0.001)	+5.3 (p=0.02)
	Versus Placebo			
	Absolute	-2.0 (p=0.36)	+8.6 (p <0.001)	+6.7 (p=0.002)
	Relative	-3.9 (p=0.21)	+12.8 (p<0.001)	+9.2 (p=0.004)

- Cohort 3 - We evaluated the 400mg (q12h) dose of lumacaftor in combination with ivacaftor in Cohort 3 in 11 patients with CF who are homozygous for the F508del mutation. Cohort 3 also included the randomization of four patients to placebo to allow for a blinded safety assessment. Three patients completed treatment in the placebo group. The pattern of lung function response observed in Cohort 3 was similar to that observed in the 600mg (QD) dose group in Cohort 2, with a decline in FEV_1 during the lumacaftor monotherapy dosing period followed by a statistically significant increase in FEV_1 during the lumacaftor and ivacaftor combination dosing period. Additional lung function results for Cohort 3 are provided below:

		Mean Absolute and Relative Changes in Percent Predicted FEV_1		
		Day 0 - 28; lumacaftor alone	Day 28 - 56; lumacaftor + ivacaftor	Day 0 - 56
lumacaftor (400mg q12h) + ivacaftor (250mg q12h)	Within Group			
	Absolute	-4.3 (p=0.04)	+6.6 (p=0.01)	+1.9 (p=0.57)
	Relative	-6.3 (p=0.08)	+8.8 (p=0.01)	+2.5 (p=0.67)

Phase 2 Clinical Trial in Patients with One Copy (heterozygous) of the F508del Mutation

We recently began enrollment in an 8-week Phase 2 clinical trial of lumacaftor in combination with ivacaftor in patients with CF who are 18 years of age and older and who have one copy of the F508del mutation in their CFTR gene and one copy of a mutation in their CFTR gene that is not expected to respond to either ivacaftor or lumacaftor alone. In the Phase 2 clinical trial that previously evaluated heterozygous patients, the improvement in lung function was smaller than the improvement seen in homozygous patients. The clinical trial we recently initiated was requested by the FDA and is designed to provide additional safety and lung function data on the combination of ivacaftor and lumacaftor in heterozygous patients. This clinical trial will evaluate a twice-daily administration of lumacaftor (400 mg) and ivacaftor (250 mg).

VX-661

Phase 2 Clinical Trial

In April 2013, we announced the data from a randomized, double-blind, placebo-controlled Phase 2 clinical trial of VX-661 alone and in combination with ivacaftor. This clinical trial enrolled 128 patients with CF who were 18 years of age and older with two copies of the F508del mutation. One group of patients was randomized to receive either VX-661 (10, 30, 100 and 150 mg dosed once daily), or placebo, alone for 28 days. A separate group of patients was randomized to receive the combination of VX-661 (10, 30, 100 and 150 mg dosed once daily) and ivacaftor (150 mg dosed twice daily), or placebo, for 28 days. The primary endpoints of the clinical trial were safety, tolerability and change in sweat chloride levels. Change in lung function (FEV_1) was measured as a secondary endpoint.

There were statistically significant mean absolute decreases in sweat chloride levels, both within group and versus placebo, across the combination and monotherapy groups. These changes generally were modest and were variable

across the dose groups.

VX-661 generally was well-tolerated when dosed alone and in combination with ivacaftor. The most common adverse events were pulmonary in nature. Most adverse events were mild to moderate in severity and similar between the treatment and placebo groups, and the types and frequency of adverse events were similar between the treatment and placebo groups. The rate of serious adverse events also was similar between the treatment arms and the placebo arm.

Lung Function Results for Combination Dosing

Mean absolute and relative improvements in lung function were observed in all the combination dosing groups (10, 30, 100 and 150 mg), both within group and versus placebo. The improvements in lung function were dose-dependent, with the greatest improvements observed in the groups that received the highest doses of VX-661 in combination with ivacaftor. A summary of these lung function results is provided in the following table:

Mean Changes in Lung Function	Mean Relative Change in Percent Predicted FEV_1 From Baseline		Mean Absolute Change in Percent Predicted FEV_1 From Baseline	
	Day 0 - 28	28 Days Post-Treatment (Within-Group Mean)*	Day 0 - 28	28 Days Post-Treatment (Within-Group Mean)*
Placebo (n=23) (within group)	0.03 (NS)	1.6	-0.4 (NS)	0.6
Combination Treatment Arms	vs. Placebo		vs. Placebo	
VX-661 (10 mg) + ivacaftor (150 mg) (n=17)	4.1 (NS)	1.7	2.3 (NS)	0.8
VX-661 (30 mg) + ivacaftor (150 mg) (n=17)	5.4 (NS)	1.2	3.4 (NS)	0.5
VX-661 (100 mg) + ivacaftor (150 mg) (n=15)	9.0 (p=0.01)	1.7	4.8 (p=0.01)	0.5
VX-661 (150 mg) + ivacaftor (150 mg) (n=16)	7.5 (p=0.02)	1.4	4.5 (p=0.01)	0.7

NS = Not Statistically Significant

* The statistical analysis plan (SAP) for this clinical trial did not include statistical comparisons for the 28-day washout period

Planned and Ongoing Phase 2 Clinical Trials

We are preparing to conduct an additional Phase 2 clinical trial of VX-661, a CFTR corrector compound, in combination with ivacaftor in patients with CF who have two copies of the F508del mutation in their CFTR gene. We have submitted the protocol for this 12-week Phase 2 clinical trial to the FDA and expect to begin enrollment in the first half of 2014. The primary endpoint of this clinical trial is safety, with secondary endpoints to assess efficacy and pharmacokinetics of the combination in order to characterize VX-661 for further clinical development. If the safety and efficacy data from this Phase 2 clinical trial is satisfactory, we expect to conduct further evaluation of VX-661. Long term, our primary strategy is to develop VX-661 as a triple-combination regimen with ivacaftor and a next-generation CFTR corrector compound. Additionally, we may consider developing VX-661 in a dual-combination regimen with ivacaftor.

We have completed enrollment in a Phase 2 clinical trial to evaluate a 4-week regimen of VX-661 in combination with ivacaftor in patients with one copy of the G551D mutation and one copy of the F508del mutation in their CFTR genes. This clinical trial is intended to explore whether the addition of a CFTR corrector to treatment with ivacaftor can provide greater clinical benefit than treatment with KALYDECO alone in these patients.

HCV INFECTION

Background

The Centers for Disease Control and Prevention, or CDC, has estimated that approximately 2.7 million to 3.9 million people in the United States are chronically infected with HCV. The World Health Organization, or WHO, has estimated that about 170 million people are chronically infected with HCV worldwide. Although exposure to HCV often leads to chronic infection, patients frequently do not have symptoms and are unaware that they have become infected with HCV. Over time, many patients develop liver inflammation. This inflammation can progress to scarring of the liver, called fibrosis, or more advanced scarring of the liver, called cirrhosis. Patients with cirrhosis may go on to develop liver failure or other

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complications, including liver cancer. The WHO estimates that HCV infection is responsible for more than 50% of all liver cancer cases and two-thirds of all liver transplants in the developed world.

Genotype 1 HCV infection is the most prevalent form of HCV infection in the United States and the most difficult to treat. There are many other less prevalent HCV infection genotypes, each of which tends to respond differently to treatment. Patients who are treated successfully maintain undetectable HCV RNA levels after treatment has been completed, which is referred to as a sustained viral response, or SVR.

In addition to our HCV protease inhibitor INCIVEK, there are three oral direct-acting antiviral drugs approved for the treatment of genotype 1 HCV infection in the United States: Gilead Sciences, Inc.'s, or Gilead's, SOVALDI™ (sofosbuvir), an HCV nucleotide analogue NS5B polymerase inhibitor that was approved by the FDA in December 2013; Janssen's OLYSIO™ (simeprevir), an HCV protease inhibitor that was approved by the FDA in November 2013, and Merck's VICTRELIS™ (boceprevir), an HCV protease inhibitor that was approved by the FDA in 2011. Each of these direct-acting antiviral drugs generally are prescribed in combination with pegylated-interferon, or peg-IFN, a drug that is administered by weekly injection, and ribavirin, or RBV.

INCIVEK/INCIVO/TELAVIC

INCIVEK (telaprevir) is an orally-administered HCV protease inhibitor for adults with genotype 1 HCV infection that is prescribed in combination with peg-IFN and RBV. We market INCIVEK in the United States and Canada, where it was approved in 2011. In 2011, our collaborators, Janssen and Mitsubishi Tanabe, also obtained marketing approval for telaprevir from the European Commission and the Japanese Ministry of Health, Labor and Welfare, respectively. Janssen markets telaprevir under the brand name INCIVO in Europe and other countries in its territories, and Mitsubishi Tanabe markets telaprevir under the brand name TELAVIC in Japan. Janssen paid us royalties on net sales of INCIVO through the fourth quarter of 2013 and beginning in the first quarter of 2014 has a fully-paid license to market INCIVO in its territories. Mitsubishi Tanabe also has a fully-paid license to market telaprevir in its territories. Telaprevir was discovered in our collaboration, now ended, with Eli Lilly and Company, and we pay Eli Lilly and Company royalties on net sales of telaprevir.

INCIVEK achieved rapid acceptance for the treatment of patients with genotype 1 HCV infection in the United States and accounted for a majority of our net product revenues in 2011, 2012 and 2013. However, INCIVEK revenues have been declining since reaching a peak in the fourth quarter of 2011. In response to the continued and rapid decline in the number of patients being treated with INCIVEK in the United States and anticipated competition resulting from the expected approval of direct-acting antivirals SOVALDI and OLYSIO, we reduced our promotion and support for INCIVEK in 2013. We expect that only a small portion of our net product revenues in 2014 will be due to INCIVEK.

VX-135

We are evaluating the development of all-oral, interferon-free regimens of 12 weeks or less in duration incorporating our HCV nucleotide analogue NS5B polymerase inhibitor VX-135. A number of pharmaceutical companies are investigating combination regimens that incorporate one or more of an HCV protease inhibitor, an HCV nucleotide analogue, an HCV non-nucleotide polymerase inhibitor and an NS5A inhibitor. Clinical trials of these investigational combination regimens are being conducted in a wide variety of patient populations, including treatment-naïve and treatment-failure patients, and across all HCV genotypes, which respond differently to different combinations of molecules employing different mechanisms.

Many of our competitors' potential all-oral treatment regimens are more advanced, including all-oral treatment regimens that are being evaluated in Phase 3 clinical trials by Gilead, Abbvie, Inc., or Abbvie, and BMS. While the development and regulatory timelines for drug candidates for the treatment of HCV infection are subject to risk and uncertainty, we believe that (i) substantial additional clinical data regarding potential all-oral treatment regimens will become available in 2014 and (ii) it is possible that one or more all-oral treatment regimens for genotype 1 HCV infection could be commercially available as soon the second half of 2014. As a result, if we are successful in developing an all-oral treatment regimen that includes VX-135, we expect that our all-oral treatment regimen would compete directly with several all-oral treatment regimens that were approved several years prior to the approval of our all-oral treatment regimen.

Partial Clinical Hold

In July 2013, the FDA placed a partial clinical hold on VX-135 in the United States. The partial clinical hold was placed on VX-135 in the United States following observation of reversible elevated liver enzymes in patients who received 400 mg

of VX-135 in combination with RBV in a Phase 2 clinical trial conducted in Europe. Until the partial clinical hold has been resolved, we cannot pursue further evaluation of VX-135 in the United States.

VX-135 in Combination with Daclatasvir

We, in collaboration with BMS, are evaluating VX-135 in combination with daclatasvir, an NS5A replication complex inhibitor being developed by BMS, in a Phase 2a clinical trial. The first two cohorts of this open-label Phase 2a study of VX-135 in combination with daclatasvir were conducted in New Zealand and evaluated 100 mg and 200 mg once-daily doses of VX-135 in combination with daclatasvir once daily (60 mg) for 12 weeks of total treatment. Twenty-three patients with genotype 1 HCV who were new to treatment (treatment-naïve) and did not have liver cirrhosis were enrolled in these cohorts. More than 75 percent of all patients enrolled had genotype 1a HCV infection.

- 200 mg of VX-135 in Combination with Daclatasvir (60 mg): Based on the intent-to-treat analysis, 58 percent (7 of 12) of patients in this treatment arm had undetectable HCV RNA levels after 4 weeks of treatment and 83 percent (10 of 12) of these patients had undetectable HCV RNA levels four weeks after the completion of treatment, or SVR4. One patient in this treatment arm experienced a serious adverse event (vomiting/nausea) and discontinued treatment after the first dose. This patient did not achieve SVR4. The eleven other patients in this arm completed 12 weeks of treatment and 91 percent (10 of 11) of these patients achieved SVR4. One patient relapsed during the follow-up period and did not achieve SVR4.
- 100 mg of VX-135 in Combination with Daclatasvir (60 mg): Based on an intent-to-treat analysis, 73 percent (8 of 11) of patients in this treatment arm achieved undetectable HCV RNA levels after 4 weeks of treatment and 73 percent (8 of 11) of patients had undetectable HCV RNA levels four weeks after the completion of treatment (SVR4). Two patients in this arm experienced viral breakthrough while receiving the combination regimen, and one patient relapsed during the follow-up period.

We are in discussions with Alios BioPharma, Inc., or Alios, and BMS regarding these data and potential next steps for further evaluation of VX-135 in combination with daclatasvir.

AUTOIMMUNE DISEASES (RHEUMATOID ARTHRITIS)

Background

Autoimmune diseases, including rheumatoid arthritis, or RA, are characterized by inflammation that is believed to be the result of an incorrectly regulated immune response. Rheumatoid arthritis is a chronic disease that affects 0.5% to 1.0% of the world's population and, according to the CDC, approximately 1.5 million adults in the United States. Rheumatoid arthritis causes destruction of joint cartilage and erosion of adjacent bone, resulting in deformity, loss of function and substantial disability. Many patients with rheumatoid arthritis also eventually require joint replacements. There are a number of approved treatments for rheumatoid arthritis, including oral and injectable disease-modifying antirheumatic drugs, or DMARDs, and a Janus kinase (JAK) inhibitor that is marketed by Pfizer in the United States. These treatments are effective in a portion of patients with rheumatoid arthritis, but a significant portion of patients do not respond adequately to currently available drugs or experience a decrease in the effectiveness of these drugs over time. We are seeking to develop an oral therapy for the treatment of rheumatoid arthritis that could be used alone or in combination with existing DMARDs.

VX-509

VX-509 is an investigational oral drug candidate intended to inhibit Janus kinase 3, or JAK3, which is involved in the modulation of a type of white blood cell, referred to as a lymphocyte, that is central to autoimmune disease pathology. Because of JAK3's role in lymphocyte biology, we believe it is a promising target for the design of immunosuppressant drugs for treatment of a variety of autoimmune diseases, including rheumatoid arthritis. Based on in vitro and in vivo data, VX-509 shows promise as a potent and selective inhibitor of JAK3.

We recently completed the evaluation of VX-509 in a double-blind, randomized, placebo-controlled 24-week Phase 2b clinical trial that enrolled and dosed 358 people with RA who had active disease despite methotrexate treatment. Patients in the clinical trial continued to receive stable doses of methotrexate during the clinical trial. Up to 20 percent of the patients in the clinical trial had previously been treated with a single tumor necrosis factor (TNF) inhibitor. Patients in the clinical trial were randomized to receive placebo or one of four dose regimens of VX-509 (100 mg once daily (QD), 150 mg once daily, 200 mg once daily or 100 mg given twice daily (BID)) for 24 weeks.

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The primary endpoints of the clinical trial were the proportion of patients who achieved a 20 percent improvement in signs and symptoms of RA, as measured by the ACR improvement criteria, or ACR20, response at week 12 and the change from baseline in Disease Activity Score for 28 joints, or DAS28, at week 12. Additional secondary endpoints were used to evaluate the clinical activity of VX-509, including the proportion of patients who achieved 50 percent and 70 percent improvement in signs and symptoms of RA, or ACR50 and ACR70, respectively, at week 12. In all VX-509 treatment arms, the proportion of patients achieving ACR20 and ACR50 and the decrease from baseline in DAS28 were significantly greater than in placebo. The three highest dose groups showed ACR20 responses of between 58 percent and 68 percent, compared to 18 percent for placebo, and statistically significant ACR70 responses versus placebo.

From week 12 to 24, data from this clinical trial showed continued improvements in the signs and symptoms of RA as measured by ACR20, ACR50 and ACR70. At week 24, all doses of VX-509 showed statistically significant ACR20, ACR50 and ACR70 responses versus placebo. Across the four VX-509 dose groups, the ACR20, ACR50 and ACR70 responses were between 61 and 63 percent, 38 and 47 percent and 15 and 25 percent, respectively, through 24 weeks of treatment. The ACR20, ACR50 and ACR70 responses for patients who received placebo were 17, 7 and 3 percent, respectively, through 24 weeks.

Safety results through 12 and 24 weeks of treatment were similar. Through 24 weeks, the discontinuation rate due to adverse events was 9.1 percent for the pooled VX-509 treatment group and 8.5 percent for the placebo group. Overall, adverse event rates through 24 weeks were 59.9 percent in the pooled VX-509 treatment groups compared to 42.3 percent for those who received placebo. There were two deaths in the clinical trial, including one death in the VX-509 200 mg QD group in a patient with pancytopenia and pneumonia and one death in the VX-509 100 mg BID group in a patient who had cardiac failure.

In addition to the Phase 2b clinical trial in RA, we have completed several drug-drug interaction studies of VX-509 in healthy volunteers. These studies demonstrate that dosing of VX-509 inhibits CYP3A4 and indicates that dose modification with frequently prescribed medicines (e.g., atorvastatin and methylprednisone) or limited concomitant use of certain medications (e.g. oral midazolam) with VX-509 may be required. We are seeking a collaborator for VX-509.

INFLUENZA

Background: Effects and Prevalence of Influenza

The CDC has estimated that in the United States more than 200,000 patients with influenza infection are hospitalized annually with respiratory and cardiac-related complications. While the number of influenza-related deaths varies significantly depending on the severity of the influenza season, the CDC has estimated the number of influenza-related deaths in the United States averages approximately 25,000 per year. In addition to vaccinations designed to prevent the spread of infection, we believe that there is a significant market for antiviral agents that could potentially be used to treat influenza. Currently, neuraminidase inhibitors oseltamivir (Tamiflu) and zanamivir (Relenza) are the antiviral agents that are used to treat influenza infection, but these drugs must be administered within 24 to 48 hours of initial infection in order to be effective and do not produce responses in a significant portion of patients.

VX-787

VX-787 is an investigational drug candidate intended for the treatment of influenza A, which is typically the predominate strain of influenza and includes H1 (pandemic) and H5 (avian) influenza strains. VX-787 aims to treat influenza A through a mechanism that is different from neuraminidase inhibitors. In March 2013, we announced data from a randomized, double-blind, placebo-controlled Phase 2 clinical trial that enrolled and dosed 104 healthy people (72 in the VX-787 arms; 32 in the placebo arm), 18 to 45 years of age, who volunteered to be experimentally exposed to an attenuated form of live H3N2 influenza A virus. In this clinical trial, we evaluated four dosing regimens of VX-787 given once daily for five days beginning 24 hours after infection with the influenza virus. The clinical trial met its primary endpoint, and patients treated with VX-787 had a statistically significant decrease in the amount of virus in nasal secretions (viral shedding) over the seven-day evaluation period as compared to patients who received placebo. Patients in the highest VX-787 dose group experienced influenza-like symptoms for a median of 1.9 days, compared to 3.7 days in the placebo group. In addition, 93 percent of patients in this dose group showed no clinical

symptoms of influenza after three days of treatment, compared to 41 percent of patients in the placebo group. In this clinical trial, VX-787 was generally well-tolerated, and all patients completed treatment. There were no serious adverse events or adverse events that led to discontinuation of treatment. Overall, the most

frequently reported class of adverse events in the VX-787 and placebo arms were those typically associated with influenza-like illness. We are seeking a collaborator to advance VX-787 development beyond this stage.

COMMERCIAL ORGANIZATION

Our commercial organization focuses on supporting sales of KALYDECO in the United States, Europe, Canada and Australia. Our sales force and managed markets organizations are responsible for promoting products to health care providers and obtaining reimbursement for products from third-party payors, including regulatory and governmental organizations in the United States and international markets. Following our October 2013 restructuring, we no longer have a U.S. field-based sales force focused on supporting sales of INCIVEK.

Our U.S. field-based CF commercial team includes approximately 15 therapeutic specialists who each have experience with CF. We focus our CF marketing efforts in the United States on a relatively small number of physicians and health care professionals who write most of the prescriptions for CF medicines. Many of these physicians and health care professionals are located at one of the approximately 110 accredited centers in the United States focused on the treatment of CF. In international markets, we have a small sales force to promote KALYDECO. We market our products and educate physicians by calling on 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.

RESEARCH

We believe that our integrated drug design approach has significantly enhanced our ability to discover and develop small molecule drug candidates directed at biologically complex targets associated with serious diseases. Our platform integrates biology, pharmacology, drug metabolism and pharmacokinetics, toxicology, material sciences, biophysics, medicinal chemistry and process chemistry, automation and information technologies in a coordinated fashion throughout the discovery process. We believe that our approach has been validated through our success in moving novel drug candidates into clinical trials and obtaining marketing approvals for KALYDECO and INCIVEK.

Currently, the disease areas of highest priority to us from a research perspective are: CF and other genetic diseases; cancer; neurological diseases and disorders and autoimmune diseases. We focus our research activities on products that would be prescribed by specialist physicians for the treatment of rare or life-threatening diseases, which are referred to as specialty markets. In CF, our research group is working to identify additional corrector compounds that could be included in future dual- and/or triple-combination treatment regimens that have the potential to provide additional benefits to patients with CF.

Driven by the complexity of the disease areas selected, we attempt to identify multiple approaches within each indication that, either as a stand-alone therapy or combination therapy, could provide treatment options that are transformational in nature. We select disease areas by mapping our research strengths onto disease areas with high unmet medical need, with an emphasis on indications, where based on scientific insights, we believe that we, independently or in collaboration with other third parties, will be able to discover, develop and commercialize important medicines for serious diseases.

Our past drug discovery efforts have produced a variety of drug candidates that have been commercialized or are in preclinical or clinical development. We believe our ongoing research programs will continue to create value for us by generating new drug candidates in areas of significant unmet medical need. We expect one or more compounds from our research programs to enter into clinical development in 2014.

To augment our internal research programs, we seek to collaborate with leading academic research institutions, government laboratories, foundations and other organizations in order to advance research in our areas of therapeutic interest as well as in areas of basic technological enablement. We have established relationships with organizations and consortia of organizations from around the world with expertise in areas of interest to us and intend to leverage that experience to further our research efforts.

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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. 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 CFFT in 1998. We entered into the current collaboration agreement with CFFT in 2004 and amended it several times to support research and development activities related to potentiator compounds and corrector compounds, including ivacaftor, lumacaftor and VX-661. Pursuant to an April 2011 amendment to the collaboration agreement, CFFT agreed to provide financial support for development activities for VX-661, a corrector compound discovered under the collaboration, and additional research and development activities directed at discovering new corrector compounds. We retain worldwide rights to develop and commercialize ivacaftor, lumacaftor, VX-661 and any other compounds discovered during the course of the research collaboration with CFFT and are obligated to pay CFFT tiered royalties ranging from single digits to sub-teens, calculated as a percentage of net sales, on ivacaftor, as well as lumacaftor, VX-661 and any other compounds discovered during the original research term or the research term that began in 2011. We have made the two commercial milestone payments required under the collaboration agreement upon achievement of certain sales levels of KALYDECO. Under the collaboration agreement, we also are obligated to make a total of two one-time commercial milestone payments upon achievement of certain sales levels for CFTR corrector compounds.

For each compound commercialized under this collaboration, we will have royalty obligations to CFFT until the expiration of patents covering that 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 patent applications in the United States and European Union covering the composition-of-matter of lumacaftor that expire in 2026, subject to potential patent life extensions. CFFT may terminate its funding obligations under the collaboration, as amended, in certain circumstances, in which case there will be a proportional reduction in the royalty rates and commercial milestone payments for certain CFTR corrector compounds. The collaboration also may be terminated by either party for a material breach by the other, subject to notice and cure provisions.

Alios BioPharma, Inc.

In June 2011, we entered into a license and collaboration agreement with Alios, a privately-held biotechnology company. Pursuant to the agreement, we are collaborating on the research, development and commercialization of VX-135, an HCV nucleotide analogue discovered by Alios. In 2012, we ended development of ALS-2158, a second HCV nucleotide analogue discovered by Alios and licensed to us pursuant to the agreement. We are responsible for all costs related to development and commercialization of VX-135. Our research program with Alios directed to the discovery of additional HCV nucleotide analogues that act on the HCV polymerase has ended.

Under the terms of the agreement, we have exclusive worldwide development and commercialization rights to VX-135. Upon entering into the agreement, we paid Alios a $60.0 million up-front payment. As of December 31, 2013, Alios had earned an aggregate of $60.0 million in development milestone payments pursuant to the agreement. The agreement provides for development milestone payments to Alios of up to an additional $312.5 million if VX-135 is approved and commercialized. Alios also is eligible to receive commercial milestone payments of up to $750.0 million, as well as tiered royalties on net sales of approved drugs.

We may terminate our agreement with Alios (i) upon 30 days' notice to Alios if we cease development of VX-135 after it has experienced a technical failure and/or (ii) upon 60 days' notice to Alios at any time after we complete Phase 2a clinical trials. The agreement also may be terminated by either party for a material breach by the other, and by Alios for our inactivity or if we challenge certain Alios patents, in each case subject to notice and cure provisions.

Unless earlier terminated, the agreement will continue in effect until the expiration of our royalty obligations, which expire on a country-by-country basis on the later of (a) the date the last-to-expire patent covering a licensed product expires or (b) ten years after the

first commercial sale in the country. In the United States and European Union, there are patent applications pending covering the composition-of-matter of VX-135 that, if granted, would expire in 2031.

Janssen Pharmaceutica NV

In June 2006, we entered into a license, development, manufacturing and commercialization agreement with Janssen. Under the agreement, we collaborated with Janssen on the development and commercialization of telaprevir. We have exclusive commercial rights to telaprevir in North America and led the development program for telaprevir in North America and the Janssen territories. Janssen has exclusive rights to commercialize INCIVO (telaprevir) outside of North America and the Far East. In the fourth quarter of 2013, we entered into an amendment to our agreement with Janssen, the 2013 Janssen Amendment. Pursuant to the 2013 Janssen Amendment, (i) Janssen paid us $152.0 million in the fourth quarter of 2013, (ii) Janssen's obligations to pay us royalties on net sales of INCIVO terminated after the fourth quarter of 2013, and (iii) Janssen received a fully-paid license to commercialize INCIVO in its territories, subject to the continued payment of certain third-party royalties on net sales of INCIVO in its territories.

The agreement will continue in effect until the later of (i) the expiration of the last-to-expire patent covering INCIVO or (ii) the last to expire third-party royalty payment on net sales of INCIVO. In the European Union, there is a patent covering the composition-of-matter of INCIVO that expires in 2026.

Mitsubishi Tanabe Pharma Corporation

We have a collaboration agreement with Mitsubishi Tanabe pursuant to which Mitsubishi Tanabe has a fully-paid license to manufacture and commercialize TELAVIC (telaprevir) to treat HCV infection in Japan and other specified countries in the Far East. This agreement was entered into in 2004 and amended in 2009. Pursuant to this agreement, Mitsubishi Tanabe provided financial and other support for the development and commercialization of telaprevir, made a $105.0 million payment to us in connection with the 2009 amendment of the collaboration agreement and made a $65.0 million payment to us in the fourth quarter of 2011 related to the commercialization of TELAVIC in Japan. There are no further payments due to us under this collaboration agreement. Mitsubishi Tanabe is responsible for its own development and manufacturing costs in its territory. Mitsubishi Tanabe may terminate the agreement at any time without cause upon 60 days’ prior written notice to us. 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 the last-to-expire patent covering TELAVIC. In Japan, we have a patent covering the composition-of-matter of TELAVIC that expires in 2021.

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 2 clinical trials. The following table sets forth the status of the 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)
KALYDECO (ivacaftor)	Granted (2027)	Application Pending (2025)
lumacaftor	Application Pending (2026)	Application Pending (2026)
VX-661	Granted (2027)	Application Pending (2027)
INCIVEK/INCIVO (telaprevir)	Granted (2025)	Granted (2026)
VX-135	Application Pending (2031)	Application Pending (2031)
VX-509	Granted (2026)	Application Pending (2025)
VX-787	Application Pending (2030)	Application Pending (2030)

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, our intellectual property holdings include:

- U.S. and foreign patent applications covering potentiator compounds and corrector compounds for the CFTR protein, including ivacaftor, lumacaftor and VX-661 and many other related compounds, and the use of those potentiators and correctors to treat CF.
- U.S. and foreign patents and patent applications covering telaprevir and other HCV protease and polymerase inhibitors and the use of these compounds to treat HCV infection.
- U.S. and foreign patent applications licensed from Alios covering VX-135 and the use of VX-135 to treat HCV infection.
- U.S. and foreign patents and patent applications covering inhibitors of a variety of kinase proteins, including VX-509, and the use of those inhibitors to treat autoimmune disease, including rheumatoid arthritis.
- U.S. and foreign patents and patent applications covering influenza virus inhibitors, including VX-787.
- U.S. and foreign patents and patent applications covering the manufacture, pharmaceutical compositions, related solid forms, formulations, dosing regimens and methods of use of these compounds, including our two marketed products ivacaftor and telaprevir.

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.

Ivacaftor was granted orphan drug status in the United States and the European Union. 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 are entitled to orphan drug exclusivity for ivacaftor in the United States, which means that the FDA may not approve another application to market ivacaftor for the same indication for a period of seven years from approval except in very limited circumstances. As a result of the seven-year orphan drug marketing exclusivity period, even if a competitor successfully challenges the ivacaftor patents, it could not obtain approval from the FDA to market ivacaftor for the treatment of patients with a G551D mutation in their CFTR gene in the United States until January 2019.

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 an international network of third parties, including sole source suppliers of certain components of our products and drug candidates, 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. We expect that we will continue for the foreseeable future to rely on third parties to meet most of our commercial supply needs and some of our clinical supply needs. We are in the process of establishing our own small-scale manufacturing capabilities, which we plan to use for clinical trial supplies and as a secondary source for 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, supply us with raw materials, and contract manufacturers in the European Union and the United States convert these raw materials into drug substance, and 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. A disruption in the clinical supply of ivacaftor could delay the completion of clinical trials and/or affect timelines for submitting an sNDA or NDA. Our supply chain includes a sole-source manufacturer that has the capability of providing its services to us from multiple sites. In 2013, we obtained an alternative source for the active ingredient of ivacaftor.

Manufacture of Co-formulated Ivacaftor/Lumacaftor

We are planning to use a continuous manufacturing process in order to manufacture co-formulated lumacaftor and ivacaftor tablets. We have established continuous manufacturing capabilities at our third-party manufacturer in the United Kingdom, which was used to produce a portion of the clinical trial supplies for our Phase 3 clinical trials of lumacaftor in combination with ivacaftor, and are in the process of establishing continuous manufacturing capabilities and seeking validation for these capabilities at our new facility located in Boston, Massachusetts. We are upgrading the continuous manufacturing process at our third-party manufacturer and are scheduled to begin producing co-formulated lumacaftor and ivacaftor intended for commercial use in mid-2014. Continuous process manufacturing connects the processes used in traditional batch manufacturing and uses on-line monitoring in order to increase control of the manufacturing process. The goal of continuous process manufacturing is to reduce material waste and cycle times and improve yield, which may result in reduced cost, reduced development and production timelines, lower inventories and increased market response flexibility. While continuous process manufacturing has been used in many industries, we believe that we would be the first company to seek approval for an NDA using a continuous manufacturing process. As a result, we also have designed and tested a non-continuous process for manufacturing co-formulated lumacaftor and ivacaftor tablets that we would seek to utilize if we experience delays associated with the continuous manufacturing process.

