VERTEX PHARMACEUTICALS INC / MA

FORM 10-K
(Annual Report)

Filed 02/16/16 for the Period Ending 12/31/15

Address	50 NORTHERN AVENUE
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Telephone	6173416393
CIK	0000875320
Symbol	VRTX
SIC Code	2834 - Pharmaceutical Preparations
Industry	Biotechnology & Drugs
Sector	Healthcare
Fiscal Year	12/31

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

WASHINGTON, D.C. 20549

FORM 10-K

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

For the Fiscal Year Ended December 31, 2015

or

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

For the transition period from _ to _

Commission file number 000-19319

Vertex Pharmaceuticals Incorporated

(Exact name of registrant as specified in its charter)

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

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

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

Title of Each Class	**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

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

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

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

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

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

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer 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 ☒	Accelerated filer ☐	Non-accelerated filer ☐	Smaller reporting company ☐

(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 ☐ No ☒

The aggregate market value of the registrant's common stock held by non-affiliates of the registrant (without admitting that any person whose shares are not included in such calculation is an affiliate) based on the last reported sale price of the common stock on June 30, 2015 (the last trading day of the registrant's second fiscal quarter of 2015) was $30.0 billion . As of January 31, 2016 , the registrant had 246,391,955 shares of common stock outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the definitive Proxy Statement for the 2016 Annual Meeting of Shareholders to be held on June 15, 2016 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 medicines for serious diseases. We use precision medicine approaches with the goal of creating transformative drugs for patients in specialty markets. Our business is focused on developing and commercializing therapies for the treatment of cystic fibrosis, or CF, and advancing our research and development programs in other indications, while maintaining our financial strength.

Cystic Fibrosis

Our goal is twofold: to develop treatment regimens that will provide benefits to as many patients with CF as possible and to enhance those benefits. Our two marketed medicines are ORKAMBI and KALYDECO, which are approved to treat patients with CF who have specific mutations in their cystic fibrosis transmembrane conductance regulator, or *CFTR,* gene.

ORKAMBI

ORKAMBI (lumacaftor in combination with ivacaftor) was approved by the United States Food and Drug Administration, or FDA, in July 2015 and by the European Commission in November 2015, for the treatment of patients with CF twelve years of age and older who have two copies (homozygous) of the F508del mutation in their *CFTR* gene. We believe that there are approximately 20,500 patients in the United States and European Union currently eligible for treatment with ORKAMBI, of which we believe more than 4,500 patients had begun treatment as of December 31, 2015. We recently completed the first of two Phase 3 clinical trials evaluating lumacaftor in combination with ivacaftor for the treatment of patients with CF six to eleven years of age who are homozygous for the F508del mutation in their *CFTR* gene. We believe that there are approximately 5,800 patients in the United States and European Union within this patient population.

KALYDECO

KALYDECO (ivacaftor) 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. Since 2012, we have increased the number of patients who are being treated with KALYDECO in the United States and non-U.S. markets by expanding the label for KALYDECO to include patients with CF who have additional mutations in their *CFTR* gene and to include patients in additional age demographics. We believe that there are approximately 4,000 patients in North America, Europe and Australia who currently are eligible for treatment with KALYDECO.

CF Development Programs

We have multiple development programs in the field of CF, including:

- VX-661, a corrector compound that we are evaluating in a Phase 3 development program in combination with ivacaftor in multiple CF patient populations who have at least one copy of the F508del mutation in their *CFTR* gene;
- VX-371, an investigational epithelial sodium channel, or ENaC, inhibitor, that is being evaluated in a Phase 2 development program and which we exclusively licensed from Parion Sciences, Inc., or Parion, in 2015; and
- VX-152 and VX-440, two next-generation CFTR corrector compounds that entered Phase 1 clinical trials in the fourth quarter of 2015 and that we plan to evaluate as part of combination treatment regimens.

Research and Development Programs

We are engaged in a number of other research and mid- and early-stage development programs, including programs in the areas of oncology, pain and neurology. We plan to continue investing in our research programs and fostering scientific innovation in order to identify and develop transformative medicines with a focus on CF and other genetic diseases, oncology, pain and neurology. We believe that pursuing research in diverse areas allows us to balance the risks inherent in drug development and may provide drug candidates that will form our pipeline in future years.

CYSTIC FIBROSIS

Background

CF is a rare, life-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. To develop CF, children must inherit two defective *CFTR* genes, which are referred to as alleles - one from each parent. 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 F508del mutation and the G551D mutation.

The F508del mutation results in a defect in the CFTR protein in which the CFTR protein does not reach the surface of cells in sufficient quantities. 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 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, a CFTR potentiator, keeps the CFTR protein channels on the cell surface open more often, to increase the flow of salt and water into and out of the cell. CFTR correctors, such as lumacaftor, VX-661, VX-152 and VX-440 are believed to help CFTR protein reach the cell surface. We believe that ENaC inhibitors, such as VX-371, may help maintain mucus hydration and accelerate pulmonary mucus clearance.

We use the brand name for our products when we refer to the product that has been approved and with respect to the indications on the approved label. Otherwise, including in discussions of our CF development programs, we refer to our compounds by their scientific (or generic) name.

ORKAMBI (lumacaftor in combination with ivacaftor)

ORKAMBI is an orally-administered combination therapy comprised of lumacaftor, a CFTR corrector, and ivacaftor, a CFTR potentiator, that is approved in the United States, European Union and Canada for the treatment of patients with CF twelve years of age and older who are homozygous for the F508del mutation in their *CFTR* gene. We have submitted regulatory applications seeking approval for lumacaftor in combination with ivacaftor in Australia based on TRAFFIC and TRANSPORT, two Phase 3 randomized, double-blind, placebo-controlled clinical trials of lumacaftor in combination with ivacaftor that we completed in 2014.

We recently completed a Phase 3 clinical trial evaluating lumacaftor in combination with ivacaftor for the treatment of patients with CF six to eleven years of age who are homozygous for the F508del mutation in their *CFTR* gene. The clinical trial, which enrolled 58 patients, met its primary safety endpoint and data from the clinical trial showed that the combination was generally well-tolerated. The most common adverse events were cough, headache, infective pulmonary exacerbation, nasal congestion, abdominal pain, increased sputum and elevated liver enzymes. Two patients (3.4%) discontinued treatment because of adverse events. In the clinical trial improvements in a secondary endpoint measuring pulmonary function, including improvements in percent predicted forced expiratory volume in one second, or ppFEV1, and an exploratory endpoint measuring lung clearance index were observed. Based on these results, we plan to submit a supplemental New Drug Application, or sNDA, to the FDA in the second quarter of 2016 seeking approval for patients with CF six to eleven years of age who are homozygous for the F508del mutation in their *CFTR* gene. A second Phase 3 clinical trial evaluating lumacaftor in combination with ivacaftor in this same patient population is ongoing. If successful, this clinical trial will be used to support approval of lumacaftor in combination with ivacaftor in this patient population in the European Union. The primary endpoint of this six-month clinical trial, which is expected to enroll 200 patients, is absolute change in lung clearance index.

KALYDECO (ivacaftor)

KALYDECO (ivacaftor) is an orally-administered CFTR potentiator that is approved in the United States, European Union, Australia and Canada for the treatment of certain patients with CF who have specific mutations in their *CFTR* gene. In the United States, KALYDECO is approved for the treatment of patients with CF two years of age and older who have one of the following mutations in their *CFTR* gene: G551D, G178R, S549N, S549R, G551S, G1244E, S1251N, S1255P, G1349D and R117H. In the European Union, KALYDECO is approved for the treatment of patients with CF (i) two years of age and older who have one of the following mutations in their *CFTR* gene: G551D, G178R, S549N, S549R, G551S,

G1244E, S1251N, S1255P and G1349D and (ii) eighteen years of age and older who have the R117H mutation in their *CFTR* gene.

In October 2015, we submitted an sNDA to the FDA for KALYDECO for patients with CF two years of age and older who have one of 23 residual function mutations. The sNDA was based on preclinical data for ivacaftor in residual function mutations, the established clinical profile of KALYDECO and on previously reported data from an exploratory Phase 2a clinical trial in patients with CF. In February 2016, we received a Complete Response Letter from the FDA regarding the sNDA pursuant to which the FDA determined that it cannot approve the sNDA in its present form. We plan to meet with the FDA regarding the sNDA to determine an appropriate path forward.

In the first quarter of 2016, we plan to commence a clinical trial for ivacaftor in patients with CF less than two years of age to evaluate the effect of ivacaftor on markers of CF disease in young children. This clinical trial will utilize a weight-based dose of ivacaftor granules that can be mixed in soft foods or liquids.

VX-661 in Combination with Ivacaftor

VX-661 is an orally-administered CFTR corrector drug candidate that we are developing in combination with ivacaftor. In the first quarter of 2015, we initiated a Phase 3 development program comprised of four separate clinical trials for VX-661 in combination with ivacaftor in multiple CF patient populations who have at least one copy of the F508del mutation in their *CFTR* gene. Details of the patient population and status of each of these clinical trials is as follows:

- *Two copies of the F508del in their CFTR gene* : We expect enrollment to be complete in mid-2016 and expect data from this clinical trial by early 2017;
- *One copy of the F508del mutation in their CFTR gene and a second mutation in their CFTR gene that results in a gating defect in the CFTR protein* : We expect enrollment to be complete by the end of 2016 and expect data from this clinical trial in the first half of 2017;
- *One copy of the F508del mutation in their CFTR gene and a second mutation in their CFTR gene that results in residual CFTR function* : We expect enrollment to be complete by the end of 2016 and expect data from this clinical trial in the first half of 2017; and
- *One copy of the F508del mutation in their CFTR gene and a second mutation that results in minimal CFTR function* : We expect enrollment in the first part of this clinical trial to be complete in mid-2016 and an interim futility analysis of efficacy data, which will be conducted by an independent third-party, to be completed by the end of 2016. If supported by data from the first part of this clinical trial, we would subsequently initiate the second part of this clinical trial.

In addition to evaluating the efficacy of the combination regimen, these four Phase 3 clinical trials will provide safety data on the combination of VX-661 and ivacaftor to support the planned development of a triple combination regimen that includes a next-generation corrector in combination with VX-661 and ivacaftor.

ENaC Inhibition

In June 2015, we entered into a collaboration with Parion to develop investigational ENaC inhibitors, including VX-371, for the potential treatment of CF and other pulmonary diseases. Preclinical evaluation in human bronchial epithelial, or HBE, cells from patients with CF who have two copies of the F508del mutation in their *CFTR* gene showed that the addition of VX-371 to lumacaftor in combination with ivacaftor resulted in an additional increase in both airway surface liquid and cilia beat frequency compared to baseline and to the use of VX-371 or lumacaftor in combination with ivacaftor alone. Improvements in airway surface liquid height and cilia beat frequency are believed to be measures of increased hydration of the cell surface.

VX-371 is being evaluated in an exploratory Phase 2a clinical trial in approximately 120 patients with CF with any mutation in their *CFTR* gene, including those who have mutations not expected to respond to ivacaftor alone. The primary endpoint of this clinical trial is safety, and we expect results from this clinical trial in mid-2016. In the first quarter of 2016, we expect to initiate a placebo-controlled Phase 2a clinical trial of VX-371 to evaluate the addition of VX-371 to treatment with ORKAMBI for patients with CF who are homozygous for the F508del mutation in their *CFTR* gene.

Next-generation CFTR Corrector Compound s

We are developing two next-generation CFTR corrector compounds, VX-152 and VX-440, that we plan to evaluate as part of triple combination treatment regimens. We initiated Phase 1 clinical trials in healthy volunteers of each of VX-152 and VX-440, alone and as part of a triple combination with VX-661 and ivacaftor, in the fourth quarter of 2015. If these clinical trials are successful, we plan to initiate Phase 2 clinical trials of VX-152 or VX-440 as part of a triple combination with VX-661 and ivacaftor in the second half of 2016 in patients with CF who have:

- Two copies of the F508del mutation in their *CFTR* gene;
- One copy of the F508del mutation in their *CFTR* gene and a second mutation in their *CFTR* gene that results in minimal CFTR function; and
- One copy of the F508del mutation in their *CFTR* gene and a second mutation in their *CFTR* gene that is known to be responsive to ivacaftor.

In HBE cells with two copies of the F508del mutation in the *CFTR* gene, as well as in HBE cells with one copy of the F508del mutation in the *CFTR* gene and a second mutation that results in minimal CFTR function, the triple combinations (VX-152/VX-661/ivacaftor and VX-440/VX-661/ivacaftor) resulted in chloride transport (measured as a percent of normal) that was approximately three-fold greater than the use of a lumacaftor/ivacaftor combination in these cells.

RESEARCH AND DEVELOPMENT PROGRAMS

Our approach to project selection and drug design aims to enhance our ability to discover and develop drug candidates by combining transformative insights into the causes of serious diseases with innovative approaches to therapeutics. The approach starts with knowledge of human genetics and human biology, and our ability to develop complex biological assays to query the underlying biology of disease. We leverage our expertise in assay automation, medicinal and process chemistry, modeling and informatics, biomarkers, pharmacology, drug metabolism and pharmacokinetics, toxicology, material sciences and formulation to develop, select and advance drug candidates. We believe that our approach has been validated through our success in moving novel drug candidates into clinical trials and obtaining marketing approvals for ORKAMBI, KALYDECO and INCIVEK (telapravir). Currently, the disease areas that are most advanced in our research labs are: CF and other genetic diseases; DNA repair in cancer; genetically validated targets for pain; and neurological diseases.

We focus our research activities on developing products that would be prescribed by specialist physicians for the treatment of rare or life-threatening diseases, which are referred to as specialty markets. Driven by these priority disease areas and by insights into the underlying mechanisms whereby diseases develop and progress, 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, where there have been breakthrough scientific insights, and where innovative therapeutic approaches are available.

To augment our internal research programs, we seek to collaborate with biopharmaceutical and technology companies, leading academic research institutions, government laboratories, foundations and other organizations as needed to advance research in our areas of therapeutic interest as well as to access technologies needed to execute on our strategy. We have established such relationships with organizations around the world and intend to extend and leverage that experience to further our research efforts to discover transformational medicines for serious diseases in specialty markets.

Our research and mid- and early-stage development programs currently are focused on the following areas:

Oncology

We have three oncology drug candidates in development that are designed to inhibit DNA repair pathways that are fundamental to the survival and proliferation of certain cancers.

VX *-970*

Our most advanced oncology drug candidate is VX-970, an inhibitor of ataxia telangiectasia and Rad3-related kinase, or ATR. We plan to evaluate VX-970, both alone and and in combination with other cancer therapies, including targeted agents, chemotherapy, radiotherapy and immuno-oncology therapies, in early-stage clinical trials in selected tumor types and patient

subtypes that are expected to be responsive to ATR inhibition based on biomarker data. We are conducting two Phase 1/2 clinical trials of VX-970 in combination with commonly used DNA-damaging chemotherapies in specific cohorts of triple-negative breast cancer patients and non-small cell lung cancer patients. We expect preliminary data from these clinical trials to be available in 2016.

We also have entered into cooperative research and development agreements with the National Cancer Institute to evaluate VX-970 across other types of cancers. The first clinical trial conducted pursuant to these agreements is ongoing, and several additional clinical trials are planned in patients who have non-small cell lung, head and neck, bladder, ovarian and other cancers.