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. 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

A number of companies are seeking to identify and develop drug candidates for the treatment of CF, including Novartis, Pfizer, Genzyme, which is a division of Sanofi, and several private companies. While we are the first company to successfully develop a drug that treats the underlying cause of CF, KALYDECO is approved to treat only a small portion of patients with CF. Our competitors have research and development programs directed at identifying and developing CFTR potentiators, CFTR correctors and drug candidates with other mechanisms of action that seek to address the underlying cause of CF, and our success in rapidly developing and commercializing KALYDECO may increase the resources that our competitors allocate to the development of these potential treatments for CF. We do not believe that any of these competitive programs yet have entered late-stage clinical development. However, in the future, if one or more competing therapies are successfully developed as a treatment for patients with CF, our revenues from KALYDECO and/or our other CF drug candidates, if then approved, could face significant competitive pressure.

HCV Infection

The number and type of treatments for HCV infection has changed, and likely will continue to change, rapidly. Factors that may affect the market for any specific HCV treatment regimen include the introduction of new competitive drugs or drug combinations, increased sales from currently-approved drugs, adverse information regarding the safety characteristics or efficacy of the regimen, significant new information regarding potential treatment regimens being evaluated in clinical trials and enrollment by patients in clinical trials being conducted by us or our competitors.

Since 2011, we have marketed INCIVEK in direct competition with Merck & Co., Inc.'s VICTRELIS (boceprevir), another HCV protease inhibitor. In the fourth quarter of 2013, the FDA approved Gilead's SOVALDI (sofosbuvir), an HCV nucleotide analogue NS5B polymerase inhibitor and Janssen's OLYSIO™ (simeprevir), the third HCV protease inhibitor. Each of these direct-acting antiviral drugs are generally prescribed in combination with peg-IFN and RBV. Due to increased competition from newly introduced competitive therapies and our reduced promotion of INCIVEK, we expect that only a small portion of our net product revenues in 2014 will be due to INCIVEK.

On the basis of clinical data reported by our competitors from numerous late-stage clinical trials, it appears likely that the recent approval of SOVALDI and OLYSIO could be quickly followed by drugs to be co-administered in all-oral regimens that do not require peg-IFN, an injectable. Many companies are seeking to develop all-oral treatment regimens for HCV infection that could render uncompetitive current and future treatment regimens that include the administration of peg-IFN by injection. Many of our competitors' potential all-oral treatment regimens are more advanced than VX-135 combination regimens, including all-oral treatment regimens that are being evaluated in Phase 3 clinical trials being conducted by Gilead, Abbvie and BMS. While the development and regulatory timelines for these drug candidates are subject to risk and uncertainty, we believe that (i) substantial additional clinical data regarding potential all-oral treatment regimens will become available in 2014 and (ii) it is possible that one or more all-oral treatment regimens for genotype 1 HCV infection could be commercially available as soon the second half of 2014. As a result, if we are successful in developing an all-oral treatment regimen that includes VX-135, we expect that our all-oral treatment regimen would compete directly with several all-oral treatment regimens that were approved several years prior to the approval of our all-oral treatment regimen.

Where companies have control of multiple drug candidates that span different mechanisms of action, they typically are investigating combination regimens of those drug candidates, with or without the addition of RBV. In addition, many companies, including us, are pursuing a strategy of evaluating drug candidates they control in combination with drug candidates controlled by third parties. For example, we entered into a non-exclusive collaboration to evaluate VX-135 in combination with BMS's HCV NS5A inhibitor daclatasvir, and BMS is evaluating daclatasvir in combination with Gilead's SOVALDI. There can be no assurance that third parties will agree to enter into or expand existing collaborative arrangements with respect to the development of combination regimens for the treatment of HCV infection that include VX-135.

GOVERNMENT REGULATION

The research, development, testing, manufacture, quality control, approval, labeling, packaging, storage, record keeping, promotion, advertising, distribution and marketing of our products and drug candidates are subject to extensive regulation by United States and foreign governmental authorities.

United States Government Regulation

New Drug Application Approval Processes

In the United States, the FDA regulates drugs under the Federal Food, Drug and Cosmetic Act, or the FDCA, and implementing regulations. The process of obtaining regulatory approvals and the subsequent compliance with applicable federal, state, local and foreign statutes and regulations require the expenditure of substantial time and financial resources. 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 to administrative or judicial sanctions, any of which could have a material adverse effect on us. These sanctions could include:

- refusal to approve pending applications;
- withdrawal of an approval;
- imposition of a clinical hold;
- warning letters;
- product seizures;
- total or partial suspension of production or distribution; or
- injunctions, fines, disgorgement, or civil or criminal penalties.

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 investigational new drug, or 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 to assure that the facilities, methods and controls are adequate to preserve the product’s identity, strength, quality and purity; 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. Preclinical or nonclinical testing typically continues even after the IND is submitted. In addition to including the results of the preclinical studies, the IND also will include a protocol detailing, among other things, the objectives of the initial clinical trial and the parameters to be used in monitoring safety. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30-day time period, places the IND on clinical hold. If an IND is placed on clinical hold, the IND sponsor and the FDA must resolve any outstanding concerns before clinical trials can begin. A clinical hold may occur at any time during the life of an IND, and may affect one or more specific clinical trials or all clinical trials conducted under the IND.

All clinical trials must be conducted under the supervision of one or more qualified investigators in accordance with GCP. They must be conducted under protocols detailing the objectives of the trial, dosing procedures, subject selection and exclusion criteria and the safety and effectiveness criteria to be evaluated. Each protocol and any amendments must be submitted to the FDA as part of the IND, and 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. An institutional review board, or IRB, at each institution participating in the clinical trial must review and approve the protocol and any amendments before a clinical trial commences or continues at that institution, approve the information regarding the clinical trial and the consent form that must be provided to each trial subject or his or her legal representative, and monitor the clinical trial until completed and otherwise comply with IRB regulations.

Clinical trials typically are conducted in three sequential phases that may overlap or be combined:

- 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. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug candidate has been associated with unexpected serious harm to healthy volunteers or patients.

We estimate that it generally takes 10 to 15 years, or possibly longer, to discover, develop and bring to market a new pharmaceutical product in the United States, as outlined below:

Phase	Estimated Duration
Discovery	2 to 4 years
Preclinical	1 to 2 years
Phase 1	1 to 2 years
Phase 2	2 to 4 years
Phase 3	2 to 4 years
FDA approval	6 months to 2 years

During the development of a new drug, sponsors are given opportunities to meet with the FDA at certain points. These points may be prior to submission of an IND, at the end of Phase 2 testing, and before an NDA is submitted. Meetings at other times may be requested. These meetings can provide an opportunity for the sponsor to share information

about the data gathered to date, for the FDA to provide advice, and for the sponsor and FDA to reach agreement on the next phase of

development. Sponsors typically use the end of Phase 2 meeting to discuss their Phase 2 clinical results and present their plans for the pivotal Phase 3 clinical trial that they believe will support approval of the drug candidate.
Concurrently with clinical trials, companies usually complete additional animal safety studies and also must develop additional information about the chemistry and physical characteristics of the drug and finalize a process for manufacturing the product in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the drug candidate, and the manufacturer must develop methods for testing the quality, purity and potency of the final products. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the drug candidate does not undergo unacceptable deterioration over its shelf-life.
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 may not approve an NDA if the applicable regulatory criteria are not satisfied or may require additional clinical or other data. Even if such data are submitted, the FDA may ultimately decide that the NDA does not satisfy the criteria for approval. 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.
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. The complete response letter usually describes all of the specific deficiencies in the NDA identified by the FDA. If a complete response letter is issued, the applicant may either resubmit the NDA, addressing all of the deficiencies identified in the letter, or withdraw the application.
Expedited Review and Approval
The FDA has various programs, including Fast Track, priority review, and accelerated approval, that are intended to expedite or simplify the process for reviewing drug candidates, and/or provide for approval on the basis of surrogate endpoints. Even if a drug candidate qualifies for one or more of these programs, the FDA may later decide that the drug candidate no longer meets the conditions for qualification or that the time period for FDA review or approval will not be shortened. Generally, drug candidates that may be eligible for these programs are those for serious or life-threatening conditions, those with the potential to address unmet medical needs, and those that offer meaningful benefits over existing treatments. For example, Fast Track is a process designed to facilitate the development, and expedite the review of drug candidates to treat serious diseases and fill an unmet medical need. Priority review is designed to give drug candidates that offer major advances in treatment or provide a treatment where no adequate therapy exists an initial review within six months as compared to a standard review time of ten months. Although Fast Track and priority review do not affect the standards for approval, the FDA will attempt to facilitate early and frequent meetings with a sponsor of a Fast Track designated drug candidate and expedite review of the application for a drug candidate designated for priority review. Accelerated approval provides an earlier approval of drugs that treat serious diseases, and that fill an unmet medical need based on a surrogate endpoint, which is a laboratory measurement or physical sign used as an indirect or substitute measurement representing a clinically meaningful outcome. As a condition of approval, the FDA may require that a sponsor of a product receiving accelerated approval perform post-marketing clinical trials.
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.

Drug manufacturers and other entities involved in the manufacture and distribution of approved products are required to register with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and some state agencies for compliance with cGMP and other laws.

We rely, and expect to continue to rely, on third parties for the production of our products. Future FDA and state 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.

From time to time, new legislation is enacted that changes the statutory provisions governing the approval, manufacturing and marketing of products regulated by the FDA. 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 changed.

Patent Term Restoration and Marketing Exclusivity

Depending upon the timing, duration and specifics of FDA approval of the use of our drugs, some of our United States patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, referred to as the Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit a patent restoration term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. However, patent term restoration cannot extend the remaining term of a patent beyond a total of 14 years from the product's approval date. The patent term restoration period is generally one-half the time between the effective date of an IND, and the submission date of an NDA, plus the time between the submission date of an NDA and the approval of that application. Only one patent applicable to an approved product is eligible for the extension and the extension must be applied for prior to expiration of the patent. The United States Patent and Trademark Office, in consultation with the FDA, reviews and approves the application for any patent term extension or restoration. In the future, we may apply for restorations of patent term for some of our currently owned or licensed patents to add patent life beyond their current expiration date, depending on the expected length of clinical trials and other factors involved in the submission of the relevant NDA.

Market exclusivity provisions under the FDCA also can delay the submission or the approval of certain applications. The FDCA provides a five-year period of non-patent marketing exclusivity within the United States to the first applicant to gain approval of an NDA for a new chemical entity. For a new chemical entity that qualifies for Orphan Drug designation, the FDCA provides such marketing exclusivity for a period of seven years. A product is a new chemical entity if the FDA has not previously approved any other new product containing the same active moiety, which is the molecule responsible for the action of the drug substance. During the exclusivity period, the FDA may not accept for review an abbreviated new drug application, or ANDA, or a 505(b)(2) NDA submitted by another

company for another version of such product where the

applicant does not own or have a legal right of reference to all the data required for approval. However, an application may be submitted after four years if it contains a certification of patent invalidity or non-infringement. The FDCA also provides three years of marketing exclusivity for an NDA, 505(b)(2) NDA or supplement to an existing NDA if new clinical investigations, other than bioavailability studies, that were conducted or sponsored by the applicant are deemed by the FDA to be essential to the approval of the application, for example, for new indications, dosages, or strengths of an existing drug. This three-year exclusivity covers only the conditions associated with the new clinical investigations and does not prohibit the FDA from approving ANDAs for drugs containing the original active agent.

Pediatric Exclusivity

Section 505A of the FDCA, as amended by the FDA Amendments Act of 2007, permits certain drugs to obtain an additional six months of exclusivity, if the sponsor submits information requested in writing by the FDA, or a written request, relating to the use of the drug in children. The FDA may not issue a written request for clinical trials on unapproved or approved indications or where it determines that information relating to the use of a drug in a pediatric population, or part of the pediatric population, may not produce health benefits in that population.

Foreign Regulation

In addition to regulations in the United States, we are subject to a variety of foreign regulations governing clinical trials and commercial sales and distribution of our products. 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. The decentralized procedure provides for approval by one or more "concerned" member states based on an assessment of an application performed by one member state, known as the "reference" member state. Under the decentralized approval procedure, an applicant submits an application, or dossier, and related materials to the reference member state and concerned member states. The reference member state prepares a draft assessment and drafts of the related materials within 120 days after receipt of a valid application. Within 90 days of receiving the reference member state's assessment report, each concerned member state must decide whether or not to approve the assessment report and related materials. If a member state does not recognize the marketing authorization, the disputed points are eventually referred to the European Commission, whose decision is binding on all member states.

Orphan Drug Designation

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, or more than 200,000 people in the United States and for which there is no reasonable expectation that the cost of developing and making available in the United States a drug for this type of disease or condition will be recovered from sales in the United States for that drug. Orphan drug designation must be requested before submitting an NDA. After the FDA grants orphan drug designation, the identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. Orphan drug designation does not convey any advantage in or shorten the duration of the regulatory review and approval process. KALYDECO and lumacaftor 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 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, except in very limited circumstances, for seven years. Orphan drug exclusivity, however, also could block the approval of our drug candidates for seven years if a competitor 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.

As in the United States, we may apply for designation of a drug candidate as an orphan drug for the treatment of a specific indication in the European Union before the application for marketing authorization is made. Orphan drugs in

Europe enjoy economic and marketing benefits, including up to 10 years of market exclusivity for the approved indication unless another applicant can show that its product is safer, more effective or otherwise clinically superior to the orphan-designated product.

The FDA and foreign regulators expect holders of exclusivity for orphan drugs, such as KALYDECO, to assure the availability of sufficient quantities of their orphan drugs to meet the needs of patients. Failure to do so could result in the withdrawal of marketing exclusivity for the orphan drug.

Breakthrough Therapy Designation

In July 2012, the Food and Drug Administration Safety and Innovation Act, or FDASIA, was enacted, amending the FDCA. As part of FDASIA, Congress created a new drug designation called "Breakthrough Therapy." This designation is intended to facilitate expedited development and review of a compound which, alone or in combination with one or more other compounds, is intended to treat a serious or life-threatening disease or condition and for which preliminary clinical evidence indicates that the compound may demonstrate substantial clinical improvement over existing therapies. Breakthrough Therapy designation may be requested at the filing of, or as an amendment to, an IND based on criteria established by the FDA.

Actions identified in FDASIA that may expedite the development and review of a Breakthrough Therapy include, as appropriate: holding meetings with the sponsor and the review team throughout the development of the drug; involving senior managers and experienced review staff, as appropriate, in a collaborative, cross-disciplinary review; and assigning a cross-disciplinary project lead for the FDA review team to facilitate efficient review of the development program and serve as a scientific liaison between the review team and the sponsor. We expect that over time the FDA will develop regulations and/or provide additional guidance regarding the development of drug candidates that receive Breakthrough Therapy designation. As this is an evolving regulatory designation, we cannot determine the specific implications of the Breakthrough Therapy designations on our development programs.

Reimbursement

Sales of our products depend, in part, 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 provides funding for the federal government to compare the effectiveness of different treatments for the same illness. A plan for the research will 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 will 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 Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act of 2010, which is referred to as the ACA, was enacted in March 2010 and is designed to expand coverage for the uninsured while at the same time containing overall health care costs. With regard to pharmaceutical products, among other things, the ACA is designed to expand and increase industry rebates for drugs covered under Medicaid programs, impose an annual fee on branded pharmaceutical manufacturers and make changes to the coverage requirements under the Medicare Part D program. In 2013, 2012 and 2011, our rebates associated with the Medicare Part D "donut hole" were $1.9 million, $1.8 million and $1.4 million, respectively. In 2013 and 2012, we recorded $10.4 million and $1.8 million, respectively, in sales, general and administrative expenses related to the branded prescription drug fee established pursuant to the ACA. We were not subject to this fee prior to 2012. The branded prescription drug fee is not tax deductible. We cannot predict all of the effects of the ACA on pharmaceutical companies as many of the ACA reforms require the promulgation of detailed regulations implementing the statutory provisions, which has not yet occurred.

In Europe and many other foreign countries, the success of KALYDECO, and any other drug candidates we may develop, depends largely on obtaining and maintaining government reimbursement, because in many foreign countries patients are unlikely to use 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 product can begin while the reimbursement rate that a company will receive in future periods 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 European Union provides options for its member states to restrict the range of drugs for which their national health insurance systems provide reimbursement and to 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 allow favorable reimbursement and pricing arrangements for any of our products.

Other United States Regulations

Pharmaceutical companies also are subject to various federal and state laws pertaining to health care "fraud and abuse," including anti-kickback laws and false claims laws, and the reporting of payments to physicians and teaching hospitals.

Anti-kickback Laws

U.S. federal laws prohibit fraud and abuse involving state and federal health care programs, such as Medicare and Medicaid. These laws are interpreted broadly and enforced aggressively by various state and federal agencies, including the Centers for Medicare & Medicaid Services, or CMS, the Department of Justice, the Office of Inspector General for HHS and various state agencies. These anti-kickback laws prohibit, among other things, 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 furnishing, arranging for or recommending of an item or service that is reimbursable, in whole or in part, by a federal health care program. Remuneration is broadly defined to include

anything of value, such as, cash payments, gifts or gift certificates, discounts, or the furnishing of services, supplies or equipment. The anti-kickback laws are broad and prohibit many arrangements and practices that are lawful in businesses outside of the health care industry.

The penalties for violating the anti-kickback laws can be severe. The sanctions include criminal and civil penalties, and possible exclusion from the federal health care programs. Many states have adopted laws similar to the federal anti-kickback laws, and some apply to items and services reimbursable by any payor, including third-party payors.

State and Federal Prohibitions on False Claims

The federal False Claims Act imposes liability on any person or entity that, among other things, knowingly presents, or causes to be presented, a false or fraudulent claim for payment to the federal government. Under the False Claims Act, a person acts knowingly if he has actual knowledge of the information or acts in deliberate ignorance or in reckless disregard of the truth or falsity of the information. Specific intent to defraud is not required. Provisions of the False Claims Act allow a private individual to bring an action on behalf of the federal government and to share in any amounts paid by the defendant to the government in connection with the action. The number of filings under these provisions has increased significantly in recent years. When an entity is determined to have violated the False Claims Act, it may be required to pay up to three times the actual damages sustained by the government, plus civil penalties for each false claim. Conduct that violates the False Claims Act may also lead to exclusion from the federal health care programs. Given the number of claims likely to be at issue, potential damages under the False Claims Act for even a single inappropriate arrangement could be significant. In addition, various states have enacted similar laws modeled after the False Claims Act that apply to items and services reimbursed under Medicaid and other state health care programs, and, in several states, such laws apply to claims submitted to all payors.

Federal Prohibitions on Health Care Fraud and False Statements Related to Health Care Matters

Under the administrative simplification provisions of the Health Insurance Portability and Accountability Act of 1996, or HIPAA, and state laws there are numerous regulations for protecting the privacy and security of protected health information. Additional administrative simplification provisions created the following federal crimes: health care fraud, false statements relating to health care matters, theft or embezzlement in connection with a health benefit program and obstruction of criminal investigation of health care offenses. The health care fraud statute prohibits knowingly and willfully executing a scheme to defraud any health care benefit program, including a private insurer. The false statements statute prohibits knowingly and willfully falsifying, concealing, or covering up a material fact or making any materially false, fictitious, or fraudulent statement in connection with the delivery of or payment for health care benefits, items, or services. The theft or embezzlement statute prohibits knowingly and willfully embezzling, stealing or otherwise converting or misapplying the money or property of a health care benefit program. The obstruction of criminal investigations of health care offenses statute prohibits willfully preventing, obstructing, misleading or delaying the communication of information and records relating to a violation of a federal health care offense to a criminal investigator. A violation of any of these laws is a felony and may result in fines, or exclusion from the federal health care programs.

Physician Payment Sunshine Act

The Physician Payment Sunshine Act will require pharmaceutical manufacturers to report annually to the Secretary of HHS payments or other transfers of value made by that entity to physicians and teaching hospitals. In February 2013, regulations were released that contain detailed guidance regarding the information that must be collected and reported. We were required to collect information regarding such payments starting in August 2013 and will be required to begin reporting such information in March 2014. Over the next several years, we will need to continue to dedicate significant resources to enhance our systems and processes in order to comply with these regulations. Failure to comply with the reporting requirements would result in significant civil monetary penalties. Similar laws have been enacted or are under consideration in foreign jurisdictions, including France which has adopted the Loi Bertrand, or French Sunshine Act, which became effective in 2013.

The Foreign Corrupt Practices Act

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.

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Other Regulations

In addition to the statutes and regulations described above, we also are subject to regulation in the United States under the Occupational Safety and Health Act, the Environmental Protection Act, the Toxic Substances Control Act, the Resource Conservation and Recovery Act and other federal, state, local and foreign statutes and regulations, now or hereafter in effect.

EMPLOYEES

As of December 31, 2013, we had approximately 1,800 employees, which was a decrease of 18% from approximately 2,200 on December 31, 2012. Of these employees, approximately 1,500 were based in the United States, approximately 200 were based in Europe and approximately 100 were based in Canada. Our scientific staff members have diversified experience and expertise in molecular and cell biology, biochemistry, synthetic organic chemistry, protein X-ray crystallography, protein nuclear magnetic resonance spectroscopy, microbiology, computational chemistry, 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 in France and Spain. Science magazine named Vertex as one of its top employers in the life sciences in 2011, 2012 and 2013. 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 X, "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 Alios as of December 31, 2013 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. We have research sites located in San Diego, California; Coralville, Iowa; Montreal, Canada and Milton Park, U.K. We also have an office in Washington, D.C. We have established our European headquarters in Switzerland and have offices in Australia, France, Germany, Ireland, Spain, the Netherlands and the United Kingdom.

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.	58	Chairman of the Board, Chief Executive Officer and President
Stuart A. Arbuckle	48	Executive Vice President and Chief Commercial Officer
Kenneth L. Horton, J.D.	47	Executive Vice President and Chief Legal Officer
Peter Mueller, Ph.D.	57	Executive Vice President, Global Research and Development, and Chief Scientific Officer
Ian F. Smith	48	Executive Vice President and Chief Financial Officer
Thomas Connolly	56	Senior Vice President, Human Resources
Megan Pace	41	Senior Vice President, Corporate Communications
Amit K. Sachdev, J.D.	46	Senior Vice President, Global Government Strategy, Market Access and Value
Paul M. Silva	48	Senior Vice President and Corporate Controller
David Altshuler, M.D., Ph.D.	49	Director
Joshua S. Boger, Ph.D.	62	Director
Terrence C. Kearney	59	Director
Yuchun Lee	48	Director
Margaret G. McGlynn	54	Director
Wayne J. Riley, M.D.	54	Director
Bruce I. Sachs	54	Director
Elaine S. Ullian	66	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 was a director and the non-executive Vice Chairman of the board of Shire plc, a specialty biopharmaceutical company, from 2006 to January 2012, and was also a member of the Board of Directors of Millennium Pharmaceuticals, Inc. from October 2007 until it was acquired in June 2008. Dr. Leiden received his M.D., Ph.D. and B.A. degrees from the University of Chicago.

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 currently is a member of the Board of Directors of the Cancer Support Community, an international non-profit organization dedicated to providing support, education and hope to people affected by cancer. Mr. Arbuckle holds a BSc in pharmacology and physiology from the University of Leeds.

Mr. Horton is our Executive Vice President and Chief Legal Officer, a position he has held since June 2012. Prior to joining us, Mr. Horton served as General Counsel and Executive Vice President of Corporate Development at Nordion Inc. (formerly MDS Inc.), a global health science company, from 2005 to 2011. He joined MDS from PerkinElmer, Inc., where he was Vice President, Acquisitions, Ventures and General Counsel for the Life and Analytical Sciences

business unit. Mr.

Horton began his legal career practicing corporate law at Ropes & Gray in Boston after working as a strategy consultant in the United States and Europe. Mr. Horton currently serves on the Board of Advisors for Beth Israel Deaconess-Needham Hospital and was formerly Chairman of Lumira Capital. Mr. Horton holds an A.B. from Dartmouth College, a J.D. from Harvard Law School and was awarded the D.A.A.D. Direktstipendium for study at the Universitaet Bonn.

Dr. Mueller is our Executive Vice President, Global Research and Development, a position he has held since May 2009, and has been our Chief Scientific Officer since July 2003. Dr. Mueller was our Executive Vice President, Drug Innovation and Realization, from February 2006 to May 2009, and our Senior Vice President, Drug Discovery and Innovation, from July 2003 to February 2006. Prior to joining us, Dr. Mueller was the Senior Vice President, Research and Development, of Boehringer Ingelheim Pharmaceuticals, Inc., with responsibility for the development of all drug candidates in the company's portfolio in North America. He led research programs in the areas of immunology, inflammatory cardiovascular disease and gene therapy on a global basis. During his time with Boehringer Ingelheim, Dr. Mueller oversaw the discovery of numerous development candidates and held several positions in basic research, medicinal chemistry and management. Dr. Mueller received both an undergraduate degree and a Ph.D. in chemistry at the Albert Einstein University of Ulm, Germany, where he also holds a Professorship in Theoretic Organic Chemistry. He completed fellowships in quantum pharmacology at Oxford University and in biophysics at Rochester University.

Mr. Smith is our Executive Vice President and Chief Financial Officer, a position he has held since February 2006. From November 2003 to February 2006, he was our Senior Vice President and Chief Financial Officer, and from October 2001 to November 2003, he served as our Vice President and Chief Financial Officer. 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 currently is a member of the Boards of Directors of Acorda Therapeutics, Inc., a drug development company, and Infinity Pharmaceuticals, Inc., a drug development company. 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. Connolly is our Senior Vice President, Human Resources, a position he has held since August 2013. Mr. Connolly served as our Vice President, Human Resources from September 2012 through August 2013. From January 2009 to September 2012, Mr. Connolly was a Senior Vice President and the Chief Human Resources Officer at MF Global. Prior to MF Global, he held human resources leadership positions at UBS, Goldman Sachs, Citibank, Aetna and Lehman Brothers. He currently serves as a special advisor on human resources and other organizational matters to Save the Children, and serves on the Advisory Board of the Center for Innovation & Change Leadership at Suffolk University. Mr. Connolly holds a B.S. in Psychology from the University of Connecticut, an M.B.A. from Leonard N. Stern School of Business at New York University, an M.S. in Industrial/Organizational Psychology from Stevens Institute of Technology and an M.S. in Health Care Administration from the University of Phoenix.

Ms. Pace is our Senior Vice President, Corporate Communications, a position she has held since July 2012. Ms. Pace served as our Vice President, Corporate Communications from May 2010 through July 2012. Prior to joining us, Ms. Pace was a Senior Director at Genentech, Inc., a biotechnology company, from 2005 through April 2010, where she led the team responsible for public affairs, product public relations and patient advocacy. Prior to Genentech, she held government affairs and public relations roles at Eli Lilly & Company, and worked at Porter Novelli, a global public relations firm, where she managed disease awareness and public health campaigns for several biopharmaceutical companies and government agencies. Ms. Pace holds a B.A. from the College of Charleston.

Mr. Sachdev is our Senior Vice President, Global Government Strategy, Market Access and Value, a role he assumed in February 2013. As a Senior Vice President, he has led our government affairs, public policy and patient advocacy functions since he joined us in July 2007 and built and managed our Canadian business operations from October 2010 through February 2013. Mr. Sachdev served as Executive Vice President, Health of the Biotechnology Industry Organization (BIO) from April 2005 through June 2007. Mr. Sachdev was the Deputy Commissioner for Policy at the FDA from April 2004 through April 2005, and held several other senior positions within the FDA from September 2002 through April 2004. From 1998 to 2002, Mr. Sachdev served as Majority Counsel to the Committee on Energy and Commerce in the United States House of Representatives. From 1993 to 1997, Mr. Sachdev practiced law, first at

the Chemical Manufacturers Association, and then with the law firm of Ropes & Gray. Mr. Sachdev holds a B.S from Carnegie Mellon University, and a J.D. from Emory University School of Law.

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. Altshuler has been a member of our Board of Directors since May 2012. Dr. Altshuler is the Director of the Program in Medical and Population Genetics at the Broad Institute of Harvard University and the Massachusetts Institute of Technology, a position he has held since 2003. He has served as the Institute's Deputy Director and Chief Academic Officer since 2009. He is one of four founding members of the Broad Institute, a research collaboration of Harvard, MIT, The Whitehead Institute and the Harvard Hospitals. Dr. Altshuler joined the faculty at Harvard Medical School and the Massachusetts General Hospital in 2000 and has held the academic rank of Professor of Genetics and Medicine since 2008. He has served as Adjunct Professor of Biology at MIT since 2012. 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.

Dr. Boger is the founder of Vertex and has been a director since our inception in 1989. He was our Chief Executive Officer from 1992 through May 2009. He was our Chairman of the Board from 1997 until May 2006 and our President from our inception until December 2000, and from 2005 through February 2009. He was our Chief Scientific Officer from 1989 until May 1992. Prior to founding Vertex in 1989, Dr. Boger held the position of Senior Director of Basic Chemistry at Merck Sharp & Dohme Research Laboratories in Rahway, New Jersey, where he headed both the Department of Medicinal Chemistry of Immunology & Inflammation and the Department of Biophysical Chemistry. Dr. Boger holds a B.A. in chemistry and philosophy from Wesleyan University and M.S. and Ph.D. degrees in chemistry from Harvard 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. 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 has served as an Executive in Residence (XIR) and Partner of General Catalyst Partners, a venture capital firm, since April of 2013. 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. Since July 2011, Ms. McGlynn has 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. 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.

Dr. Riley has been a member of our Board of Directors since July 2010. Dr. Riley is Clinical Professor of Medicine, Vanderbilt University School of Medicine and Adjunct Professor of Healthcare Management, Owen Graduate School of Management at Vanderbilt University. From January 2007 until July 2013, Dr. Riley was President and Chief Executive Officer of Meharry Medical College. At Meharry he held the rank of tenured Professor of Internal Medicine and was a Senior Health Policy Associate at the Robert Wood Johnson Center for Health Policy at Meharry. From May 2004 to

December 2006, Dr. Riley served as a corporate officer and member of the executive management team as Vice President and Vice Dean for Health Affairs and Governmental Relations and Associate Professor of Medicine at Baylor College of Medicine, and Assistant Chief of Medicine at Ben Taub General Hospital. Dr. Riley is a member of the Board of Directors of HCA Holdings, Inc., the parent company of Hospital Corporation of America, a leading operator of hospitals and health facilities, where he serves on the Audit & Compliance Committee and the Nominating and Corporate Governance Committee and is the Chair of the Patient Safety and Quality Committee. Dr. Riley formerly served as a Director of Pinnacle Financial Partners and of the Nashville Branch Board of the Federal Reserve Bank of Atlanta. Dr. Riley earned a B.A. from Yale University, an M.P.H. in health systems management from Tulane University School of Public Health & Tropical Medicine, an M.D. from the Morehouse School of Medicine and an M.B.A. from Rice University's Jones Graduate School of Management.

Mr. Sachs has been a member of our Board of Directors since 1998. He 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 at Xylogics, Inc. Mr. Sachs was a director of BigBand Networks, Inc., a network-based platform company, from 2005 through June 2009. 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. From 1996 through January 2010, she 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 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.

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

We are investing significant resources in our development program for lumacaftor (VX-809) in combination with ivacaftor and, if the results of clinical trials of this combination therapy, the anticipated or actual timing of marketing approvals for this combination therapy, or the market acceptance of this combination therapy, if approved, including treatment reimbursement levels agreed to by third-party payors, are unfavorable or do not meet the expectations of investors or public market analysts, our business will be materially harmed and the market price of our common stock would likely decline.

We are investing significant resources in our development program for lumacaftor in combination with ivacaftor as a potential treatment for patients with CF who have two copies (homozygous) of the F508del mutation in their CFTR gene. In February 2013, we initiated the Phase 3 clinical development program for lumacaftor in combination with ivacaftor. We initiated this program based primarily on data from a Phase 2 clinical trial in which a relatively small number of patients received lumacaftor as a monotherapy for 28 days, followed by lumacaftor in combination with ivacaftor for 28 days. The pattern of lung function response observed in both Cohort 2 and Cohort 3 of our Phase 2 clinical trial was similar, with a decline in FEV_1 during the lumacaftor monotherapy dosing period followed by a statistically significant increase in FEV_1 during the lumacaftor and ivacaftor combination dosing period. In addition, the increase in FEV_1 observed in our Phase 2 clinical trial of lumacaftor in combination with ivacaftor was less than the increase in FEV_1 observed in comparable Phase 2 clinical trials of ivacaftor in patients with CF who have one copy of the G551D mutation in their CFTR gene.

We have enrolled approximately 550 patients with CF who are homozygous for the F508del mutation in each of the two Phase 3 clinical trials evaluating lumacaftor in combination with ivacaftor, which are referred to as TRAFFIC and TRANSPORT, for a total of approximately 1,100 patients. We expect that we will obtain data from this Phase 3 clinical development program in mid-2014. In TRAFFIC and TRANSPORT, lumacaftor is being evaluated in combination with ivacaftor over a significantly longer dosing period of 24 weeks and without the monotherapy lead-in period that was part of the Phase 2 clinical trial. In order to obtain approval for lumacaftor in combination with ivacaftor, we will need to show that lumacaftor in combination with ivacaftor is safe and effective in a significantly larger number of patients than were involved in the Phase 2 clinical trial, over the significantly longer 24-week combination dosing period.

If the data from our ongoing clinical trials or non-clinical studies of lumacaftor in combination with ivacaftor regarding the safety or efficacy of this combination are not favorable, the FDA and comparable foreign regulatory authorities may not approve this combination regimen and/or we may be forced to delay or terminate the development of this combination regimen, which would materially harm our business. Further, even if we gain marketing approvals for this combination therapy from the FDA and comparable foreign regulatory authorities in a timely manner, we cannot be sure that this combination therapy will be commercially successful. If the results of TRAFFIC and TRANSPORT, the anticipated or actual timing of marketing approvals for this combination therapy, or the market acceptance of this combination therapy, 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 expect to incur future losses, and we may not become profitable in future periods.

Over the past three years a majority of our revenues have been due to sales of INCIVEK. As a result of declines in INCIVEK revenues, we expect to incur a significant operating loss in 2014 and expect to continue to incur operating losses until we are able to substantially increase product revenues from the sale of therapies for the treatment of CF. There can be no assurance that we will be successful in expanding the label for ivacaftor or obtaining approval for

lumacaftor in combination with ivacaftor. Our net losses will have an adverse effect on, among other things, our shareholders' equity, total assets and working capital. We expect that losses will fluctuate from quarter to quarter and year to year, and that such fluctuations may be substantial. We cannot predict when we will become profitable, if ever.

Our future revenues from KALYDECO are dependent, among other factors, on the outcomes of reimbursement discussions in international markets, our ongoing clinical trials and discussions with regulatory authorities regarding the potential for ivacaftor as a treatment for additional patient populations.

In 2012, we obtained approval to market KALYDECO (ivacaftor) for the treatment of patients with CF six years of age and older with the G551D mutation in the CFTR gene. Since its approval in the first quarter of 2012, most patients six years of age and older in the United States and Europe who have the G551D mutation in the CFTR gene have started treatment with KALYDECO. We are in discussions with relevant agencies in Australia and Canada regarding public reimbursement for the cost of KALYDECO for patients with CF six years of age and older in these countries who have the G551D mutation in their CFTR gene. There can be no assurance that we will be able to obtain, or obtain on a timely basis, appropriate reimbursement for KALYDECO in these international markets.

In order to expand the market for ivacaftor, we need to demonstrate that ivacaftor is safe and effective in additional patient populations. We submitted an sNDA to the FDA and an MAA variation in the European Union in September 2013 and October 2013, respectively, seeking approval to market ivacaftor for the treatment of patients with CF six years of age and older who have specified other mutations in their CFTR gene. These submissions incorporated clinical data from our first ivacaftor label-expansion Phase 3 clinical trial. In December 2013, we announced data from a Phase 3 clinical trial evaluating ivacaftor as a potential treatment for patients with CF who have the R117H mutation in their CFTR gene. This clinical trial did not meet its primary endpoint. However, we believe that a pre-specified subgroup analysis demonstrated a clinical benefit for patients 18 years of age and older with CF who have the R117H mutation on at least one allele. We plan to meet with the FDA in early 2014 to discuss these results and the potential submission of an sNDA for patients with CF who have the R117H mutation on at least one allele. We also are conducting a Phase 3 clinical trial to evaluate ivacaftor as a potential treatment for patients two to five years of age with CF who have specific mutations in their CFTR gene and a Phase 2 clinical trial to evaluate ivacaftor in patients with CF who have residual CFTR function.

These clinical trials and our discussions with regulatory authorities are subject to the same risks and uncertainties that are described in these risk factors with respect to the development of our drug candidates. There can be no assurance that the results from our clinical trials of ivacaftor or the data included in our submissions to regulatory authorities will be sufficient to obtain approval for use of ivacaftor in patients with other mutations in their CFTR gene or in any children two to five years of age with CF.

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

KALYDECO and any drugs we develop in the future may not be able to compete effectively with marketed drugs or new drugs that may be developed by competitors. 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. Many of our competitors, including major pharmaceutical companies such as Abbvie, Bristol-Myers Squibb, Gilead, Johnson & Johnson, Merck, Novartis, Pfizer, Sanofi and Roche, possess substantially greater financial, technical and human resources than we possess.

A number of companies are seeking to identify and develop drug candidates for the treatment of CF, including Novartis, Pfizer, Genzyme, which is a division of Sanofi, and several private companies. Our competitors have research and development programs directed at identifying CFTR potentiators, CFTR correctors and drug candidates with other mechanisms of action that seek to address the underlying cause of CF, and our success in rapidly developing and commercializing KALYDECO may increase the resources that our competitors allocate to the development of these potential treatments for CF. While we do not believe that any of these competitive programs have entered late-stage clinical development, if one or more competing therapies are successfully developed as a treatment for patients with CF, our revenues from KALYDECO and/or other compounds, if then approved, could face competitive pressures.

We are aware of a number of companies that are developing new treatments for HCV infection, including HCV nucleotide analogues, HCV protease inhibitors, non-nucleoside HCV polymerase inhibitors and HCV NS5A inhibitors. We expect that over the next several years several all-oral treatment treatment regimens for HCV infection

will be approved in the United States and elsewhere in the world. Due in part to these competitive factors, two drug candidates, VX-135 and VX-222, that we were developing as treatments for HCV infection became impaired in 2013 resulting in aggregate intangible asset impairment charges of $663.5 million. The commercial prospects for VX-135, if approved, will depend on, among

other factors, the efficacy, safety, tolerability and other characteristics of any combination therapy including VX-135 relative to existing and future treatments for HCV infection, and the clinical data obtained and timing of marketing approvals for drug candidates being developed by our competitors. If we develop an all-oral treatment regimen that includes VX-135, we expect that our all-oral treatment regimen would compete directly with several all-oral treatment regimens that were approved several years prior to the approval of any all-oral treatment regimen that includes VX-135.

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. For example, in December 2012, we updated the INCIVEK label in the United States to include a Boxed Warning stating that fatal and non-fatal serious skin reactions have been reported in patients taking INCIVEK combination treatment. 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. 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, patients and third-party payors do not accept our drugs, we may be unable to generate significant revenues in future periods.

Our drugs may not gain or maintain market acceptance among physicians and patients. Effectively marketing our products 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 request or take them, for a variety of reasons including:

- lower demonstrated efficacy, safety and/or tolerability compared to other drugs;
- prevalence and severity of adverse side-effects;
- lack of cost-effectiveness;
- lack of reimbursement availability from third-party payors;
- 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 marketing and/or distribution support.

If our drugs fail to achieve or maintain market acceptance, we will 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.

In both domestic and foreign markets, 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. Governments and other third-party payors seek to contain or reduce the costs of health care through various means, and in certain foreign markets, pricing or profitability of therapeutic and other pharmaceutical products is subject to governmental control. For example, KALYDECO has been approved in Australia and Canada, but we are still in discussions with relevant agencies regarding public reimbursement for the cost of KALYDECO in these countries. 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. The ACA requires discounts under the Medicare drug benefit program and increases 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.

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 our products is a specialty pharmaceutical product, and our research and development programs are 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. 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 we market any of our products in a manner that violates federal or state 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 state and federal laws and regulations. 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 practices that involve remuneration intended to induce prescribing, purchasing or recommending may be subject to scrutiny or penalty if they do not qualify for an exemption or safe harbor.

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; and submitting inflated “best price” information to the Medicaid Rebate Program.

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 KALYDECO for patients six years of age and older with CF who have the G551D mutation in their CFTR gene and INCIVEK for adults with genotype 1 HCV infection and provide promotional materials and training programs to physicians regarding the use of KALYDECO and INCIVEK in these patient populations. 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 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.

Also applicable to some of our practices is HIPAA and its implementing regulations, which created federal criminal laws that prohibit executing a scheme to defraud any health care benefit program or making false statements relating to health care matters and which also imposes certain regulatory and contractual requirements regarding the privacy, security and transmission of individually identifiable health information.

The majority of states also have statutes or regulations similar to the federal anti-kickback law and false claims laws, which apply to items and services reimbursed under Medicaid and other state programs, or, in several states, apply regardless of the payor. In addition, certain states have laws governing the privacy of certain health information, which may differ from each other in significant ways and often are not preempted by HIPAA, complicating compliance efforts. Sanctions under these federal and state laws may include civil monetary penalties, exclusion of a pharmaceutical manufacturer’s products from reimbursement under government programs and criminal fines. 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 recent years, several states and localities have enacted legislation requiring pharmaceutical companies to establish marketing compliance programs, file periodic reports with the state or make periodic public disclosures on sales, marketing, pricing, clinical trials, health care provider payments and other activities. Additionally, as part of the ACA, the federal government recently enacted the Physician Payment Sunshine Act provisions. The Physician Payment Sunshine Act provisions require pharmaceutical manufacturers to report annually to the Secretary of HHS payments or other transfers of value made by that entity to physicians and teaching hospitals. In February 2013, regulations were released that contain detailed guidance regarding the information that must be collected and reported. We were required to begin collecting information regarding such payments starting in August 2013 and will be required to begin reporting such information in March 2014. We are dedicating significant resources to enhance our 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 ACA also includes various provisions designed to strengthen significantly fraud and abuse enforcement, such as increased funding for enforcement efforts and the lowering of the intent requirement of the federal anti-kickback statute and criminal health

care fraud statute such that a person or entity no longer needs to have actual knowledge of this statute or specific intent to violate it.

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. 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. Any action against us for violation of these laws, even if we successfully defend against them, could cause us to incur significant legal expenses and divert our management's attention from the operation of our business.

The sales and marketing practices of our industry have been the subject of increased scrutiny from federal and state government agencies, and we believe that this trend will continue. We have in place policies to govern how we may retain health care professionals as consultants that reflect the current climate on this issue and are providing training on these policies. 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 health care systems could hinder or prevent commercial success of our products and drug candidates.

The United States federal government and other governments are pursuing various changes in the health care system. Any government-adopted measures could adversely affect the pricing of health care products, including our approved products and/or any future drug candidates approved for sale. The continuing efforts of governments, insurance companies, managed care organizations and other payors for health care products to contain or reduce health care costs may adversely affect our ability to set prices we believe are fair for our products or any drugs we may develop and commercialize.

New laws, regulations and judicial decisions, or new interpretations of existing laws, regulations and decisions, relating to health care availability, methods of delivery or payment for drugs, or sales, marketing or pricing, may limit our potential revenues, and we may need to revise our research and development or commercialization programs. The pricing and reimbursement environment may change in the future and become more challenging for any of several reasons, including policies advanced by the U.S. government or foreign governments, new health care legislation or fiscal challenges faced by government health administration authorities. Specifically, 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. Some of these proposed and implemented reforms have resulted, or could result, in reduced reimbursement rates for our current or future products, which would adversely affect our business, operations and financial results. The ACA has far-reaching consequences for biopharmaceutical companies like us. As a result of this legislation, substantial changes are being made to the current system for paying for health care in the United States, including changes made in order to extend medical benefits to those who would otherwise lack health insurance coverage. If reimbursement for our products is substantially less than we expect in the future, or rebate obligations associated with them are substantially increased, our business could be materially and adversely affected.

Further federal and state proposals and health care reforms in and outside of the United States could limit the prices that can be charged for our products and may further limit our commercial opportunity. Our results of operations could be materially adversely affected by the ACA, by the Medicare prescription drug coverage legislation, by the possible effect of such current or future legislation on amounts that private insurers will pay and by other health care reforms that may be enacted or adopted in the future.

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. If we are unable to successfully develop additional drug candidates, our business will be materially harmed.

Our business depends upon the successful development and commercialization of additional 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 drugs;
- 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 ongoing or planned clinical trials for ivacaftor, ivacaftor in combination with lumacaftor and ivacaftor in combination with VX-661. 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 combination treatments for CF that include ivacaftor in combination with (i) lumacaftor or VX-661 and/or (ii) a next-generation CFTR corrector compound. 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. 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 us, 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.

We are planning to develop co-formulated lumacaftor/ivacaftor using a continuous manufacturing process, and any failure to establish and validate our manufacturing process could adversely affect our ability to obtain approval for and launch lumacaftor in combination with ivacaftor.

We are planning to use a continuous manufacturing process to manufacture co-formulated lumacaftor/ivacaftor tablets. Continuous process manufacturing connects the processes used in traditional batch manufacturing and uses on-line monitoring in order to increase control of the manufacturing process. We have not previously designed, implemented or utilized a continuous manufacturing process to produce commercial quantities of a pharmaceutical product and believe that we would be the first company to seek approval for an NDA or an MAA using this method of manufacturing. As a result, there is a risk that we will encounter technical difficulties in the design, implementation or use of our continuous manufacturing process for the manufacture of co-formulated lumacaftor/ivacaftor that we will not be able to overcome, or overcome in a timely manner. In addition, it may be more difficult to satisfy regulators that our process is capable of consistently producing commercial quantities of co-formulated lumacaftor/ivacaftor and that our methods for testing the quality, purity and potency of the final products are sufficient. We also initially plan to primarily rely on a single validated third-party source to produce lumacaftor in combination with ivacaftor, and to use the new manufacturing facility we are establishing as a secondary source. Our continuous manufacturing process will be subject to inspections by or under the authority of the FDA and by or under the authority of other federal, state and foreign regulatory authorities. Any failure to establish and validate our continuous manufacturing process for co-formulated lumacaftor/ivacaftor or any disruption in our supply chain could increase costs or adversely affect our ability to launch lumacaftor in combination with ivacaftor in a timely manner. In addition, there can be no assurance that if we fail, or encounter delays with respect to our continuous manufacturing process of lumacaftor/ivacaftor, that we will be able to establish and validate, or establish and validate in a timely manner, a non-continuous manufacturing process to manufacture lumacaftor/ivacaftor.

If we are unable to obtain regulatory approval, we will be unable to commercialize our drug candidates.

Our drug candidates are subject to extensive governmental regulations relating to their development, clinical evaluation, manufacturing and commercialization. Rigorous nonclinical testing and clinical trials and an extensive regulatory approval process are required in the United States and in most other countries prior to the commercial sale of drug candidates. Satisfaction of these and other regulatory requirements is costly, time-consuming, uncertain and subject to unanticipated delays. It is possible that none of the drug candidates we are developing will be approved for

marketing.

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.

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. Foreign 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, the FDA may not favorably consider data from clinical trials conducted in foreign jurisdictions.

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. Any of the following could delay our development programs:

- 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.

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.

In July 2013, the FDA placed our U.S. clinical trial evaluating VX-135, a drug candidate for the treatment of HCV infection, on partial clinical hold, and our business may be adversely affected if we cannot develop VX-135.

We have a collaboration for the development of our HCV nucleotide analogue VX-135 as a potential treatment for HCV infection. In July 2013, the FDA placed a partial clinical hold on our ongoing Phase 2 clinical trial in the United States of VX-135 in combination with RBV in patients with genotype 1 HCV infection following observation of reversible elevated liver enzymes in patients who received 400 mg of VX-135 in combination with RBV in a Phase 2 clinical trial in Europe. Until the partial clinical hold has been resolved, we cannot pursue further evaluation of VX-135 in the United States. There is no assurance that the FDA will lift the partial clinical hold or that we will be able to successfully develop VX-135. If we are not able to develop VX-135, or if our progress in developing VX-135 continues to be slowed significantly, our business may be adversely affected.

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. 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 Collaborators, Manufacturing and Reliance on Third Parties

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 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.
- 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.

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

We in-license VX-135 from Alios, and any loss of this license would materially harm our efforts to develop an all-oral treatment regimen for HCV infection.

We depend on third-party manufacturers, including a sole source manufacturer, 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 and distribute KALYDECO (ivacaftor) and INCIVEK (telaprevir) for commercial sale, and our drug candidates for clinical trials. As a result of our reliance on these third-party manufacturers and suppliers, including a sole source supplier of one of our manufacturing processes, 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, supply us with raw materials, and contract manufacturers in the European Union and the United States convert these raw materials into drug substance and 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 effectively 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. Furthermore, we may be required to modify our production methods to permit us to economically manufacture our drugs for sale and our drug candidates for clinical trials. These modifications may require us to re-evaluate our resources and the resources of our third-party manufacturers, which could result in abrupt changes in our production methods and supplies.

We require a supply of ivacaftor for commercial sale (as KALYDECO) and ivacaftor, lumacaftor and our other drug candidates for use in our clinical trials. We obtain ivacaftor and lumacaftor to meet our commercial and clinical supply needs through a third-party manufacturing network. Our supply chain for KALYDECO includes a sole source supplier for one of our manufacturing processes. A disruption in the commercial supply of KALYDECO for patients would have a significant impact on patients, our business and our product revenues. A disruption in the clinical supply of ivacaftor or ivacaftor in combination with lumacaftor could delay the completion of clinical trials and impact timelines for filing an sNDA, NDA and comparable foreign regulatory submissions. There can be no assurance that we will be able to establish a secondary manufacturer for all of our ivacaftor supply needs 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 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, and we have entered into a non-exclusive collaboration agreement with BMS to evaluate VX-135 in combination with daclatasvir. 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. 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 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 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.

We rely on third parties to conduct our clinical trials, and those third parties may not perform satisfactorily, including failing to meet established deadlines for the completion of such trials or regulatory requirements.

We rely on third parties such as contract research organizations to help manage our clinical trial process and on medical institutions and clinical investigators to enroll qualified patients and conduct our clinical trials. Our reliance on these third parties for clinical development activities reduces our control over these activities. Accordingly, these third-party contractors may not complete activities on schedule, or may not conduct our clinical trials in accordance with regulatory requirements or our trial design. 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 trial. 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 trials or in specific circumstances might result in a requirement that a 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 and substantial liabilities.

We have numerous issued patents and patent applications pending in the United States, as well as counterparts in other countries. Our success will depend, in significant part, on our ability to obtain and maintain U.S. and foreign patent protection for our drugs, their uses and our processes, to preserve our trade secrets and to operate without infringing the proprietary rights of third parties. In particular, we believe that composition-of-matter claims are the most significant patent claims for companies in our segment of the pharmaceutical industry, which focuses on small molecules that are new chemical compounds. While we have patents or patent applications with composition-of-matter claims for each of our products and clinical drug candidates, only a portion of these patents have been granted. We cannot be certain that any patents will issue from our patent applications or, even if patents issue or have issued, that the issued claims will provide us with any significant protection against competitive products or otherwise be valuable commercially.

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 maintain, obtain and enforce patents is uncertain and involves complex legal and factual questions. 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. Similarly, publication of discoveries in the scientific literature often lag behind actual discoveries. Consequently, we cannot be certain that we or our licensors 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 products or drug candidates or a similar invention, we may have to participate in interference proceedings to determine priority of invention and could lose our patent position. Furthermore, we may not have

identified all U.S. and foreign patents or published applications that affect our business by blocking our ability to commercialize our drugs or drug candidates.

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 products 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.

The laws of many foreign jurisdictions do not protect intellectual property rights to the same extent as in the United States and many companies 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 development, testing and regulatory review of a drug candidate, it is possible that, before a drug candidate can be commercialized, the related patent may expire or remain in force for only a short period following commercialization of such drug candidate, thereby reducing any advantages of the patent. 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 other patent protection on such drug candidates, those drug candidates would not be protected by patents, and we would then rely solely on other forms of exclusivity, such as regulatory exclusivity provided by the FDCA.

Risks Related To Our Operations

If we are unable to successfully implement our strategic plan, our business may be materially harmed.

Our strategy is to make focused investments to invent and develop innovative drugs, while we continue to market our products to eligible patients to generate revenues and maintain a strong financial position. We expect our total revenues to decline significantly in 2014 as compared to 2013 as a result of expected decreases in INCIVEK and INCIVO revenues. While we are seeking to increase our revenues from KALYDECO, we do not believe that in the near term these potential increased revenues will be sufficient to offset expected declines in INCIVEK and INCIVO revenues. In order to maintain a strong financial position, we are focusing our investment on CF and advancing our other research and early-stage development programs.

We may not be able increase or sustain our revenues from therapies for the treatment of CF, which would make it difficult to maintain a strong financial position and continue our research and development investments at the levels we currently plan. In addition, there can be no assurance that our development programs will be successful or that our research programs will result in drugs that we can successfully develop and commercialize.

If we fail to manage our operations effectively, our business may suffer.

We have expanded 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.

Our transition to our new corporate headquarters in Boston, Massachusetts could materially disrupt our business operations.

Our transition to our new corporate headquarters in Boston, Massachusetts is complicated and requires us to expend significant logistical and financial resources in 2014. Our corporate headquarters and primary research facilities were located in Cambridge, Massachusetts in close proximity to numerous other biotechnology companies since our founding in 1989. While we do not expect the move to result in significant turnover, we cannot be sure that we will be able to retain all our key scientific, commercial and management employees.

We are conducting a staggered move of employees, office and laboratory supplies and certain equipment from our previous facilities to our new corporate headquarters. The transition may cause disruptions to our business operations in Massachusetts, including disruptions to our use of certain laboratories and other research and development facilities that were not included in the January 2014 move of a majority of our employees. We also need to complete the decommissioning of our existing facilities in Cambridge, Massachusetts in a timely and cost-effective manner. Our business operations could be materially harmed if the disruptions to our use of certain laboratories and other research and development facilities are more significant than expected.

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

Our business exposes us to significant potential product liability risks that are inherent in the development, clinical testing, manufacturing and sales and marketing of human therapeutic products. 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 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 damages 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.

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 KALYDECO and expand our research and development capabilities. In 2013, a substantial portion of our revenues and expenses were associated with our foreign operations. In addition, a significant portion of our commercial supply chain, including sourcing of raw materials and manufacturing, is located in China, Japan and the European Union. 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;
- collectibility of accounts receivable;
- unexpected changes in tariffs, trade barriers and regulatory requirements;
- economic weakness, including inflation, or political instability in particular foreign economies and markets;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;
- foreign taxes, including withholding of payroll taxes;
- foreign currency fluctuations, which could result in increased operating expenses or reduced revenues, 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;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad; and
- business interruptions resulting from geo-political actions, including war and terrorism.

These and other risks associated with our international operations could materially adversely affect our business.
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 acquire or license technologies, resources or drug candidates, we will incur a variety of costs and may never realize benefits from the transaction.
If appropriate opportunities become available, we might license or acquire technologies, resources, drugs or drug candidates. We might never realize the anticipated benefits of such a transaction, and we may later incur impairment charges related to assets acquired in any such transaction. In particular, due to the risks inherent in drug development, we may not successfully develop or obtain marketing approval for the drug candidates we acquire. For example, in 2013 we incurred intangible asset impairment charges of $663.5 million relating to drug candidates for the treatment of HCV infection. 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.
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. 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, our October 2013 restructuring activities may make it more difficult to attract and retain qualified employees. 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 and restricted stock—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 controlled use of hazardous materials, chemicals and various 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 accidental contamination or

injury from these materials can not 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.

Risks Related to Holding Our Common Stock and Potential Financing Activities

Our stock price may fluctuate.

Market prices for securities of companies such as ours are highly volatile. From January 1, 2012 to December 31, 2013, our common stock traded between $32.04 and $89.96 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 of 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.

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. Factors that have caused quarterly fluctuations in the past include variable amounts of net product revenues and collaborative revenues, impairment charges, charges for excess and obsolete inventories, changes in the fair value of derivative instruments and the deconsolidation of Alios. We cannot accurately predict our future revenues from our products, and our revenues from our products could vary on a quarterly basis. Our revenues from our products may be affected by, among other factors, seasonality and the timing of orders from our significant customers. Our quarterly results also could be significantly 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 proportionately reduce operating expenses 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.

We could be negatively affected by securities class action complaints.

On September 6, 2012, a purported securities class action lawsuit was commenced in the United States District Court for the District of Massachusetts under the caption City of Bristol Pension Fund v. Vertex Pharmaceuticals Incorporated, et al., naming as defendants us and certain of our current and former officers and directors. The lawsuit alleges that we made material misrepresentations and/or omissions of material fact in our public disclosures during the period from May 7, 2012 through June 28, 2012, all in violation of Section 10(b) of the Securities Exchange Act of 1934, as amended, and Rule 10b-5 promulgated thereunder. By order dated December 12, 2012, the court appointed the City of Bristol lead plaintiff and appointed the City of Bristol's attorneys lead counsel. The plaintiffs filed an amended complaint on February 11, 2013. We filed a motion to dismiss the complaint on April 12, 2013. On May 28, 2013, the plaintiffs filed an opposition to our motion to dismiss the complaint. On June 27, 2013, we filed a reply in further support of our motion to dismiss the plaintiffs' complaint. The court conducted a hearing on our motion to dismiss on November 25, 2013. The plaintiffs seek unspecified monetary damages on behalf of the putative class and an award of costs and expenses, including attorney's fees, as well as disgorgement of the proceeds from certain individual defendants' sales of our common stock. We believe that this action is without merit and intend to defend it vigorously. This action will take time and money to defend and may distract us from more productive activities. No assurance can be provided that we will be successful in defending this claim or that insurance proceeds will be sufficient to cover any liability under such claims.

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

We expect to incur significant losses in 2014 and, although we do not have any plans to do so in the near term, we may in the future need to raise additional capital. Any potential public offering or private placement may or may not be similar to the transactions that we have completed in the past. Any debt financing may be on terms that, among other things, include conversion features that could result in dilution to our then-existing security holders and restrict our ability to pay interest and dividends—although we do not intend to pay dividends for the foreseeable future. Any equity financings would result in dilution to our then-existing security holders. If adequate funds are not available on acceptable terms, or at all, we may be required to curtail significantly or discontinue one or more of our research, drug discovery or development programs, including clinical trials, incur significant cash exit costs, or attempt to obtain funds through arrangements with collaborators or others that may require us to relinquish rights to certain of our technologies, drugs or drug candidates. Based on many factors, including general economic conditions, additional financing may not be available on acceptable terms, if at all.

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

As of December 31, 2013, we had 233.8 million shares of common stock issued and outstanding. As of December 31, 2013, we also had outstanding options to purchase 15.7 million shares of common stock with a weighted-average exercise price of $44.40 per share. Outstanding vested options are likely to be exercised if the market price of our common stock exceeds the applicable exercise price, and, in the future, we expect to issue additional options and

restricted stock 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.

We have adopted anti-takeover provisions and are subject to Massachusetts corporate laws that may frustrate any attempt to remove or replace our current management or effectuate a business combination involving Vertex.

Our corporate charter and by-law provisions and Massachusetts state laws may discourage certain types of transactions involving an actual or potential change of control of Vertex that might be beneficial to us or our security holders. Our charter provides for staggered terms for the members of the Board of Directors. 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 net product revenues from KALYDECO and INCIVEK;
- our expectations regarding clinical trials, development timelines and regulatory authority filings and submissions for ivacaftor, lumacaftor, VX-135 and VX-661;
- our expectations regarding the timing of data from our clinical trials of ivacaftor and lumacaftor in combination with ivacaftor, the possibility of using that data to support regulatory submissions and the timing of those potential submissions;
- our ability to successfully market our products 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, VX-135 and VX-661, 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;
- our estimates regarding the charges associated with our October 2013 workforce reduction and our other restructuring activities;

- 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, 2013 regarding our filings under the Securities Exchange Act of 1934, as amended, that have not been resolved.

ITEM 2. PROPERTIES

Corporate Headquarters

In the first quarter of 2014, we relocated our corporate headquarters from Cambridge, Massachusetts to two connected buildings that were built in Boston, Massachusetts. We lease approximately 1.1 million square feet of office and laboratory space in these 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 will complement the office and laboratory facilities at our corporate headquarters.

Transition to Corporate Headquarters

We are completing the transition to our new corporate headquarters in Boston from our previous facilities, which were located in Cambridge, Massachusetts. A majority of our Massachusetts-based employees were relocated to the new corporate headquarters in January 2014. We expect to complete the relocation of our Massachusetts-based employees to our new facilities in the first half of 2014.

Existing Facilities in Cambridge, Massachusetts

We currently lease approximately 100,000 square feet of laboratory and office space for our former corporate headquarters, which were located at 130 Waverly Street, and approximately 192,000 square feet of laboratory and office space at 200 Sidney Street, located adjacent to our former corporate headquarters. The 130 Waverly Street and 200 Sidney Street leases expire on December 31, 2015. We lease approximately 145,000 square feet at 88 Sidney Street, Cambridge, Massachusetts under a lease that expires in June 2014. We are in the process of decommissioning our existing laboratory facilities at these locations.

The lease for our Kendall Square, Cambridge, Massachusetts facility will expire in 2018. We have subleased approximately 145,000 square feet of the Kendall Square facility, and used the remaining 147,000 square feet of space we

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lease for our research operations prior to the relocation. The subleases are for terms ending in 2015, with one sublease having an extension option to 2018.

Additional United States and Worldwide Locations

In addition to our facilities in Massachusetts, we lease an aggregate of approximately 242,000 square feet of space in facilities located in California, Washington D.C., Iowa, Canada, Switzerland, the United Kingdom, France, Germany, Australia, Ireland, Spain and the Netherlands. This includes laboratory and office space to support our research and development organizations in San Diego, California, Montreal, Canada, Coralville, Iowa and Milton Park, Abingdon, England.