VX-803 and VX-984

We are in Phase 1 development of two additional oncology drug candidates, VX-803 and VX-984. We are evaluating escalating doses of VX-803, an ATR inhibitor, alone and in combination with chemotherapy in an ongoing Phase 1 clinical trial. We recently initiated a Phase 1 clinical trial of VX-984, an inhibitor of DNA-dependent protein kinase, to evaluate escalating doses of VX-984 alone and in combination with pegylated liposomal doxorubicin.

Pain

We have two drug candidates, VX-150 and VX-241, that are designed to inhibit sodium channels involved in pain sensation. In the fourth quarter of 2015, we initiated a Phase 2 clinical trial to evaluate VX-150, an inhibitor of a sodium channel known as NaV 1.8, which is expected to enroll approximately 100 patients who have symptomatic osteoarthritis of the knee. We expect to begin clinical development of VX-241, an inhibitor of a sodium channel known as NaV 1.7, in the first half of 2016.

Acute Spinal Cord Injury

We have exclusively licensed VX-210, a drug candidate for the treatment of acute spinal cord injury, from BioAxone BioSciences, Inc. VX-210 is designed to inhibit a protein known as Rho that blocks neural regeneration after injury. We expect to initiate a Phase 2b/3 clinical trial in the first half of 2016 to evaluate the efficacy and safety of VX-210 in patients who have certain acute cervical spinal cord injuries.

COMMERCIAL ORGANIZATION

Our commercial organization focuses on supporting sales of ORKAMBI and KALYDECO in the markets where such products are approved. Our sales and marketing organizations are responsible for promoting products to health care providers and obtaining reimbursement for products from third-party payors, including governmental organizations in the United States and non-U.S. markets.

Our U.S. field-based CF commercial team is comprised of a small number of individuals whom we believe will be sufficient to support future needs. We focus our CF marketing efforts in the United States on a relatively small number of physicians and health care professionals who write most of the prescriptions for CF medicines. Many of these physicians and health care professionals are located at a limited number of accredited centers in the United States focused on the treatment of CF. In international markets, we currently have a small sales force that has been promoting KALYDECO but we expect to increase the size of this sales force moderately as we launch ORKAMBI and continue to expand geographically.

We market our products through personal interactions with individual physicians, advertising, sending direct mail, public relations activities and other activities. In addition, our government affairs and public policy group advocates for policies that promote life sciences innovation and increase awareness of the diseases on which we are focusing, with state and federal legislatures, government agencies, public health officials and other policy-makers. We also have established programs in the United States that provide our products to qualified uninsured or underinsured patients at no charge or at a reduced charge, based on specific eligibility criteria.

COLLABORATIONS

We have entered into collaborations with pharmaceutical and other companies and organizations that provide us financial and other resources, including capabilities in research, development, manufacturing and sales and marketing, and licenses to intellectual property. These collaborations have provided us with drug candidates and/or important financial and non-

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

Cystic Fibrosis Foundation Therapeutics Incorporated

We began working with CFFT in 1998. We entered into a collaboration agreement with CFFT in 2004 and have amended it several times to support research and development activities. We are obligated to pay CFFT tiered royalties ranging from single digits to sub-teens, calculated as a percentage of net sales, on ivacaftor, lumacaftor and VX-661. 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 sales of lumacaftor, the first of which was earned in the fourth quarter of 2015 and the second of which we expect to be earned in the first quarter of 2016.

For ivacaftor, lumacaftor and VX-661, 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 patents in the United States and European Union covering the composition-of-matter of lumacaftor that expire in 2030 and 2026, respectively, subject to potential patent life extensions. We have patents in the United States and European Union covering the composition-of-matter of VX-661 that expire in 2027 and 2028, respectively, subject to potential patent life extensions.

Parion Sciences, Inc.

In June 2015, we entered into a strategic collaboration and license agreement with Parion pursuant to which we are collaborating with Parion to develop ENaC inhibitors, including VX-371 (formerly P-1037) and VX-551 (formerly P-1055), for the potential treatment of CF and other pulmonary diseases.

We are leading development activities for VX-371 and are responsible for all costs, subject to certain exceptions, related to its development and commercialization. We also will lead development activities for VX-551, which is in pre-clinical development. Under the terms of the agreement, we received worldwide development and commercial rights to VX-371 and VX-551 for the potential treatment of CF and all other pulmonary diseases and have the option to select additional compounds discovered in Parion's research program. Parion received an $80.0 million up-front payment and has the potential to receive up to an additional (i) $490.0 million in development and regulatory milestone payments for development of ENaC inhibitors in CF, including $360.0 million related to global filing and approval milestones, (ii) $370.0 million in development and regulatory milestones for VX-371 and VX-551 in non-CF pulmonary indications and (iii) $230.0 million in development and regulatory milestones if we elect to develop an additional ENaC inhibitor from Parion's research program. Parion will receive tiered royalties on potential sales of licensed products that range from the low double digits to mid-teens as a percentage of sales.

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

CRISPR Therapeutics AG

In October 2015, we entered into a strategic collaboration, option and license agreement with CRISPR Therapeutics AG, or CRISPR, and its affiliates to collaborate on the discovery and development of potential new treatments aimed at the underlying genetic causes of human diseases using CRISPR-Cas9 gene editing technology. We have the exclusive right to license up to six CRISPR-Cas9-based targets. In connection with the CRISPR agreement, we paid CRISPR an upfront

payment of $75.0 million and made a $30.0 million investment in CRISPR pursuant to a convertible loan agreement that converted into preferred stock in January 2016.

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

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

BioAxone Biosciences, Inc.

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

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

Outlicense Arrangements

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

Janssen Pharmaceuticals, Inc.

In 2014, we entered into an agreement with Janssen Pharmaceuticals, Inc., or Janssen Inc. Pursuant to this agreement, Janssen Inc. has an exclusive worldwide license to develop and commercialize certain drug candidates for the treatment of influenza, including VX-787. We received non-refundable payments of $35.0 million from Janssen Inc. in 2014 and have the potential to receive development, regulatory and commercial milestone payments as well as royalties on future product sales, if any. Janssen Inc. is responsible for costs related to the development and commercialization of the compounds. Janssen Inc. may terminate the agreement, subject to certain exceptions, upon six months' notice.

INTELLECTUAL PROPERTY

We actively seek protection for our products and proprietary information by means of U.S. and foreign patents, trademarks and copyrights, as appropriate. In addition, we rely upon trade secret protection and contractual arrangements to protect certain of our proprietary information and products. We have patents and pending patent applications that relate to potential drug targets, compounds we are developing to modulate those targets, methods of making or using those compounds and proprietary elements of our drug discovery platform.

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

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

Drug/Drug Candidate	Status of United States Patent (Anticipated Expiration, Subject to Potential Extensions)	Status of European Union Patent (Anticipated Expiration, Subject to Potential Extensions)
Ivacaftor	Granted (2027)	Granted (2025)
Lumacaftor	Granted (2030)	Granted (2026)
VX-661	Granted (2027)	Granted (2028)

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

- U.S. and foreign patent applications covering CF potentiators, correctors and ENaC inhibitors, including ivacaftor, lumacaftor, VX-661, VX-371, VX-152 and VX-440 and many other related compounds, and the use of those potentiators, correctors and ENaC inhibitors to treat CF.
- U.S. and foreign patents and patent applications covering VX-970, VX-803 and VX-984 and the use of VX-970, VX-803 and VX-984 to treat oncology indications.
- U.S. and foreign patents and patent applications covering VX-150 and VX-241 and the use of VX-150 and VX-241 to treat pain indications.
- U.S. and foreign patents and patent applications covering VX-210 and the use of VX-210 to treat neurology indications.
- U.S. and foreign patents and patent applications covering the manufacture, pharmaceutical compositions, related solid forms, formulations, dosing regimens and methods of use of these compounds, including ivacaftor and lumacaftor.

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 have a European patent that covers the composition-of-matter of ivacaftor that we expect will provide intellectual property protection in the European Union through its expiration date in 2025, subject to potential extension. We are entitled to orphan drug exclusivity for ivacaftor in the United States and the European Union, which means that the FDA may not approve another application to market ivacaftor for the same indication for a period of seven years following approval, and the EMA cannot accept an MAA for a drug similar to ivacaftor for a period of ten years following approval. As a result of the orphan drug exclusivity, even if a competitor successfully challenges the ivacaftor patents, it could not obtain approval from the FDA to market ivacaftor in the United States for the treatment of patients who

have one of the mutations to the *CFTR* gene for which KALYDECO is currently approved until 2019, or submit an MAA in the European Union for the treatment of patients who have one of the mutations to the *CFTR* gene for which KALYDECO is currently approved until 2022, except in very limited circumstances.

Lumacaftor, and the fixed dose combination of lumacaftor and ivacaftor, were granted orphan drug status in the United States. We have patents in the United States and European Union that cover the composition of matter of lumacaftor that we expect will provide intellectual property protection in these jurisdictions through their expiration dates in 2030 and 2026, respectively, subject to potential extension.

VX-661 was granted orphan drug status in the United States and the European Union. We have patents in the United States and European Union that cover the composition of matter of VX-661 that we expect will provide intellectual property protection in these jurisdictions through their expiration dates in 2027 and 2028, respectively, subject to potential extension.

MANUFACTURING

Manufacturing Approach and Philosophy

As we market and sell our approved products and advance our drug candidates through clinical development toward commercialization, we continue to build and maintain our supply chain and quality assurance resources. We rely on internal capabilities and an international network of third parties to manufacture and distribute our products for commercial sale and post-approval clinical trials and to manufacture and distribute our drug candidates for clinical trials. Wherever possible, we seek to establish multiple suppliers for each raw material and step in the manufacturing process, however our supply chain includes a single-source manufacturer for (i) one step in the ivacaftor manufacturing process and (ii) the manufacture of the oral granule formulation of KALYDECO that is used for patients with CF two to five years of age.

We expect that we will continue for the foreseeable future to rely on third parties to meet most of our commercial supply needs and a significant portion of our clinical supply needs. We have established our own small-scale manufacturing capabilities, which we use for clinical trial supplies and as an additional 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 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 regulatory filings.

Manufacture of ORKAMBI (lumacaftor/ivacaftor)

We have developed several manufacturing processes to produce commercial quantities of ORKAMBI, including a process utilizing continuous manufacturing technology as well as a batch manufacturing process. We have established manufacturing capabilities at our third-party manufacturer in the United Kingdom that is producing commercial quantities of ORKAMBI using a batch manufacturing process we designed. We have established continuous manufacturing capabilities and obtained validation for these capabilities at our facility located in Boston, Massachusetts. Continuous process drug product manufacturing may result in reduced cost, reduced development and production timelines and increased market

response flexibility. While continuous process manufacturing has been used in many industries, we believe that we are the first company to obtain FDA approval for a fully-continuous drug product manufacturing process.

Manufacture of VX-661/Ivacaftor

We are using both a batch manufacturing process and a continuous drug product manufacturing process to obtain a supply of VX-661 tablets to be used in our Phase 3 clinical trials of VX-661 in combination with ivacaftor. If we successfully complete development and obtain approval for VX-661 in combination with ivacaftor, we plan to produce our commercial supply of VX-661 using a continuous drug product 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. Potential competitors also include academic institutions, government agencies, other public and private research organizations and charitable venture philanthropy organizations that conduct research, seek patent protection and/or establish collaborative arrangements for research, development, manufacturing and commercialization. Many of our competitors have substantially greater financial, technical and human resources than we do. We face competition based on the safety and efficacy of our products and drug candidates, the timing and scope of regulatory approvals, the availability and cost of supply, marketing and sales capabilities, reimbursement coverage, price, patent protection and other factors. Our competitors may develop or commercialize more effective, safer or more affordable products than we are able to develop or commercialize or obtain more effective patent protection. As a result, our competitors may commercialize products more rapidly or effectively than we do, which would adversely affect our competitive position, the likelihood that our drug candidates, if approved, would achieve and maintain market acceptance and our ability to generate meaningful revenues from our products. Future competitive products may render our products, or future products, obsolete or noncompetitive.

Cystic Fibrosis

An increasing number of companies are seeking to identify and develop drug candidates for the treatment of CF, including companies such as Concert Pharmaceuticals, Genzyme, which is a division of Sanofi, Novartis, Pfizer, ProQR Therapeutics, PTC Therapeutics, Shire and several private companies. Although we are the first company to successfully develop drugs that treat the underlying cause of CF, ORKAMBI and KALYDECO are collectively approved to treat only a portion of patients with CF. Our competitors have research and development programs directed at identifying and developing CFTR potentiators, CFTR correctors, ENaC inhibitors and drug candidates with other mechanisms of action or that utilize new therapeutic approaches that seek to address the underlying cause of CF. Our success in rapidly developing and commercializing KALYDECO and ORKAMBI may increase the resources that our competitors allocate to the development of these potential treatments for CF. If one or more competing therapies are successfully developed as a treatment for patients with CF, our revenues from ORKAMBI, KALYDECO and/or our other CF drug candidates, if then approved, could face significant competitive pressure.

GOVERNMENT REGULATION

The research, development, testing, manufacture, quality control, approval, labeling, packaging, storage, safety monitoring, 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, including small molecules, 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 or delay in review of pending applications;
- withdrawal of an approval or the implementation of limitations on a previously approved indication for use;
- imposition of a clinical hold, a risk mitigation and evaluation strategy or other safety-related limitations;
- warning letters or "untitled letters";
- product seizures;
- total or partial suspension of production or distribution; or
- injunctions, fines, disgorgement, 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.

As part of the development process, companies usually complete 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.

Biologics License Application Process

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

Expedited Review and Approval

The FDA has 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.

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 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.

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 later of the effective date of an IND or the issuance date of the patent, 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.

Exclusivity of Biologics

Biologics are entitled to exclusivity under the Biologics Price Competition and Innovation Act, which was passed as Title VII to the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act of 2010, which we refer to as the ACA. The law provides a pathway for approval of biosimilars following the expiration of 12 years of exclusivity for the innovator biologic plus any extension term for pediatrics as discussed above. Historically, a biologic approved under a BLA was not subject to the generic drug review and approval provisions of the FDCA. However, the ACA created a regulatory pathway for the abbreviated approval for biological products that are demonstrated to be "biosimilar" or "interchangeable" with an FDA-approved biological product. In order to meet the standard of interchangeability, a sponsor must demonstrate that the biosimilar product can be expected to produce the same clinical result as the reference product, and for a product that is administered more than once, that the risk of switching between the reference product and biosimilar product is not greater than the risk of maintaining the patient on the reference product. Such biosimilars would reference biological products approved in the United States. The law establishes a period of 12 years of data exclusivity for reference products, which protects the data in the original BLA by prohibiting sponsors of biosimilars from gaining FDA approval based in part on reference to data in the original BLA.

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, ORKAMBI and VX-661 have been granted designation as orphan drugs by the FDA.

If a drug candidate that has orphan drug designation subsequently receives the first FDA approval for that drug for the disease for which it has such designation, the product is entitled to orphan drug exclusivity, which means that the FDA may not approve any other applications to market the same drug for the same indication, 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 first obtains approval of the same product as defined by the FDA or if our drug candidate is determined to be contained within the competitor's product for the same indication or disease.

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 ensure 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.

Reimbursement

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

The Medicare Prescription Drug, Improvement, and Modernization Act of 2003, or the MMA, established the Medicare Part D program to provide a voluntary prescription drug benefit to Medicare beneficiaries. Under Part D, Medicare beneficiaries may enroll in prescription drug plans offered by private entities, which will provide coverage of outpatient prescription drugs. Unlike Medicare Part A and B, Part D coverage is not standardized. Part D prescription drug plan sponsors are not required to pay for all covered Part D drugs, and each drug plan can develop its own drug formulary that identifies which drugs it will cover and at what tier or level. However, Part D prescription drug formularies must include drugs within each therapeutic category and class of covered Part D drugs, though not necessarily all the drugs in each category or class. Any formulary used by a Part D prescription drug plan must be developed and reviewed by a pharmacy and therapeutic committee. Government payment for some of the costs of prescription drugs may increase demand for products for which we receive marketing approval. However, any negotiated prices for our products covered by a Part D

prescription drug plan likely will be lower than the prices we might otherwise obtain. Moreover, while the MMA applies only to drug benefits for Medicare beneficiaries, private payors often follow Medicare coverage policy and payment limitations in setting their own payment rates. Any reduction in payment that results from the MMA may result in a similar reduction in payments from non-governmental payors.

The American Recovery and Reinvestment Act of 2009 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 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. 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 ORKAMBI, KALYDECO and of any other drug candidates we may develop, depends largely on obtaining and maintaining government reimbursement, because in many foreign countries patients are unable to access prescription pharmaceutical products that are not reimbursed by their governments. Negotiating reimbursement rates in foreign countries can delay the commercialization of a pharmaceutical product and generally results in a reimbursement rate that is lower than the net price that companies can obtain for the same product in the United States.

In some countries, such as Germany and France, commercial sales of a new product can 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 were 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.

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, 2015 , we had approximately 1,950 employees, as compared to approximately 1,830 employees as of December 31, 2014 . Of these employees, approximately 1,600 were based in the United States, approximately 275 were based in Europe and approximately 75 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 ex-U.S. countries. Science magazine named Vertex as one of its top employers in the life sciences in each of the last five years. We consider our relations with our employees to be good.

OTHER MATTERS

Financial Information and Significant Customers

Financial information about (i) our net product revenues and other revenues generated in the principal geographic regions in which we operate and our significant customers is set forth in Note T, “Segment Information,” to our consolidated financial statements included in this Annual Report on Form 10-K, (ii) net income (loss) per share attributable to Vertex common shareholders and our total assets are provided in our consolidated financial statements included in this Annual Report on Form 10-K and (iii) our research and development expenses in each of the last three fiscal years and our deconsolidation of Alios as of December 31, 2014 is provided in Item 7, “Management’s Discussion and Analysis of Financial Condition and Results of Operations.” A discussion of the risks attendant to our international operations is set forth in the “Risk Factors” section of this Annual Report on Form 10-K.

Information Available on the Internet

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

Corporate Information

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

DIRECTORS AND EXECUTIVE OFFICERS OF THE REGISTRANT

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

Name	Age	Position
Jeffrey M. Leiden, M.D., Ph.D.	60	Chairman of the Board, Chief Executive Officer and President
David Altshuler, M.D., Ph.D.	51	Executive Vice President, Global Research and Chief Scientific Officer
Stuart A. Arbuckle	50	Executive Vice President and Chief Commercial Officer
Jeffrey A. Chodakewitz, M.D.	60	Executive Vice President, Global Medicines Development and Medical Affairs, and Chief Medical Officer
Michael Parini, J.D.	41	Executive Vice President and Chief Legal Officer
Amit K. Sachdev, J.D.	48	Executive Vice President, Global Government Strategy, Market Access and Value
Ian F. Smith	50	Executive Vice President and Chief Financial Officer
Paul M. Silva	49	Senior Vice President and Corporate Controller
Sangeeta M. Bhatia, M.D., Ph.D.	47	Director
Joshua S. Boger, Ph.D.	64	Director
Terrence C. Kearney	61	Director
Yuchun Lee	50	Director
Margaret G. McGlynn	56	Director
Bruce I. Sachs	56	Director
Elaine S. Ullian	68	Director
William Young	71	Director

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

Dr. Altshuler has been our Executive Vice President, Global Research and Chief Scientific Officer since January 2015 and was a member of our Board of Directors from May 2012 through December 2014. Dr. Altshuler was one of four founding members of the Broad Institute, a research collaboration of Harvard, MIT, The Whitehead Institute and the Harvard Hospitals. He served as the Director of the Institute's Program in Medical and Population Genetics from 2003 through December 2014 and as the Institute's Deputy Director and Chief Academic Officer from 2009 through December 2014. Dr. Altshuler joined the faculty at Harvard Medical School and the Massachusetts General Hospital in 2000 and held the academic rank of Professor of Genetics and Medicine from 2008 through December 2014. He served as Adjunct Professor of Biology at MIT from 2012 through December 2014. Dr. Altshuler earned a B.S. from MIT, a Ph.D. from Harvard University and an M.D. from Harvard Medical School. Dr. Altshuler completed his clinical training in Internal Medicine, and in Endocrinology, Diabetes and Metabolism, at the Massachusetts General Hospital.

Mr. Arbuckle is our Executive Vice President and Chief Commercial Officer, a position he has held since September 2012. Prior to joining us, Mr. Arbuckle held multiple commercial leadership roles at Amgen, Inc., a 17,000 person biotechnology company, from July 2004 through August 2012. Mr. Arbuckle has worked in the biopharmaceuticals industry since 1986, including more than 15 years at GlaxoSmithKline plc, where he held sales and marketing roles of increasing responsibility for medicines aimed at treating respiratory, metabolic, musculoskeletal, cardiovascular and other diseases. He has served as a member of the Board of Directors of Cerulean Pharma, Inc. since June 2015. Mr. Arbuckle holds a BSc in pharmacology and physiology from the University of Leeds.

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

Mr. Parini is our Executive Vice President and Chief Legal Officer, a position he has held since January 2016. From 2004 until he joined Vertex, Mr. Parini served in various roles of increasing responsibility at Pfizer Inc., most recently as Senior Vice President and Associate General Counsel. Prior to Pfizer, Mr. Parini was an attorney at Akin, Gump, Strauss, Hauer & Feld, L.L.P. Mr. Parini holds a B.A. from Georgetown University and a J.D. from the Georgetown University Law Center.

Mr. Sachdev is our Executive Vice President, Policy, Access and Value, a role he assumed in October 2014. In this role, Mr. Sachdev manages our global market access, health economics and outcomes research efforts for our drugs and drug candidates. In 2007, he joined us as a Senior Vice President, and has led our government affairs and public policy activities, as well as our patient advocacy programs. From 2010 through 2013 he established our first international commercial operations in Canada. Prior to joining us, Mr. Sachdev served as Executive Vice President, Health of the Biotechnology Industry Organization (BIO) and was the Deputy Commissioner for Policy at the FDA where he also served in several other senior positions within the FDA. Prior to the FDA, Mr. Sachdev served as Majority Counsel to the Committee on Energy and Commerce in the United States House of Representatives and practiced law at the Chemical Manufacturers Association, and subsequently at the law firm of Ropes & Gray LLP. Mr. Sachdev holds a B.S from Carnegie Mellon University, and a J.D. from Emory University School of Law.

Mr. Smith is our Executive Vice President and Chief 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. Silva is our Senior Vice President and Corporate Controller, a position he has held since April 2011. Mr. Silva joined us in August 2007 as Senior Director, Accounting Operations and was our Vice President and Corporate Controller from September 2008 through April 2011. Prior to joining us, he was the Vice President, Internal Reporting at Iron Mountain Incorporated from July 2006 until August 2007 and a consultant to Iron Mountain's financing department from April 2005 until July 2006. He was the Finance Director of the Bioscience Technologies Division of Thermo Electron Corporation from 2002 to April 2005. Mr. Silva holds a B.S. in accounting from Assumption College.

Dr. Bhatia has been a member of our Board of Directors since June 2015. Dr. Bhatia is a professor at the Massachusetts Institute of Technology, where she currently serves as the John J. and Dorothy Wilson Professor of Health Sciences & Technology/Electrical Engineering & Computer Science. Prior to joining the Massachusetts Institute of Technology in 2005,

Dr. Bhatia was a professor of bioengineering and medicine at the University of California at San Diego from 1998 through 2005. Dr. Bhatia also is an investigator for the Howard Hughes Medical Institute, a member of the Department of Medicine at Brigham and Women's Hospital, a member of the Broad Institute and a member of the Koch Institute for Integrative Cancer Research. Dr. Bhatia holds an Sc.B. in biomedical engineering from Brown University, an S.M. and Ph.D. in Mechanical Engineering from the Massachusetts Institute of Technology and an M.D. from Harvard Medical School.

Dr. 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 our board of directors 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. Mr. Kearney serves as a member of the Board of Directors at Acceleron Pharma Inc., a biopharmaceutical company, and Innoviva, Inc. (formerly known as Theravance, Inc.), a royalty management company. 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 also serves as the Chief Executive Officer of two software companies, Clarabridge, Inc. and Allego Inc. Mr. Lee was the Vice President of IBM's Enterprise Marketing Management Group from November 2010 through January 2013. Mr. Lee co-founded Unica Corporation, a provider of software and services used to automate marketing processes, in 1992, and was Unica's President and/or Chief Executive Officer from 1992 through November 2010, when Unica was acquired by IBM. From 1989 to 1992, Mr. Lee was a senior consultant at Digital Equipment Corporation, a supplier of general computing technology and consulting services. Mr. Lee holds a B.S. and an M.S. in electrical engineering and computer science from the Massachusetts Institute of Technology and an M.B.A. from Babson College.

Ms. McGlynn has been a member of our Board of Directors since May 2011. Ms. McGlynn served as the President and Chief Executive Officer of the International AIDS Vaccine Initiative, a global not-for-profit organization whose mission is to ensure the development of safe, effective and accessible HIV vaccines for use throughout the world, from July 2011 until September 2015. Ms. McGlynn served as President, Vaccines and Infectious Diseases of Merck & Co., Inc. from 2005 until 2009. Ms. McGlynn joined Merck in 1983 and served in a variety of marketing, sales and managed care roles. Ms. McGlynn serves as a member of the Board of Directors for Air Products and Chemicals, Inc., a company specializing in gases and chemicals for industrial uses, and Amicus Therapeutics, Inc., a biopharmaceutical company. She is also a member of the National Industrial Advisory Committee at the University at Buffalo School of Pharmacy and Pharmaceutical Sciences. Ms. McGlynn holds a B.S. in Pharmacy and an M.B.A. in Marketing from the State University of New York at Buffalo.

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

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

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

ITEM 1A. RISK FACTORS

RISK FACTORS

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

Risks Related to Our Business

Our business and future revenues depend heavily on our ability to successfully commercialize ORKAMBI. If we are unable to do so, or if reimbursement levels agreed to by third-party payors are unfavorable or do not meet the expectations of investors or public equity market analysts, our business will be materially harmed and the market price of our common stock would likely decline .

We believe that a significant portion of the value attributed to our company by investors is based on the commercial potential of ORKAMBI, which was approved in the United States in July 2015 and the European Union in November 2015 for the treatment of patients with CF twelve years of age and older who are homozygous for the F508del mutation in their *CFTR* gene. While we recognized our first net product revenues from sales of ORKAMBI in the United States in the second half of 2015, we are in the early stages of the commercial launch of this product and are unable to predict the future level of net product revenues we will recognize from sales of ORKAMBI in the United States. Outside of the United States, we do not expect to recognize significant ORKAMBI net product revenues in 2016 other than in Germany due to the time it takes to complete the reimbursement discussions in many ex-U.S. countries.

If ORKAMBI were to become subject to problems such as safety or efficacy issues, the introduction or greater acceptance of competing products, changes in reimbursement policies of payors and other third parties, or adverse legal, administrative, regulatory or legislative developments, our ability to commercialize ORKAMBI would be impaired and our stock price would likely decline. In addition, our ability to successfully commercialize ORKAMBI is dependent on, among other things, the rate at which patients initiate treatment of ORKAMBI, the proportion of initiated patients who remain on treatment and the compliance rate for patients who remain on treatment. Since the regulations that govern pricing, coverage and reimbursement for drugs vary widely from country to country, there is no assurance that coverage and reimbursement will be available outside of the United States and, even if it is available, the level of reimbursement may not be satisfactory. Adverse pricing limitations or a delay in obtaining coverage and reimbursement would decrease our future net product revenues and harm our business.

Our future success also is dependent on our ability to expand the number of CF patients who are eligible for treatment with ORKAMBI. We recently completed a Phase 3 clinical trial evaluating lumacaftor in combination with ivacaftor for the treatment of patients with CF six to eleven years of age who are homozygous for the F508del mutation in their *CFTR* gene. The clinical trial met its primary safety endpoint and data from the clinical trial showed that the combination was generally well-tolerated. Based on these results, we plan to submit a sNDA to the FDA in the second quarter of 2016 seeking approval for patients with CF six to eleven years of age who are homozygous for the F508del mutation in their *CFTR* gene. A second Phase 3 clinical trial evaluating lumacaftor in combination with ivacaftor in this same patient population to support approval in the European Union is ongoing. In order to expand the market to this patient population in the European Union, the clinical trial will need to demonstrate that ORKAMBI is both safe and effective for the treatment of these patients. 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 these clinical trials, or the data included in our submissions to regulatory authorities, will be sufficient to obtain approval for the use of lumacaftor in combination with ivacaftor in this additional patient population.

Our business is dependent on KALYDECO net product revenues and if we are unable to sustain our KALYDECO net product revenues, our business will be materially harmed and the market price of our common stock would decline .

KALYDECO net product revenues represented approximately 61.2% and 79.9% of our total revenues in 2015 and 2014, respectively, and we expect KALYDECO net product revenues to continue to represent a substantial portion of our total revenues in future periods. If we are unable to sustain KALYDECO net products revenues for any reason, such as safety or efficacy issues, the introduction or greater acceptance of competing products, changes in reimbursement policies of payors

and other third parties, or adverse legal, administrative, regulatory or legislative developments, our ability to commercialize KALYDECO would be impaired and our product revenues would decrease and our financial position and stock price would be materially harmed.

In addition, our success is dependent on our ability to continue to expand the label for KALYDECO and to increase the number of patients eligible and reimbursed for treatment with KALYDECO in the United States and ex-U.S. markets. In the first quarter of 2016, we expect to initiate a clinical trial for ivacaftor in patients with CF less than two years of age to evaluate the effect of ivacaftor on markers of CF disease in young children. There can be no assurance that the data from this clinical trial will be sufficient to obtain approval for ivacaftor in this patient population. Additionally, in February 2016, we received a Complete Response Letter from the FDA regarding our sNDA for ivacaftor for patients with CF two years of age and older who have one of 23 residual function mutations. The FDA determined that it cannot approve the sNDA in its present form. While we plan to meet with the FDA regarding the sNDA to determine an appropriate path forward, there can be no assurance that the outcome from these discussions will be sufficient to obtain approval for ivacaftor in this patient population.

We have a history of incurring losses, and we cannot predict the extent of our future profitability.

We have incurred significant operating losses in each of the last three years. Our future revenues will be dependent on our ability to successfully commercialize ORKAMBI and on continued sales of KALYDECO. Our ability to achieve and sustain profitability depends on the extent to which we can increase our revenue and control our costs in order to, among other things, counter any unforeseen difficulties, complications or other unknown factors that may impair future revenue or require additional expenditures. Because of the numerous risks and uncertainties associated with pharmaceutical product development, we are unable to predict the extent of our future profitability or losses. As an example, we briefly achieved profitability in 2011 based on strong initial sales of INCIVEK but subsequently returned to incurring losses after experiencing a rapid decline in the number of patients being treated with INCIVEK. If we are unable to sustain sales of KALYDECO and increase sales of ORKAMBI, we may not achieve and/or sustain profitability.