ITEM 3. LEGAL PROCEEDINGS

On September 6, 2012, a purported shareholder class action, City of Bristol Pension Fund v. Vertex Pharmaceuticals Incorporated, et al., was filed in the United States District Court for the District of Massachusetts, naming us and certain of our current and former officers and directors as defendants. The lawsuit alleges that we made material misrepresentations and/or omissions of material fact in our public disclosures during the period from May 7, 2012 through June 28, 2012, all in violation of Section 10(b) of the Securities Exchange Act of 1934, as amended, and Rule 10b-5 promulgated thereunder. By order dated December 12, 2012, the court appointed the City of Bristol lead plaintiff and appointed the City of Bristol's attorneys lead counsel. The plaintiffs filed an amended complaint on February 11, 2013. We filed a motion to dismiss the complaint on April 12, 2013. On May 28, 2013, the plaintiffs filed an opposition to our motion to dismiss the complaint. On June 27, 2013, we filed a reply in further support of our motion to dismiss the plaintiffs' complaint. The court conducted a hearing on our motion to dismiss on November 25, 2013. The plaintiffs seek unspecified monetary damages on behalf of the putative class and an award of costs and expenses, including attorney's fees, as well as disgorgement of the proceeds from certain individual defendants' sales of our common stock. We believe that this action is without merit and intend to defend it vigorously.

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, 2013:	High	Low
First quarter	$55.93	$42.72
Second quarter	87.47	51.28
Third quarter	89.96	73.43
Fourth quarter	78.38	58.06

Year Ended December 31, 2012:	High	Low
First quarter	$43.13	$32.04
Second quarter	66.10	35.26
Third quarter	59.98	46.03
Fourth quarter	60.00	38.44

Shareholders

As of January 31, 2014, there were 1,844 holders of record of our common stock.

Performance Graph

CUMULATIVE TOTAL RETURN
Based on Initial Investment of $100 on December 31, 2008
with dividends reinvested (fiscal years ended December 31)

In 2013, we became part of the Standard & Poor's 500 ("S&P 500®") Stock Index. As a result, this year we are including the cumulative total return of that index in addition to the broad equity market indexes we included in our annual report on Form 10-K for the year ended December 31, 2012.

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.

Issuer Repurchases of Equity Securities

The table set forth below shows all repurchases of securities by us during the three months ended December 31, 2013:

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, 2013 to Oct. 31, 2013	21,833	$0.01	—	—
Nov. 1, 2013 to Nov. 30, 2013	462,198	$0.01	—	—
Dec. 1, 2013 to Dec. 31, 2013	20,287	$0.01	—	—

The repurchases were made under the terms of our Amended and Restated 2006 Stock and Option Plan. Under this plan, 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 returned to the Amended and Restated 2006 Stock and Option Plan are available for future awards under the terms of the plan.

ITEM 6. SELECTED FINANCIAL DATA

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

	Year Ended December 31,				
	2013	2012	2011	2010	2009
	(in thousands, except per share amounts)				
Consolidated Statements of Operations Data:					
Product revenues, net	$837,645	$1,333,458	$950,889	$—	$—
Royalty revenues	156,592	141,498	50,015	30,244	28,320
Collaborative revenues (1)	217,738	52,086	409,722	113,126	73,569
Total revenues	1,211,975	1,527,042	1,410,626	143,370	101,889
Total costs and expenses (2)	2,115,423	1,524,710	1,296,806	839,447	715,901
Income (loss) from operations	(903,448)	2,332	113,820	(696,077)	(614,012)
Net loss (income) attributable to noncontrolling interest (Alios) (3)	242,522	(55,897)	(11,605)	—	—
Net income (loss) attributable to Vertex (4)	$(445,028)	$(107,032)	$29,574	$(754,626)	$(642,178)
Net income (loss) per diluted share attributable to Vertex common shareholders	$(1.98)	$(0.50)	$0.14	$(3.77)	$(3.71)
Shares used in per diluted share calculations	224,906	211,946	208,807	200,402	173,259

	As of December 31,				
	2013	2012	2011	2010	2009
	(in thousands)				
Consolidated Balance Sheet Data:					
Cash, cash equivalents and marketable securities	$1,465,076	$1,321,215	$968,922	$1,031,411	$1,284,913
Total assets	2,319,041	2,759,288	2,204,280	1,725,446	1,955,488
Total current liabilities	397,829	432,624	392,348	474,783	284,883
Long-term debt obligations (5)	—	400,000	400,000	400,000	159,972
Construction financing lease obligation (6)	440,937	268,031	55,950	—	—
Other long-term obligations	123,870	424,251	390,470	346,690	414,287

(1) In 2013, we recorded $203.4 million of collaborative revenues from Janssen Pharmaceutica NV, which was primarily attributable to a 2013 amendment to our collaboration agreement with Janssen. In 2011, we recognized $318.5 million in milestone revenues from Janssen and Mitsubishi Tanabe Pharma Corporation. See Note B, "Collaborative Arrangements."

(2) In 2013 and 2012, total costs and expenses included an aggregate of $10.4 million and $133.2 million, respectively, of write-offs for excess and obsolete inventories. See Note G, "Inventories." In 2013, total costs and expenses included intangible asset impairment charges of $663.5 million. In 2011, total costs and expenses included an intangible asset impairment charge of $105.8 million. See Note J, "Intangible Assets and Goodwill."

(3) Net loss (income) attributable to noncontrolling interest (Alios) relates to our collaboration with Alios BioPharma, Inc, which we deconsolidated as of December 31, 2013. See Note B, "Collaborative Arrangements," and Note J, "Intangible Assets and Goodwill."

(4) In 2013, net loss attributable to Vertex included a deconsolidation gain of $68.2 million related to Alios. See Note B, "Collaborative Arrangements."

(5) In 2013, $400.0 million in aggregate principal amount of convertible senior subordinated notes (due 2015) was converted into common stock or redeemed. See Note L, "Convertible Senior Subordinated Notes."

(6) In 2011, we entered into two leases for our corporate headquarters, which we occupied in December 2013. We are deemed for accounting purposes to be the owner of the buildings. See Note I, "Fan Pier Leases."

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

OVERVIEW

We are in the business of discovering, developing, manufacturing and commercializing small molecule drugs. We invest in scientific innovation to create transformative medicines for patients with serious diseases in specialty markets. Our business is focused on developing and commercializing therapies for the treatment of cystic fibrosis, or CF, and advancing our other research and early-stage development programs, while maintaining our financial strength.

Since mid-2011, we have obtained approval for, and initiated commercial sales of, our first two products: KALYDECO (ivacaftor) and INCIVEK (telaprevir). KALYDECO is approved in the United States and international markets for the treatment of patients six years of age and older with CF who have a specific genetic mutation in their cystic fibrosis transmembrane conductance regulator, or CFTR, gene, which is referred to as the G551D mutation. INCIVEK is approved in the United States and Canada for the treatment of adults with genotype 1 hepatitis C virus, or HCV, infection. Our collaborators, Janssen Pharmaceutica NV, or Janssen, and Mitsubishi Tanabe Pharma Corporation, or Mitsubishi Tanabe, market telaprevir in other international markets. Our fourth quarter 2013 net product revenues included KALYDECO net product revenues of $109.4 million and INCIVEK net product revenues of $19.4 million.

Cystic Fibrosis

Our plan is to (i) increase the number of patients eligible for treatment with ivacaftor, (ii) evaluate ivacaftor in combination with lumacaftor for the treatment of patients with CF who have the most prevalent mutation in their CFTR gene and (iii) research and develop earlier-stage compounds for the treatment of CF.

Our net product revenues from KALYDECO have increased on a quarterly basis since we obtained marketing approval in the first quarter of 2012. KALYDECO was approved in 2012 in the United States and European Union as a treatment for patients with CF six years of age and older who have the G551D mutation in their CFTR gene. We believe that most patients with CF six years of age and older who have the G551D mutation in the United States and Europe have started treatment with KALYDECO. In 2013, we submitted a supplemental New Drug Application, or sNDA, to the U.S. Food and Drug Administration, or FDA, and a Marketing Authorization Application, or MAA, variation in the European Union seeking approval to market ivacaftor for the treatment of patients with CF six years of age and older who have specified other mutations in their CFTR gene, which were studied in our first label-expansion clinical trial for ivacaftor. The FDA has set a target date of March 27, 2014 to complete its review of this sNDA under the Prescription Drug User Fee Act (PDUFA). We also are seeking to expand the number of patients eligible for treatment with ivacaftor by (i) evaluating ivacaftor as a potential treatment for patients with CF who have residual CFTR function, including patients with CF who have the R117H mutation in their CFTR gene, and (ii) evaluating ivacaftor as a potential treatment for patients with CF two to five years of age who have specific mutations in their CFTR genes. In addition, we are in discussions with relevant agencies in Australia and Canada regarding public reimbursement of the cost of KALYDECO for patients with CF six years of age and older in these countries who have the G551D mutation in their CFTR gene.

In October 2013, we completed enrollment in a Phase 3 development program to evaluate combinations of ivacaftor and lumacaftor, our most advanced investigational CFTR corrector compound. The Phase 3 development program includes two Phase 3 clinical trials, referred to as TRAFFIC and TRANSPORT, that each enrolled patients 12 years of age and older with CF who have two copies (homozygous) of the F508del mutation in their CFTR gene. We expect data from TRAFFIC and TRANSPORT in mid-2014. If TRAFFIC and TRANSPORT are successful, we plan to submit a New Drug Application, or NDA, to the FDA and an MAA in the European Union, in the second half 2014.

We are evaluating VX-661, a second investigational CFTR corrector, in combination with ivacaftor, in Phase 2 clinical development. We also are seeking to identify and develop next-generation CFTR corrector compounds that could be evaluated in regimens combining ivacaftor with two CFTR corrector compounds.

HCV Infection

Over the past several years, we have obtained most of our product revenues from INCIVEK sales and focused a large portion of our resources on commercializing INCIVEK and seeking to develop other drug candidates for the treatment

of HCV infection. Our INCIVEK net product revenues have been declining on a quarterly basis since reaching a peak in the fourth quarter of 2011, and declined rapidly over the course of 2013, including a 77% decline in INCIVEK net product

revenues in the fourth quarter of 2013 as compared to the third quarter of 2013. We expect this trend to continue as a result of the introduction in the fourth quarter of 2013 of new competitive therapies for the treatment of HCV infection.

In 2013, in response to declining sales of INCIVEK and increased competition, we reduced our focus on INCIVEK, and based on additional information regarding our HCV drug development candidates and advances made by our competitors, we incurred significant impairment charges related to our HCV drug development candidates, as follows:

Impairment of VX-222. In the first quarter of 2013, we recorded a $412.9 million intangible asset impairment charge based on a determination that the fair value of our indefinite-lived in-process research and development asset related to VX-222, a drug we were developing for the treatment of HCV infection, had decreased to zero. In connection with this impairment charge, we recorded a credit of $127.6 million in our provision for income taxes, and the net effect of this impairment charge was an increase in the net loss attributable to Vertex of $285.3 million in 2013.

Workforce Reduction. In the fourth quarter of 2013, we reduced our workforce by eliminating approximately 370 full-time positions globally, representing an approximately 15% reduction in our workforce. The eliminated positions included the portion of our U.S. field-based sales force focused on promoting INCIVEK. In the second half of 2013, we incurred approximately $39.0 million in restructuring charges related to this workforce reduction. We expect the restructuring to result in a significant reduction in our sales, general and administrative expenses in 2014 as compared to 2013.

VX-135. In the fourth quarter of 2013, we recorded a $250.6 million intangible asset impairment charge, based on a determination that the fair value of our indefinite-lived in-process research and development asset related to our HCV nucleotide analogue (VX-135) program was impaired. In connection with this impairment charge, a benefit for income taxes was recorded related to the reversal of a deferred tax liability, and we deconsolidated our variable interest entity, Alios BioPharma, Inc., or Alios, as of December 31, 2013. The consolidation of Alios into our financial statements from June 2011 through December 2013, the impairment charge related to our HCV nucleotide analogue program in the fourth quarter of 2013 and the related deconsolidation of Alios have had a material effect on our consolidated statements of operations. The impairment charge resulted in the deconsolidation of Alios and a gain of $68.2 million attributable to Vertex in 2013. The gain of $68.2 million is approximately equal to the difference between (i) losses we recorded in 2011 and 2012 based on increases in the fair value of contingent milestone payments and royalties payable by us to Alios and (ii) an aggregate of $120.0 million in up-front and milestone payments that we made to Alios. We are in discussions with Alios and Bristol-Myers Squibb, or BMS, regarding potential next steps for further clinical evaluation of VX-135 in combination with BMS's daclatasvir.

In 2014, we expect that only a small portion of our net product revenues will be due to INCIVEK and that a relatively small portion of our research and development expenses will be related to our drugs and drug candidates for the treatment of HCV infection.

Research and Early-Stage Development

We are engaged in a number of other research and early-stage development programs, including programs in the areas of oncology, multiple sclerosis and other serious and rare diseases. Over the last year, we have evaluated in Phase 2 clinical trials: VX-509, our JAK3 inhibitor, in patients with rheumatoid arthritis and VX-787, a drug candidate for the treatment of influenza A. We are seeking collaborators to advance the clinical development of VX-509 and VX-787. We plan to continue investing in our research programs as well as our early-stage development programs, and fostering scientific innovation in order to identify and develop transformative medicines. We believe that pursuing research in diverse areas allows us to balance the risks inherent in drug development and may provide drug candidates that will form our pipeline in future years.

Balance Sheet

As of December 31, 2013, we had cash, cash equivalents and marketable securities of approximately $1.47 billion, which represented an increase of $143.9 million from $1.32 billion as of December 31, 2012. This increase was the result of cash received from product sales, royalties, issuances of common stock pursuant to employee benefit plans and other financing activities, offset by cash expenditures to operate our business. We amended our collaboration agreement with Janssen to provide Janssen a fully-paid license to market INCIVO in return for a $152.0 million payment. Beginning in 2014, we will no longer receive royalties based on sales of INCIVO. In order to further

strengthen our balance sheet, we converted $400.0 million in aggregate principal amount of our 3.35% convertible senior subordinated notes due 2015, or 2015 Notes, into 8.3

million shares of our common stock in 2013, reducing our future cash commitments by the principal amount of the 2015 Notes plus the associated future interest payments.

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 relatively abrupt changes in focus and priority as new information becomes available and 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, which began in 2011, 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 the promotion of a culture of compliance. Among other laws, regulations and standards, we are subject to various U.S. federal and state and comparable foreign laws pertaining to health care fraud and abuse, including anti-kickback and false claims statutes, 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 in exchange for, or to induce, the referral of business, including the purchase or prescription of a particular drug. False claims laws prohibit anyone from 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 expect to continue to devote substantial resources to maintain, administer and expand these compliance programs globally.

Continuous Manufacturing

We are planning to use a continuous manufacturing process to manufacture co-formulated lumacaftor and ivacaftor tablets. We have established continuous manufacturing capabilities at our third-party manufacturer in the United Kingdom, which was used to produce a portion of the clinical trial supplies for our Phase 3 clinical trials of lumacaftor in combination with ivacaftor, and are in the process of establishing continuous manufacturing capabilities and seeking validation for these capabilities at our new facility located in Boston, Massachusetts. We are upgrading the continuous manufacturing process at our third-party manufacturer and are scheduled to begin producing co-formulated lumacaftor and ivacaftor intended for commercial use in mid-2014. Continuous process manufacturing connects the processes used in traditional batch manufacturing and uses on-line monitoring in order to increase control of the manufacturing process. While we believe continuous process manufacturing has a number of benefits, we have not

previously designed a continuous manufacturing process to produce commercial quantities of a pharmaceutical product, and we believe that we would be the first company to seek approval for an NDA or an MAA using this method of manufacturing. As a result, we also have designed and tested a

non-continuous process for manufacturing co-formulated lumacaftor and ivacaftor tablets that we would seek to utilize if we experience delays associated with the continuous manufacturing process.

Operations

We are moving our corporate headquarters from a number of buildings in Cambridge, Massachusetts into our new facility in Boston, Massachusetts. A majority of our Massachusetts-based employees were relocated to our new corporate headquarters in January 2014. We expect to complete the relocation of our Massachusetts-based employees to our new facilities in the first half of 2014. This move allows us to consolidate our headquarters into one campus and update our physical infrastructure, including our laboratories and other research facilities. In order to manage the expansion of our international operations and move to our new headquarters, we will need to enhance our cross-functional operational, financial and management processes while continuing to attract and maintain highly skilled employees. We are decommissioning our existing laboratory facilities at our Cambridge locations. We expect to incur restructuring charges related to lease obligations for facilities in Cambridge through 2018, with the majority of these charges being incurred during 2014.

RESULTS OF OPERATIONS

				2013/2012 Comparison Increase/(Decrease)		2012/2011 Comparison Increase/(Decrease)	
	2013	2012	2011	$	%	$	%
	(in thousands)			(in thousands, except percentages)			
Revenues	$1,211,975	$1,527,042	$1,410,626	$(315,067)	(21)%	$116,416	8 %
Operating costs and expenses	2,115,423	1,524,710	1,296,806	590,713	39 %	227,904	18 %
Other income (loss), net	215,898	(53,467)	(72,641)	n/a	n/a	19,174	26 %
Net loss (income) attributable to noncontrolling interest (Alios)	242,522	(55,897)	(11,605)	n/a	n/a	44,292	382 %
Net income (loss) attributable to Vertex	$(445,028)	$(107,032)	$29,574	(337,996)	(316)%	n/a	n/a

Net Income (Loss) Attributable to Vertex

Net income (loss) attributable to Vertex, revenues and operating expenses have been affected by rapidly fluctuating INCIVEK and KALYDECO net revenues and significant intangible asset impairment charges and inventory write-offs during the three year period ended December 31, 2013. In 2014, we expect most of our revenues will be due to KALYDECO sales and that we will incur a substantial net loss.

Comparison of Net Income (Loss) Attributable to Vertex 2013 vs. 2012

Net loss attributable to Vertex was $445.0 million in 2013 compared to net loss attributable to Vertex of $107.0 million in 2012. Our revenues decreased in 2013 as compared to 2012 due to a $695.5 million decrease in INCIVEK revenues partially offset by a $199.6 million increase in KALYDECO revenues and a $165.7 million increase in collaborative revenues. Our operating costs and expenses increased in 2013 as compared to 2012 primarily due to an aggregate of $663.5 million in intangible asset impairment charges related to VX-222 and VX-135 and a $112.6 million increase in research and development expenses, partially offset by a $74.5 million decrease in sales, general and administrative expenses and an aggregate of $133.2 million in cost of product revenues due to charges for excess and obsolete INCIVEK inventories that we incurred in 2012.

In 2013, the deconsolidation of Alios resulted in a gain of $68.2 million attributable to Vertex. The $68.2 million gain is approximately equal to the difference between (i) losses we recorded in 2011 and 2012 based on increases in the fair value of contingent milestone payments and royalties payable by us to Alios and (ii) the aggregate of $120.0 million in upfront and milestone payments that we made to Alios. In 2012, the fair value of contingent milestone and royalty payments payable by us to Alios increased by $115.0 million, which increased net loss attributable to Vertex in 2012 on a dollar-for-dollar basis.

Comparison of Net Income (Loss) Attributable to Vertex 2012 vs. 2011

Net loss attributable to Vertex was $107.0 million in 2012 compared to net income attributable to Vertex of $29.6 million in 2011. Our revenues increased in 2012 as compared to 2011 due to a $210.9 million increase in INCIVEK net product revenues and a $171.6 million increase in KALYDECO net product revenues, partially offset by a significant decrease in collaborative revenues. Our operating costs and expenses increased in 2012 as compared to 2011 primarily due to a $98.5 million increase in research and development expenses, a $36.1 million increase in sales, general and administrative expenses and an aggregate of $133.2 million in cost of product revenues due to charges for excess and obsolete INCIVEK inventories that we incurred in 2012. These increases were partially offset by a $105.8 million intangible asset impairment charge in 2011 that had a net effect on net income attributable to Vertex of $73.1 million. In 2012 and 2011, the fair value of contingent milestone payments and royalties payable by us to Alios increased by $115.0 million and $70.0 million, respectively, which increased the net loss attributable to Vertex in 2012 and decreased net income attributable to Vertex in 2011 on a dollar-for-dollar basis.

Stock-based Compensation

Stock-based compensation expense was $127.3 million, $114.3 million and $118.2 million in 2013, 2012 and 2011, respectively.

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Net Income (Loss) Attributable to Vertex per Diluted Share

In 2013 and 2012, net loss attributable to Vertex was $1.98 and $0.50, respectively, per diluted share. In 2011, we had net income attributable to Vertex of $0.14 per diluted share.

Common Shares Outstanding

Our shares of outstanding common stock increased by 16.5 million shares from 217.3 million shares on December 31, 2012 to 233.8 million shares on December 31, 2013 due to our issuance in 2013 of approximately 8.3 million shares of common stock in connection with the conversions of our 2015 Notes and 8.2 million shares of common stock issued pursuant to our employee equity programs. Our shares of outstanding common stock increased by 8.0 million shares from 209.3 million shares on December 31, 2011 to 217.3 million shares on December 31, 2012 as a result of shares issued pursuant to our employee equity programs.

Revenues

				2013/2012 Comparison Increase/(Decrease)		2012/2011 Comparison Increase/(Decrease)	
	2013	2012	2011	$	%	$	%
	(in thousands)			(in thousands, except percentages)			
Product revenues, net	$837,645	$1,333,458	$950,889	$(495,813)	(37)%	$382,569	40 %
Royalty revenues	156,592	141,498	50,015	15,094	11 %	91,483	183 %
Collaborative revenues	217,738	52,086	409,722	165,652	318 %	(357,636)	(87)%
Total revenues	$1,211,975	$1,527,042	$1,410,626	$(315,067)	(21)%	$116,416	8 %

Product Revenues, Net

	2013	2012	2011
	(in thousands)		
INCIVEK	$466,360	$1,161,813	$950,889
KALYDECO	371,285	171,645	—
Total product revenues, net	$837,645	$1,333,458	$950,889

Our total net product revenues decreased by 37% in 2013 as compared to 2012 due to decreased INCIVEK net product revenues, partially offset by increased KALYDECO net product revenues. Our total net product revenues increased by 40% in 2012 as compared to 2011 due to increased INCIVEK net product revenues and KALYDECO net product revenues in 2012 for which there were no comparable revenues in 2011. In 2014, we expect that total net product revenues will decline due to significant expected decreases in INCIVEK net product revenues, partially offset by expected increases in KALYDECO net product revenues.

Our KALYDECO net product revenues have increased on a quarterly basis since we began marketing KALYDECO in the first quarter of 2012. We believe that most patients with CF six years of age and older who have the G551D mutation in the United States and Europe have started treatment with KALYDECO. We expect that KALYDECO net product revenues will increase further in 2014 as a result of geographic expansion, including potentially obtaining public reimbursement for the cost of KALYDECO in Australia and/or Canada, and potential label expansions that could increase the number of patients with CF who are eligible for treatment with KALYDECO.

We began recognizing net product revenues from sales of INCIVEK in the second quarter of 2011. INCIVEK net product revenues have been declining on a quarterly basis since reaching a peak in the fourth quarter of 2011 and were $19.4 million in the fourth quarter of 2013. Our net product revenues from sales of INCIVEK declined steeply over the course of 2013, including a 77% decline in INCIVEK net product revenues in the fourth quarter of 2013 as compared to the third quarter of 2013. We expect INCIVEK net product revenues to continue to decrease due to increased competition from the two competitive direct-acting antiviral therapies for the treatment of HCV infection that were approved by the FDA in the fourth quarter of 2013.

Royalty Revenues

Janssen obtained approval to market INCIVO in the European Union in the third quarter of 2011. Our royalty revenues increased by $15.1 million in 2013 as compared to 2012 principally due to a $13.1 million increase in royalty revenues from sales of INCIVO by Janssen. Our royalty revenues increased by $91.5 million in 2012 as compared to 2011 due to $117.6 million of revenues recognized in 2012 from sales of INCIVO by Janssen for which there were limited comparable revenues in 2011. Beginning in the first quarter of 2014, Janssen has a fully-paid license to market INCIVO in its territories, subject to continued payment of certain third-party royalties. In future periods, these third-party royalties will result in royalty revenues and corresponding offsetting royalty expenses. As a result, we expect our royalty revenues to decrease significantly in 2014 as compared to 2013. Mitsubishi Tanabe's license to market telaprevir in Japan is fully paid.

We recognized royalty revenues related to sales by GlaxoSmithKline of an HIV protease inhibitor that was discovered and developed pursuant to our collaboration with GlaxoSmithKline of $25.6 million, $23.9 million and $29.7 million in 2013, 2012 and 2011, respectively. We sold our rights to these HIV royalties in 2008 for a one-time cash payment of $160.0 million.

Collaborative Revenues

Our collaborative revenues have fluctuated significantly on an annual basis. This variability has been due to, among other things: the 2013 amendment of our collaboration agreement with Janssen that resulted in significant collaborative revenues in the fourth quarter of 2013; the recognition of significant milestone revenues from Janssen and Mitsubishi Tanabe in 2011; the 2009 amendment of our collaboration agreement with Mitsubishi Tanabe, which provided for an up-front payment that was recognized over the period from the third quarter of 2009 through the second quarter of 2012; and variable revenues we received from services we provided to Janssen and Mitsubishi Tanabe through our third-party manufacturing network.

The table presented below is a summary of our collaborative revenues for 2013, 2012 and 2011:

	2013	2012	2011
	(in thousands)		
Collaborative revenues:			
Janssen	$203,437	$16,178	$274,393
CFFT	14,322	16,960	13,654
Mitsubishi Tanabe	—	18,879	121,675
Other	(21)	69	—
Total collaborative revenues	$217,738	$52,086	$409,722

We recognized $203.4 million in Janssen collaborative revenues in 2013, which were primarily attributable to the $152.0 million payment we received in the fourth quarter of 2013 pursuant to our amendment to the Janssen collaboration agreement. These collaborative revenues also included the acceleration of the remaining deferred revenues related to the up-front payment we received from Janssen in 2006. In 2011, we recognized $250.0 million in milestone revenues under our collaboration agreement with Janssen for which there were no corresponding milestone revenues in 2012 or 2013. As of December 31, 2013, there was $5.0 million in deferred revenues related to the Janssen collaboration. We do not expect to recognize significant collaborative revenues related to the Janssen collaboration in future periods.

In 2011, we recognized a $65.0 million commercial milestone payment from Mitsubishi Tanabe. In addition, from the beginning of 2011 through the first quarter of 2012, we recognized $9.6 million per quarter in collaborative revenues related to a one-time payment that we received from Mitsubishi Tanabe in 2009. In 2011 and the first half of 2012, we also recognized revenues related to manufacturing services we provided to Mitsubishi Tanabe through our third-party manufacturing network. We have not recognized any collaborative revenues from Mitsubishi Tanabe since the first half of 2012 and will not recognize any future collaborative revenues pursuant to our collaboration agreement with Mitsubishi Tanabe.

Operating Costs and Expenses

				2013/2012 Comparison Increase/(Decrease)		2012/2011 Comparison Increase/(Decrease)	
	2013	2012	2011	$	%	$	%
	(in thousands)			(in thousands, except percentages)			
Cost of product revenues	$88,979	$236,742	$63,625	$(147,763)	(62)%	$173,117	272 %
Royalty expenses	41,298	43,143	16,880	(1,845)	(4)%	26,263	156 %
Research and development expenses	918,783	806,185	707,706	112,598	14 %	98,479	14 %
Sales, general and administrative expenses	362,342	436,796	400,721	(74,454)	(17)%	36,075	9 %
Restructuring expenses	40,521	1,844	2,074	38,677	2,097 %	(230)	(11)%
Intangible asset impairment charges	663,500	—	105,800	663,500	n/a	(105,800)	(100)%
Total costs and expenses	$2,115,423	$1,524,710	$1,296,806	$590,713	39 %	$227,904	18 %

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 INCIVEK and KALYDECO. In addition, cost of product revenues in 2013 and 2012 included an aggregate of $10.4 million and $133.2 million, respectively, in write-offs for excess and obsolete inventories.

Our cost of product revenues decreased in 2013 compared to 2012 as a result of decreased product revenues and the $133.2 million in charges for excess and obsolete INCIVEK inventories that we incurred in 2012. Our cost of product revenues increased in 2012 compared to 2011 due to our increased product revenues and the charges for excess and obsolete INCIVEK inventories that we incurred in 2012. As of December 31, 2013, we had $0.9 million in remaining INCIVEK inventories.

Royalty Expenses

Royalty expenses include third-party royalties payable upon net sales of telaprevir by our collaborators and royalty expenses related to a subroyalty payable to a third party on net sales of an HIV protease inhibitor sold by GlaxoSmithKline. Royalty expenses in 2013 decreased slightly as compared to 2012. Royalty expenses in 2012 increased compared to 2011 primarily due to increased third-party royalties payable on net sales of INCIVO by Janssen. Our royalty expenses in future periods will be dependent on our collaborators' net sales of telaprevir in their territories. Royalty expenses also include a subroyalty payable to a third party on net sales of an HIV protease inhibitor sold by GlaxoSmithKline. The subroyalty expense is offset by a corresponding amount of royalty revenues on sales by GlaxoSmithKline of an HIV protease inhibitor, the rights to which we sold to a third party in 2008.

Research and Development Expenses

				2013/2012 Comparison Increase/(Decrease)		2012/2011 Comparison Increase/(Decrease)	
	2013	2012	2011	$	%	$	%
	(in thousands)			(in thousands, except percentages)			
Research expenses	$252,989	$235,588	$216,903	$17,401	7 %	$18,685	9 %
Development expenses	665,794	570,597	490,803	95,197	17 %	79,794	16 %
Total research and development expenses	$918,783	$806,185	$707,706	$112,598	14 %	$98,479	14 %

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 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 do allocate by individual program. All research and development costs for our drugs and drug candidates are expensed as incurred.

To date, we have incurred in excess of $6.4 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.

Over the three year period ended December 31, 2013, costs related to our CF and HCV programs have 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 data from a Phase 3 clinical development program to evaluate lumacaftor in combination with ivacaftor in mid-2014. If this clinical development program is successful, we plan to submit an NDA to the FDA and an MAA in the European Union in the second half of 2014. We cannot make a meaningful estimate when, if ever, our other clinical development programs will generate revenues and cash flows.

Research Expenses

				2013/2012 Comparison Increase/(Decrease)		2012/2011 Comparison Increase/(Decrease)	
	2013	2012	2011	$	%	$	%
	(in thousands)			(in thousands, except percentages)			
Research Expenses:							
Salary and benefits	$86,499	$78,488	$76,355	$8,011	10 %	$2,133	3 %
Stock-based compensation expense	27,599	25,147	25,305	2,452	10 %	(158)	(1)%
Laboratory supplies and other direct expenses	46,173	40,005	35,641	6,168	15 %	4,364	12 %
Contractual services	23,600	21,471	13,213	2,129	10 %	8,258	62 %
Infrastructure costs	69,118	70,477	66,389	(1,359)	(2)%	4,088	6 %
Total research expenses	$252,989	$235,588	$216,903	$17,401	7 %	$18,685	9 %

Over the past three years we have maintained a substantial investment in research activities resulting in a 7% increase in research expenses in 2013 as compared to 2012 and a 9% increase in research expenses in 2012 as compared to 2011. We expect to continue to invest in our research programs with a focus on identifying drug candidates for specialty markets.