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

ORKAMBI, KALYDECO and any drugs that we develop in the future may not be able to compete effectively with marketed drugs or new drugs that may be developed by competitors. 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. Potential competitors also include other public and private companies, academic institutions, government agencies, other public and private research organizations and charitable venture philanthropy organizations that conduct research, seek patent protection and/or establish collaborative arrangements for research, development, manufacturing and commercialization. As an example, we experienced a rapid decline in the number of patients being treated with INCIVEK in 2013 and 2014.

Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller and other early-stage companies also may prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These third parties compete with us in recruiting and retaining qualified scientific and management personnel, establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs.

A number of companies are seeking to identify and develop drug candidates for the treatment of CF, including Concert Pharmaceuticals, Genzyme, which is a division of Sanofi, Novartis, Pfizer, ProQR Therapeutics, PTC Therapeutics, Shire and several private companies. Our competitors have research and development programs directed at identifying CFTR potentiators, CFTR correctors, ENaC inhibitors and drug candidates with other mechanisms of action or that utilize new therapeutic approaches that seek to address the underlying cause of CF. Our success in rapidly developing and commercializing KALYDECO and ORKAMBI may increase the resources that our competitors allocate to the development of these potential treatments for CF. If one or more competing therapies are successfully developed as a treatment for patients with CF, our revenues from ORKAMBI, KALYDECO and/or other compounds, if then approved, could face

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

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

Our products are subject to continuing regulatory oversight, including the review of additional safety information. Drugs are more widely used by patients once approval has been obtained and therefore side-effects and other problems may be observed after approval that were not seen or anticipated, or were not as prevalent or severe, during pre-approval clinical trials or nonclinical studies. 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. Each of our two commercial products and our most advanced drug candidates, contain ivacaftor, either alone or in combination with one or more other compounds. As a result, if either of our products were to experience safety issues, both ORKAMBI and KALYDECO, as well as one or more of our drug candidates, may be adversely affected. The reporting of adverse safety events involving our products or public speculation about such events could cause our stock price to decline or experience periods of volatility.

If we or our collaborators fail to comply with applicable continuing regulatory requirements, we or our collaborators may be subject to fines, suspension or withdrawal of regulatory approvals for specific products, product recalls and seizures, operating restrictions and/or criminal prosecutions. In addition, the manufacturers we engage to make our products and the manufacturing facilities in which our products are made are subject to periodic review and inspection by the FDA and foreign regulatory authorities. If problems are identified during the review or inspection of these manufacturers or manufacturing facilities, it could result in our inability to use the facility to make our product or a determination that inventories are not safe for commercial sale.

If physicians, 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 drugs and any of our drug candidates, if approved, requires substantial efforts, both prior to launch and after approval. Physicians may elect not to prescribe our drugs, and patients may elect not to request or take them, for a variety of reasons including:

- prevalence and severity of adverse side-effects;
- lack of reimbursement availability from third-party payors;
- lower demonstrated efficacy, safety and/or tolerability compared to other drugs;
- lack of cost-effectiveness;
- a decision to wait for the approval of other therapies in development that have significant perceived advantages over our drug;
- convenience and ease of administration;
- other potential advantages of alternative treatment methods; and
- ineffective sales, marketing and/or distribution support.

If our drugs fail to achieve or maintain market acceptance, we 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. The trend in the U.S. health care industry and elsewhere is cost containment and efforts of third-party payors to contain or reduce health care costs that may adversely affect our ability to establish or maintain appropriate prices for our products or any drugs that we may develop and commercialize. In certain foreign markets, pricing or profitability of therapeutic and other pharmaceutical products is subject to governmental control. Reimbursement agencies in Europe are often more conservative than those in the United States and the reimbursement process is often slower since reimbursement decisions are made on a country-by-country basis. In the United States, there have been, and we expect that there will continue to be, a number of federal and state proposals to implement similar governmental control as currently exists in Europe. Moreover, certain presidential candidates in the United States have announced an interest in further regulation of the prices of pharmaceutical products. The ACA requires discounts under the Medicare drug benefit program and increased the rebates paid by pharmaceutical companies on drugs covered by Medicaid. The ACA also imposes an annual fee, which increases annually, on sales by branded pharmaceutical manufacturers.

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

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

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 primarily focused on developing additional specialty pharmaceutical products. The increasing availability and use of innovative specialty pharmaceuticals, combined with their relative higher cost as compared to other types of pharmaceutical products, is beginning to generate significant third-party payor interest in developing cost-containment strategies targeted to this sector. Government regulations in both non-U.S. and U.S markets could limit the prices that can be charged for our products and may limit our commercial opportunity. The increasing use of health technology assessments in markets around the world and the financial challenges faced by many governments may lead to significant adverse effects on our business.

Any legislation or regulatory changes or relaxation of laws that restrict imports of drugs from other countries also could reduce the net price we receive for our products.

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

We are subject to health care fraud and abuse laws, such as the federal False Claims Act and the anti-kickback provisions of the federal Social Security Act, laws prohibiting off-label product promotion and other similar laws and regulations both in United States and in non-U.S. markets. While we have a corporate compliance program designed to actively identify, prevent and mitigate risk through the implementation of compliance policies and systems and the promotion of a culture of compliance, if we are found not to be in full compliance with these laws our business could be materially harmed.

The federal anti-kickback law prohibits knowingly and willfully offering, paying, soliciting, receiving or providing remuneration, directly or indirectly, in exchange for or to induce either the referral of an individual, or the ordering, furnishing, arranging for or recommending of an item or service that is reimbursable, in whole or in part, by a federal health care program, such as Medicare or Medicaid. The federal statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on the one hand and prescribers, patients, purchasers and formulary managers on the other hand, and therefore constrains our marketing practices and our various service arrangements with physicians, including physicians who make clinical decisions to use our products. Although there are a number of statutory exemptions and regulatory safe harbors protecting certain common activities from prosecution, the exemptions and safe harbors are drawn narrowly and courts generally will apply a "one purpose test" and find a violation of the law if any part of the intent in providing the remuneration was to induce referrals, even if it also was intended to compensate for professional services or other legitimate purposes.

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

Although physicians are permitted, based on their medical judgment, to prescribe products for indications other than those approved by the FDA, manufacturers are prohibited from promoting their products for such off-label uses. We market ORKAMBI and KALYDECO to eligible CF patients for whom the applicable product has been approved and provide promotional materials and training programs to physicians regarding the use of ORKAMBI and KALYDECO in these patient populations. These eligible patients represent only a portion of the total patients with CF. If the FDA determines that our promotional materials, training or other activities constitute off-label promotion, it could request that we modify our training or promotional materials or other activities, conduct corrective advertising or subject us to regulatory enforcement actions, including the issuance of a warning letter, injunction, seizure, civil fine and criminal penalties. It also is possible that other federal, state or foreign enforcement authorities might take action if they believe that the alleged improper promotion led to the submission and payment of claims for an off-label use, which could result in significant fines or penalties under other statutory authorities, such as laws prohibiting false claims for reimbursement. Even if it is later determined we were not in violation of these laws, we may be faced with negative publicity, incur significant expenses defending our actions and have to divert significant management resources from other matters.

Also applicable to some of our practices is the Health Insurance Portability and Accountability Act, or 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.

In addition to HIPAA, numerous other federal and state laws, including state security breach notification laws, state health information privacy laws and federal and state consumer protection laws, govern the collection, use and disclosure of personal information. Various foreign countries also have, or are developing, laws governing the collection, use and transmission of personal information. The legislative and regulatory landscape for privacy and data protection continues to evolve, and there has been an increasing amount of focus on privacy and data protection issues with the potential to affect our business. We have in the past relied on adherence to the U.S.-EU Safe Harbor Framework as agreed to and set forth by the

U.S. Department of Commerce and the European Union, which established a means for legitimizing the transfer of personal information by U.S. companies doing business in Europe from the European Economic Area to the United States. As a result of a recent opinion of the European Union Court of Justice, the U.S.-EU Safe Harbor Framework is now deemed to be an invalid method of compliance with restrictions regarding the transfer of data outside of the European Economic Area. While we are engaging in efforts to address the implications of this opinion, we may be unsuccessful in these efforts. Failure to comply with laws regarding data protection would expose us to risk of enforcement actions taken by data protection authorities in the European Union and the potential for significant penalties if we are found to be non-compliant. 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 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. We also now have similar reporting obligations in certain European countries and the European Federation of Pharmaceutical Industries and Associations has adopted a code that will require us to begin reporting such information throughout the European Union in 2016. We will also have similar reporting obligations in Australia beginning in 2016. We expended significant efforts to establish, and are continuing to devote significant resources to maintain and enhance, systems and processes in order to comply with these regulations. Failure to comply with the reporting requirements would result in significant civil monetary penalties. The 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.

On January 1, 2015, the EMA adopted a new policy on publication of clinical data whereby it will publish clinical reports submitted as part of MAAs for drugs. The policy applies to all clinical reports submitted after January 1, 2015 and the reports will be released as soon as a decision on the application has been made by the EMA. While implementation of this policy is ongoing and its full effect on our business is not yet known, the ability of third-parties to review and/or analyze the raw data from our clinical trials may increase the risk of patient confidentiality breaches and could result in enhanced scrutiny of our clinical trials results. Such scrutiny could result in misconceptions being spread about our drugs and drug candidates, even if the underlying analysis of such review turns out to be flawed. These publications could also result in the disclosure of information to our competitors that we might otherwise deem confidential, which could harm our competitive position.

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 governmental entities in the United Sates and other countries in which we market our products, 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.

The increasing use of social media platforms presents new risks and challenges.

Social media increasingly is being used by third parties to communicate about our products and drug candidates and the diseases our therapies are designed to treat. We believe that members of the CF community may be more active on social media as compared to other patient populations due to the demographics of this patient population. Social media practices in the pharmaceutical and biotechnology industries are evolving, which creates uncertainty and risk of noncompliance with regulations applicable to our business. For example, patients may use social media platforms to comment on the

effectiveness of, or adverse experiences with, a drug or a drug candidate, which could result in reporting obligations. In addition, there is a risk of inappropriate disclosure of sensitive information or negative or inaccurate posts or comments about us on any social networking website. If any of these events were to occur or we otherwise fail to comply with applicable regulations, we could incur liability, face restrictive regulatory actions or incur other harm to our business.

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

Our drug candidates remain subject to clinical testing and regulatory approval. If we are unable to successfully develop additional drug candidates, and in particular our next-generation CFTR combination regimens, our business will be materially harmed.

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

- offer therapeutic or other improvement over existing competitive therapies;
- be proven safe and effective in clinical trials;
- meet applicable regulatory standards;
- be capable of being produced in commercial quantities at acceptable costs; or
- if approved for commercial sale, be successfully marketed as pharmaceutical products.

We have recently completed and/or have ongoing or planned clinical trials for several of our drug candidates, including drug candidates for the treatment of CF, oncology, pain and neurology. The strength of our company's product portfolio and pipeline will depend in large part upon the outcomes of these clinical trials and our ability to develop and commercialize combination treatments for CF that include ivacaftor in combination with (i) VX-661 and/or (ii) our next-generation CFTR corrector compounds, including VX-152 and VX-440. Results of our clinical trials and findings from our nonclinical studies, including toxicology findings in nonclinical studies conducted concurrently with clinical trials, could lead to abrupt changes in our development activities, including the possible cessation of development activities associated with a particular drug candidate or program. Moreover, clinical data are often susceptible of varying interpretations and analyses, and many companies that have believed their drug candidates performed satisfactorily in clinical trials have nonetheless failed to obtain marketing approval of their drug candidate. Furthermore, results from our clinical trials may not meet the level of statistical significance required by the FDA or other regulatory authorities for approval of a drug candidate.

Many companies in the pharmaceutical and biotechnology industries, including our company, have suffered significant setbacks in later-stage clinical trials even after achieving promising results in earlier-stage clinical trials. Accordingly, the results from completed preclinical studies and clinical trials may not be replicated in later clinical trials, and ongoing clinical trials for our drug candidates may not be predictive of the results we may obtain in later-stage clinical trials or of the likelihood of approval of a drug candidate for commercial sale. In addition, from time to time we report interim data from our clinical trials. Interim data from a clinical trial may not be predictive of final results from the clinical trial.

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

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

We may seek a fast track and/or breakthrough therapy designation for some of our drug candidates. For example, ivacaftor was granted fast-track designation in the United States and a number of our drugs and drug candidates, including

ivacaftor and the combination regimens of lumacaftor with ivacaftor and VX-661 with ivacaftor, were designated as breakthrough therapies. Drug candidates that receive one or both of these designations may be eligible for, among other things, an accelerated regulatory review. Each of these designations is within the discretion of the FDA. Accordingly, even if we believe one of our drug candidates meets the criteria for fast track and/or breakthrough therapy designation, the FDA may disagree and instead determine not to make such designation. The receipt of one or both of these designations for a drug candidate does not guarantee a faster development process, review or approval compared to drugs considered for approval under conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, even if one or more of our drugs or drug candidates qualifies for fast track and/or breakthrough therapy designation, the FDA may later decide to withdraw such designation if it determines that the drug or drug candidate no longer meets the conditions for qualification.

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

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

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

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

- ongoing discussions with the FDA or comparable foreign authorities regarding the scope or design of our clinical trials and the number of clinical trials we must conduct;
- delays in enrolling volunteers or patients into clinical trials, including as a result of low numbers of patients that meet the eligibility criteria for the trial;
- a lower than anticipated retention rate of volunteers or patients in clinical trials;
- the need to repeat clinical trials as a result of inconclusive results, unforeseen complications in testing or clinical investigator error;
- inadequate supply or deficient quality of drug candidate materials or other materials necessary for the conduct of our clinical trials;
- unfavorable FDA or foreign regulatory authority inspection and review of a manufacturing facility that supplied clinical trial materials or its relevant manufacturing records or a clinical trial site or records of any clinical or preclinical investigation;

- unfavorable scientific results from clinical trials;
- serious and unexpected drug-related side-effects experienced by participants in our clinical trials or by participants in clinical trials being conducted by our competitors to evaluate drug candidates with similar mechanisms of action or structures to drug candidates that we are developing;
- favorable results in testing of our competitors' drug candidates, or FDA or foreign regulatory authority approval of our competitors' drug candidates; or
- action by the FDA or a foreign regulatory authority to place a clinical hold or partial clinical hold on a trial or compound or deeming the clinical trial conduct as problematic.

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

We, our collaborators, the FDA or other applicable regulatory authorities may suspend clinical trials of a drug candidate at any time if we or they believe the healthy volunteers or patients participating in such clinical trials are being exposed to unacceptable health risks or for other reasons. For example, in July 2013, the FDA placed a partial clinical hold on VX-135, a drug candidate we were developing for the treatment of patients with hepatitis C virus infection. Any such suspension could materially adversely affect the development of a particular drug candidate and our business.