Development Expenses

				2013/2012 Comparison Increase/(Decrease)		2012/2011 Comparison Increase/(Decrease)	
	2013	2012	2011	$	%	$	%
	(in thousands)			(in thousands, except percentages)			
Development Expenses:							
Salary and benefits	$170,042	$147,574	$126,441	$22,468	15%	$21,133	17%
Stock-based compensation expense	53,868	46,386	50,269	7,482	16%	(3,883)	(8)%
Laboratory supplies and other direct expenses	47,794	36,585	33,588	11,209	31%	2,997	9%
Contractual services	244,778	217,406	149,033	27,372	13%	68,373	46%
Drug supply costs	38,767	14,044	34,133	24,723	176%	(20,089)	(59)%
Infrastructure costs	110,545	108,602	97,339	1,943	2%	11,263	12%
Total development expenses	$665,794	$570,597	$490,803	$95,197	17%	$79,794	16%

Our development expenses increased by $95.2 million, or 17%, in 2013 as compared to 2012 and by $79.8 million, or 16%, in 2012 as compared to 2011. The increases in 2013 compared to 2012 were principally due to the expansion of clinical development programs in cystic fibrosis, including the initiation of the Phase 3 program for the combination of lumacaftor and ivacaftor, and increased drug supply costs primarily related to lumacaftor. The increases in 2012 in comparison to 2011 were principally due to increases in headcount and the expansion of our development efforts as we completed the registration programs for ivacaftor, prepared the regulatory filings needed to obtain approval for ivacaftor and continued the development of our other drug candidates.

Sales, General and Administrative Expenses

				2013/2012 Comparison Increase/(Decrease)		2012/2011 Comparison Increase/(Decrease)	
	2013	2012	2011	$	%	$	%
	(in thousands)			(in thousands, except percentages)			
Sales, general and administrative expenses	$362,342	$436,796	$400,721	$(74,454)	(17)%	$36,075	9%

Sales, general and administrative expenses decreased by 17% in 2013 compared to 2012, primarily due to decreased INCIVEK commercial expenses and our October 2013 restructuring activities, partially offset by increased KALYDECO commercial expenses. Sales, general and administrative expenses increased by 9% in 2012 compared to 2011, primarily due to the expansion of our global commercial organization to support the launch of KALYDECO in North America and Europe and increased INCIVEK marketing expenses. We expect that our sales, general and administrative expenses will decrease in 2014 as compared to 2013 due to decreased commercial support for INCIVEK.

Restructuring Expense

We reduced our workforce primarily related to commercial support of INCIVEK in the fourth quarter of 2013, and we recorded $39.0 million of restructuring charges related to these restructuring activities. We estimate that we will incur aggregate restructuring charges of approximately $2.0 million to $2.5 million in the future related to this restructuring. In 2013, we also began incurring restructuring charges related to the relocation of our corporate headquarters to Boston, Massachusetts from Cambridge, Massachusetts. These charges were not significant in 2013, but we expect to incur approximately $50.0 million in restructuring charges related to this relocation in 2014.

Prior to the third quarter of 2013, our restructuring expense primarily related to remaining lease obligations following restructuring activities in 2003. As of December 31, 2013, our accrued restructuring liability related to these lease obligations was $19.1 million. In 2013, 2012 and 2011, we recorded restructuring expense related to our 2003 restructuring activities of $0.4 million, $1.8 million and $2.1 million, respectively.

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Intangible Asset Impairment Charges

In 2013, we recorded a $412.9 million impairment charge related to VX-222, a non-nucleoside HCV polymerase inhibitor. In connection with this impairment charge, we recorded a credit of $127.6 million in our provision for income taxes, resulting in a net effect on net loss attributable to Vertex related to this impairment charge of $285.3 million in 2013. In 2013, we also recorded a $250.6 million impairment charge related to the HCV nucleotide analogue (VX-135) program and a benefit for income taxes of $102.1 million.

In 2011, we recorded a $105.8 million impairment charge related to VX-759, a non-nucleoside HCV polymerase inhibitor. In connection with this impairment charge, we recorded a credit of $32.7 million in our provision for income taxes resulting in a net effect on net income attributable to Vertex related to this impairment charge of $73.1 million in 2011.

There were no corresponding intangible asset impairment charges in 2012.

Other Income (Loss), Net

Interest Expense, Net

Net interest expense increased by $7.7 million, or 51%, in 2013 from $15.0 million in 2012. Net interest expense decreased by $22.7 million, or 60%, in 2012 from $37.7 million in 2011.

Other Income (Expense), Net

In 2013, we recorded net other expense of $49.9 million, primarily related to the deconsolidation of Alios. In 2011, we recorded net other expense of $15.7 million, primarily related to the embedded and free-standing derivatives associated with two financial transactions that we entered into in September 2009. Net other income in 2012 was approximately $0.3 million.

Provision for (Benefit from) Income Taxes

In 2013, we recorded a benefit from income taxes of $288.6 million. This benefit from income taxes was principally due to a benefit of $166.1 million attributable to noncontrolling interest (Alios) and a benefit of $127.6 million related to our impairment charge for the VX-222 intangible asset.

In 2012, we recorded a provision for income taxes of $38.8 million. This provision for income taxes was primarily due to a provision of $39.0 million attributable to noncontrolling interest (Alios).

In 2011, we recorded a provision for income taxes of $19.3 million. This provision for income taxes was due to a provision of $48.8 million attributable to noncontrolling interest (Alios) related to the accounting for the collaboration between Alios and us, partially offset by a benefit from income taxes of $32.7 million related to our impairment charge related to the VX-759 intangible asset.

Noncontrolling Interest (Alios)

A summary of net loss (income) attributable to noncontrolling interest (Alios) in 2013, 2012, and 2011 is as follows:

	2013	2012	2011
	(in thousands)		
Loss before provision for (benefit from) income taxes	$283,747	$20,044	$9,536
Decrease (increase) in fair value of contingent milestone and royalty payments	124,920	(114,970)	(69,950)
Provision for (benefit from) income taxes	(166,145)	39,029	48,809
Net loss (income) attributable to noncontrolling interest (Alios)	$242,522	$(55,897)	$(11,605)

In 2013, the impairment charge related to VX-135 and related tax credit and the decrease in fair value of the contingent milestone payments and royalties payable by us to Alios of $124.9 million resulted in a net loss attributable to Alios of $242.5 million.

The fair value of the contingent milestone payments and royalties payable by us to Alios increased by $115.0 million and $70.0 million, in 2012 and 2011, respectively, due to the advancement of our HCV nucleotide analogue program. Increases

in the fair value of the contingent milestone payments and royalties payable by us to Alios resulted in a decrease in net income attributable to Vertex (or an increase in net loss attributable to Vertex) on a dollar-for-dollar basis.

LIQUIDITY AND CAPITAL RESOURCES

As of December 31, 2013 we had cash, cash equivalents and marketable securities of approximately $1.47 billion, which represented an increase of $143.9 million from approximately $1.32 billion as of December 31, 2012. This increase was due to cash receipts from product sales and royalties, the $152.0 million payment we received from Janssen in the fourth quarter of 2013 and $265.9 million in cash we received from issuances of common stock pursuant to employee benefit plans, partially offset by cash expenditures we made during 2013 related to, among other things, research and development expenses and sales, general and administrative expenses, approximately $64.8 million in build-out costs for our new corporate headquarters, and $135.0 million for capital expenditures for property and equipment. In addition, in 2013, we began supporting $31.9 million in irrevocable stand-by letters of credit issued in support of property leases and other similar agreements with an unsecured credit facility with a one-year term. We previously had cash-collateralized these stand-by letters of credit. As a result of this credit facility, our restricted cash decreased by $31.8 million net of other activity recorded during 2013 and our cash and cash equivalents increased by a corresponding amount.

As of December 31, 2012, we had $400.0 million in aggregate principal amount of 2015 Notes. In addition to the $400.0 million in aggregate principal amount, which was scheduled to mature on October 1, 2015, we were scheduled to make interest payments in an aggregate amount of $33.5 million during the period from June 30, 2013 through October 1, 2015. In the second quarter of 2013, we called the 2015 Notes for redemption. In response, the holders of the 2015 Notes converted their notes into 8.2 million shares of our common stock and received an additional 0.1 million shares of our common stock to compensate them for the semi-annual interest payment that would have been payable on October 1, 2013. As of December 31, 2013, we had no 2015 Notes outstanding and our future cash commitments have been reduced by the $400.0 million in aggregate principal of the 2015 Notes plus the associated future interest payments.

Sources of Liquidity

We intend to rely on cash flows from product sales as our primary source of liquidity. Our cash flows from product sales have been decreasing in recent periods and, beginning in 2014, we will no longer receive cash flows from royalties based on sales of INCIVO by Janssen. Our near-term cash flows from product sales will be dependent on continued sales of KALYDECO, the outcomes of our reimbursement discussions with regulatory authorities in Australia and Canada, the outcomes of ongoing label-expansion programs for ivacaftor and the Phase 3 clinical trials of lumacaftor in combination with ivacaftor. In recent periods, we also have received significant proceeds from the issuance of common stock under our employee benefit plans, but 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.

Future Capital Requirements

We are incurring substantial operating expenses to conduct research and development activities and operate our organization. In addition, we have substantial facility and capital lease obligations, including leases for two buildings in Boston, Massachusetts that continue through 2028.

We expect that cash flows from our products together with our current cash, cash equivalents and marketable securities will be sufficient to fund our operations for at least the next twelve months. The adequacy of our available funds to meet our future operating and capital requirements will depend on many factors, including the amounts of future revenues generated by our products and the potential introduction or one or more of our other drug candidates to the market, and the number, breadth, cost and prospects of our research and development programs.

Financing Strategy

Although we do not have any plans to do so in the near term, we may raise additional capital through public offerings or private placements of our securities. In addition, we may raise additional capital through securing new collaborative agreements or other methods of financing. We will continue to manage our capital structure and to 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, 2013:

	Payments Due by Period				
	2014	2015-2016	2017-2018	2019 and later	Total
	(in thousands)				
Fan Pier Leases	$67,206	$134,412	$134,412	$752,798	$1,088,828
Facility operating leases, excluding Fan Pier Leases	60,641	87,590	52,341	75,344	275,916
Capital lease obligations	19,957	30,155	21,326	2,121	73,559
Research, development and drug supply costs	17,617	—	—	—	17,617
Other	6,760	5,040	84	—	11,884
Total contractual commitments and obligations	$172,181	$257,197	$208,163	$830,263	$1,467,804

Leases

In 2011, we entered into leases for two buildings that were constructed at Fan Pier in Boston, Massachusetts during the period from 2011 through 2013. These two buildings became our corporate headquarters in January 2014. We commenced lease payments in December 2013 and the initial lease periods end in December 2028.

Our future minimum commitments under our Kendall Square lease are included in "Facility operating leases, excluding Fan Pier Leases." We have entered into two subleases for a portion of the rentable square footage at the Kendall Square facility to offset our on-going contractual lease obligations. The future minimum committed income from the subleases is $8.5 million for 2014 and $4.0 million for 2015. These amounts are not offset against our obligations set forth in the table above. See Note R, "Restructuring Expenses," to our consolidated financial statements for further information.

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

Research, Development and Drug Supply Costs

"Research, development and drug supply costs," does 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, 2013, we had accrued $30.8 million related to these contracts for costs incurred for services provided through December 31, 2013, and we have approximately $139.9 million in cancelable future commitments based on existing contracts as of December 31, 2013. 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

We have entered into certain research and development collaboration agreements with third parties 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. Pursuant to our collaboration with Alios, Alios is eligible to receive development milestone payments from us of up to $312.5 million if VX-135 is approved and commercialized. As of December 31, 2013, Alios had earned $60.0 million of these milestone payments, all of which had been paid as of December 31, 2013. Alios also is eligible to receive commercial milestone payments from us of up to $750.0 million, as well as tiered royalties on net sales of approved drugs. We also have royalty and milestone obligations to the Cystic Fibrosis Foundation Therapeutics Incorporated. 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, 2013, we have $2.0 million of liabilities associated with uncertain tax positions. As of December 31, 2013, we cannot reasonably estimate the amount we expect to pay within the next twelve months in connection with 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 is 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;
- consolidation and deconsolidation of variable interest entity;
- accruals;
- commercial supplies and inventories;
- income taxes; and
- leases.

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 major and selected regional wholesalers and 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. Separately, we have arrangements with numerous third-party payors in North America that provide for government-mandated and privately-negotiated rebates, chargebacks and discounts. 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. 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 incentives offered to certain indirect customers, including patients. 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.

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.

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. Typically, government-mandated discounts in the United States and Canada are significantly larger than discounts provided to 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 frequently are submitted to us significantly after the related sales, potentially resulting in adjustments in the period in which the new information becomes known. If we increased our estimate of the percentage of patients receiving our products covered by third-party payors entitled to government-mandated discounts by two percentage points, our net product revenues would decrease by less than one percent for the three months ended December 31, 2013.

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.

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; payments for services we provide through our third-party manufacturing network; 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 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. For arrangements entered into or materially modified after January 1, 2011, 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.

In the fourth quarter of 2013, we amended our collaboration agreement with Janssen, and were required to make significant estimates regarding (i) the determination of whether or not the agreement was materially modified and (ii) the

estimated selling price for the remaining telaprevir development activities. We recognized $182.4 million of collaborative revenues pursuant to the collaboration agreement in the fourth quarter of 2013. This amount was primarily attributable to (i) the new consideration received from Janssen, including the $152.0 million fourth quarter 2013 payment and the remaining deferred revenues related to the 2006 up-front payment less (ii) our best estimate of selling price for the remaining telaprevir development activities. As of December 31, 2013, the remaining deferred revenue balance related to Janssen was $5.0 million, which will be recognized as collaborative revenues as telaprevir development program activities are completed.

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 acquired 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.

In 2013, we incurred intangible asset impairment charges totaling $663.5 million that all related to drug candidates for the treatment of HCV infection. As of December 31, 2013, we had no intangible assets.

ViroChem Acquisition

As of December 31, 2010, the intangible assets acquired from ViroChem that were reflected on our consolidated balance sheet related to two drug candidates, VX-222 and VX-759. VX-222 and VX-759 had estimated fair values on the acquisition date and December 31, 2010 of $412.9 million and $105.8 million, respectively. The estimated fair values ascribed to VX-222 and VX-759 on the acquisition date were based on the estimated fair value that would have been ascribed to each of these drug candidates by a market participant that acquired both drug candidates in a single transaction.

In the third quarter of 2011, we recorded a $105.8 million intangible asset impairment charge related to VX-759 and in the first quarter of 2013, we recorded a $412.9 million intangible asset impairment charge related to VX-222. The timing of these impairment charges were based on changes in our estimates regarding the potential to develop these assets and the competitive landscape, which were reflected in the reported results for the period in which they became known.

Alios Collaboration

We recorded $250.6 million of intangible assets on our consolidated balance sheet based on our estimate of the fair value of Alios' HCV nucleotide analogue program as of June 13, 2011 and made significant estimates regarding: the probability of obtaining regulatory approval of an HCV nucleotide analogue; the timing and expected costs of clinical trials and other development activities; future potential cash flows from sales of drugs and the appropriate discount and tax rates. In the fourth quarter of 2013, a $250.6 million intangible asset impairment charge related to the HCV nucleotide analogue (VX-135) program was recorded. The timing of this impairment charge was based on changes in

our estimates regarding the potential to develop this asset and the competitive landscape, which were reflected in our reported results in the period in which they became known.

Consolidation and Deconsolidation of Variable Interest Entity

In 2011, we entered into an agreement with Alios pursuant to which we agreed to collaborate on the research, development and commercialization of ALS-2200 (now formulated as VX-135) and ALS-2158, two HCV nucleotide analogues discovered by Alios. In 2012, we received data from Phase 1 clinical trials in which Alios evaluated ALS-2200 and ALS-2158. Based on data from these clinical trials, we ended all development activities related to ALS-2158 and continued to develop VX-135. We are responsible for all expenses related to the development and commercialization of VX-135. We paid Alios a $60.0 million up-front payment in connection with the execution of the agreement and $60.0 million in milestone payments through December 31, 2013. Alios is eligible to receive research and development milestone payments, commercial milestone payments and tiered royalties on net sales of any approved drugs licensed by us under the collaboration agreement. Our interests in Alios are limited to those accorded to us pursuant to our collaboration agreement with Alios, and we have no equity interest, or right to acquire any equity interest, in Alios. In addition to Alios' activities related to HCV nucleotide analogues, Alios is engaged in separate programs directed at developing novel drugs.

Our collaboration with Alios requires us to apply accounting policies that involve significant judgments and that have a material effect on our consolidated financial statements. Under applicable accounting guidance, as a result of the relationship established through the collaboration agreement, Alios was deemed to be a variable interest entity, or VIE, our license to ALS-2200 (VX-135) and ALS-2158 was deemed to be a variable interest in Alios as a whole, and we were deemed to be Alios' primary beneficiary. As a result, we were required to consolidate Alios' financial statements into our financial statements for the period from June 2011 through December 31, 2013. As a result of the impairment of our HCV nucleotide analogue program in the fourth quarter of 2013, we determined that we no longer had a variable interest in Alios as a whole and deconsolidated Alios effective as of December 31, 2013.

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

- In 2013, the deconsolidation of Alios resulted in a gain of $68.2 million attributable to Vertex. The $68.2 million gain is approximately equal to the difference between (i) losses we recorded in 2011 and 2012 based on increases in the fair value of contingent milestone payments and royalties payable by us to Alios and (ii) the aggregate of $120.0 million in up-front and milestone payments that we made to Alios pursuant to the Alios collaboration.
- In each period, we recorded net loss (income) attributable to the Alios noncontrolling interest. This net loss (income) reflected Alios' net loss (income) for the period as adjusted for gains and losses in the fair value of the contingent milestone payments and royalties payable by us to Alios. Determining the fair value of the contingent milestone payments and royalties payable by us to Alios required 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 the HCV nucleotide analogues licensed from Alios and appropriate discount and tax rates. We based our estimate 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 represented a measure of credit risk associated with settling the liability. Significant judgment was used in determining the appropriateness of these assumptions at each reporting period. Increases in 2011 and 2012 in the fair value of the contingent milestone payments and royalties payable by us to Alios resulted in a decrease in net income attributable to Vertex (or an increase in net loss attributable to Vertex) on a dollar-for-dollar basis.
- From June 2011 through December 31, 2013, we consolidated all of Alios' expenses and revenues into our consolidated statements of operations, eliminating all intercompany balances and transactions. As of December 31, 2013, our consolidated balance sheet excludes Alios' balances.
- We continue to have significant involvement with Alios due to the Alios agreement; therefore, the deconsolidation of Alios does not qualify for discontinued operations presentation in our consolidated financial statements as of December 31, 2013. We will evaluate whether we continue to have significant involvement with Alios for a period of one year from the December 31, 2013 deconsolidation date. If we determine that we no longer have significant continuing involvement with Alios during the year following the deconsolidation of Alios, we will retroactively adjust our consolidated financial statements to reflect discontinued operations presentation.

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Accruals

Research and development expenses, including amounts funded through research and development collaborations, and sales, general and administrative expenses 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, past history for 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 INCIVEK inventories on January 1, 2011 and the costs of our KALYDECO inventories on January 1, 2012. 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 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.

Treatment of HCV infection is a highly competitive field characterized by rapid technological advances. In 2013 and 2012, following periodic assessments of the recoverability of our inventories, we recorded within cost of product revenues an aggregate of $10.4 million and $133.2 million, respectively in charges primarily related to excess and obsolete INCIVEK inventories based on our analysis of our INCIVEK inventory levels in relation to our commercial outlook for INCIVEK. Periodic assessments of the recoverability of capitalized costs involve significant estimates and judgments on the part of management. As of December 31, 2013, we had $0.9 million in remaining INCIVEK inventories.

Income Taxes

We maintain a valuation allowance on our net operating losses and other deferred tax assets because we have an extended history of annual losses. Our U.S. federal net operating loss carryforwards totaled approximately $2.7 billion as of December 31, 2013. On an annual basis, we reassess the valuation allowance for deferred income tax assets. After consideration of all the evidence, both positive and negative, we continue to maintain a valuation allowance on the deferred tax asset as of December 31, 2013 because it is more likely than not that the deferred tax asset will not be realized. In future periods, if we determine that it is more likely than not that the deferred tax asset will be realized, (i) the valuation allowance would be decreased, (ii) a portion or all of the deferred tax asset would be reflected on our consolidated balance sheet and (iii) we would record non-cash benefits in our consolidated statements of operations related to the reflection of the deferred tax asset on our consolidated balance sheet.

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.

We evaluated the leases in the fourth quarter of 2013 and determined that the leases did not meet the criteria for “sale-leaseback” treatment. Accordingly, we began depreciating the asset and incurring interest expense related to the financing obligation during the fourth quarter of 2013. 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. The portion of the lease obligations allocated to the land is treated as an operating lease that commenced in 2011. In connection with the leases for our corporate headquarters, in 2014, we expect to incur approximately $60.0 million in interest expense, $14.0 million in depreciation expense and $6.5 million in operating expenses.

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. There were no new accounting pronouncements adopted during 2013 that had a material effect on our financial statements.

ITEM 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

As part of our investment portfolio, we own financial instruments that are sensitive to market risks. The investment portfolio is used to preserve our capital until it is required to fund operations, including our research and development activities. None of these market risk-sensitive instruments are held for trading purposes. We do not have derivative financial instruments in our investment portfolio.

Interest Rate Risk

We invest our cash in a variety of financial instruments, principally securities issued by the U.S. government and its agencies, investment-grade corporate bonds and commercial paper, and money market funds. These investments are denominated in U.S. dollars. All of our interest-bearing securities are subject to interest rate risk and could decline in value if interest rates fluctuate. Substantially all of our investment portfolio consists of marketable securities with active secondary or resale markets to help ensure portfolio liquidity, and we have implemented guidelines limiting the term-to-maturity of our investment instruments. Due to the conservative nature of these instruments, we do not believe that we have a material exposure to interest rate risk.

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, payables 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.

In December 2013, we implemented a foreign currency management program with the objective of reducing the impact of exchange rate fluctuations on our operating results and forecasted revenues and expenses denominated in foreign currencies. The change in fair value of these foreign currency forward contracts included in accumulated other comprehensive loss and the gross fair value of foreign currency forward assets and liabilities included on the consolidated balance sheet as of December 31, 2013 were not material.

ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA

The information required by this Item 8 is contained on pages F-1 through F-45 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, 2013. 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 (1992 framework)(COSO). Based on its assessment, the Company’s management has concluded that, as of December 31, 2013, 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, 2013, 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

The Board of Directors and Shareholders of

Vertex Pharmaceuticals Incorporated

We have audited Vertex Pharmaceuticals Incorporated's internal control over financial reporting as of December 31, 2013, based on criteria established in Internal Control—Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (1992 framework)(the COSO criteria). Vertex Pharmaceuticals Incorporated'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 conducted our audit in accordance with the standards of the Public Company Accounting Oversight Board (United States). 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.

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.

In our opinion, Vertex Pharmaceuticals Incorporated maintained, in all material respects, effective internal control over financial reporting as of December 31, 2013, based on the COSO criteria.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), the consolidated balance sheets of Vertex Pharmaceuticals Incorporated as of December 31, 2013 and 2012, and 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, 2013 of Vertex Pharmaceuticals Incorporated and our report dated February 11, 2014 expressed an unqualified opinion thereon.

/s/ Ernst & Young LLP

Boston, Massachusetts

February 11, 2014

ITEM 9B. OTHER INFORMATION

Not applicable.

PART III

Portions of our definitive Proxy Statement for the 2014 Annual Meeting of Shareholders, or 2014 Proxy Statement, during which, we expect to, among other things, (i) elect our Class I Directors, (ii) conduct the non-binding advisory vote on our executive compensation program and (iii) ratify the appointment of our independent registered accounting firm, 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 2014 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 2014 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 2014 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 2014 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 2014 Proxy Statement and is incorporated herein by reference. We expect this information to be provided under “ Election of Directors,” “Corporate Governance and Risk Management,” “Approval of Related Person Transactions” and “Transactions with Related Persons.”

ITEM 14. PRINCIPAL ACCOUNTANT FEES AND SERVICES

The information required by this Item 14 will be included in the 2014 Proxy Statement and is incorporated herein by reference. We expect this information to be provided under “Ratification of the Appointment of Independent Registered Public Accounting Firm.”

PART IV

ITEM 15. EXHIBITS AND FINANCIAL STATEMENT SCHEDULES

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

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

(a)(3) Exhibits.

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

Exhibit Number	Exhibit Description	Filed with this report	Incorporated by Reference herein from—Form or Schedule	Filing Date/ Period Covered	SEC File/ Reg. Number
3.1	Restated Articles of Organization of Vertex Pharmaceuticals Incorporated, as amended.		10-Q (Exhibit 3.1)	August 11, 2008	000-19319
3.2	By-laws of Vertex Pharmaceuticals Incorporated, as amended and restated as of February 5, 2014.		8-K (Exhibit 3.1)	February 5, 2014	000-19319
4.1	Specimen stock certificate.		S-1 (Exhibit 4.1)	July 18, 1991	33-40966
Collaboration Agreements					
10.1	License, Development, Manufacturing and Commercialization Agreement, dated June 30, 2006, by and between Vertex Pharmaceuticals Incorporated and Janssen Pharmaceutica, N.V.†		10-K (Exhibit 10.1)	February 22, 2012	000-19319
10.2	2013 Amendment, dated November 19, 2013, to the License, Development, Manufacturing and Commercialization Agreement by and between Vertex Pharmaceuticals Incorporated and Janssen Pharmaceutica NV.†	X			
10.3	License, Development and Commercialization Agreement, dated as of June 11, 2004, between Vertex Pharmaceuticals Incorporated and Mitsubishi Pharma Corporation.†		10-Q (Exhibit 10.1)	November 9, 2009	000-19319
10.4	Second Amendment to License, Development and Commercialization Agreement, dated July 30, 2009, between Mitsubishi Tanabe Pharma Corporation and Vertex Pharmaceuticals Incorporated.†		10-Q (Exhibit 10.2)	November 9, 2009	000-19319

10.5	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, 2011000-19319
10.6	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
10.7	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, 2011000-19319

Exhibit Number	Exhibit Description	Filed with this report	Incorporated by Reference herein from—Form or Schedule	Filing Date/ Period Covered	SEC File/ Reg. Number
10.8	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
10.9	License and Collaboration Agreement, dated June 13, 2011, by and between Alios BioPharma, Inc. and Vertex Pharmaceuticals Incorporated and Vertex Pharmaceuticals (Switzerland) LLC.†		10-Q (Exhibit 10.1)	August 9, 2011	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 as of January 18, 2001, between Kendall Square, LLC and Vertex Pharmaceuticals Incorporated.†		10-K (Exhibit 10.16)	March 26, 2001	000-19319
Equity Plans					
10.13	1996 Stock and Option Plan, as amended and restated as of March 14, 2005.*		10-K (Exhibit 10.3)	March 16, 2005	000-19319
10.14	Form of Stock Option Grant under 1996 Stock and Option Plan.*		8-K (Exhibit 10.1)	February 9, 2005	000-19319
10.15	Amended and Restated 2006 Stock and Option Plan.*		10-Q (Exhibit 10.3)	August 8, 2012	000-19319
10.16	Form of Stock Option Grant under 2006 Stock and Option Plan.*		8-K (Exhibit 10.2)	May 15, 2006	000-19319
10.17	Form of Restricted Stock Award under 2006 Stock and Option Plan.*		8-K (Exhibit 10.3)	May 15, 2006	000-19319
10.18	Form of Restricted Stock Award (Performance Accelerated Restricted Stock) under 2006 Stock and Option Plan.*		8-K (Exhibit 10.4)	May 15, 2006	000-19319
10.19	Form of Stock Option Grant-Performance Accelerated 2009 Stock-Options.*		10-K (Exhibit 10.33)	February 19, 2010	000-19319
10.20	2013 Stock and Option Plan.*		8-K (Exhibit 10.1)	May 8, 2013	000-19319
10.21	Form of Non-Qualified Stock Option Agreement under 2013 Stock and Option Plan.*	X			000-19319
10.22	Form of Restricted Stock Agreement under 2013 Stock and Option Plan.*	X			000-19319
10.23	Form of Restricted Stock Unit Agreement under 2013 Stock and Option Plan.*	X			000-19319
10.24		X			000-19319

	Form of Non-Qualified Stock Option Agreement under Amended and Restated 2006 Stock and Option Plan (granted on or after July 30, 2013).*				
10.25	Form of Restricted Stock Agreement under Amended and Restated 2006 Stock and Option Plan (granted on or after July 30, 2013).*	X			000-19319
10.26	Form of Restricted Stock Unit Agreement under Amended and Restated 2006 Stock and Option Plan (granted on or after July 30, 2013).*	X			000-19319
10.27	Vertex Pharmaceuticals Incorporated Employee Stock Purchase Plan, as amended and restated.*		10-Q (Exhibit 10.4)	August 8, 2012	000-19319
Agreements with Executive Officers and Directors					
10.28	Agreement between Jeffrey M. Leiden and Vertex, dated December 14, 2011.*		10-K (Exhibit 10.34)	February 22, 2012	000-19319
10.29	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
10.30	Transition Agreement between Matthew W. Emmens and Vertex, dated December 14, 2011.*		10-K (Exhibit 10.38)	February 22, 2012	000-19319
10.31	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
10.32	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
10.33	Employment Agreement, dated as of June 11, 2012, between Vertex Pharmaceuticals Incorporated and Kenneth L. Horton.*		10-Q (Exhibit 10.1)	August 8, 2012	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
10.34	Change of Control Agreement, dated as of June 11, 2012, between Vertex Pharmaceuticals Incorporated and Kenneth L. Horton.*		10-Q (Exhibit 10.2)	August 8, 2012	000-19319
10.35	Second Amended and Restated Employment Agreement, dated November 15, 2012, between Peter Mueller and Vertex Pharmaceuticals Incorporated.*		10-K (Exhibit 10.38)	March 1, 2013	000-19319
10.36	Second Amended and Restated Change of Control Agreement, dated November 15, 2012, between Vertex Pharmaceuticals Incorporated and Peter Mueller.*		10-K (Exhibit 10.39)	March 1, 2013	000-19319
10.37	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
10.38	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
10.39	Form of Employee Non-Disclosure and Inventions Agreement.*		S-1 (Exhibit 10.4)	May 30, 1991	33-40966
10.40	Vertex Employee Compensation Plan.*	X			
10.41	Vertex Pharmaceuticals Non-Employee Board Compensation.*		10-K (Exhibit 10.57)	February 22, 2012	000-19319
Subsidiaries					
21.1	Subsidiaries of Vertex Pharmaceuticals Incorporated.	X			
Consent					
23.1	Consent of Independent Registered Public Accounting Firm, Ernst & Young LLP.	X			
Certifications					
31.1	Certification of the Chief Executive Officer under Section 302 of the Sarbanes-Oxley Act of 2002.	X			
31.2	Certification of the Chief Financial Officer under Section 302 of the Sarbanes-Oxley Act of 2002.	X			
32.1	Certification of the Chief Executive Officer and the Chief Financial Officer under Section 906 of the Sarbanes-Oxley Act of 2002.	X			
101.INS	XBRL Instance	X			
101.SCH	XBRL Taxonomy Extension Schema	X			
101.CAL	XBRL Taxonomy Extension Calculation	X			
101.LAB	XBRL Taxonomy Extension Labels	X			
101.PRE	XBRL Taxonomy Extension Presentation	X			
101.DEF	XBRL Taxonomy Extension Definition	X			

* Management contract, compensatory plan or agreement.