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

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

Risks Related to Collaborations and other Business Development Activities

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

In order to achieve our long-term business objectives, our strategy is to supplement our internal pipeline by acquiring rights to additional drugs, drug candidates and other technologies that have the potential to provide us with new commercial opportunities. We may not be able to acquire, in-license or otherwise obtain rights to additional drugs, drug candidates or other technologies on acceptable terms or at all. We have faced and will continue to face significant competition for these types of drugs, drug candidates and other technologies from a variety of other companies with interests in the specialty pharmaceutical marketplace, many of which have significantly more financial resources and experience in business

development activities than we have. In addition, non-profit organizations may be willing to provide capital to the companies that control additional drugs, drug candidates or technologies, which may provide incentives for companies to advance these drugs, drug candidates or technologies independently. Because of these competitive pressures, the cost of acquiring, in-licensing or otherwise obtaining rights to such drugs, drug candidates or other technologies has grown dramatically in recent years and may be at levels that we cannot afford or that we believe are not justified by market potential. This competition is most intense for approved drugs and late-stage drug candidates, which have the lowest risk and would have the most immediate effect on our financial performance.

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

We may acquire a business or the rights to drugs, drug candidates or other technologies. For example, in 2015, we entered into a collaboration with Parion pursuant to which we exclusively licensed investigational ENaC inhibitors, including VX-371 (formerly P-1037), for the potential treatment of CF and other pulmonary diseases. We also entered into an agreement with CRISPR to collaborate on the discovery and development of potential new treatments aimed at the underlying genetic causes of human diseases using CRISPR-Cas9 gene editing technology. With respect to each of these transactions and any additional acquisition of a business or rights to drugs, drug candidates or other technologies, we may not realize the anticipated benefits of such transaction, each of which involves numerous risks. These risks include:

- failure to successfully further develop the acquired or licensed drugs or technology or to achieve strategic objectives, including successfully developing and commercializing the drugs, drug candidates or technologies that we acquire or license;
- inadequate or unfavorable data from clinical trials evaluating the acquired or licensed drug or drug candidates;
- entry into markets in which we have no or limited direct prior experience or where competitors in such markets have stronger market positions;
- disruption of our ongoing business and distraction of our management and employees from other opportunities and challenges;
- potential failure of the due diligence processes to identify significant problems, liabilities or other shortcomings or challenges of an acquired company, or acquired or licensed product or technology, including but not limited to, problems, liabilities or other shortcomings or challenges with respect to intellectual property, product quality, safety, accounting practices, employee, customer or third party relations and other known and unknown liabilities;
- liability for activities of the acquired company or licensor before the acquisition or license, including intellectual property infringement claims, violations of laws, commercial disputes, tax liabilities, and other known and unknown liabilities;
- exposure to litigation or other claims in connection with, or inheritance of claims or litigation risk as a result of an acquisition or license, including but not limited to, claims from terminated employees, customers, former equity holders or other third-parties;
- difficulty in integrating the drugs, drug candidates, technologies, business operations and personnel of an acquired company; and
- difficulties in the integration of the acquired company's departments, systems, including accounting, human resource and other administrative systems, technologies, books and records, and procedures, as well as in maintaining uniform standards, controls, including internal control over financial reporting required by the Sarbanes-Oxley Act of 2002 and related procedures and policies.

Acquisitions and licensing arrangements are inherently risky, and ultimately, if we do not complete an announced acquisition or license transaction or integrate an acquired business, or an acquired or licensed drug, drug candidate or other technology successfully and in a timely manner, we may not realize the benefits of the acquisition or license to the extent anticipated and the perception of the effectiveness of our management team and our company may suffer in the marketplace. Additionally, we may later incur impairment charges related to assets acquired in any such transaction. For example, we

acquired or licensed several drug candidates for the treatment of HCV infection, but due to adverse clinical data regarding these drug candidates and competitive pressures, we incurred significant costs and impairment charges but did not realize the expected benefits from these transactions. In addition, even if we achieve the long-term benefits associated with strategic transactions, our expenses and short-term costs may increase materially and adversely affect our liquidity and short-term net income (loss). Future licenses or acquisitions could result in potentially dilutive issuances of equity securities, the incurrence of debt, the creation of contingent liabilities, impairment expenses related to goodwill, and impairment or amortization expenses related to other intangible assets, which could harm our financial condition.

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

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

- Our collaborators may change the focus of their development and commercialization efforts or may have insufficient resources to effectively develop our drug candidates. The ability of some of our products and drug candidates to reach their potential could be limited if collaborators decrease or fail to increase development or commercialization efforts related to those products or drug candidates. Our collaboration agreements provide our collaborators with a level of discretion in determining the amount and timing of efforts and resources that they will apply to these collaborations.
- Any future collaboration agreements may have the effect of limiting the areas of research and development that we may pursue, either alone or in collaboration with third parties.
- Collaborators may develop and commercialize, either alone or with others, drugs that are similar to or competitive with the drugs or drug candidates that are the subject of their collaborations with us.
- Disagreements with collaborators, including disagreements over proprietary rights, contract interpretation or the preferred course of development, might cause delays or termination of the research, development or commercialization of drug candidates, might lead to additional responsibilities for us with respect to drug candidates, or might result in litigation or arbitration. Any such disagreements would divert management attention and resources and be time-consuming and expensive.
- Collaborators may not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential litigation.
- Collaborators may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability.
- Investigations and/or compliance or enforcement actions against a collaborator, which may expose us to indirect liability as a result of our partnership with such collaborator.
- Our collaboration agreements are subject to termination under various circumstances.

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

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

As part of our ongoing strategy, we may seek additional collaborative arrangements or external funding for certain of our development programs and/or seek to expand existing collaborations to cover additional commercialization and/or development activities. We have a number of research programs and early-stage clinical development programs, some of which are being developed in collaboration with a third party. For example, in June 2014, we granted Janssen Pharmaceuticals, Inc. an exclusive license to develop and commercialize VX-787, a drug candidate discovered by us for the treatment of influenza. At any time, we may determine that in order to continue development of a drug candidate or program

or successfully commercialize a drug we need to identify a collaborator or amend or expand an existing collaboration. Whether we reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator's evaluation of a number of factors. Those factors may include the design or results of clinical trials, the likelihood of approval by the FDA or similar regulatory authorities outside the United States, the potential market for the subject drug candidate, the costs and complexities of manufacturing and delivering such drug candidate to patients, the potential of competing products, the existence of uncertainty with respect to our ownership of the applicable intellectual property, which can exist if there is a challenge to such ownership without regard to the merits of the challenge, and industry and market conditions generally. Potentially, and depending on the circumstances, we may desire that a collaborator either agree to fund portions of a drug development program led by us, or agree to provide all of the funding and directly lead the development and commercialization of a program. No assurance can be given that any efforts we make to seek additional collaborative arrangements will be successfully completed on a timely basis or at all. If we elect to fund and undertake development or commercialization activities on our own, we may need to obtain additional expertise and additional capital, which may not be available to us on acceptable terms or at all. If we are unable to enter into acceptable collaborative relationships, one or more of our development programs could be delayed or terminated and the possibility of our receiving a return on our investment in the program could be impaired.

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

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

We rely on a worldwide network of third-party manufacturers and in rare circumstances, compounders, to manufacture some of our drugs for commercial use and our drug candidates for clinical trials. As a result of our reliance on these third-party manufacturers and suppliers, we could be subject to significant supply disruptions outside of our control. Our supply chain for sourcing raw materials and manufacturing drug product ready for distribution is a multi-step international endeavor. Third-party contract manufacturers, including some in China, supply us with raw materials, and 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 manage the business relationships with companies in our supply chain, we do not have control over their operations. Supply disruptions may result from a number of factors, including shortages in product raw materials, labor or technical difficulties, regulatory inspections or restrictions, shipping or customs delays or any other performance failure by any third-party manufacturer on which we rely. Any supply disruptions could disrupt sales of our products and/or the timing of our clinical trials.

We require a supply of ivacaftor and lumacaftor for commercial sale (as KALYDECO and/or ORKAMBI). We also require a supply of ivacaftor, lumacaftor, VX-661, VX-371, VX-152 and VX-440 and our other drug candidates for use in our clinical trials. We obtain ivacaftor and lumacaftor (and the combinations thereof) to meet our commercial and clinical supply needs through a third-party manufacturing network. Our supply chain includes a single-source manufacturer for (i) one step in the ivacaftor manufacturing process and (ii) the manufacture of the oral granule formulation of KALYDECO that is used for patients with CF two to five years of age. As a result, if these manufacturers become unable or unwilling to continue manufacturing product on our behalf and we are not able to promptly identify another manufacturer, we would experience a disruption in the commercial supply of KALYDECO and/or ORKAMBI, which would have a significant effect on patients, our business and our product revenues. Similarly, a disruption in the clinical supply of drug products could delay the completion of clinical trials and affect timelines for regulatory filings. There can be no assurance that we will be able to establish and maintain secondary manufacturers for all of our ivacaftor or lumacaftor 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 rely on third parties to conduct certain pre-clinical work and clinical trials, and those third parties may not perform satisfactorily, including failing to meet established deadlines for the completion of such studies and/or trials or failing to satisfy regulatory requirements.

We rely on third parties such as contract research organizations to help manage certain pre-clinical work and our clinical trials and on medical institutions 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 but does not relieve us of our responsibilities. For example, we remain responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocols for the clinical trial. Moreover, the FDA requires us to comply with standards, commonly referred to as good laboratory practices and good clinical practices for conducting, recording and reporting the results of pre-clinical and clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity and confidentiality of trial participants are protected. If these third parties do not successfully carry out their contractual duties or meet expected deadlines, we may be required to replace them. Although we believe that there are a number of other third-party contractors we could engage to continue these activities, it may result in a delay of the affected clinical trial or drug development program. If clinical trials are not conducted in accordance with our contractual expectations or regulatory requirements, action by regulatory authorities might significantly and adversely affect the conduct or progress of these clinical trials or in specific circumstances might result in a requirement that a clinical trial be redone. Accordingly, our efforts to obtain regulatory approvals for and commercialize our drug candidates could be delayed.

Risks Related to Intellectual Property

If our patents do not protect our drugs, or our drugs infringe third-party patents, we could be subject to litigation and substantial liabilities.

We have numerous issued patents and pending patent applications in the United States, as well as counterparts in other countries. Our success will depend, in significant part, on our ability to obtain and defend U.S. and foreign patents covering our drugs, their uses and our processes, to preserve our trade secrets and to operate without infringing the proprietary rights of third parties. We cannot be certain that any patents will issue from our pending patent applications or, even if patents issue or have issued, that the issued claims will provide us with adequate protection against competitive products or otherwise be commercially valuable.

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

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

breadth or strength of protection provided by our patents and patent applications is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize current or future products.

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

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

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

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

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

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

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

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

In addition, while it is our policy to require our employees and contractors who may be involved in the development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who in fact develops intellectual property that we regard as our own. Our and their

assignment agreements may not be self-executing or may be breached, and we may be forced to bring claims against third parties, or defend claims they may bring against us, to determine the ownership of what we regard as our intellectual property.

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

Risks Related To Our Operations

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

We have expanded and are continuing to expand our global operations and capabilities, which has placed, and will continue to place, significant demands on our management and our operational, research and development and financial infrastructure. To effectively manage our business, we need to:

- implement and clearly communicate our corporate-wide strategies;
- enhance our operational and financial infrastructure, including our controls over records and information;
- enhance our operational, financial and management processes, including our cross-functional decision-making processes and our budget prioritization systems;
- train and manage our global employee base;
- transition from a U.S.-centric company into an organization capable of developing and commercializing multiple drug candidates in international markets; and
- enhance our compliance and legal resources.

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 ORKAMBI and expand our research and development capabilities. In 2015, a substantial portion of our revenues and expenses were associated with our foreign operations and we expect that portion to increase over time. New laws and industry codes in the European Union and elsewhere have expanded transparency requirements regarding payments and transfers of value as well as patient-level clinical trial data. New laws in the European Union also have expanded protections related to personal data and provided for increased sanctions for violations. Collectively, our expansion and these new requirements are adding to our compliance costs and expose us to potential sanctions for failing to meet the enhanced safeguards and reporting demands in these jurisdictions. In addition, a significant portion of our commercial supply chain, including sourcing of raw materials and manufacturing, is located in China and the 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;
- differing levels of enforcement and/or recognition of contractual and intellectual property rights;
- complying with local laws and regulations, which are interpreted and enforced differently across jurisdictions and which can change significantly over time;
- foreign taxes, including withholding of payroll taxes;

- foreign currency fluctuations, which could result in reduced revenues or increased operating expenses, and other obligations incident to doing business or operating in another country;
- workforce uncertainty in countries where labor unrest is more common than in the United States;
- import and export licensing requirements, tariffs, and other trade and travel restrictions;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad; and
- business interruptions resulting from geo-political actions, including war and terrorism.

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

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

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

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

We maintain and rely extensively on information technology systems and network infrastructures for the effective operation of our business. In the course of our business, we collect, store and transmit confidential information (including personal information and intellectual property), and it is critical that we do so in a secure manner to maintain the confidentiality and integrity of such confidential information. The size and complexity of our information technology and information security systems makes such systems potentially vulnerable to service interruptions or to security breaches. A disruption, infiltration or failure of our information technology systems or any of our data centers as a result of software or hardware malfunctions, computer viruses, cyber attacks, employee theft or misuse, power disruptions, natural disasters, floods or accidents could cause breaches of data security and loss of critical data, which in turn could materially adversely affect our business and subject us to both private and governmental causes of action. While we have implemented security measures in an attempt to minimize these risks to our data and information technology systems and have adopted a business continuity plan to deal with a disruption to our information technology systems, there can be no assurance that our efforts will prevent breakdowns or breaches in our systems that could adversely affect our business.

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

Because our drug discovery and development activities are highly technical in nature, we require the services of highly qualified and trained scientists who have the skills necessary to conduct these activities. In addition, we need to attract and retain employees with experience in marketing and commercialization of medicines. We face intense competition for our personnel from our competitors and other companies throughout our industry. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. Moreover, the growth of local biotechnology companies and the expansion of major pharmaceutical companies into the Boston area have increased competition for the available pool of skilled employees, especially in technical fields, and the high cost of living in Massachusetts makes it difficult to attract employees from other parts of the country to Massachusetts. Our ability to commercialize our products, and achieve our research and development objectives, depends on our ability to respond effectively to these demands. If we are unable to hire and retain qualified personnel, there could be a material adverse effect on our business.

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

Our future success will depend in large part on our ability to retain the services of our key scientific and management personnel and to integrate new scientific and management personnel into our business. A loss of key personnel or a failure to properly integrate new personnel could be disruptive. We have entered into employment agreements with some executives and provide compensation-related benefits to all of our key employees that vest over time and therefore induce them to remain with us. However, the employment agreements can be terminated by the executive on relatively short notice. The value to employees of stock-related benefits that vest over time—such as options, restricted stock and restricted stock units—is significantly affected by movements in our stock price, and may at any point in time be insufficient to counteract more lucrative offers from other companies. A failure to retain, as well as hire, train and effectively integrate into our organization a sufficient number of qualified scientists, professionals, sales personnel and senior management would negatively affect our business.

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

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

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

Most of our operations, including our research and development activities, are conducted in a limited number of facilities. If any of our major facilities were to experience a catastrophic loss, due to a fire, earthquake or similar event, our operations could be seriously harmed. For example, our corporate headquarters, as well as additional leased space that we use for certain logistical and laboratory operations and manufacturing, are located in a flood zone along the Massachusetts coast. We have adopted a business continuity plan to address most events of a crisis nature. However, if we are unable to fully implement our disaster recovery plans, we may experience delays in recovery of data and/or an inability to perform vital corporate functions, which could result in a significant disruption in our research, development, manufacturing and/or commercial activities, the loss or critical data and/or large expenses to repair or replace the facility, which would have a material adverse effect on our business.