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

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SIGNATURES

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

Vertex Pharmaceuticals Incorporated

February 11, 2014 By: /s/ Jeffrey M. Leiden
Jeffrey M. Leiden
Chief Executive Officer

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

Name	Title	Date
/s/ Jeffrey M. Leiden Jeffrey M. Leiden	Chair of the Board, President and Chief Executive Officer (Principal Executive Officer)	February 11, 2014
/s/ Ian F. Smith Ian F. Smith	Executive Vice President and Chief Financial Officer (Principal Financial Officer)	February 11, 2014
/s/ Paul M. Silva Paul M. Silva	Senior Vice President and Corporate Controller (Principal Accounting Officer)	February 11, 2014
/s/ David Altshuler David Altshuler	Director	February 11, 2014
/s/ Joshua S. Boger Joshua S. Boger	Director	February 11, 2014
/s/ Terrence C. Kearney Terrence C. Kearney	Director	February 11, 2014
/s/ Yuchun Lee Yuchun Lee	Director	February 11, 2014
/s/ Margaret G. McGlynn Margaret G. McGlynn	Director	February 11, 2014
/s/ Wayne J. Riley Wayne J. Riley	Director	February 11, 2014
/s/ Bruce I. Sachs Bruce I. Sachs	Director	February 11, 2014
/s/ Elaine S. Ullian Elaine S. Ullian	Director	February 11, 2014

Report of Independent Registered Public Accounting Firm

The Board of Directors and Shareholders of

Vertex Pharmaceuticals Incorporated

We have audited the accompanying consolidated balance sheets of Vertex Pharmaceuticals Incorporated as of December 31, 2013 and 2012, and 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, 2013. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits.

We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements. An audit also includes assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the financial statements referred to above present fairly, in all material respects, the consolidated financial position of Vertex Pharmaceuticals Incorporated at December 31, 2013 and 2012, and the consolidated results of its operations and its cash flows for each of the three years in the period ended December 31, 2013, 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), Vertex Pharmaceuticals Incorporated's internal control over financial reporting as of December 31, 2013, based on the criteria established in Internal Control—Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (1992 framework) and our report dated February 11, 2014 expressed an unqualified opinion thereon.

/s/ Ernst & Young LLP

Boston, Massachusetts

February 11, 2014

VERTEX PHARMACEUTICALS INCORPORATED
Consolidated Statements of Operations
(in thousands, except per share amounts)

	Year Ended December 31,		
	2013	2012	2011
Revenues:			
Product revenues, net	$837,645	$1,333,458	$950,889
Royalty revenues	156,592	141,498	50,015
Collaborative revenues	217,738	52,086	409,722
Total revenues	1,211,975	1,527,042	1,410,626
Costs and expenses:			
Cost of product revenues	88,979	236,742	63,625
Royalty expenses	41,298	43,143	16,880
Research and development expenses	918,783	806,185	707,706
Sales, general and administrative expenses	362,342	436,796	400,721
Restructuring expenses	40,521	1,844	2,074
Intangible asset impairment charges	663,500	—	105,800
Total costs and expenses	2,115,423	1,524,710	1,296,806
Income (loss) from operations	(903,448)	2,332	113,820
Interest expense, net	(22,730)	(15,022)	(37,681)
Other income (expense), net	(49,939)	309	(15,694)
Income (loss) before provision for (benefit from) income taxes	(976,117)	(12,381)	60,445
Provision for (benefit from) income taxes	(288,567)	38,754	19,266
Net income (loss)	(687,550)	(51,135)	41,179
Net loss (income) attributable to noncontrolling interest (Alios)	242,522	(55,897)	(11,605)
Net income (loss) attributable to Vertex	$(445,028)	$(107,032)	$29,574
Net income (loss) per share attributable to Vertex common shareholders:			
Basic	$(1.98)	$(0.50)	$0.14
Diluted	$(1.98)	$(0.50)	$0.14
Shares used in per share calculations:			
Basic	224,906	211,946	204,891
Diluted	224,906	211,946	208,807

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,		
	2013	2012	2011
Net income (loss)	$(687,550)	$(51,135)	$41,179
Changes in other comprehensive income (loss):			
Unrealized holding gains (losses) on marketable securities	(154)	305	(119)
Unrealized losses on foreign currency forward contracts	(23)	—	—
Foreign currency translation adjustment	421	198	133
Total changes in other comprehensive income (loss)	244	503	14
Comprehensive income (loss)	(687,306)	(50,632)	41,193
Comprehensive loss (income) attributable to noncontrolling interest (Alios)	242,522	(55,897)	(11,605)
Comprehensive income (loss) attributable to Vertex	$(444,784)	$(106,529)	$29,588

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, 2013(1)	2012(1)
Assets		
Current assets:		
Cash and cash equivalents	$569,299	$489,407
Marketable securities, available for sale	895,777	831,808
Restricted cash and cash equivalents (Alios)	—	69,983
Accounts receivable, net	85,517	143,250
Inventories	14,147	30,464
Prepaid expenses and other current assets	23,836	24,673
Total current assets	1,588,576	1,589,585
Restricted cash	130	31,934
Property and equipment, net	696,911	433,609
Intangible assets	—	663,500
Goodwill	30,992	30,992
Other assets	2,432	9,668
Total assets	$2,319,041	$2,759,288
Liabilities and Shareholders' Equity		
Current liabilities:		
Accounts payable	$49,327	$101,292
Accrued expenses	271,077	264,884
Deferred revenues, current portion	21,510	27,566
Accrued restructuring expense, current portion	14,286	4,758
Capital lease obligations, current portion	16,893	13,707
Income taxes payable (Alios)	—	715
Other liabilities, current portion	24,736	19,702
Total current liabilities	397,829	432,624
Deferred revenues, excluding current portion	49,459	96,242
Accrued restructuring expense, excluding current portion	14,067	18,570
Capital lease obligations, excluding current portion	48,754	15,170
Convertible senior subordinated notes (due 2015)	—	400,000
Deferred tax liability	—	280,367
Construction financing lease obligation	440,937	268,031
Other liabilities, excluding current portion	11,590	13,902
Total liabilities	962,636	1,524,906
Commitments and contingencies (Note T and Note V)		
Redeemable noncontrolling interest (Alios)	—	38,530
Shareholders' equity:		
Preferred stock, $0.01 par value; 1,000,000 shares authorized; none issued and outstanding at December 31, 2013 and 2012	—	—
Common stock, $0.01 par value; 300,000,000 shares authorized at December 31, 2013 and 2012; 233,788,852 and 217,286,868 shares issued and outstanding at December 31, 2013 and 2012, respectively	2,320	2,149
Additional paid-in capital	5,321,286	4,519,448
Accumulated other comprehensive loss	(306)	(550)
Accumulated deficit	(3,966,895)	(3,521,867)

Total Vertex shareholders' equity	1,356,405	999,180
Noncontrolling interest (Alios)	—	196,672
Total shareholders' equity	1,356,405	1,195,852
Total liabilities and shareholders' equity	$2,319,041	$2,759,288

(1) Amounts as of December 31, 2012 include the assets and liabilities of Vertex's variable interest entity ("VIE"), Alios BioPharma, Inc. ("Alios"). The Company deconsolidated Alios as of December 31, 2013. Vertex's interests and obligations with respect to the VIE's assets and liabilities are limited to those accorded to Vertex in its agreement with Alios. See Note B, "Collaborative Arrangements," to these consolidated financial statements for amounts.

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 Loss	Accumulated Deficit	Total Vertex Shareholders' Equity	Noncontrolling Interest (Alios)	Total Shareholders' Equity	Redeemable Noncontrolling Interest (Alios)
	Shares	Amount							
Balance, December 31, 2010	203,523	$2,016	$3,947,433	$(1,067)	$(3,444,409)	$503,973	$—	$503,973	$—
Unrealized holding losses on marketable securities				(119)		(119)		(119)	
Foreign currency translation adjustment				133		133		133	
Net income					29,574	29,574	11,605	41,179	
Issuance of common stock under benefit plans	5,781	56	133,362			133,418	(25)	133,393	
Stock-based compensation expense			118,964			118,964	304	119,268	
Tax benefit from equity compensation			900			900		900	
Alios noncontrolling interest upon consolidation							130,486	130,486	36,299
Change in liquidation value of noncontrolling interest							(737)	(737)	737
Balance, December 31, 2011	209,304	$2,072	$4,200,659	$(1,053)	$(3,414,835)	$786,843	$141,633	$928,476	$37,036
Unrealized holding gains on marketable securities				305		305		305	
Foreign currency translation adjustment				198		198		198	
Net income (loss)					(107,032)	(107,032)	55,897	(51,135)	
Issuance of common stock under benefit plans	7,983	77	201,760			201,837	155	201,992	
Stock-based compensation			115,058			115,058	481	115,539	

expense									
Tax benefit from equity compensation			1,971			1,971		1,971	
Change in liquidation value of noncontrolling interest							(1,494)	(1,494)	1,494
Balance, December 31, 2012	217,287	$2,149	$4,519,448	$(550)	$(3,521,867)	$999,180	$196,672	$1,195,852	$38,530
Unrealized holding losses on marketable securities				(154)		(154)		(154)	
Unrealized losses on foreign currency forward contracts				(23)		(23)		(23)	
Foreign currency translation adjustment				421		421		421	
Net loss					(445,028)	(445,028)	(242,522)	(687,550)	
Issuance of common stock under benefit plans	8,226	88	271,713			271,801	(63)	271,738	
Convertible senior subordinated notes (due 2015) conversion	8,276	83	402,182			402,265		402,265	
Stock-based compensation expense			127,883			127,883	468	128,351	
Restructuring expense related to benefit plans			1,312			1,312		1,312	
Tax benefit from equity compensation			(1,252)			(1,252)		(1,252)	
Alios noncontrolling interest upon deconsolidation						—	45,445	45,445	(38,530)
Balance, December 31, 2013	233,789	$2,320	$5,321,286	$(306)	$(3,966,895)	$1,356,405	$—	$1,356,405	$—

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,		
	2013	2012	2011
Cash flows from operating activities:			
Net income (loss)	$(687,550)	$(51,135)	$41,179
Adjustments to reconcile net income (loss) to net cash provided by (used in) operating activities:			
Depreciation and amortization expense	48,365	38,191	35,041
Stock-based compensation expense	127,303	114,285	118,226
Other non-cash based compensation expense	5,860	10,261	8,525
Intangible asset impairment charges	663,500	—	105,800
Secured notes (due 2012) discount amortization expense	—	—	18,409
Change in fair value of derivative instruments	—	—	16,801
Deferred income taxes	(285,053)	36,660	(7,501)
Non-cash restructuring charges	7,594	—	—
Deconsolidation of variable interest entity (Alios)	55,110	—	—
Write-downs of inventories to net realizable value	10,358	133,189	—
Excess tax benefit from share-based payment arrangements	1,252	(1,971)	(900)
Other non-cash items, net	6,742	178	319
Changes in operating assets and liabilities, excluding the effects of the acquisition and deconsolidation of a variable interest entity (Alios):			
Accounts receivable, net	53,363	39,912	(170,606)
Inventories	7,142	(29,925)	(111,388)
Prepaid expenses and other current assets	(12,061)	(23,619)	10,358
Accounts payable	(49,234)	14,892	37,468
Accrued expenses and other liabilities	43,725	29,232	116,822
Accrued restructuring expense	5,025	(2,985)	(3,282)
Deferred revenues	(53,011)	(39,324)	(71,536)
Net cash provided by (used in) operating activities	(51,570)	267,841	143,735
Cash flows from investing activities:			
Purchases of marketable securities	(2,412,418)	(1,705,829)	(721,545)
Sales and maturities of marketable securities	2,348,295	1,367,927	1,016,040
Payment for acquisition of variable interest entity (Alios)	—	—	(60,000)
Expenditures for property and equipment	(51,393)	(71,140)	(34,595)
Decrease in restricted cash and cash equivalents	31,804	2,156	—
Decrease (increase) in restricted cash and cash equivalents (Alios)	27,884	(18,105)	12,695
Decrease (increase) in other assets	1,698	(826)	(183)
Net cash provided by (used in) investing activities	(54,130)	(425,817)	212,412
Cash flows from financing activities:			
Excess tax benefit from share-based payment arrangements	(1,252)	1,971	900
Issuances of common stock under benefit plans	265,878	191,721	124,862
Payments to redeem secured notes	(158)	—	(155,000)
Settlement of milestone derivatives	—	—	(95,000)
Payments on capital lease obligations	(16,057)	(2,615)	—
Payments on construction financing lease obligation	(67,527)	(18,873)	—
Net cash provided by (used in) financing activities	180,884	172,204	(124,238)
Effect of changes in exchange rates on cash	4,708	(141)	214

Net increase in cash and cash equivalents	79,892	14,087	232,123
Cash and cash equivalents—beginning of period	489,407	475,320	243,197
Cash and cash equivalents—end of period	$569,299	$489,407	$475,320
Supplemental disclosure of cash flow information:			
Cash paid for interest	$11,015	$13,400	$13,512
Cash paid for income taxes	$2,840	$9,318	$—
Conversion of convertible senior subordinated notes (due 2015) for common stock	$399,842	$—	$—
Capitalization of construction in-process related to construction financing lease obligation	$215,013	$235,594	$54,655
Assets acquired under capital lease obligations	$50,972	$30,101	$—
Unamortized deferred debt issuance costs exchanged	$4,230	$—	$—

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") is in the business of discovering, developing, manufacturing and commercializing small molecule drugs for patients with serious diseases in specialty markets. The Company's two products are: KALYDECO (ivacaftor), which the Company markets in the United States and international markets for the treatment of patients six years of age and older with cystic fibrosis ("CF"), who have the G551D mutation in their cystic fibrosis transmembrane conductance regulator ("CFTR") gene, and INCIVEK (telaprevir), which is approved in the United States and Canada for the treatment of adults with genotype 1 hepatitis C virus ("HCV") infection.
The Company began recognizing net product revenues from sales of INCIVEK and KALYDECO in the second quarter of 2011 and first quarter of 2012, respectively. The Company's collaborator, Janssen Pharmaceutica NV ("Janssen"), began marketing telaprevir in its territories under the brand name INCIVO in September 2011. The Company's net loss attributable to Vertex for 2013 was $445.0 million, or $1.98 per share. As of December 31, 2013, the Company had cash, cash equivalents and marketable securities of approximately $1.47 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 KALYDECO, competition, uncertainty about clinical trial outcomes and regulatory approvals, uncertainties relating to pharmaceutical pricing and reimbursement, rapid technological change, 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 and (ii) its wholly-owned subsidiaries. In addition, the consolidated financial statements for the period from June 13, 2011 through December 31, 2013, reflect the operations of Alios BioPharma, Inc. ("Alios"), a collaborator that is a variable interest entity (a "VIE") for which the Company was deemed under applicable accounting guidance to have a variable interest and be the primary beneficiary. As of December 31, 2013, the Company deconsolidated Alios, and the Company's consolidated balance sheet as of December 31, 2013 excludes Alios. All material intercompany balances and transactions have been eliminated. The Company operates in one segment, pharmaceuticals. Please refer to Note X, "Segment Information," for enterprise-wide disclosures regarding the Company's revenues, major customers and long-lived assets by geographic area.
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, restructuring expense, the fair value of intangible assets, noncontrolling interest (Alios), the consolidation and deconsolidation of a VIE, leases and the income tax provision. 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.

VERTEX PHARMACEUTICALS INCORPORATED

Notes to Consolidated Financial Statements (Continued)

Revenue Recognition

Product Revenues, Net

The Company sells its products principally to a limited number of major and selected regional wholesalers and specialty pharmacy providers in North America as well as government-owned and supported customers in Europe (collectively, its “Customers”). The Company's Customers in North America subsequently resell the products to patients and health care providers. The Company recognizes 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 incentives offered to certain indirect customers, including patients.

The Company makes significant estimates and judgments that materially affect the Company’s recognition of net product revenues. 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 revenues associated with the units in which revenue recognition was deferred.

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 generally include a 2% 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 with government agencies and various private organizations (collectively, 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 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, 2013:

	Trade Allowances	Rebates, Chargebacks and Discounts	Product Returns	Other Incentives	Total
	(in thousands)				
2013					
Beginning Balance	$5,416	$63,560	$2,852	$3,565	$75,393
Provision related to current period sales	31,395	204,459	5,795	9,295	250,944
Adjustments related to prior period sales	343	4,474	15,149	(228)	19,738
Credits/payments made	(35,619)	(204,249)	(7,997)	(11,077)	(258,942)
Ending Balance	$1,535	$68,244	$15,799	$1,555	$87,133
2012					
Beginning Balance	$11,162	$52,659	$340	$5,202	$69,363
Provision related to current period sales	55,913	216,942	2,067	19,103	294,025
Adjustments related to prior period sales	29	3,883	1,498	72	5,482
Credits/payments made	(61,688)	(209,924)	(1,053)	(20,812)	(293,477)
Ending Balance	$5,416	$63,560	$2,852	$3,565	$75,393
2011					
Beginning Balance	$—	$—	$—	$—	$—
Provision related to current period sales	38,228	75,145	553	9,692	123,618
Credits/payments made	(27,066)	(22,486)	(213)	(4,490)	(54,255)
Ending Balance	$11,162	$52,659	$340	$5,202	$69,363

Based on the current information available to the Company, cumulative adjustments related to prior period sales represent 0.7% and 1.3%, respectively, of the gross product revenues that were recorded in the years ended December 31, 2012 and 2011.

Royalty Revenues

The Company’s royalty revenues on commercial sales of INCIVO (telaprevir) by Janssen are based on net sales of licensed products in licensed territories as provided by Janssen. The Company recognizes royalty revenues in the period the sales occur.

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. In the circumstance where the Company has sold its rights to future royalties under a license agreement and also maintains 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 defers recognition of the proceeds it receives for the royalty stream and recognizes these deferred revenues over the life of the license agreement pursuant to the units-of-revenue method. The Company’s estimates regarding the estimated remaining royalty payments due to the purchaser have changed in the past and may change in the future.

Collaborative Revenues

The Company recognizes 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; payments for services the Company provides through its third-party manufacturing network; 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.

VERTEX PHARMACEUTICALS INCORPORATED

Notes to Consolidated Financial Statements (Continued)

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 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 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.

Collaborative research, development and/or commercialization agreements entered into prior to January 1, 2011 that contained multiple elements of revenue were divided into separate units of accounting if certain criteria were met, including whether the delivered element had stand-alone value to the collaborator and whether there was objective and reliable evidence of the fair value of the undelivered obligation(s). The Company allocated consideration it received among the separate units either on the basis of each unit's fair value or using the residual method, and applied the revenue recognition criteria to each of the separate units.

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

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

Research and Development Activities/Manufacturing Services: If the Company was entitled to reimbursement from its collaborators for specified research and development expenses and/or was entitled to payments for specified manufacturing services that the Company provided through its third-party manufacturing network, the Company determined whether the research and development funding would result in collaborative revenues or an offset to research and development expenses.

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 has not experienced any credit losses in these accounts and does not believe it is exposed to any significant credit risk on these funds. The Company implemented a foreign exchange hedging program in December 2013. As of December 31, 2013, the notional amount and fair value of these

hedges was not significant.

VERTEX PHARMACEUTICALS INCORPORATED

Notes to Consolidated Financial Statements (Continued)

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 and Italy were not material in 2013, and the Company had no receivables from Spain or Portugal in 2013. The Company believes that its allowance for doubtful accounts was adequate at December 31, 2013. Please refer to Note X, "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.

Restricted Cash

Restricted cash consists of balances held in deposit with certain banks to collateralize conditional stand-by letters of credit in the names of the Company’s landlords pursuant to certain operating lease agreements. The Company also separately disclosed on its consolidated balance sheet restricted cash and cash equivalents (Alios) as of December 31, 2012. The Company deconsolidated Alios as of December 31, 2013. Please refer to Note B, "Collaborative Arrangements," for further information.

Marketable Securities

The Company's marketable securities consist of investments in government-sponsored enterprise securities, corporate debt securities and commercial paper that are classified as available-for-sale. 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 other comprehensive 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.

There were no charges recorded for other-than-temporary declines in fair value of marketable securities in 2013, 2012 or 2011. 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. There were no gross realized gains or losses recognized in 2013, 2012 or 2011.

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. For awards with performance conditions, 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. Stock-based compensation expense is determined based on the fair value of the award at the grant date, including estimated forfeitures, and is adjusted each period to reflect actual forfeitures and the outcomes of certain performance conditions.

VERTEX PHARMACEUTICALS INCORPORATED

Notes to Consolidated Financial Statements (Continued)

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; contractual services costs, including clinical trial and pharmaceutical development costs; 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 $19.6 million, $58.6 million and $30.8 million in 2013, 2012 and 2011, respectively.

Inventories

The Company values its inventories at the lower-of-cost or market. 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 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 useful life of the improvements or the estimated remaining life of the associated lease. Maintenance and repairs to an asset that do not improve or extend its life are charged to operations. When assets are retired or otherwise disposed of, the assets and related accumulated depreciation are eliminated from the accounts and any resulting gain or loss is reflected in the Company’s consolidated statements of operations. The Company performs an assessment of the fair value of the assets if indicators of impairment are identified during a reporting period and records the assets at the lower of the net book value or the fair value of the assets.

The Company capitalizes internal costs incurred to develop software for internal use during the application development stage. 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.

VERTEX PHARMACEUTICALS INCORPORATED

Notes to Consolidated Financial Statements (Continued)

The Company records certain construction costs incurred by a landlord as an asset and corresponding financing obligation on the Company's consolidated balance sheets as the owner of the buildings for accounting purposes.

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 amortized using the straight-line method over the estimated 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.

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 the Company licenses assets owned by a collaborator in order to determine whether or not the collaborator is a VIE. If the collaborator is a VIE, 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 or the right to receive benefits from 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.

Business Combinations

The Company assigns the value of consideration, including contingent consideration, transferred in business combinations to the appropriate accounts on the Company's consolidated balance sheet based on their fair value as of the effective date of the transaction. If a collaboration has been treated as a business combination and there are contingent payments, increases in the fair value of the contingent payments pursuant to collaborations accounted for as business combinations result in a decrease in net income attributable to Vertex (or an increase in net loss attributable to Vertex) on a dollar-for-dollar basis. Transaction costs and any restructuring costs associated with these transactions are expensed as incurred.

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

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

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Notes to Consolidated Financial Statements (Continued)

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.

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.

Goodwill

The difference between the purchase price and the fair value of assets acquired and liabilities assumed in a business combination is allocated to goodwill. Goodwill is evaluated for impairment on an annual basis as of October 1, and more frequently if indicators are present or changes in circumstances suggest that impairment may exist.

Deconsolidation and Discontinued Operations

Upon the occurrence of certain events and on a regular basis, the Company evaluates whether it no longer has a controlling financial interest in its subsidiaries, including deemed subsidiaries such as consolidated VIEs. If it is determined that the Company 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 (i) the operations and cash flows to the former subsidiary have been or will be eliminated from the Company's ongoing operations as a result of the deconsolidation event and (ii) the Company will have any significant continuing involvement in the operations of the former subsidiary after the deconsolidation event. 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 because 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 these derivatives, particularly with respect to derivatives related to the achievement of milestones in the development of telaprevir, included significant assumptions regarding the estimates market participants would make in order to evaluate these derivatives.

The Company recognizes the fair value of hedging instruments that are designated and qualify as hedging instruments pursuant to GAAP, primarily foreign currency forward contracts, as either assets or liabilities on the consolidated balance sheets. Changes in the fair value of hedging instruments are recorded each period in accumulated other comprehensive loss until the date of settlement, at which point the cumulative change in the fair value since the inception of the hedge is

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Notes to Consolidated Financial Statements (Continued)

recognized in "Product revenues, net," in its consolidated statements of operations. The Company classifies the cash flows from hedging instruments in the same category as the cash flows from the hedged items.

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 income (expense), net" in the consolidated statements of operations.

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. 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 at least on a quarterly basis.

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 does not record tax provisions or benefits, as the Company intends to permanently reinvest undistributed earnings in its foreign subsidiaries.

Foreign Currency Translation and Transactions

All material consolidated entities have the U.S. dollar as their functional currency. Non-U.S. dollar 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, which is a separate component of shareholders’ equity. Included in accumulated other comprehensive loss are net unrealized losses related to foreign currency translation of $0.3 million, $0.7 million and $0.9 million at December 31, 2013, 2012, and 2011, 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 gains were $5.1 million and $0.7 million for 2013 and 2011, respectively, and net transaction losses were $0.4 million in 2012.

Net Income (Loss) Per Share Attributable to Vertex Common Shareholders

Basic and diluted net income 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) and the assumed conversion of convertible notes.

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

The Company did not adopt any new accounting pronouncements during 2013 that had a material effect on the Company’s consolidated financial statements.

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Notes to Consolidated Financial Statements (Continued)

B. Collaborative Arrangements

Janssen Pharmaceutica NV

In 2006, the Company entered into a collaboration agreement with Janssen (the "2006 Janssen Agreement") for the development, manufacture and commercialization of telaprevir, which Janssen began marketing under the brand name INCIVO in certain of its territories in September 2011. Under the collaboration agreement, Janssen has exclusive rights to commercialize telaprevir in its territories including Europe, South America, the Middle East, Africa and Australia. In November 2013, the Company and Janssen amended the collaboration agreement (the "2013 Janssen Amendment," as amended the "Janssen Agreement").

Janssen made a $165.0 million up-front license payment to the Company in 2006. The Company amortized the up-front license payment over the Company’s estimated period of performance under the Janssen Agreement through November 2013. As of November 2013, the effective date of the 2013 Janssen Amendment, there was $32.1 million remaining in deferred revenues related to this up-front license payment.

In addition to the up-front license payment, Janssen made contingent milestone payments for successful development, approval and launch of telaprevir as a product in its territories. At the inception of the 2006 Janssen Agreement, the Company determined that all of the contingent milestones were substantive and would result in revenues in the period in which the milestone was achieved. The Company earned $350.0 million of these contingent milestone payments, including a $50.0 million milestone payment earned in the first quarter of 2011 in connection with the European Medicines Agency’s acceptance of the marketing authorization application for INCIVO and an aggregate of $200.0 million in milestone payments earned in the third quarter of 2011 related to the approval of INCIVO by the European Commission and the launch of INCIVO in the European Union. The Company will not receive any further milestone payments under the Janssen Agreement.

Under the Janssen Agreement, each party incurs internal and external reimbursable expenses and is reimbursed by the other party for 50% of these expenses. The Company recognized the full amount of the reimbursable costs it incurred as research and development expenses on its consolidated statements of operations. The Company recognized, including in 2013, the amounts Janssen was obligated to pay the Company with respect to reimbursable expenses, net of reimbursable expenses incurred by Janssen, as collaborative revenues. During 2012 and 2011, Janssen incurred more reimbursable costs than the Company, and the net amounts payable by the Company to reimburse Janssen were recorded as a reduction of collaborative revenues. Each of the parties were responsible for drug supply in its territories. Until December 31, 2013, the Company provided Janssen certain services through the Company’s third-party manufacturing network for telaprevir.

Janssen paid the Company a tiered royalty averaging in the mid-20% range as a percentage of net sales of INCIVO in Janssen’s territories through the fourth quarter of 2013. In addition, Janssen is responsible for certain third-party royalties on net sales of INCIVO in its territories.

Pursuant to the 2013 Janssen Amendment, (i) Janssen made a payment of $152.0 million to the Company in the fourth quarter of 2013; (ii) Janssen's obligations to pay the Company royalties on net sales of INCIVO (telaprevir) terminated after the fourth quarter of 2013; and (iii) Janssen received a fully-paid license to commercialize INCIVO in its territories, subject to the continued payment of certain third-party royalties on its net sales of INCIVO. The Company and Janssen continue to perform activities related to the telaprevir development program.

The Company determined the 2013 Janssen Amendment was a material modification to the 2006 Janssen Agreement because there was a material change to the consideration and deliverables under the agreement and determined that there is one undelivered element under the agreement, as amended, which is the continuation of certain telaprevir development activities. The Company recognized $182.4 million of collaborative revenues pursuant to the Janssen Agreement in the fourth quarter of 2013. This amount was primarily attributable to (i) the residual consideration received from Janssen, including the $152.0 million fourth quarter 2013 payment and the remaining deferred revenues related to the 2006 up-front payment less (ii) the best estimate of selling price for the remaining telaprevir development activities. As of December 31, 2013, the remaining deferred revenue balance related to the Janssen

collaboration was $5.0 million and will be recognized as collaborative revenues as telaprevir development program activities are completed.

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Notes to Consolidated Financial Statements (Continued)

The agreement will continue in effect until the expiration of Janssen's third-party royalty obligations, which expire on a country-by-country basis on the later of (a) the last-to-expire patent covering INCIVO or (b) the last required payment by Janssen to the Company pursuant to the agreement. In the European Union, the Company has a patent covering the composition-of-matter of INCIVO that expires in 2026.

During the three years ended December 31, 2013, the Company recognized the following revenues attributable to the Janssen collaboration:

	2013	2012	2011
	(in thousands)		
Royalty revenues	$130,724	$117,592	$20,289
Collaborative revenues:			
Up-front and amendment payments revenues	$190,345	$12,428	$12,428
Milestone revenues	—	—	250,000
Net reimbursement (payment) for telaprevir development costs	2,793	(3,507)	(8,418)
Reimbursement for manufacturing services	10,299	7,257	20,383
Total collaborative revenues attributable to the Janssen collaboration	$203,437	$16,178	$274,393
Total revenues attributable to the Janssen collaboration	$334,161	$133,770	$294,682

Mitsubishi Tanabe Pharma Corporation

The Company has a collaboration agreement (the "MTPC Agreement") with Mitsubishi Tanabe Pharma Corporation ("Mitsubishi Tanabe") pursuant to which Mitsubishi Tanabe has a fully-paid license to manufacture and commercialize TELAVIC (the brand name under which Mitsubishi Tanabe is marketing telaprevir) in Japan and other specified countries in Asia. In September 2011, Mitsubishi Tanabe obtained approval to market TELAVIC in Japan. The parties entered into the MTPC Agreement in 2004 and amended it in 2009. Pursuant to the MTPC Agreement, Mitsubishi Tanabe provided financial and other support for the development and commercialization of telaprevir, made a $105.0 million payment in connection with the 2009 amendment of the collaboration agreement and made a $65.0 million commercial milestone payment recognized as collaborative revenues in the fourth quarter of 2011. There are no further payments under this collaboration agreement. Mitsubishi Tanabe is responsible for its own development and manufacturing costs in its territory.

Mitsubishi Tanabe may terminate the MTPC Agreement at any time without cause upon 60 days' prior written notice to the Company. The MTPC 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 MTPC Agreement will continue in effect until the expiration of the last-to-expire patent covering telaprevir in Mitsubishi Tanabe's territories. In Japan, the Company has a patent covering the composition-of-matter of telaprevir that expires in 2021.

The $105.0 million payment that the Company received in the third quarter of 2009 in connection with the amendment to the MTPC Agreement was a nonrefundable, up-front license fee, and revenues related to the 2009 payment were recognized on a straight-line basis over the period of performance of the Company's obligations under the amended agreement. The final deferred revenues related to the 2009 up-front license payment were recognized in April 2012. In connection with the amendment to the MTPC Agreement, the Company supplied manufacturing services to Mitsubishi Tanabe, until April 2012, through the Company's third-party manufacturing network for telaprevir.

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Notes to Consolidated Financial Statements (Continued)

The Company did not record any collaborative revenues attributable to the MTPC Agreement in 2013. The table below sets forth the total collaborative revenues attributable to the MTPC Agreement for 2012 or 2011:

	2012	2011
	(in thousands)	
Amortized portion of up-front payments	$12,744	$38,232
Milestone revenues	485	68,515
Payments for manufacturing services	5,650	14,928
Total collaborative revenues attributable to the Mitsubishi Tanabe collaboration	$18,879	$121,675

Cystic Fibrosis Foundation Therapeutics Incorporated

In April 2011, the Company entered into an amendment (the “April 2011 Amendment”) to its existing collaboration agreement with Cystic Fibrosis Foundation Therapeutics Incorporated (“CFFT”) pursuant to which CFFT agreed to provide financial support for (i) development activities for VX-661, a corrector compound discovered under the collaboration, and (ii) additional research and development activities directed at discovering new corrector compounds.