Risks Related to Holding Our Common Stock

Our stock price may fluctuate.

Market prices for securities of companies such as ours are highly volatile. From January 1, 2015 to December 31, 2015, our common stock traded between $97.45 and $143.45 per share. The market for our stock, like that of other companies in the biotechnology industry, has experienced significant price and volume fluctuations. The future market price of our securities could be significantly and adversely affected by factors such as:

- the information contained in our quarterly earnings releases, including our net product revenues and operating expenses for completed periods and guidance regarding future periods;
- announcements of FDA actions with respect to our drugs or our competitors' drugs, or regulatory filings for our drug candidates or those of our competitors, or announcements of interim or final results of clinical trials or nonclinical studies relating to our drugs, drug candidates or those of our competitors;
- prescription data and other information disclosed by third parties regarding our business or products;
- technological innovations or the introduction of new drugs by our competitors;
- government regulatory action;
- public concern as to the safety of drugs developed by us or our competitors;
- developments in patent or other intellectual property rights or announcements relating to these matters;
- developments in domestic and international governmental policy or regulation, for example, relating to intellectual property rights;
- developments relating specifically to other companies and market conditions for pharmaceutical and biotechnology stocks or stocks in general;
- business development, capital structuring or financing activities; and
- general worldwide or national economic, political and capital market conditions.

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

In July 2014, we entered into a credit agreement that provides for a $300.0 million senior secured term loan. We are required to repay principal on the loan beginning in the fourth quarter of 2016 with us repaying $75.0 million on each of October 1, 2016, January 1, 2017, April 1, 2017 and July 9, 2017.

Our indebtedness could have important consequences to our business, including increasing our vulnerability to general adverse financial, business, economic and industry conditions, as well as other factors that are beyond our control. In October 2016, we will be required to begin repayment of the principal amount of our indebtedness, thereby reducing the availability of future cash flows to fund working capital, capital expenditures, acquisitions, research and development efforts and other general corporate purposes.

The credit agreement requires that we maintain, on a quarterly basis, a minimum level of KALYDECO net revenues. Further, the credit agreement includes negative covenants, subject to exceptions, restricting or limiting our ability and the ability of our subsidiaries to, among other things, incur additional indebtedness, grant liens, engage in certain investment, acquisition and disposition transactions, pay dividends, repurchase capital stock and enter into transactions with affiliates. As a result, we may be restricted from engaging in business activities that may otherwise improve our business. Failure to comply with the covenants could result in an event of default that could trigger acceleration of our indebtedness, which would require us to repay all amounts owing under the credit agreement and/or our capital leases and could have a material adverse effect on our business.

Additionally, our obligations under the credit agreement are unconditionally guaranteed by certain of our domestic subsidiaries. All obligations under the credit agreement, and the guarantees of those obligations, are secured, subject to

certain exceptions, by substantially all of our assets and the assets of all guarantors, including the pledge of all or a portion of the equity interests of certain of our subsidiaries. If we fail to satisfy our obligations under the credit agreement or are unable to obtain sufficient funds to make payments, the lenders could foreclose on our pledged collateral.

Our quarterly operating results are subject to significant fluctuation.

Our operating results have fluctuated from quarter to quarter in the past, and we expect that they will continue to do so in the future. Our future revenues will be dependent on the level of net product revenues from sales of ORKAMBI, which is reliant on the number of patients for whom treatment with ORKAMBI is initiated, the proportion of initiated patients who remain on treatment, patient compliance with the recommended treatment regimen and the level of rebates, chargebacks, discounts and other adjustments to our ORKAMBI gross product revenues. Additional factors that have caused quarterly fluctuations in recent years include variable amounts of revenues, impairment charges, charges for excess and obsolete inventories, changes in the fair value of derivative instruments and the consolidation or deconsolidation of variable interest entities. We cannot accurately predict our future net product revenues from ORKAMBI and our total net product revenues could vary on a quarterly basis. Our total net product revenues may be affected by, among other factors, the timing of orders from our significant customers. Our revenues also are subject to foreign exchange rate fluctuations due to the global nature of our operations. Although we have foreign currency forward contracts to hedge forecasted product revenues denominated in foreign currencies, our efforts to reduce currency exchange losses may not be successful. As a result, currency fluctuations among our reporting currency, the U.S. dollar, and the currencies in which we do business may affect our operating results, often in unpredictable ways. Our quarterly results also could be materially affected by significant charges, which may or may not be similar to charges we have experienced in the past. Most of our operating expenses relate to our research and development activities, do not vary directly with the amount of revenues and are difficult to adjust in the short term. As a result, if revenues in a particular quarter are below expectations, we are unlikely to reduce operating expenses proportionately for that quarter. These examples are only illustrative and other risks, including those discussed in these "Risk Factors," could also cause fluctuations in our reported financial results. Our operating results during any one period do not necessarily suggest the results of future periods.

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

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

We could be negatively affected by securities class action complaints.

On May 28, 2014, a purported shareholder class action *Local No. 8 IBEW Retirement Plan & Trust 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 alleged that we made material misrepresentations and/or omissions of material fact in our disclosures during the period from May 7, 2012 through May 29, 2012, all in violation of Section 10(b) of the Securities Exchange Act of 1934, as amended, and Rule 10b-5 promulgated thereunder. The purported class consists of all persons (excluding defendants) who purchased our common stock between May 7, 2012 and May 29, 2012. The plaintiffs seek unspecified monetary damages, costs and attorneys' fees as well as disgorgement of the proceeds from certain individual defendants' sales of our stock. On October 8, 2014, the Court approved Local No. 8 IBEW Retirement Fund as lead plaintiff, and Scott and Scott LLP as lead counsel for the plaintiff and the putative class. We filed a motion to dismiss the complaint on December 8, 2014 and the plaintiffs filed their opposition to our motion to dismiss on January 22, 2015. On February 23, 2015, we filed a reply to the plaintiffs' opposition to our motion to dismiss. The court heard oral argument on our motion to dismiss on March 6, 2015 and took the motion under advisement. On September 30, 2015, the court granted our motion to dismiss. On October 15, 2015, the plaintiff filed a notice of appeal.

We believe that this action is without merit and intend to vigorously defend the litigation. 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 could be negatively affected by government investigations.

In the third quarter of 2015, we received a subpoena from the United States Department of Justice related to our marketed medicines. This subpoena requests documents relating primarily to our Good Laboratory Practices in a bioanalytical laboratory. We are in the process of responding to the subpoena and intend to continue to cooperate. If we are unable to resolve this matter in a satisfactory manner, our business could be adversely affected.

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

A change in tax laws, treaties or regulations, or their interpretation, of any country in which we operate could materially affect us if we generate taxable income in a future period. We continue to assess the impact of various tax reform proposals and modifications to existing tax treaties in all jurisdictions where we have operations to determine the potential effect on our business and any assumptions we have made about our future taxable income. We cannot predict whether any specific proposals will be enacted, the terms of any such proposals or what effect, if any, such proposals would have on our business if they were to be enacted.

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

We have a history of operating losses and may in the future need to raise additional capital. We have borrowed $300.0 million under a credit agreement that we entered into in the third quarter of 2014. 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. Any potential public offering, private placement or debt financing may or may not be similar to the transactions that we entered into in the past. Any debt financing may be on terms that, among other things, include conversion features that could result in dilution to our then-existing security holders and restrict our ability to pay interest and dividends—although we do not intend to pay dividends for the foreseeable future. Additionally, our pledge of our assets as collateral to secure our obligations under our credit agreement may limit our ability to obtain additional debt financing. Any equity financings would result in dilution to our then-existing security holders. If adequate funds are not available on acceptable terms, or at all, we may be required to curtail significantly or discontinue one or more of our research, drug discovery or development programs, including clinical trials, incur significant cash exit costs, or attempt to obtain funds through arrangements with collaborators or others that may require us to relinquish rights to certain of our technologies, drugs or drug candidates. Based on many factors, including general economic conditions, additional financing may not be available on acceptable terms, if at all.

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

As of December 31, 2015 , we had 246.3 million shares of common stock issued and outstanding. As of December 31, 2015 , we also had outstanding options to purchase 11.1 million shares of common stock with a weighted-average exercise price of $75.99 per share. Outstanding vested options are likely to be exercised if the market price of our common stock exceeds the applicable exercise price, and, in the future, we expect to issue additional options, restricted stock and restricted stock units to directors and employees. In addition, we may issue additional common stock or restricted securities in the future as part of financing activities or business development activities and any such issuances may have a dilutive effect on our then-existing shareholders. Sales of substantial amounts of our common stock in the open market, or the availability of such shares for sale, could adversely affect the price of our common stock. The issuance of restricted common stock or common stock upon exercise of any outstanding options would be dilutive, and may cause the market price for a share of our common stock to decline.

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. Additionally, one of our collaboration agreements includes a change in control provision that could reduce the potential acquisition price an acquirer is willing to pay or discourage a takeover attempt that may otherwise be viewed as beneficial to shareholders.

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 ORKAMBI;
- our expectations regarding clinical trials, development timelines and regulatory authority filings and submissions for ivacaftor, lumacaftor, VX-661, VX-371 (formerly P-1037), VX-152, VX-440, VX-970, VX-803, VX-984, VX-150, VX-241 and VX-210, as well as the sNDA for KALYDECO for patients with CF two years of age and older who have one of 23 residual function mutations;
- future interactions with the FDA regarding our sNDA for KALYDECO for patients with CF two years of age and older who have one of 23 residual function mutations that the FDA determined it could not approve in its present form;
- our expectations regarding planned clinical trials for next-generation correctors based upon pre-clinical data;
- our ability to successfully market KALYDECO and ORKAMBI 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-661, VX-371 (formerly P-1037), VX-152, VX-440, VX-970, VX-803, VX-984, VX-150, VX-241 and VX-210, and the expected timing of our receipt of data from our ongoing and planned clinical trials;
- the data that will be generated by ongoing and planned clinical trials and the ability to use that data to advance compounds, continue development or support regulatory filings;
- our beliefs regarding the support provided by clinical trials and preclinical and nonclinical studies of our drug candidates for further investigation, clinical trials or potential use as a treatment;
- our plan to continue investing in our research and development programs and our strategy to develop our drug candidates, alone or with third party-collaborators;
- the establishment, development and maintenance of collaborative relationships;
- potential business development activities;
- potential fluctuations in foreign currency exchange rates;
- our ability to use our research programs to identify and develop new drug candidates to address serious diseases and significant unmet medical needs; and
- our liquidity and our expectations regarding the possibility of raising additional capital.

Any or all of our forward-looking statements in this Annual Report on Form 10-K may turn out to be wrong. They can be affected by inaccurate assumptions or by known or unknown risks and uncertainties. Many factors mentioned in this

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

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

ITEM 1B. UNRESOLVED STAFF COMMENTS

We did not receive any written comments from the Securities and Exchange Commission prior to the date 180 days before the end of the fiscal year ended December 31, 2015 regarding our filings under the Securities Exchange Act of 1934, as amended, that have not been resolved.

ITEM 2. PROPERTIES

Corporate Headquarters

We lease approximately 1.1 million square feet of office and laboratory space at our corporate headquarters in Boston, Massachusetts in two buildings pursuant to two leases that we entered into in May 2011. The leases commenced in December 2013 and will extend until December 2028. We have an option to extend the term of the leases for an additional ten years. In addition, in connection with our relocation to Boston, we entered into a lease in June 2012 for approximately 100,000 square feet of space in the Boston Marine Industrial Park, in close proximity to our corporate headquarters. We are using this additional space for certain logistical and laboratory operations and manufacturing equipment that will complement the office and laboratory facilities at our corporate headquarters.

Existing Facility in Cambridge, Massachusetts

We currently lease approximately 290,000 square feet of laboratory and office space at our former Kendall Square facility in Cambridge, Massachusetts that will expire in 2018. We have subleased approximately 267,000 square feet of the approximately 290,000 square feet of the Kendall Square facility under subleases, each with terms ending in 2018.

Additional United States and Worldwide Locations

In addition to our facilities in Massachusetts, we lease an aggregate of approximately 275,000 square feet of space. This includes laboratory and office space to support our research and development organizations in San Diego, California, Montreal, Canada, and Milton Park, Abingdon, England and office space in many of the countries in which we sell our products. In addition, in December 2015, we entered into a lease for approximately 170,000 square feet of office and laboratory space in a building to be built in San Diego, California. The lease will commence upon completion of the building, scheduled for the second half of 2017, and will extend for 16 years from the commencement date.

ITEM 3. LEGAL PROCEEDINGS

Local No. 8 IBEW Retirement Plan & Trust v. Vertex Pharmaceuticals Incorporated, et al.

On May 28, 2014, a purported shareholder class action *Local No. 8 IBEW Retirement Plan & Trust 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 alleged that we made material misrepresentations and/or omissions of material fact in our disclosures during the period from May 7, 2012 through May 29, 2012, all in violation of Section 10(b) of the Securities Exchange Act of 1934, as amended, and Rule 10b-5 promulgated thereunder. The purported class consists of all persons (excluding defendants) who purchased our common stock between

May 7, 2012 and May 29, 2012. The plaintiffs seek unspecified monetary damages, costs and attorneys' fees as well as disgorgement of the proceeds from certain individual defendants' sales of our stock. On October 8, 2014, the Court approved Local No. 8 IBEW Retirement Fund as lead plaintiff, and Scott and Scott LLP as lead counsel for the plaintiff and the putative class. We filed a motion to dismiss the complaint on December 8, 2014 and the plaintiffs filed their opposition to our motion to dismiss on January 22, 2015. On February 23, 2015, we filed a reply to the plaintiffs' opposition to our motion to dismiss. The court heard oral argument on our motion to dismiss on March 6, 2015 and took the motion under advisement. On September 30, 2015, the court granted our motion to dismiss. On October 15, 2015, the plaintiff filed a notice of appeal. We believe the claims to be without merit and intend to vigorously defend the litigation.

DOJ Subpoena

In the third quarter of 2015, we received a subpoena from the United States Department of Justice related to our marketed medicines. This subpoena requests documents relating primarily to our Good Laboratory Practices in a bioanalytical laboratory. We are in the process of responding to the subpoena and intend to continue to cooperate.