The Company entered into the original collaboration agreement with CFFT in 2004 and amended it several times prior to 2011 to, among other things, provide partial funding for its cystic fibrosis drug discovery and development efforts. In 2006, the Company received a $1.5 million milestone payment from CFFT. There are no additional milestones payable by CFFT to the Company pursuant to the collaboration agreement, as amended. Under the April 2011 Amendment, CFFT agreed to provide the Company with up to $75.0 million in funding over approximately 5 years for corrector-compound research and development activities. The Company retains the right to develop and commercialize KALYDECO (ivacaftor), VX-809, VX-661 and any other compounds discovered during the course of the research collaboration with CFFT. The Company recognized collaborative revenues from this collaboration of $14.3 million, $17.0 million and $13.7 million, respectively, in 2013, 2012 and 2011.

In the original agreement, as amended prior to the April 2011 Amendment, the Company agreed to pay CFFT tiered royalties calculated as a percentage, ranging from single digits to sub-teens, of annual net sales of any approved drugs discovered during the research term that ended in 2008, including KALYDECO, lumacaftor and VX-661. The April 2011 Amendment provides for a tiered royalty in the same range on net sales of corrector compounds discovered during the research term that began in 2011. In each of the third quarter of 2012 and the first quarter of 2013, CFFT earned a commercial milestone payment of $9.3 million from the Company upon achievement of certain sales levels for KALYDECO. These milestones were reflected in the Company's cost of product revenues. There are no additional commercial milestone payments payable by the Company to CFFT related to sales levels for KALYDECO. The Company also is obligated to make a total of two one-time commercial milestone payments upon achievement of certain sales levels for corrector compounds such as lumacaftor or VX-661.

The Company began marketing KALYDECO in the United States in the first quarter of 2012 and began marketing KALYDECO in certain countries in the European Union in the third quarter of 2012. The Company has royalty obligations to CFFT for each compound commercialized pursuant to this collaboration until the expiration of patents covering that compound. The Company has 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. The Company has patent applications in the United States and European Union covering the composition-of-matter of lumacaftor that expire in 2026, subject to potential patent life extensions. CFFT may terminate its funding obligations under the collaboration, as amended, in certain circumstances, in which case there will be a proportional adjustment to the royalty rates and commercial milestone payments for certain corrector compounds. The collaboration also may be terminated by either party for a material breach by the other, subject to notice and cure provisions.

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Notes to Consolidated Financial Statements (Continued)

Alios BioPharma, Inc.
License and Collaboration Agreement
In June 2011, the Company entered into a license and collaboration agreement (the "Alios Agreement") with Alios, a privately-held biotechnology company. The Company and Alios are collaborating on the research, development and commercialization of an HCV nucleotide analogue discovered by Alios, ALS-2200 (now formulated as VX-135), which is designed to act on the HCV polymerase.
Under the terms of the Alios Agreement, the Company received exclusive worldwide rights to ALS-2200 (VX-135) and ALS-2158, a second HCV nucleotide analogue discovered by Alios that was developed pursuant to the Alios agreement through the third quarter of 2012. Alios and the Company began clinical development of ALS-2200 (VX-135) and ALS-2158 in December 2011. The Company is responsible for all costs related to development, commercialization and manufacturing of each compound licensed to the Company pursuant to the Alios Agreement and provided funding to Alios to conduct the Phase 1 clinical trials for ALS-2200 and ALS-2158. In addition, the Company provided funding for a research program, which ended in 2013, directed to the discovery of additional HCV nucleotide analogues that act on the HCV polymerase.
Upon entering into the Alios Agreement, the Company paid Alios a $60.0 million up-front payment. As of December 31, 2013, Alios had earned an aggregate of $60.0 million in development milestone payments pursuant to the Alios Agreement. The Alios Agreement provides for development milestone payments to Alios of up to an additional $312.5 million if VX-135 is approved and commercialized. In addition, Alios is eligible to receive commercial milestone payments of up to $750.0 million, as well as tiered royalties on net sales of VX-135.
The Company may terminate the Alios Agreement (i) upon 30 days' notice to Alios if the Company ceases development after VX-135 has experienced a technical failure and/or (ii) upon 60 days' notice to Alios at any time after the Company completes Phase 2a clinical trials. The Alios Agreement also may be terminated by either party for a material breach by the other, and by Alios for the Company's inactivity or if the Company challenges certain Alios patents, in each case subject to notice and cure provisions. Unless earlier terminated, the Alios 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 (a) the date the last-to-expire patent covering a licensed product expires or (b) 10 years after the first commercial sale in the country.
Alios is continuing to operate as a separate entity, is engaged in other programs directed at developing novel drugs that are not covered by the Alios Agreement and maintains ownership of the underlying patent rights that are licensed to the Company pursuant to the Alios Agreement. Under applicable accounting guidance, the Company determined that Alios was a VIE, its license to VX-135 and ALS-2158 was a variable interest in Alios, that Alios was a business and that the Company was Alios' primary beneficiary for the period from June 13, 2011 through December 31, 2013. The Company based these determinations on, among other factors, the significance to Alios of the licensed compounds and on the Company's power, through the joint steering committee for the licensed compounds established under the Alios Agreement, to direct the activities that most significantly affect the economic performance of Alios. Accordingly, the Company consolidated Alios' financial statements with the Company's consolidated financial statements from June 13, 2011 through December 31, 2013. However, the Company's interests in Alios were limited to those accorded to the Company in the Alios Agreement. In particular, the Company did not acquire any equity interest in Alios, any interest in Alios' cash and cash equivalents or any control over Alios' activities that do not relate to the Alios Agreement. Alios does not have any right to the Company's assets except as provided in the Alios Agreement.
As of December 31, 2013, the Company determined that it no longer had a variable interest in Alios as a whole and did not possess the power to direct the activities that most significantly affect the economic performance of Alios based on, among other factors, the decline in significance to Alios of the licensed HCV nucleotide analogue program. A full impairment charge of $250.6 million related to the Alios collaboration and a benefit for income taxes of $102.1 million was recorded attributable to Alios. The Company deconsolidated Alios based on this conclusion as of December 31, 2013. The deconsolidation resulted in a gain of $68.2 million recorded in other income (expense), net

attributable to Vertex in the consolidated statement of operations for the year ended December 31, 2013. The gain of $68.2 million was approximately the difference between (i) losses the Company recorded in 2011 and 2012 based on increases in the fair value of contingent

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Notes to Consolidated Financial Statements (Continued)

milestone and royalty payments payable by the Company to Alios and (ii) the aggregate of $120.0 million in up-front and milestone payments that the Company has made to Alios to date pursuant to the Alios Agreement.

The Company continues to have significant continuing involvement with Alios due to the Alios Agreement; therefore, the deconsolidation of Alios is not presented as discontinued operations in the Company's consolidated financial statements as of December 31, 2013. The Company will evaluate whether it continues to have significant continuing involvement with Alios for a period of one year from the December 31, 2013 deconsolidation date.

Please refer to Note J, "Intangible Assets and Goodwill," for further information regarding the impairment of the HCV nucleotide analogue program.

Noncontrolling Interest (Alios)

Prior to the deconsolidation, the Company recorded noncontrolling interest (Alios) on two lines on its consolidated balance sheets. The noncontrolling interest (Alios) was reflected on two separate lines because Alios has both common shareholders and preferred shareholders that are entitled to redemption rights in certain circumstances. The Company recorded net loss (income) attributable to noncontrolling interest (Alios) on its consolidated statements of operations, reflecting Alios' net loss (income) for the reporting period, adjusted for changes in the fair value of contingent milestone payments and royalties payable by the Company to Alios, which was evaluated each reporting period. A summary of net loss (income) attributable to noncontrolling interest (Alios) for the three years ended December 31, 2013 is as follows:

	2013	2012	2011
	(in thousands)		
Loss before provision for (benefit from) income taxes	$283,747	$20,044	$9,536
Decrease (increase) in fair value of contingent milestone and royalty payments	124,920	(114,970)	(69,950)
Provision for (benefit from) income taxes	(166,145)	39,029	48,809
Net loss (income) attributable to noncontrolling interest (Alios)	$242,522	$(55,897)	$(11,605)

In 2012 and 2011, the fair value of the contingent milestone payments and royalties payable by Vertex to Alios related to the in-licensed HCV nucleotide analogue program increased by $115.0 million and $70.0 million, respectively, due to the advancement of the Company's HCV nucleotide program, including the positive data the Company received in 2012 from a Phase 1 clinical trial that evaluated ALS-2200. As of December 31, 2013, the Company concluded that the fair value of the contingent milestone and royalty payments was zero. This determination was based on, among other factors, (a) safety, tolerability and efficacy data from a Phase 2a clinical trial of VX-135 in combination with daclatasvir that the Company received in late December 2013 and analyzed and announced in January 2014, (b) the continuing partial clinical hold on VX-135 by the U.S. Food and Drug Administration ("FDA"), (c) a review of the existing and emerging data regarding all-oral regimens for HCV infection being developed by the Company's competitors, and (d) the risks associated with establishing collaborations for the potential late-stage development of a combination regimen containing VX-135 and drug candidates controlled by third parties.

The Company used present-value models to determine the estimated fair value of the contingent milestone and royalty payments until it deconsolidated Alios, based on assumptions regarding the probability of achieving the relevant milestones, estimates regarding the time to develop drug candidates, estimates of future product sales and the appropriate discount and tax rates. The Company based its estimate 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 represented a measure of credit risk associated with settling the liability. Significant judgment was used in determining the appropriateness of these assumptions at each reporting period.

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Notes to Consolidated Financial Statements (Continued)

Alios Balance Sheet Information

The Company included items related to Alios on the Company's consolidated balance sheet as of December 31, 2012. Due to the deconsolidation of Alios as of December 31, 2013, these items were not included on the Company's consolidated balance sheet as of December 31, 2013. The following table summaries items related to the Alios included on the Company's consolidated balance sheet as of December 31, 2012.

	As of December 31, 2012 (in thousands)
Restricted cash and cash equivalents (Alios)	$69,983
Prepaid expenses and other current assets	$672
Property and equipment, net	$1,728
Intangible assets	$250,600
Other assets	$861
Accounts payable	$1,054
Accrued expenses	$6,099
Income taxes payable (Alios)	$715
Deferred tax liability	$152,781
Other liabilities, excluding current portion	$910
Redeemable noncontrolling interest (Alios)	$38,530
Noncontrolling interest (Alios)	$196,672

As of December 31, 2012, the Company recorded Alios' cash and cash equivalents as restricted cash and cash equivalents (Alios) because (i) the Company did not have any interest in or control over Alios' cash and cash equivalents and (ii) the Alios Agreement did not provide for these assets to be used for the development of the assets that the Company licenses from Alios pursuant to the Alios Agreement. Assets recorded as a result of consolidating Alios' financial condition into the Company's consolidated balance sheet did not represent additional assets that could have been used to satisfy claims against the Company's general assets.

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Notes to Consolidated Financial Statements (Continued)

C. Net Income (Loss) Per Share Attributable to Vertex Common Shareholders

The following table sets forth the computation of basic and diluted net income (loss) per share for the three years ended December 31, 2013:

	2013	2012	2011
	(in thousands, except per share amounts)		
Basic net income (loss) attributable to Vertex per common share calculation:			
Net income (loss) attributable to Vertex common shareholders	$(445,028)	$(107,032)	$29,574
Less: Undistributed earnings allocated to participating securities	—	—	(291)
Net income (loss) attributable to Vertex common shareholders—basic	$(445,028)	$(107,032)	$29,283
Basic weighted-average common shares outstanding	224,906	211,946	204,891
Basic net income (loss) attributable to Vertex per common share	$(1.98)	$(0.50)	$0.14
Diluted net income (loss) attributable to Vertex per common share calculation:			
Net income (loss) attributable to Vertex common shareholders	$(445,028)	$(107,032)	$29,574
Less: Undistributed earnings allocated to participating securities	—	—	(285)
Net income (loss) attributable to Vertex common shareholders—diluted	$(445,028)	$(107,032)	$29,289
Weighted-average shares used to compute basic net income (loss) per common share	224,906	211,946	204,891
Effect of potentially dilutive securities:			
Stock options	—	—	3,863
Other	—	—	53
Weighted-average shares used to compute diluted net income (loss) per common share	224,906	211,946	208,807
Diluted net income (loss) attributable to Vertex per common share	$(1.98)	$(0.50)	$0.14

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

	2013	2012	2011
	(in thousands)		
Stock options	15,729	19,726	9,626
Convertible senior subordinated notes	—	8,192	8,192
Unvested restricted stock and restricted stock units	2,165	2,350	8

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:

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.

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Notes to Consolidated Financial Statements (Continued)

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, 2013, the Company's investments were in money market funds, short-term government-sponsored enterprise securities, corporate debt securities and commercial paper. As of December 31, 2013, all of the Company's financial assets 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 a money market funds and government-sponsored enterprise securities. The Company's financial assets valued based on Level 2 inputs consisted of corporate debt securities and commercial paper, which consisted of investments in highly-rated investment-grade corporations. During 2013, 2012 and 2011, 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 subject to fair value measurements:

	Fair Value Measurements as of December 31, 2013			
		Fair Value Hierarchy		
	Total	Level 1	Level 2	Level 3
	(in thousands)			
Financial assets carried at fair value:				
Cash equivalents:				
Money market funds	$255,689	$255,689	$—	$—
Marketable securities:				
Government-sponsored enterprise securities	600,450	600,450	—	—
Commercial paper	83,493	—	83,493	—
Corporate debt securities	211,834	—	211,834	—
Total	$1,151,466	$856,139	$295,327	$—

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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, 2013				
Cash and cash equivalents:				
Cash and money market funds	$569,299	$—	$—	$569,299
Total cash and cash equivalents	$569,299	$—	$—	$569,299
Marketable securities:				
Government-sponsored enterprise securities (due within 1 year)	$600,496	$7	$(53)	$600,450
Commercial paper (due within 1 year)	83,384	109	—	83,493
Corporate debt securities (due within 1 year)	189,674	14	(34)	189,654
Corporate debt securities (due after 1 year through 5 years)	22,181	6	(7)	22,180
Total marketable securities	$895,735	$136	$(94)	$895,777
Total cash, cash equivalents and marketable securities	$1,465,034	$136	$(94)	$1,465,076
December 31, 2012				
Cash and cash equivalents:				
Cash and money market funds	$489,407	$—	$—	$489,407
Total cash and cash equivalents	$489,407	$—	$—	$489,407
Marketable securities:				
U.S. Treasury securities (due within 1 year)	$111,350	$2	$(2)	$111,350
Government-sponsored enterprise securities (due within 1 year)	440,181	49	(5)	440,225
Commercial paper (due within 1 year)	225,294	155	—	225,449
Corporate debt securities (due within 1 year)	15,429	1	(1)	15,429
Corporate debt securities (due after 1 year through 5 years)	39,358	10	(13)	39,355
Total marketable securities	$831,612	$217	$(21)	$831,808
Total cash, cash equivalents and marketable securities	$1,321,019	$217	$(21)	$1,321,215

Alios' $70.0 million of cash and money market funds as of December 31, 2012, recorded on the Company's consolidated balance sheet in "Restricted cash and cash equivalents (Alios)," are not included in the above table.

In December 2013, the Company initiated a hedging program intended to mitigate the changes in foreign exchange rates for a portion of the Company's product revenues denominated in Euros, which included foreign currency forward contracts that were designated as cash flow hedges. The notional amount of Euro denominated foreign currency forward contracts as of December 31, 2013 was $17.5 million. The changes in fair value of these foreign currency forward contracts included in accumulated other comprehensive loss and the gross fair value of foreign currency forward assets and liabilities included on the consolidated balance sheet as of December 31, 2013 were not material.

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Notes to Consolidated Financial Statements (Continued)

F. Accumulated Other Comprehensive Loss

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

	Foreign currency translation adjustment	Unrealized holding gains on marketable securities	Unrealized losses on foreign currency forward contracts	Total
	(in thousands)			
Balance at December 31, 2012	$(746)	$196	$—	$(550)
Other comprehensive income (loss) before reclassifications	421	(154)	(23)	244
Amounts reclassified from accumulated other comprehensive loss	—	—	—	—
Net current period other comprehensive income (loss)	421	(154)	(23)	244
Balance at December 31, 2013	$(325)	$42	$(23)	$(306)

For the year ended December 31, 2013, there were no amounts reclassified from accumulated other comprehensive loss.

G. Inventories

Inventories consisted of the following:

	As of December 31, 2013	2012
	(in thousands)	
Raw materials	$489	$3,754
Work-in-process	9,981	11,317
Finished goods	3,677	15,393
Total	$14,147	$30,464

In 2013, the Company recorded within cost of product revenues $10.4 million of write-offs for excess and obsolete inventories. In 2012, the Company recorded within cost of product revenues $133.2 million of write-offs for excess and obsolete INCIVEK inventories related to declining sales. The write-offs for excess and obsolete inventories of $10.4 million and $133.2 million in 2013 and 2012, respectively, affected the net loss attributable to Vertex per share, net of tax, by $0.05 and $0.61 in 2013 and 2012, respectively.

H. Property and Equipment

Property and equipment, net consisted of the following:

	As of December 31, 2013	2012
	(in thousands)	
Buildings	$506,056	$—
Furniture and equipment	190,555	173,766
Leasehold improvements	163,019	123,770
Software	102,520	101,276
Computers	43,096	40,779
Construction-in-process	—	290,703
Total property and equipment, gross	1,005,246	730,294
Less: accumulated depreciation	(308,335)	(296,685)

Total property and equipment, net	$696,911	$433,609

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Notes to Consolidated Financial Statements (Continued)

Buildings as of December 31, 2013 and construction-in-process as of December 31, 2012, related to construction costs for the buildings at Fan Pier, which were placed in service in 2013. Please refer to Note I, "Fan Pier Leases," for further information.

Total property and equipment, gross, as of December 31, 2013 and 2012, included $76.4 million and $30.1 million, respectively, for property and equipment recorded under capital leases. Accumulated depreciation, as of December 31, 2013 and 2012, included $3.8 million and $1.1 million, respectively, for property and equipment recorded under capital leases. Included in property and equipment, net as of December 31, 2013 were $5.5 million and $0.5 million in capitalized internally developed software costs and related amortization, respectively. There were no such costs included in property and equipment, net as of December 31, 2012.

The Company recorded depreciation expense of $47.3 million, $35.7 million and $28.9 million, respectively, in 2013, 2012 and 2011.

I. 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, including having responsibility to pay for a portion of the costs of finish work and structural elements of the Buildings, the Company was deemed for accounting purposes to be the owner of the Buildings during the construction period. Therefore, the Company recorded project construction costs incurred by the landlord as an asset and a related financing obligation during the construction period. The Company evaluated the Fan Pier Leases in the fourth quarter of 2013 and determined that the Fan Pier Leases did not meet the criteria for “sale-leaseback” treatment. This determination was based on, among other things, the Company's continuing involvement with the property in the form of non-recourse financing to the lessor. Accordingly, the Company began depreciating the asset and incurring interest expense related to the financing obligation during the fourth quarter of 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.

Property and equipment, net, included $506.1 million and $290.7 million as of December 31, 2013 and 2012, respectively, related to construction costs for the Buildings. The construction financing lease obligations related to the Buildings on the Company's consolidated balance sheets were $440.9 million and $268.0 million, respectively, as of December 31, 2013 and 2012.

J. Intangible Assets and Goodwill

Intangible Assets

As of December 31, 2013, the Company had no intangible assets recorded on its consolidated balance sheet. The intangible assets that were previously reflected on the Company's consolidated balance sheets related to drug candidates for the treatment of HCV infection. The field of HCV infection treatment is highly competitive and characterized by rapid technological advances and the development of drug candidates for the treatment of HCV infection is subject to numerous risks. Two of the Company's competitors received approval in the fourth quarter of 2013 for new treatment regimens for HCV infection that include pegylated-interferon and ribavirin, and several of the Company's competitors are conducting Phase 3 clinical trials evaluating all-oral combinations of their drug candidates for the treatment of HCV infection.

ViroChem Acquisition

As of December 31, 2010, the intangible assets acquired from ViroChem that were reflected on the Company's consolidated balance sheet related to two drug candidates, VX-222 and VX-759. VX-222 and VX-759 had estimated

fair

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Notes to Consolidated Financial Statements (Continued)

values on December 31, 2010 of $412.9 million and $105.8 million, respectively. In the third quarter of 2011, the Company determined that the fair value of VX-759 had become impaired and that its fair value was zero. As a result, the Company recorded an impairment charge in 2011 of $105.8 million that was reflected as an intangible asset impairment charge on the Company's consolidated statement of operations. In connection with this impairment charge, the Company recorded a benefit from income taxes of $32.7 million. In 2011, the decrease to the Company's net income attributable to Vertex related to this impairment charge, net of tax credit, was $73.1 million, and the net decrease to the Company's net income per share attributable to Vertex common shareholders was $0.35 per diluted share.

In 2013, the Company determined that there were indicators that the value of the VX-222 intangible asset had become impaired. This determination was based on (a) preliminary safety, tolerability and efficacy data from a Phase 2 clinical trial of VX-222, telaprevir and ribavirin, which was received in March 2013 and analyzed through April 2013 and (b) a review of the existing and emerging data regarding all-oral regimens for HCV infection being developed by the Company's competitors that appeared to be generally well tolerated with high sustained viral response rates for treatment-naïve patients with genotype 1 HCV infection. After evaluating the data from this Phase 2 clinical trial, the Company determined that regimens containing VX-222 were unlikely to be competitive with the treatment regimens being developed by the Company's competitors. The Company evaluated the fair value of VX-222 from the perspective of a market participant and based on this analysis determined that the fair value of VX-222 was zero as of March 31, 2013. Accordingly, the Company recorded a $412.9 million impairment charge in 2013. In connection with this impairment charge, the Company recorded a credit of $127.6 million in its provision for income taxes. In 2013, the increase to the Company's net loss attributable to Vertex related to this impairment charge, net of the tax credit, was $285.3 million, and the net increase to the Company's net loss per share attributable to Vertex common shareholders was $1.27 per share.

Alios Collaboration

In June 2011, the Company recorded $250.6 million of intangible assets on its consolidated balance sheet based on the Company's estimate of the fair value of Alios' HCV nucleotide analogue program, including the intellectual property related to ALS-2200 and ALS-2158. In the third quarter of 2012, after the Company discontinued the development of ALS-2158, the Company evaluated the Alios HCV nucleotide analogue program for impairment. The Company determined that there was no impairment to the program in the third quarter of 2012 because of the advancement of ALS-2200 (now formulated as VX-135).

In July 2013, the FDA placed a partial clinical hold on VX-135, which is being evaluated in Phase 2 clinical development. The partial clinical hold, which prevents the Company from further evaluation of VX-135 in the United States, remains in place as of the date of this filing.

In connection with preparing its financial statements for 2013, the Company determined that there were indicators that the value of the HCV nucleotide analogue program intangible asset had become impaired. This determination was based on, among other factors, (a) safety, tolerability and efficacy data from a Phase 2a clinical trial of VX-135 in combination with daclatasvir that the Company received in late December 2013 and analyzed and announced in January 2014, (b) the continuing partial clinical hold on VX-135 by the FDA, (c) a review of the existing and emerging data regarding all-oral regimens for HCV infection being developed by the Company's competitors, and (d) the risks associated with establishing collaborations for the potential late-stage development of a combination regimen containing VX-135 and drug candidates controlled by third parties. Based on these revised estimates, the Company evaluated the fair value of VX-135 from the perspective of a market participant and determined that the fair value of VX-135 was zero as of December 31, 2013. Accordingly, a $250.6 million impairment charge and a benefit from income taxes of $102.1 million was recorded in the fourth quarter of 2013.

Goodwill

As of December 31, 2013 and 2012, goodwill of $31.0 million was recorded on the Company's consolidated balance sheets. There was no change to goodwill during the year ended December 31, 2013.

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Notes to Consolidated Financial Statements (Continued)

K. Accrued Expenses and Other Liabilities, Current Portion

Accrued expenses consisted of the following:

	As of December 31, 2013	2012
	(in thousands)	
Product revenue allowances	$85,510	$69,936
Payroll and benefits	76,785	62,140
Research, development and commercial contract costs	52,468	63,960
Royalty payable	18,334	29,007
Other	16,241	18,932
Professional fees	10,593	11,226
Taxes payable	8,362	2,182
Unrecognized tax benefits	2,784	4,106
Interest	—	3,395
Total	$271,077	$264,884

Other liabilities, current portion consisted of the following:

	As of December 31, 2013	2012
	(in thousands)	
Deferred rent	$16,652	$14,302
Customer deposits	7,692	—
Other	392	5,400
Total	$24,736	$19,702

L. Convertible Senior Subordinated Notes

In September 2010, the Company completed an offering of $400.0 million in aggregate principal amount of 3.35% convertible senior subordinated notes due 2015 Notes (the "2015 Notes"). This offering resulted in $391.6 million of net proceeds to the Company. The underwriting discount and other expenses of $8.4 million were recorded as debt issuance costs and were included in other assets on the Company’s consolidated balance sheets. The 2015 Notes bore interest at the rate of 3.35% per annum, and the Company was required to make semi-annual interest payments on the outstanding principal balance of the 2015 Notes on April 1 and October 1 of each year.

The 2015 Notes were convertible at any time, at the option of the holder, into common stock at a price equal to approximately $48.83 per share, or 20.4794 shares of common stock per $1,000 principal amount of the 2015 Notes, subject to adjustment. If the closing price of the Company’s common stock exceeded 130% of the conversion price for at least 20 trading days within a period of 30 consecutive trading days, the Company had the right to redeem the 2015 Notes at its option at a redemption price equal to 100% of the principal amount of the 2015 Notes to be redeemed.

In the second quarter of 2013, the Company's common stock exceeded 130% of the conversion price of the 2015 Notes for at least 20 trading days within a period of 30 consecutive trading days, and the Company notified the holders of the 2015 Notes that it would redeem the 2015 Notes on June 17, 2013. In response to the Company's call of the 2015 Notes for redemption, in accordance with the provisions of the 2015 Notes, the holders of $399.8 million in aggregate principal amount of 2015 Notes elected to convert their 2015 Notes into the Company's common stock at the conversion price of approximately $48.83 per share. As a result of these conversions, the Company issued 8,188,448 shares of common stock. The remaining $0.2 million in aggregate principal amount of 2015 Notes was redeemed on June 17, 2013.

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Notes to Consolidated Financial Statements (Continued)

Pursuant to the terms of the 2015 Notes, the Company made an additional payment of $16.75 per $1,000 principal amount, payable in shares of the Company's common stock, to the holders of the 2015 Notes that converted or redeemed their 2015 Notes after the Company called the 2015 Notes for redemption. These payments resulted in the issuance of an additional 87,109 shares of the Company's common stock. In the second quarter of 2013, the Company recognized an aggregate of $6.7 million in interest expense related to the 2015 Notes. Unamortized debt issuance costs for the 2015 Notes of $4.2 million were recorded as an offset to additional paid-in capital.

M. Common Stock, Preferred Stock and Equity Plans

The Company is authorized to issue 300,000,000 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, 2013 and 2012, the Company had no shares of preferred stock issued or outstanding.

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") or other equity-based awards, as specified in the individual plans.

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

			As of December 31, 2013	
Title of Plan	Group Eligible	Type of Award Granted	Awards Outstanding	Additional Awards Authorized for Grant
2013 Stock and Option Plan	Employees, Non-employee Directors and Consultants	NSO, ISO, RS and RSU	1,170,827	2,129,173
2006 Stock and Option Plan	Employees, Non-employee Directors and Consultants	NSO, ISO, RS and RSU	15,748,949	3,282,178
1996 Stock and Option Plan	Employees, Non-employee Directors, Advisors and Consultants	NSO, ISO and RS	974,303	—
Total			17,894,079	5,411,351

All options granted under the Company's 2013 Stock and Option Plan ("2013 Plan"), 2006 Stock and Option Plan ("2006 Plan") and 1996 Stock and Option 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, 2013, the stock and option plans under which the Company makes new equity awards are the Company's 2006 Plan and 2013 Plan. Under the 2006 Plan and the 2013 Plan, no stock options can be awarded with an exercise price less than the fair market value on the date of grant. The Company's shareholders authorized 3,300,000 shares for issuance pursuant to the 2013 Plan in 2013 and approved an increase in the number of shares authorized for issuance pursuant to the 2006 Plan of 3,000,000 shares in 2012.

During the three years ended December 31, 2013, grants to current employees and directors 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, 2013, for grants to new employees and directors, the date of grant for awards was the employee's first day of employment or

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Notes to Consolidated Financial Statements (Continued)

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 ten years from the grant date.

During the three years ended December 31, 2013, all shares of outstanding restricted stock and restricted stock units have been granted at a price equal to $0.01, the par value of the Company's common stock. Vesting of options, restricted stock and restricted stock units generally is ratable over specified periods, usually four years, and is determined by the Company's Board of Directors.

The following table summarizes information related to the outstanding and exercisable options during the year ended December 31, 2013:

	Stock Options	Weighted-average Exercise Price	Weighted-average Remaining Contractual Life	Aggregate Intrinsic Value
	(in thousands)	(per share)	(in years)	(in thousands)
Outstanding at December 31, 2012	19,726	$ 38.09		
Granted	4,840	$ 57.87		
Exercised	(6,995)	$ 35.28		
Forfeited	(1,822)	$ 46.89		
Expired	(20)	$ 46.64		
Outstanding at December 31, 2013	15,729	$ 44.40	6.67	$481,311
Exercisable at December 31, 2013	7,950	$ 38.84	5.13	$283,146
Exercisable and Expected to Vest at December 31, 2013	14,967	$ 43.95	6.56	$463,885

The aggregate intrinsic value in the table above represents the total pre-tax amount, net of exercise price, that would have been received by option holders if all option holders had exercised all options with an exercise price lower than the market price on December 31, 2013, which was $74.21 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 2013, 2012 and 2011 was $291.6 million, $148.7 million and $90.5 million, respectively. The total cash received by the Company as a result of employee stock option exercises during 2013, 2012 and 2011 was $246.8 million, $172.8 million and $109.6 million, respectively.

The following table summarizes information about stock options outstanding and exercisable at December 31, 2013:

	Options Outstanding			Options Exercisable	
Range of Exercise Prices	Number Outstanding	Weighted-average Remaining Contractual Life	Weighted-average Exercise Price	Number Exercisable	Weighted-average Exercise Price
	(in thousands)	(in years)	(per share)	(in thousands)	(per share)
$ 9.09–$20.00	432	2.37	$ 15.37	432	$ 15.37
$20.01–$30.00	1,055	5.74	$ 29.38	812	$ 29.23
$30.01–$40.00	6,842	5.07	$ 36.55	4,773	$ 36.06
$40.01–$50.00	4,136	8.74	$ 46.32	787	$ 46.62
$50.01–$60.00	1,713	7.16	$ 53.78	874	$ 54.35
$60.01–$70.00	80	9.08	$ 65.54	14	$ 63.20
$70.01-$80.00	87	9.31	$ 77.55	9	$ 77.73
$80.01–$88.18	1,384	9.50	$ 83.11	249	$ 82.13
Total	15,729	6.67	$ 44.40	7,950	$ 38.84

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Notes to Consolidated Financial Statements (Continued)

The following table summarizes the restricted stock activity of the Company during the year ended December 31, 2013:

	Restricted Stock	Weighted-average Grant-date Fair Value
	(in thousands)	(per share)
Unvested at December 31, 2012	2,270	$42.92
Granted	1,356	$62.16
Vested	(800)	$42.27
Cancelled	(780)	$51.47
Unvested at December 31, 2013	2,046	$52.66

The total fair value of restricted stock that vested during 2013, 2012 and 2011 (measured on the date of vesting) was $50.9 million, $41.1 million and $34.6 million, respectively.