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, 2015:	High	Low
First quarter	$ 136.33	$ 103.75
Second quarter	137.50	113.68
Third quarter	143.45	97.45
Fourth quarter	134.71	101.49

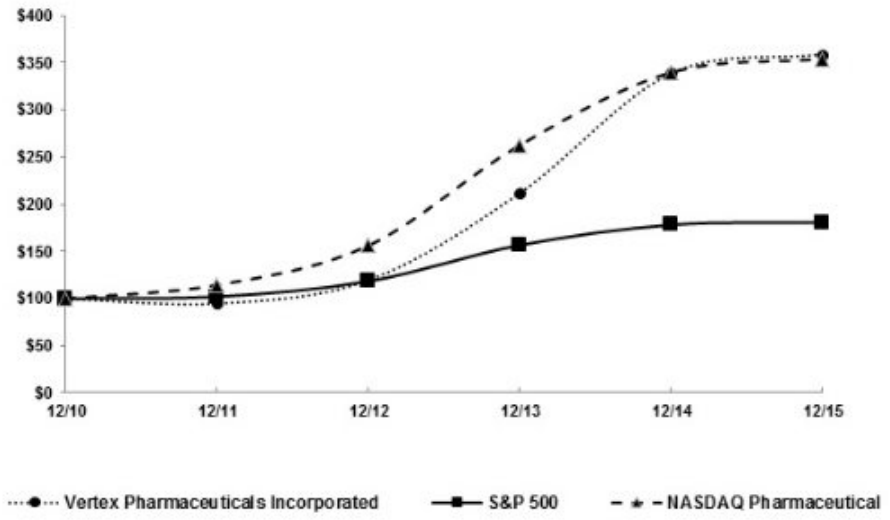
Year Ended December 31, 2014:	High	Low
First quarter	$ 87.77	$ 67.49
Second quarter	98.80	59.79
Third quarter	116.88	84.41
Fourth quarter	124.35	96.43

Shareholders

As of January 29, 2016 , there were 1,666 holders of record of our common stock.

Performance Graph

CUMULATIVE TOTAL RETURN
Based on Initial Investment of $100 on December 31, 2010
with dividends reinvested (fiscal years ended December 31)



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

Dividends

We have never declared or paid any cash dividends on our common stock, and we currently expect that any future earnings will be retained for use in our business. Any future determination to declare cash dividends will be subject to the discretion of our board of directors and applicable law and will depend on various factors, including our results of operations, financial condition, prospects and any other factors deemed relevant by our board of directors. In addition, our credit agreement limits our ability to pay cash dividends on our common stock.

Issuer Repurchases of Equity Securities

The table set forth below shows all repurchases of securities by us during the three months ended December 31, 2015 :

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, 2015 to Oct. 31, 2015	56,036	$ 0.01	—	—
Nov. 1, 2015 to Nov. 30, 2015	53,704	$ 0.01	—	—
Dec. 1, 2015 to Dec. 31, 2015	21,158	$ 0.01	—	—

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

ITEM 6. SELECTED FINANCIAL DATA

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

	Year Ended December 31,				
	2015	2014	2013	2012	2011
	(in thousands, except per share amounts)				
Consolidated Statements of Operations Data:					
Product revenues, net					
KALYDECO product revenues, net	$ 631,674	$ 463,750	$ 371,285	$ 171,645	$ —
ORKAMBI product revenues, net	350,663	—	—	—	—
INCIVEK product revenues, net	17,987	24,071	466,360	1,161,813	950,889
Total product revenues, net	1,000,324	487,821	837,645	1,333,458	950,889
Royalty revenues	23,959	40,919	156,592	141,498	50,015
Collaborative revenues (1)	8,053	51,675	217,738	52,086	409,722
Total revenues	1,032,336	580,415	1,211,975	1,527,042	1,410,626
Total costs and expenses (2)	1,499,215	1,272,827	1,821,983	1,480,315	1,277,355
(Loss) income from continuing operations attributable to Vertex	(556,334)	(737,643)	(503,622)	32,271	109,797
(Loss) income from discontinued operations attributable to Vertex (3)	—	(912)	58,594	(139,303)	(80,223)
Net (loss) income attributable to Vertex	$ (556,334)	$ (738,555)	$ (445,028)	$ (107,032)	$ 29,574
Diluted (loss) income from continuing operations attributable to Vertex per common share	$ (2.31)	$ (3.14)	$ (2.24)	$ 0.15	$ 0.52
Shares used in per diluted share calculations	241,312	235,307	224,906	215,262	208,807

	As of December 31,				
	2015	2014	2013	2012	2011
	(in thousands)				
Consolidated Balance Sheet Data:					
Cash, cash equivalents and marketable securities	$ 1,042,462	$ 1,387,106	$ 1,465,076	$ 1,321,215	$ 968,922
Total assets	2,498,875	2,334,679	2,319,041	2,759,288	2,204,280
Total current liabilities	506,349	368,254	397,829	432,624	392,348
Long-term debt obligations, excluding current portion (4)	223,969	280,569	—	400,000	400,000
Construction financing lease obligation, excluding current portion (5)	472,611	473,073	440,937	268,031	55,950
Other long-term obligations	202,318	116,600	123,870	424,251	390,470

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

(2) Total costs and expenses included (i) in 2013 and 2012, an aggregate of $10.4 million and $133.2 million, respectively, of write-offs for excess and obsolete inventories, (ii) in 2013 and 2012, total costs and expenses included intangible asset impairment charges of $412.9 million and $105.8 million , respectively and (iii) in 2015, 2014 and 2013, $2.2 million , $50.9 million and $40.5 million , respectively, of restructuring charges. See Note H, "Inventories," Note J, "Intangible Assets and Goodwill" and Note Q, "Restructuring Expenses."

(3) (Loss) income from discontinued operations attributable to Vertex relates to our collaboration with Alios BioPharma, Inc., in 2011 through 2013, which we deconsolidated as of December 31, 2013. See Note B, "Collaborative Arrangements."

(4) In 2014, we borrowed $300.0 million in the form of a senior secured term loan that matures in July 2017. In 2013, our convertible senior subordinated notes (due 2015) with an aggregate principal amount of $400.0 million were converted into common stock or redeemed. See Note L, "Long Term Obligations."

(5) 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 L, "Long Term Obligations."

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 medicines for serious diseases. We use precision medicine approaches with the goal of creating transformative medicines for patients in specialty markets. Our business is focused on developing and commercializing therapies for the treatment of cystic fibrosis, or CF, and advancing our research and development programs in other indications, while maintaining our financial strength. Our two marketed products are ORKAMBI and KALYDECO.

In 2012, we obtained approval for, and initiated commercial sales of, KALYDECO (ivacaftor), and in 2015, we obtained approval for, and initiated commercial sales of ORKABMI (lumacaftor in combination with ivacaftor). KALYDECO net product revenues have been increasing on an annual basis and ORKAMBI net product revenues commenced in the United States in the second half of 2015. Our total net product revenues increased by 105% from $487.8 million in 2014 to $1.0 billion in 2015 , primarily due to ORKAMBI net product revenues, which commenced in the third quarter of 2015, and an increase in KALYDECO net product revenues. In the fourth quarter of 2015, our total net product revenues were $406.6 million , including $219.9 million in ORKAMBI net product revenues and $180.7 million in KALYDECO net product revenues. We expect our net income (loss) and total net product revenues in 2016 will be largely dependent on our ORKAMBI net product revenues in the United States.

Cystic Fibrosis

ORKAMBI

ORKAMBI (lumacaftor in combination with ivacaftor) was approved by the United States Food and Drug Administration, or FDA, in July 2015 and by the European Commission in November 2015, for the treatment of patients with CF twelve years of age and older who are homozygous for the F508del mutation in their cystic fibrosis transmembrane conductance regulator, or *CFTR,* gene. We recognized our first net product revenues from ORKAMBI in the second half of 2015. Our future ORKAMBI net product revenues in the United States will reflect the number of patients for whom treatment with ORKAMBI is initiated, the proportion of initiated patients who remain on treatment, patient compliance with the recommended treatment regimen and the level of rebates, chargebacks, discounts and other adjustments to our ORKAMBI gross product revenues. We believe that there currently are approximately 8,500 patients in the United States who are eligible for treatment with ORKAMBI and that as of December 31, 2015 more than 4,500 patients in the United States had started treatment with ORKAMBI. Following the approval in the European Union in November 2015, we have begun the country-by-country reimbursement approval process. We believe that there are approximately 12,000 patients with CF twelve years of age and older who are homozygous for the F508del mutation in Europe.

We recently completed the first of two Phase 3 clinical trials evaluating ORKAMBI for the treatment of patients with CF six to eleven years of age who are homozygous for the F508del mutation in their *CFTR* gene. We believe that there are approximately 6,000 patients in the United States and European Union within this patient population.

KALYDECO

KALYDECO (ivacaftor) 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. Since 2012, we have increased the number of patients who are being treated with KALYDECO in the United States and non-U.S. markets by expanding the label for KALYDECO to include patients with CF who have additional mutations in their *CFTR* gene and to include patients in additional age demographics. We believe that there are approximately 4,000 patients in North America, Europe and Australia who are currently eligible for treatment with KALYDECO.

CF Development Programs

We have multiple development programs in the field of CF, including:

- VX-661, a corrector compound that we are evaluating in a Phase 3 development program in combination with ivacaftor in multiple CF patient populations who have at least one copy of the F508del mutation in their *CFTR* gene;
- VX-371, an investigational epithelial sodium channel, or ENaC, inhibitor, that is being evaluated in a Phase 2 development program and which we exclusively licensed from Parion Sciences, Inc. in 2015; and
- VX-152 and VX-440, two next-generation CFTR corrector compounds that entered Phase 1 clinical trials in the fourth quarter of 2015 and that we plan to evaluate as part of combination treatment regimens.

Research and Development

We are engaged in a number of other research and mid- and early-stage development programs, including in the areas of oncology, pain and neurology.

Oncology

We are conducting two Phase 1/2 clinical trials of VX-970, a protein kinase inhibitor of ataxia telangiectasia and Rad3-related, or ATR, in combination with commonly used DNA-damaging chemotherapies across a range of solid tumor types, including triple negative breast cancer and non-small cell lung cancer. We also are in Phase 1 development of VX-803, a second ATR inhibitor, alone and in combination with chemotherapy. We recently initiated Phase 1 clinical development of VX-984, a third oncology drug candidate, alone and in combination with pegylated liposomal doxorubicin.

Pain

We are developing VX-150 and VX-241, two drug candidates for the treatment of pain. In the fourth quarter of 2015, we initiated a Phase 2 clinical trial to evaluate VX-150 in patients with symptomatic osteoarthritis of the knee. We expect to begin clinical development of VX-241 in the first half of 2016.

Acute Spinal Cord Injury

We are developing VX-210, a drug candidate for the treatment of acute spinal cord injury, that we exclusively licensed from BioAxone BioSciences, Inc. VX-210 is designed to inhibit a protein known as Rho that blocks neural regeneration after injury. We expect to initiate a Phase 2b/3 clinical trial in the first half of 2016 to evaluate the efficacy and safety of VX-210 in patients with certain acute cervical spinal cord injuries.

Research

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.

Drug Discovery and Development

Discovery and development of a new pharmaceutical product is a difficult and lengthy process that requires significant financial resources along with extensive technical and regulatory expertise and can take 10 to 15 years or more. Potential drug candidates are subjected to rigorous evaluations, driven in part by stringent regulatory considerations, designed to generate information concerning efficacy, side-effects, proper dosage levels and a variety of other physical and chemical characteristics that are important in determining whether a drug candidate should be approved for marketing as a pharmaceutical product. Most chemical compounds that are investigated as potential drug candidates never progress into development, and most drug candidates that do advance into development never receive marketing approval. Because our investments in drug candidates are subject to considerable risks, we closely monitor the results of our discovery, research, clinical trials and nonclinical studies and frequently evaluate our drug development programs in light of new data and scientific, business and commercial insights, with the objective of balancing risk and potential. This process can result in abrupt changes in focus and priorities as new information becomes available and as we gain additional understanding of our ongoing programs and potential new programs, as well as those of our competitors.

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

Regulatory Compliance

Our marketing of pharmaceutical products is subject to extensive and complex laws and regulations. We have a corporate compliance program designed to actively identify, prevent and mitigate risk through the implementation of compliance policies and systems, and through the promotion of a culture of compliance. Among other laws, regulations and standards, we are subject to various U.S. federal and state laws, and comparable foreign laws pertaining to health care fraud and abuse, including anti-kickback and false claims 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 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.

Reimbursement

Sales of our products depend, to a large degree, on the extent to which our products are covered by third-party payors, such as government health programs, commercial insurance and managed health care organizations. We dedicate substantial management and other resources in order to obtain and maintain appropriate levels of reimbursement for our products from third-party payors, including governmental organizations in the United States and ex-U.S. markets. Following the FDA's July 2015 approval of ORKAMBI in the United States, we are engaging in discussions with numerous commercial insurers and managed health care organizations, along with government health programs that are typically managed by authorities in the individual states. Following the European Commission's November 2015 approval of ORKAMBI in Europe, we are working to obtain government reimbursement for ORKAMBI on a country-by-country basis, because in many foreign countries patients are unable to access prescription pharmaceutical products that are not reimbursed by their governments. Consistent with our experience with KALYDECO when it was first approved, we expect reimbursement discussions in ex-U.S. markets may take a significant period of time.

RESULTS OF OPERATIONS

	2015	2014	2013	2015/2014 Comparison Increase/(Decrease) $	2015/2014 Comparison Increase/(Decrease) %	2014/2013 Comparison Increase/(Decrease) $	2014/2013 Comparison Increase/(Decrease) %
	(in thousands)			(in thousands, except percentages)			
Revenues	$ 1,032,336	$ 580,415	$ 1,211,975	$ 451,921	78 %	$ (631,560)	(52)%
Operating costs and expenses	1,499,215	1,272,827	1,821,983	226,388	18 %	(549,156)	(30)%
Other items, net	(89,455)	(45,231)	106,386	$ 44,224	98 %	n/a	n/a
Loss from continuing operations attributable to Vertex	(556,334)	(737,643)	(503,622)	(181,309)	(25)%	234,021	46 %
(Loss) income from discontinued operations attributable to Vertex	—	(912)	58,594	n/a	n/a	n/a	n/a
Net loss attributable to Vertex	$ (556,334)	$ (738,555)	$ (445,028)	$ (182,221)	(25)%	$ 293,527	66 %

Net Loss Attributable to Vertex

Comparison of Net Loss Attributable to Vertex 2015 vs. 2014

Net loss attributable to Vertex was $556.3 million in 2015 as compared to a net loss attributable to Vertex of $738.6 million in 2014 . Our revenues increased significantly in 2015 as compared to 2014 primarily due to ORKAMBI net product revenues, which commenced in the third quarter of 2015, and a $167.9 million increase in KALYDECO net product revenues, partially offset by a $43.6 million decrease in our collaborative revenues. Our operating costs and expenses increased in 2015 as compared to 2014 primarily due to increases in research and development expenses, sales, general and administrative expenses and cost of product revenues, partially offset by decreased restructuring expenses and royalty expenses.

Comparison of Net Loss Attributable to Vertex 2014 vs. 2013

Net loss attributable to Vertex was $738.6 million in 2014 as compared to a net loss attributable to Vertex of $445.0 million in 2013 . Our revenues decreased in 2014 as compared to 2013 due to a $442.3 million decrease in INCIVEK net product revenues, a $166.1 million decrease in collaborative revenues and a $115.7 million decrease in royalty revenues, partially offset by a $92.5 million increase in KALYDECO net product revenues. Our operating costs and expenses decreased in 2014 as compared to 2013 primarily due to an intangible asset impairment charge related to VX-222 of $412.9 million recorded in 2013 and decreases in cost of product revenues, royalty expenses, research and development expenses and sales, general and administrative expenses. In 2014, the $45.2 million loss reflected in other items, net was primarily due to interest expense associated with the leases for our corporate headquarters. In 2013 the $106.4 million gain reflected in other items, net was primarily due to a benefit from income taxes we recorded related to the VX-222 impairment charge. The income (loss) from discontinued operations in 2014 and 2013 related to a collaboration with Alios that was terminated in 2014.