Employee Stock Purchase Plan

The Company has an employee stock purchase plan (the “ESPP”). The ESPP permits eligible employees to enroll in a twelve-month offering period comprising two six-month purchase periods. Participants may purchase shares of the Company’s common stock, through payroll deductions, at a price equal to 85% of the fair market value of the common stock on the first day of the applicable twelve-month offering period, or the last day of the applicable six-month purchase period, whichever is lower. Purchase dates under the ESPP occur on or about May 14 and November 14 of each year. In 2012, the Company's shareholders approved an increase in the number of shares of common stock authorized for issuance pursuant to the ESPP. As of December 31, 2013, there were 1,753,381 shares of common stock authorized for issuance pursuant to the ESPP.

In 2013, the following shares were issued to employees under the ESPP:

	Year Ended December 31, 2013 (in thousands, except per share amount)
Number of shares	527
Average price paid per share	$36.21

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 typically 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 service period. The expense recognized over the service period includes an estimate of awards that will be forfeited.

The effect of stock-based compensation expense during the three years ended December 31, 2013 was as follows:

	2013	2012	2011
	(in thousands)		
Stock-based compensation expense by line item:			
Research and development expenses	$81,467	$71,533	$75,574
Sales, general and administrative expenses	45,836	42,752	42,652
Total stock-based compensation expense included in costs and expenses	$127,303	$114,285	$118,226

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Notes to Consolidated Financial Statements (Continued)

The stock-based compensation expense by type of award during the three years ended December 31, 2013 was as follows:

	2013	2012	2011
	(in thousands)		
Stock-based compensation expense by type of award:			
Stock options	$85,067	$79,047	$83,098
Restricted stock and restricted stock units	36,479	29,194	30,708
ESPP share issuances	6,805	7,298	5,462
Less: stock-based compensation expense capitalized to inventories	(1,048)	(1,254)	(1,042)
Total stock-based compensation expense included in costs and expenses	$127,303	$114,285	$118,226

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

The following table sets forth the Company’s unrecognized stock-based compensation expense, net of estimated forfeitures, as of December 31, 2013, by type of award and the weighted-average period over which that expense is expected to be recognized:

	As of December 31, 2013	
	Unrecognized Expense Net of Estimated Forfeitures (in thousands)	Weighted-average Recognition Period (in years)
Type of award:		
Stock options	$141,283	2.56
Restricted stock and restricted stock units	$73,490	2.47
ESPP share issuances	$5,956	0.67

Stock Options

The Company issues stock options with service conditions, which are generally the vesting periods of the awards. In 2009, the Company also issued, to certain members of senior management, stock options with performance conditions that vested upon the satisfaction of the performance conditions by the end of the first quarter of 2012. 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 2013, 2012 and 2011 had a weighted-average grant-date fair value per share of $25.79, $19.72 and $20.88, respectively.

The fair value of each option granted during 2013, 2012 and 2011 was estimated on the date of grant using the Black-Scholes option pricing model with the following weighted-average assumptions:

	2013	2012	2011
Expected stock price volatility	46.20%	47.93%	49.53%
Risk-free interest rate	1.25%	0.95%	2.09%
Expected term of options (in years)	5.81	5.78	5.74
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: Options to purchase the Company's stock with remaining terms of greater than one year are regularly traded in the market. Expected stock price volatility is calculated using the trailing one month average of daily implied volatilities prior to grant date.
- 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 and Restricted Stock Units

The Company issues restricted stock and restricted stock units with service conditions, which are generally the vesting periods of the awards. The Company also issues, to certain members of senior management, restricted stock and restricted stock units that vest upon the earlier of the satisfaction of (i) a performance condition or (ii) a service condition.

Employee Stock Purchase Plan

The weighted-average fair value of each purchase right granted during 2013, 2012 and 2011 was $21.08, $12.90 and $9.80, respectively. The following table reflects the weighted-average assumptions used in the Black-Scholes option pricing model for 2013, 2012 and 2011:

	2013		2012		2011	
Expected stock price volatility	54.69	%	46.90	%	51.32	%
Risk-free interest rate	0.08	%	0.16	%	0.08	%
Expected term (in years)	0.74		0.74		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 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. September 2009 Financial Transactions

2012 Notes

In September 2009, the Company sold $155.0 million in aggregate of secured notes due 2012 (the "2012 Notes") for an aggregate of $122.2 million pursuant to a note purchase agreement with Olmsted Park S.A. (the "Purchaser"). The 2012 Notes were issued at a discount and did not pay current interest prior to maturity. The 2012 Notes were scheduled to mature on October 31, 2012, subject to earlier mandatory redemption to the extent that specified milestone events set forth in the Company's collaboration with Janssen occurred prior to October 31, 2012. In February 2011, the Company received a milestone payment of $50.0 million and subsequently redeemed $50.0 million of 2012 Notes pursuant to their terms. The remaining $105.0 million of 2012 Notes were redeemed on October 31, 2011, with the proceeds of milestone payments received from Janssen in October 2011. The 2012 Notes contained an embedded derivative related to the potential mandatory redemption or early repayment of the 2012 Notes at the face amount prior to their maturity date. The fair value of this

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Notes to Consolidated Financial Statements (Continued)

embedded derivative was evaluated quarterly, with changes in the fair value of the embedded derivative resulting in a corresponding gain or loss. The Company recorded quarterly interest expense related to the 2012 Notes using the effective interest rate method.

Sale of Contingent Milestone Payments

In September 2009, the Company entered into two purchase agreements with the Purchaser pursuant to which the Company sold its rights to an aggregate of $95.0 million in contingent milestone payments under the Janssen agreement related to the launch of telaprevir in the European Union, for nonrefundable payments totaling $32.8 million. The Purchaser received the $95.0 million in milestone payments from Janssen in the fourth quarter of 2011. The Company determined that this sale of a future revenue stream should be accounted for as a liability. The fair value of the rights sold to the Purchaser pursuant to the purchase agreements was evaluated each reporting period until the payments were received in the fourth quarter of 2011, with changes in the fair value of the derivative instruments based on the probability of achieving the milestones, the timing of achieving the milestones or discount rates resulting in a corresponding gain or loss.

Expenses Related to September 2009 Financial Transactions

The Company had no expenses related to these transactions in 2013 or 2012. The table below sets forth the total expenses related to the September 2009 financial transactions for 2011:

	2011 (in thousands)
Expenses and Losses (Gains):	
Interest expense related to 2012 Notes	$21,687
Change in fair value of embedded derivative related to 2012 Notes	(400)
Change in fair value of free-standing derivatives related to the sale of milestone payments	17,201
Total September 2009 financial transaction expenses	$38,488

P. 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. As of December 31, 2013, the Company had $63.5 million in deferred revenues related to the one-time cash payment, which it is recognizing over the life of the collaboration agreement with GlaxoSmithKline plc based on the units-of-revenue method. In addition, the Company continues to recognize royalty revenues equal to the amount of the third-party subroyalty and an offsetting royalty expense for the third-party subroyalty payment.

Q. Income Taxes

The components of income (loss) before provision for (benefit from) income taxes during the three years ended December 31, 2013 consisted of the following:

	2013	2012	2011
	(in thousands)		
United States	$(390,009)	$256,816	$343,515
Foreign	(586,108)	(269,197)	(283,070)
Income (loss) before provision for (benefit from) income taxes	$(976,117)	$(12,381)	$60,445

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Notes to Consolidated Financial Statements (Continued)

The components of the provision for (benefit from) income taxes during the three years ended December 31, 2013 consisted of the following:

	2013	2012	2011
	(in thousands)		
Current taxes:			
United States	$(11,420)	$2,057	$22,275
Foreign	1,084	(1,865)	(561)
State	2,136	1,902	8,655
Total current taxes	$(8,200)	$2,094	$30,369
Deferred taxes:			
United States	$(131,281)	$31,308	$19,629
Foreign	(127,587)	—	(32,692)
State	(21,499)	5,352	1,960
Total deferred taxes	$(280,367)	$36,660	$(11,103)
Provision for (benefit from) income taxes	$(288,567)	$38,754	$19,266

The difference between the Company's "expected" tax provision (benefit), as computed by applying the U.S. federal corporate tax rate of 35% to income (loss) before provision for (benefit from) income taxes, and actual tax is reconciled as follows:

	2013	2012	2011
	(in thousands)		
Income (loss) before provision for (benefit from) income taxes	$(976,117)	$(12,381)	$60,445
Expected tax provision (benefit)	(341,641)	(4,333)	21,156
State taxes, net of federal benefit	(19,268)	7,075	10,624
Foreign rate differential	72,961	62,425	43,629
Tax credits	(16,775)	(1,980)	(51,086)
Unbenefited operating losses	(43,570)	(30,364)	(6,286)
Non-deductible expenses	9,614	3,198	1,953
Rate change	50,076	3,275	—
Other	36	(542)	(724)
Provision for (benefit from) income taxes	$(288,567)	$38,754	$19,266

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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,	
	2013	2012
	(in thousands)	
Deferred tax assets:		
Net operating loss	$850,946	$777,687
Tax credit carryforwards	180,380	147,074
Property and equipment	—	10,701
Intangible assets	26,105	63,353
Deferred revenues	25,158	44,867
Stock-based compensation	63,521	83,979
Inventories	26,278	56,564
Accrued expenses	52,470	27,945
Currency translation adjustment	217	—
Construction financing lease obligation	152,688	—
Gross deferred tax assets	1,377,763	1,212,170
Valuation allowance	(1,243,664)	(1,211,561)
Total deferred tax assets	134,099	609
Deferred tax liabilities:		
Property and equipment	(134,099)	—
Unrealized gain	—	(376)
Contingent milestone and royalty payment obligation	—	(50,904)
Acquired intangibles	—	(229,696)
Net deferred tax liabilities	$—	$(280,367)

For federal income tax purposes, as of December 31, 2013, the Company has net operating loss carryforwards of approximately $2.7 billion and tax credits of $120.1 million, which may be used to offset future federal income and tax liability, respectively. Approximately $694.8 million of the federal net operating loss carryforward will result in an increase to additional paid-in capital if and when these carryforwards are used to reduce income taxes payable.

For state income tax purposes, the Company has net operating loss carryforwards of approximately $966.8 million and tax credits of $66.9 million, which may be used to offset future state income and tax liability, respectively. Approximately $204.5 million of the state net operating loss carryforward will result in an increase to additional paid-in capital if and when these carryforwards are used to reduce state income taxes payable.

These federal and state operating loss carryforwards and tax credits expire at various dates through 2033. After consideration of all the evidence, both positive and negative, the Company continues to maintain a valuation allowance for the full amount of the 2013 deferred tax asset because it is more likely than not that the deferred tax asset will not be realized. In future periods, if management determines that it is more likely than not that the deferred tax asset will be realized, (i) the valuation allowance would be decreased, (ii) a portion or all of the deferred tax asset would be reflected on the Company’s consolidated balance sheet and (iii) the Company would record non-cash benefits in its consolidated statements of operations related to the reflection of the deferred tax asset on its consolidated balance sheets.

The valuation allowance increased by $32.1 million from December 31, 2012 to December 31, 2013 primarily due to an increase in net operating losses and credits.

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Notes to Consolidated Financial Statements (Continued)

Unrecognized tax benefits during the two years ended December 31, 2013 consisted of the following:

	2013	2012
	(in thousands)	
Unrecognized tax benefits beginning of year	$4,106	$4,360
Gross change for current year positions	1,325	598
Increase for prior period positions	—	—
Decrease for prior period positions	(290)	—
Decrease due to settlements and payments	—	—
Decrease due to statute limitations	(185)	(852)
Deconsolidation of Alios	(2,932)	—
Unrecognized tax benefits end of year	$2,024	$4,106

The Company had gross unrecognized tax benefits of $2.0 million and $4.1 million, respectively, as of December 31, 2013 and 2012. At December 31, 2013, $2.0 million represented the amount of unrecognized tax benefits that, if recognized, would result in a reduction of the Company's effective tax rate. The Company recognizes interest and penalties related to income taxes as a component of income tax expense. As of December 31, 2013, no interest and penalties have been accrued. In 2014, it is reasonably possible that the Company will reduce the balance of its unrecognized tax benefits by approximately $0.5 million due to the application of statute of limitations and settlements with taxing authorities, all of which would reduce the Company's effective tax rate.

The Company files United States federal income tax returns and income tax returns in various state, local and foreign jurisdictions. The Company is no longer subject to any tax assessment from an income tax examination in the United States before 2008 or any other major taxing jurisdiction for years before 2006, except where the Company has net operating losses or tax credit carryforwards that originate before 2006. The Company is currently under examination by Revenue Quebec and the Canada Revenue Agency for the year ended December 31, 2011. No adjustments have been reported. The Company is not under examination by any other jurisdictions for any tax year.

At December 31, 2013, foreign earnings, which were not significant, have been retained indefinitely by foreign subsidiary companies for reinvestment; therefore, no provision has been made for income taxes that would be payable upon the distribution of such earnings, and it would not be practicable to determine the amount of the related unrecognized deferred income tax liability. Upon repatriation of those earnings, in the form of dividends or otherwise, the Company would be subject to U.S. federal income taxes (subject to an adjustment for foreign tax credits) and withholding taxes payable to the various foreign countries.

R. Restructuring Expenses

2003 Restructuring

In June 2003, Vertex adopted a plan to restructure its operations to coincide with its increasing internal emphasis on advancing drug candidates through clinical development to commercialization. The restructuring was designed to re-balance the Company's relative investments in research and development to better support the Company's long-term strategy. At that time, the restructuring plan included a workforce reduction, write-offs of certain assets and a decision not to occupy approximately 290,000 square feet of specialized laboratory and office space in Cambridge, Massachusetts under lease to Vertex (the "Kendall Square Lease"). The Kendall Square Lease commenced in January 2003 and has a 15-year term. In the second quarter of 2005, the Company revised its assessment of its real estate requirements and decided to use approximately 120,000 square feet of the facility subject to the Kendall Square Lease (the "Kendall Square Facility") for its operations, beginning in 2006. The remaining rentable square footage of the Kendall Square Facility currently is subleased to third parties.

The Company's initial estimate of its liability for net ongoing costs associated with the Kendall Square Lease obligation was recorded in the second quarter of 2003 at fair value. The restructuring expense incurred from the second quarter of 2003 through the end of the first quarter of 2005 (i.e., immediately prior to the Company's decision to use a portion of the Kendall

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Notes to Consolidated Financial Statements (Continued)

Square Facility for its operations) relates to the estimated incremental net ongoing lease obligations associated with the entire Kendall Square Facility, together with imputed interest costs relating to the restructuring liability. The restructuring expense incurred in the period beginning in the second quarter of 2005 relates only to the portion of the Kendall Square Facility that the Company was not occupying and did not intend to occupy for its operations. The remaining lease obligations, which are associated with the portion of the Kendall Square Facility that the Company occupies and uses for its operations, are recorded as rental expense in the period incurred. In 2014, the Company expects to cease using this portion of the Kendall Square Facility for its operations, and to incur related cease use charges. The Company reviews its assumptions and estimates quarterly and updates its estimates of this liability as changes in circumstances require. The expense and liability recorded is calculated using probability-weighted discounted cash-flows of the Company's estimated ongoing lease obligations, including contractual rental and build-out commitments, net of estimated sublease rentals, offset by related sublease costs.

In estimating the expense and liability under its Kendall Square Lease obligation, the Company estimated (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 of approximately 10% to discount the estimated cash flows. The Company reviews its estimates and assumptions on at least a quarterly basis, intends to continue such reviews until the termination of the Kendall Square Lease, and will make whatever modifications the Company believes necessary, based on the Company's best judgment, to reflect any changed circumstances. The Company's estimates have changed in the past, and may change in the future, resulting in additional adjustments to the estimate of the liability. Changes to the Company's estimate of the liability are recorded as additional restructuring expenses (credits). In addition, because the Company's estimate of the liability includes the application of a discount rate to reflect the time-value of money, the Company records imputed interest costs related to the liability each quarter. These costs are included in restructuring expenses on the Company's consolidated statements of operations.

The activity related to restructuring and other liability for 2003 was as follows:

	Restructuring Expense	Cash Payments	Non-cash Expense	Liability as of December 31, 2003
	(in thousands)			
Lease restructuring and other operating lease expense	$84,726	$(15,200)	$—	$69,526
Employee severance, benefits and related costs	2,616	(2,616)	—	—
Leasehold improvements and asset impairments	4,482	—	(4,482)	—
Total	$91,824	$(17,816)	$(4,482)	$69,526

In 2003, the lease restructuring and other operating lease expense included $78.7 million of lease restructuring expense and $6.0 million of lease operating expense incurred prior to the decision not to occupy the Kendall Square Facility. The restructuring accrual as of December 31, 2003 related only to the lease restructuring expense.

The activity related to 2003 restructuring for 2004 through 2013 was as follows:

	2013	2012	2011	2004-2013
	(in thousands)			
Liability, beginning of the period	$23,328	$26,313	$29,595	$69,526
Cash payments	(15,255)	(14,853)	(14,904)	(178,952)
Cash received from subleases	10,670	10,024	9,548	75,708
Credit for portion of facility Vertex decided to occupy in 2005	—	—	—	(10,018)
Restructuring expense	372	1,844	2,074	62,851
Liability, end of the period	$19,115	$23,328	$26,313	$19,115

In each period, the Company records lease restructuring expense attributable to imputed interest related to the restructuring liability. In certain periods, the restructuring expense also reflects the revision of certain key estimates and assumptions about building operating expenses and sublease income.

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Fan Pier Move Restructuring

In connection with the relocation of its Massachusetts operations to Fan Pier in Boston, Massachusetts, the Company expects to incur restructuring charges related to its remaining lease obligations at its facilities in Cambridge, Massachusetts, including lease obligations related to the 120,000 square feet of the facility subject to the Kendall Square lease that the Company began using for its operations in 2006. The Company started incurring these charges in the fourth quarter of 2013 and expects them to continue through April 2018. Most of these restructuring charges will relate to cease use charges that will be incurred during the first half of 2014. The Company incurred $1.2 million of charges related to this restructuring during 2013. The continuing charges will relate to the difference between the Company's estimated future cash flows related to its lease obligations and the actual cash flows that it incurs.

2013 Strategic Restructuring

In October 2013, the Company adopted a restructuring plan. The restructuring plan included (i) a workforce reduction primarily related to the commercial support of INCIVEK following the continued and rapid decline in the number of patients being treated with INCIVEK as new medicines for the treatment of HCV infection neared approval and (ii) the write-off of certain assets. This action resulted from the Company's decision to focus its investment on future opportunities in cystic fibrosis and other research and development programs.

The restructuring charges recorded during 2013 for each major type of cost associated with this restructuring plan were as follows:

	Restructuring Expense	Cash Payments	Non-cash Expense	Liability as of December 31, 2013
	(in thousands)			
Employee severance, benefits and related costs	$25,060	$(21,458)	$(1,312)	$2,290
Asset impairments	6,282	—	(6,282)	—
Contract termination and other associated costs	7,609	(1,458)	—	6,151
Total	$38,951	$(22,916)	$(7,594)	$8,441

The Company estimates that it will incur aggregate restructuring charges of approximately $2.0 million to $2.5 million in 2014 and 2015 related to this restructuring plan. The Company anticipates cash payments of $7.9 million and $0.5 million will be made in 2014 and 2015, respectively, related to the restructuring liability as of December 31, 2013.

S. 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. Employees have the ability to transfer funds from the stock fund invested in Vertex common stock, subject to certain restrictions. As of December 31, 2013, 755,000 shares of common stock remained available for grant under the Vertex 401(k) Plan. Through mid-2013, the Company paid matching contributions in Vertex common stock in the form of fully-vested interests in a Vertex common stock fund. Beginning in mid-2013, the Company began paying matching contributions in the form of cash.

The Company declared matching contributions paid in fully-vested interests in the Vertex common stock fund to the Vertex 401(k) Plan as follows:

	2013	2012	2011
	(in thousands)		
Discretionary matching contributions during the year ended December 31,	$5,930	$10,261	$8,619
Shares issued during the year ended December 31,	99	242	183
Shares issuable as of the year ended December 31,	0	53	62

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Notes to Consolidated Financial Statements (Continued)

In 2013, the Company declared matching contributions paid in fully-vested interests in the Vertex common stock fund of $5.9 million, paid matching contributions in the form of cash of $5.0 million and accrued $2.4 million related to matching contributions for the fourth quarter of 2013, which will be paid in the first quarter of 2014.

T. Commitments

The Company moved into its new corporate headquarters in January 2014. Please refer to Note I, "Fan Pier Leases," for additional information regarding this commitment. The leases for the Company's former headquarters expire in December 2015.

The term of the Kendall Square Lease began in January 2003. The Company occupies and uses for its operations approximately 120,000 square feet of the Kendall Square Facility and plans to cease using for its operations this portion of the Kendall Square Facility in 2014. The Company has sublease arrangements in place for the remaining rentable square footage of the Kendall Square Facility, with terms that expire in April 2015 and August 2015. The Kendall Square Lease will expire in 2018. Please refer to Note R, "Restructuring Expenses," for further information.

As of December 31, 2013, future minimum commitments under the Fan Pier Leases, facility operating leases with terms of more than one year and contractual sublease income under the Company's subleases for the Kendall Square Facility were as follows:

Year	Fan Pier Leases	Kendall Square Lease	Kendall Sublease Income	Other Operating Leases	Total Lease Commitments (Net of Sublease Income)
	(in thousands)				
2014	$67,206	$19,879	$(8,546)	$40,762	$119,301
2015	67,206	19,879	(3,996)	33,398	116,487
2016	67,206	19,879	—	14,434	101,519
2017	67,206	19,879	—	12,995	100,080
2018	67,206	6,626	—	12,841	86,673
Thereafter	752,798	—	—	75,344	828,142
Total minimum lease payments	$1,088,828	$86,142	$(12,542)	$189,774	$1,352,202

During 2013, 2012 and 2011, rental expense was $57.7 million, $57.1 million and $49.4 million, respectively.

The Company has outstanding capital leases for equipment, leasehold improvements and software licenses with terms through 2019. The leases were accounted for as capital leases. The capital leases bear interest at rates ranging from 2% to 7% per year. The following table sets forth the Company's future minimum payments due under capital leases as of December 31, 2013:

Year	(in thousands)
2014	$19,957
2015	18,346
2016	11,809
2017	10,714
2018	10,612
Thereafter	2,121
Total payments	73,559
Less: amount representing interest	(7,912)
Present value of payments	$65,647

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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," for further information.

In the second quarter of 2013, the Company began supporting $31.9 million in irrevocable stand-by letters of credit issued in support of property leases and other similar agreements with an unsecured credit facility with a one-year term. The Company previously had cash-collateralized these stand-by letters of credit. As a result of this credit facility, the restricted cash reflected on the Company's consolidated balance sheets decreased by $31.8 million net of other activity during 2013, and the Company's cash and cash equivalents increased by a corresponding amount during 2013.

U. Legal Proceedings

On September 6, 2012, a purported shareholder class action, City of Bristol Pension Fund v. Vertex Pharmaceuticals Incorporated, et al., was filed in the United States District Court for the District of Massachusetts, naming the Company and certain of the Company's current and former officers and directors as defendants. The lawsuit alleges that the Company made material misrepresentations and/or omissions of material fact in the Company's disclosures during the period from May 7, 2012 through June 28, 2012, all in violation of Section 10(b) of the Securities Exchange Act of 1934, as amended, and Rule 10b-5 promulgated thereunder. By order dated December 12, 2012, the court appointed the City of Bristol lead plaintiff and appointed the City of Bristol's attorneys lead counsel. The plaintiffs filed an amended complaint on February 11, 2013. The Company filed a motion to dismiss the complaint on April 12, 2013. On May 28, 2013, the plaintiffs filed an opposition to the Company's motion to dismiss the complaint. On June 27, 2013, the Company filed a reply in further support of the Company's motion to dismiss the plaintiffs' complaint. The court conducted a hearing on the Company's motion to dismiss on November 25, 2013. The plaintiffs seek unspecified monetary damages on behalf of the putative class and an award of costs and expenses, including attorney's fees, as well as disgorgement of the proceeds from certain individual defendants' sales of the Company's common stock. The Company believes that this action is without merit and intends to defend it vigorously. As of December 31, 2013, the Company has not recorded any reserves for this purported class action.

V. 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, 2013 or 2012.

W. Guarantees

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

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Notes to Consolidated Financial Statements (Continued)

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.

X. Segment Information

The Company operates in one segment, pharmaceuticals. Enterprise-wide disclosures about revenues, significant customers, and property and equipment, net by location are presented below.

Revenues by Product

Product revenues, net consisted of the following:

	2013	2012	2011
	(in thousands)		
INCIVEK	$466,360	$1,161,813	$950,889
KALYDECO	371,285	171,645	—
Total product revenues, net	$837,645	$1,333,458	$950,889

Revenues by Geographic Location

Total revenues from external customers and collaborators by geographic region consisted of the following. Product revenues are attributed to countries based on the location of the customer. Collaborative revenues are attributed to the operations of the Company in the United States. Royalty revenues are attributed to countries based on the location of the collaborator.

	2013	2012	2011
	(in thousands)		
United States	$896,952	$1,373,516	$1,389,568
Outside of the United States			
Europe	279,557	129,786	20,289
Other	35,466	23,740	769
Total revenues outside of the United States	315,023	153,526	21,058
Total revenues	$1,211,975	$1,527,042	$1,410,626

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:

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Notes to Consolidated Financial Statements (Continued)

	Percent of Total Gross Revenues			Percent of Gross Accounts Receivable	
	Year Ended December 31,			As of December 31,	
	2013	2012	2011	2013	2012
Janssen	22%	<10%	19%	28%	26%
AmerisourceBergen Drug Corporation	21%	32%	25%	<10%	22%
McKesson Corporation	21%	29%	24%	<10%	26%
Cardinal Health Incorporated	<10%	15%	15%	<10%	<10%
Bupa Home Healthcare Limited	<10%	N/A	N/A	14%	N/A

Property and Equipment, Net by Location

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

	As of December 31,	
	2013	2012
	(in thousands)	
United States	$657,587	$400,102
Outside of the United States		
United Kingdom	29,970	30,622
Other	9,354	2,885
Total property and equipment, net outside of the United States	39,324	33,507
Total property and equipment, net	$696,911	$433,609

VERTEX PHARMACEUTICALS INCORPORATED

Notes to Consolidated Financial Statements (Continued)

Y. Quarterly Financial Data (unaudited)

	Three Months Ended			
	March 31, 2013	June 30, 2013	September 30, 2013	December 31, 2013
	(in thousands, except per share amounts)			
Revenues:				
Product revenues, net	$267,381	$254,789	$186,653	$128,822
Royalty revenues	43,573	49,120	27,012	36,887
Collaborative revenues (1)	17,414	6,841	8,035	185,448
Total revenues	328,368	310,750	221,700	351,157
Costs and expenses:				
Cost of product revenues (2)	30,955	24,695	20,048	13,281
Royalty expenses	11,788	13,236	7,291	8,983
Research and development expenses	218,095	222,455	228,624	249,609
Sales, general and administrative expenses	92,879	106,521	87,754	75,188
Restructuring expenses	39	776	12,048	27,658
Intangible asset impairment charges (3)(4)	412,900	—	—	250,600
Total costs and expenses	766,656	367,683	355,765	625,319
Loss from operations	(438,288)	(56,933)	(134,065)	(274,162)
Interest expense, net	(3,465)	(6,551)	(95)	(12,619)
Other income (expense), net (4)	(1,187)	(27)	4,747	(53,472)
Loss before benefit from income taxes	(442,940)	(63,511)	(129,413)	(340,253)
Benefit from income taxes (3)(4)	(130,313)	(1,799)	(751)	(155,704)
Net loss	(312,627)	(61,712)	(128,662)	(184,549)
Net loss attributable to noncontrolling interest (Alios)	4,611	4,547	4,530	228,834
Net income (loss) attributable to Vertex	$(308,016)	$(57,165)	$(124,132)	$44,285
Net income (loss) per share attributable to Vertex common shareholders:				
Basic	$(1.43)	$(0.26)	$(0.54)	$0.19
Diluted	$(1.43)	$(0.26)	$(0.54)	$0.19
Shares used in per share calculations:				
Basic	215,421	222,053	230,505	231,264
Diluted	215,421	222,053	230,505	235,717

VERTEX PHARMACEUTICALS INCORPORATED

Notes to Consolidated Financial Statements (Continued)

	Three Months Ended			
	March 31, 2012	June 30, 2012	September 30, 2012	December 31, 2012
	(in thousands, except per share amounts)			
Revenues:				
Product revenues, net	$375,375	$373,273	$303,501	$281,309
Royalty revenues	38,981	33,480	25,586	43,451
Collaborative revenues	24,381	11,552	6,919	9,234
Total revenues	438,737	418,305	336,006	333,994
Costs and expenses:				
Cost of product revenues (2)	25,918	104,549	30,680	75,595
Royalty expenses	13,293	9,874	7,856	12,120
Research and development expenses	196,371	196,544	200,161	213,109
Sales, general and administrative expenses	111,146	117,514	97,684	110,452
Restructuring expenses	360	594	696	194
Intangible asset impairment charge	—	—	—	—
Total costs and expenses	347,088	429,075	337,077	411,470
Income (loss) from operations	91,649	(10,770)	(1,071)	(77,476)
Interest expense, net	(3,891)	(3,814)	(4,054)	(3,263)
Other income (expense), net	150	179	13	(33)
Income (loss) before provision for (benefit from) income taxes	87,908	(14,405)	(5,112)	(80,772)
Provision for (benefit from) income taxes	32	20,063	21,355	(2,696)
Net income (loss)	87,876	(34,468)	(26,467)	(78,076)
Net loss (income) attributable to noncontrolling interest (Alios)	3,714	(30,463)	(31,076)	1,928
Net income (loss) attributable to Vertex	$91,590	$(64,931)	$(57,543)	$(76,148)
Net income (loss) per share attributable to Vertex common shareholders:				
Basic	$0.44	$(0.31)	$(0.27)	$(0.35)
Diluted	$0.43	$(0.31)	$(0.27)	$(0.35)
Shares used in per share calculations:				
Basic	208,018	211,344	213,767	214,607
Diluted	219,264	211,344	213,767	214,607

1. During the fourth quarter of 2013, the Company recorded $182.4 million of collaborative revenue related to its Janssen collaboration, which was primarily attributable to an amendment to its collaboration agreement with Janssen. See Note B, "Collaborative Arrangements," for further information.

2. During 2013 and 2012, the Company recorded within cost of product revenues lower-of-cost or market charges for excess or obsolete inventories. See Note G, "Inventories," for further information.

3. During the first quarter of 2013, the Company recorded a $412.9 million intangible asset impairment charge related to its VX-222 indefinite-lived in-process research and development asset. In connection with this impairment charge, the Company recorded a credit of $127.6 million in its provision for income taxes. See Note J, "Intangible Assets and Goodwill," for further information.

4. During the fourth quarter of 2013, the Company deconsolidated Alios, which included certain charges related to deconsolidation recorded in other income (expense), net, and was preceded by a $250.6 million intangible asset impairment charge related to the HCV nucleotide analogue program indefinite-lived

in-process research and development asset. In connection with this impairment charge, a credit of $102.1 million was recorded to the provision for income taxes attributable to Alios. See Note B, "Collaborative Arrangements," and Note J, "Intangible Assets and Goodwill," for further information.