In 2016, we expect that our net income (loss) will be largely dependent on the level of ORKAMBI net product revenues.

Earnings Per Share

In 2015 , 2014 and 2013 , net loss attributable to Vertex was $2.31 , $3.14 and $1.98 , respectively, per diluted share. In 2015 , 2014 and 2013 , net loss from continuing operations attributable to Vertex was $2.31 , $3.14 and $2.24 , respectively, per diluted share.

Common Shares Outstanding

Our shares of outstanding common stock increased from 241.8 million shares on December 31, 2014 to 246.3 million shares on December 31, 2015 due to our issuance in 2015 of approximately 4.5 million shares of common stock pursuant to our employee equity programs. Our shares of outstanding common stock increased from 233.8 million shares on December 31, 2013 to 241.8 million shares on December 31, 2014 due to our issuance in 2014 of approximately 8.0 million shares of common stock issued pursuant to our employee equity programs.

Stock-based Compensation

Stock-based compensation expense was $231.0 million , $177.5 million and $126.8 million in 2015 , 2014 and 2013 , respectively. Our stock-based compensation expense has been increasing due to the increase in our stock price and the associated increase in the grant-date fair value of equity awards.

Revenues

				2015/2014 Comparison		2014/2013 Comparison	
				Increase/(Decrease)		Increase/(Decrease)	
	2015	2014	2013	$	%	$	%
	(in thousands)			(in thousands, except percentages)			
Product revenues, net	$ 1,000,324	$ 487,821	$ 837,645	$ 512,503	105 %	$ (349,824)	(42)%
Royalty revenues	23,959	40,919	156,592	(16,960)	(41)%	(115,673)	(74)%
Collaborative revenues	8,053	51,675	217,738	(43,622)	(84)%	(166,063)	(76)%
Total revenues	$ 1,032,336	$ 580,415	$ 1,211,975	$ 451,921	78 %	$ (631,560)	(52)%

Product Revenues, Net

	2015	2014	2013
	(in thousands)		
KALYDECO	$ 631,674	$ 463,750	$ 371,285
ORKAMBI	350,663	—	—
INCIVEK	17,987	24,071	466,360
Total product revenues, net	$ 1,000,324	$ 487,821	$ 837,645

Our total net product revenues increased by 105% in 2015 as compared to 2014 due to net product revenues from ORKAMBI, which was approved by the FDA in July 2015, and increased KALYDECO net product revenues.

In 2015, KALYDECO net product revenues were $631.7 million , including $266.1 million of net product revenues from ex-U.S. markets, compared to KALYDECO net product revenues of $463.8 million in 2014, including $201.4 million of net product revenues from ex-U.S. markets. In 2013, KALYDECO net product revenues were $371.3 million , including $154.7 million of net product revenues from ex-U.S. markets. The increase s were primarily due to additional patients being treated with KALYDECO as we completed reimbursement discussions in various jurisdictions and increased the number of patients eligible to receive KALYDECO through label expansions. We expect KALYDECO net product revenues to increase in 2016 as compared to 2015.

ORKAMBI net product revenues increased from $130.8 million in the third quarter of 2015 to $219.9 million in the fourth quarter of 2015. As of December 31, 2015, more than 4,500 patients, out of the approximately 8,500 eligible patients, had begun treatment with ORKAMBI in the United States. We expect ORKAMBI net product revenues to increase in 2016 as compared to 2015 as we recognize revenues over a full fiscal year. We believe that our ORKAMBI revenues in 2016, will be dependent on:

- the total number of eligible patients in the United States who begin treatment with ORKAMBI;
- the rate at which additional patients initiate treatment in 2016;
- the proportion of initiated patients who remain on treatment; and
- the compliance rate for patients who remain on treatment.

Initially, we expect that our ex-U.S. ORKAMBI net product revenues will be primarily from Germany due to the time it will take to complete the reimbursement discussions in other European countries following ORKAMBI's European approval in the fourth quarter of 2015.

INCIVEK net product revenues were $18.0 million , $24.1 million and $466.4 million in 2015, 2014 and 2013. We have withdrawn INCIVEK from the market. We may continue to recognize insignificant INCIVEK revenues in 2016 as we adjust our INCIVEK reserves for rebates, chargebacks and discounts.

Royalty Revenues

Our royalty revenues were $24.0 million , $40.9 million and $156.6 million in 2015 , 2014 and 2013 , respectively. Since the beginning of 2014, our royalty revenues have consisted of (i) revenues related to a cash payment we received in 2008 when we sold our rights to certain HIV royalties and (ii) revenues related to certain third-party royalties payable by our collaborators on sales of HIV drugs and telaprevir that also result in corresponding royalty expenses. In 2013, we received significant royalties from Janssen NV based on INCIVO (telaprevir) net product sales. Our rights to receive royalties on INCIVO sales ended at the beginning of 2014, and Janssen NV currently has a fully-paid license to market INCIVO in its territories, subject to the continued payment of certain third-party royalties.

Collaborative Revenues

	2015	2014	2013
		(in thousands)	
Collaborative revenues:			
Janssen Inc.	$ —	$ 35,000	$ —
Janssen NV	1,946	7,104	203,437
CFFT	—	6,455	14,322
Other (1)	6,107	3,116	(21)
Total collaborative revenues	$ 8,053	$ 51,675	$ 217,738

(1) 2015 includes $2.9 million of revenues related to variable interest entities consolidated for accounting purposes.

Our collaborative revenues have fluctuated significantly on an annual basis and may continue to fluctuate in the future. In 2015, we did not have significant collaborative revenues. In 2014 , the majority of our collaborative revenues related to $35.0 million in payments we received from Janssen Inc. related to our outlicense of VX-787. In 2013 , we recognized $203.4 million in Janssen NV collaborative revenues, which were primarily attributable to a $152.0 million payment we received pursuant to our amendment to the Janssen NV collaboration agreement. These collaborative revenues also included the acceleration of the remaining deferred revenues related to the up-front payment we received from Janssen NV in 2006.

Operating Costs and Expenses

				2015/2014 Comparison		2014/2013 Comparison	
				Increase/(Decrease)		Increase/(Decrease)	
	2015	2014	2013	$	%	$	%
	(in thousands)			(in thousands, except percentages)			
Cost of product revenues	$ 117,151	$ 39,725	$ 88,979	$ 77,426	195 %	$ (49,254)	(55)%
Royalty expenses	7,361	21,262	41,298	(13,901)	(65)%	(20,036)	(49)%
Research and development expenses	995,922	855,506	882,097	140,416	16 %	(26,591)	(3)%
Sales, general and administrative expenses	376,575	305,409	356,188	71,166	23 %	(50,779)	(14)%
Restructuring expenses	2,206	50,925	40,521	(48,719)	(96)%	10,404	26 %
Intangible asset impairment charges	—	—	412,900	n/a	n/a	(412,900)	(100)%
Total costs and expenses	$ 1,499,215	$ 1,272,827	$ 1,821,983	$ 226,388	18 %	$ (549,156)	(30)%

Cost of Product Revenues

Our cost of product revenues includes the cost of producing inventories that corresponded to product revenues for the reporting period, plus the third-party royalties payable on our net sales of our products. Pursuant to our agreement with Cystic Fibrosis Foundation Therapeutics Incorporated, or CFFT, our tiered third-party royalties on sales of KALYDECO and ORKAMBI, calculated as a percentage of net sales, range from the single digits to the sub-teens.

Our cost of product revenues increased in 2015 as compared to 2014 due primarily to increased net product revenues. Our cost of product revenues decreased in 2014 as compared to 2013 due primarily to decreased net product revenues and the charges incurred in 2013 for excess and obsolete INCIVEK inventories. We expect our cost of product revenues to increase in 2016 as compared to 2015 due to increased net product revenues.

Royalty Expenses

Royalty expenses include third-party royalties payable upon net sales of telaprevir by our collaborators in their territories and expenses related to a subroyalty payable to a third party on net sales of an HIV protease inhibitor sold by GlaxoSmithKline. Royalty expenses do not include royalties we pay to CFFT on sales of KALYDECO and ORKAMBI, which instead are included in cost of product revenues. Royalty expenses in 2015 decreased by $13.9 million , or 65% , as compared to 2014 , primarily as a result of decreased INCIVO (telaprevir) sales by our collaborator Janssen NV. Our royalty expenses with respect to telaprevir and the HIV protease inhibitor are offset by corresponding royalty revenues.

Research and Development Expenses

				2015/2014 Comparison		2014/2013 Comparison	
				Increase/(Decrease)		Increase/(Decrease)	
	2015	2014	2013	$	%	$	%
	(in thousands)			(in thousands, except percentages)			
Research expenses	$ 337,797	$ 257,483	$ 233,651	$ 80,314	31%	$ 23,832	10 %
Development expenses	658,125	598,023	648,446	60,102	10%	(50,423)	(8)%
Total research and development expenses	$ 995,922	$ 855,506	$ 882,097	$ 140,416	16%	$ (26,591)	(3)%

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

Over the past three years, we have incurred $2.7 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 of varying interpretations, which could delay, limit or prevent regulatory approval. The duration and cost of discovery, nonclinical studies and clinical trials may vary significantly over the life of a project and are difficult to predict. Therefore, accurate and meaningful estimates of the ultimate costs to bring our drug candidates to market are not available.

In 2013 , 2014 and 2015 , costs related to our CF programs represented the largest portion of our development costs. Any estimates regarding development and regulatory timelines for our drug candidates are highly subjective and subject to change. In 2015, we obtained approval for ORKAMBI in the United States and Europe, and began generating revenues from ORKAMBI in the United States in the second half of 2015. We cannot make a meaningful estimate when, if ever, our other clinical development programs will generate revenues and cash flows.

Research Expenses

	2015	2014	2013	2015/2014 Comparison Increase/(Decrease) $	2015/2014 Comparison Increase/(Decrease) %	2014/2013 Comparison Increase/(Decrease) $	2014/2013 Comparison Increase/(Decrease) %
	(in thousands)			(in thousands, except percentages)			
Research Expenses:							
Salary and benefits	$ 81,752	$ 82,975	$ 80,957	$ (1,223)	(1)%	$ 2,018	2 %
Stock-based compensation expense	49,744	40,531	27,426	9,213	23 %	13,105	48 %
Laboratory supplies and other direct expenses	37,058	38,082	35,981	(1,024)	(3)%	2,101	6 %
Outsourced services	24,210	17,401	20,169	6,809	39 %	(2,768)	(14)%
Collaboration payments	75,000	—	—	75,000	n/a	n/a	n/a
Infrastructure costs	70,033	78,494	69,118	(8,461)	(11)%	9,376	14 %
Total research expenses	$ 337,797	$ 257,483	$ 233,651	$ 80,314	31 %	$ 23,832	10 %

Over the past three years we have maintained a substantial investment in research activities resulting in increases in research expenses. Our research expenses in 2015 included a one-time $75.0 million upfront payment we made to CRISPR Therapeutics AG, or CRISPR, in connection with entry into our collaboration in the fourth quarter of 2015. Excluding the upfront payment we made to CRISPR, our research expenses increased by 2% in 2015 as compared to 2014. We expect to continue to invest in our research programs with a focus on identifying drug candidates with the goal of creating transformative medicines.

Development Expenses

	2015	2014	2013	2015/2014 Comparison Increase/(Decrease) $	2015/2014 Comparison Increase/(Decrease) %	2014/2013 Comparison Increase/(Decrease) $	2014/2013 Comparison Increase/(Decrease) %
	(in thousands)			(in thousands, except percentages)			
Development Expenses:							
Salary and benefits	$ 164,466	$ 161,718	$ 167,945	$ 2,748	2 %	$ (6,227)	(4)%
Stock-based compensation expense	103,211	76,467	53,757	26,744	35 %	22,710	42 %
Laboratory supplies and other direct expenses	30,611	34,689	38,526	(4,078)	(12)%	(3,837)	(10)%
Outsourced services	248,506	197,743	238,906	50,763	26 %	(41,163)	(17)%
Drug supply costs	9,799	10,026	38,767	(227)	(2)%	(28,741)	(74)%
Infrastructure costs	101,532	117,380	110,545	(15,848)	(14)%	6,835	6 %
Total development expenses	$ 658,125	$ 598,023	$ 648,446	$ 60,102	10 %	$ (50,423)	(8)%

Our development expenses increased by $60.1 million , or 10% , in 2015 as compared to 2014 and decreased by $50.4 million , or 8% , in 2014 as compared to 2013 . The increase in 2015 as compared to 2014 was primarily due to an increase in outsourced services related to ongoing clinical trials, including our Phase 3 development program for VX-661 in combination with ivacaftor and an increase in stock-based compensation expense, partially offset by decreased infrastructure costs and decreased laboratory supplies and other direct expenses. We expect our development expenses to increase in 2016 as compared to 2015 due to activities related to clinical trials, including the Phase 3 clinical development program for VX-661 in combination with ivacaftor.

The decreased development expenses in 2014 as compared to 2013 were principally due to decreased outsourced services expenses and drug supply costs, partially offset by increased stock-based compensation expense. The significant decrease in outsourced services expenses in 2014 was largely attributable to decreased clinical trial expenses resulting from the completion of the TRAFFIC and TRANSPORT clinical trials in the first half of 2014.

Sales, General and Administrative Expenses

	2015	2014	2013	2015/2014 Comparison Increase/(Decrease) $	2015/2014 Comparison Increase/(Decrease) %	2014/2013 Comparison Increase/(Decrease) $	2014/2013 Comparison Increase/(Decrease) %
	(in thousands)			(in thousands, except percentages)			
Sales, general and administrative expenses	$ 376,575	$ 305,409	$ 356,188	$ 71,166	23%	$ (50,779)	(14)%

Sales, general and administrative expenses increased by 23% in 2015 as compared to 2014 , primarily due to increased investment in commercial support for ORKAMBI and KALYDECO and costs incurred to prepare for the launch of ORKAMBI in ex-U.S. markets. Sales, general and administrative expenses decreased by 14% in 2014 as compared to 2013 , primarily due to decreased headcount following our October 2013 restructuring activities. We expect sales, general and administrative expenses to increase in 2016 as compared to 2015 due to the continued expansion of our commercial infrastructure to support sales of ORKAMBI.

Restructuring Expense

In 2015 , 2014 and 2013 , we recorded restructuring expenses of $2.2 million , $50.9 million and $40.5 million , respectively. Our restructuring expenses in 2014 primarily related to the relocation of our corporate headquarters in Massachusetts to Boston from Cambridge. Our restructuring expenses in 2013 primarily related to our October 2013 reduction in headcount. As of December 31, 2015 , our accrued restructuring liability related to our lease obligation in Cambridge was $13.9 million . This lease obligation expires on April 30, 2018.

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. There were no corresponding intangible asset impairment charges recorded related to continuing operations in 2014 or 2015.

In 2013, we also recorded a $250.6 million impairment charge related to the Alios HCV nucleotide analogue program and a benefit for income taxes of $102.1 million that is included in loss from discontinued operations attributable to noncontrolling interest for 2013.

Other Items, Net

Interest Expense, Net

In 2015 , 2014 and 2013 , interest expense, net was $84.2 million , $72.9 million and $22.9 million , respectively. The increase in interest expense, net in 2015 as compared to 2014 was primarily due to the interest expense we incurred for the full fiscal year in 2015 on the $300.0 million that we borrowed in mid-2014 pursuant to our credit agreement. The increase in interest expense in 2014 as compared to 2013 was primarily due to interest expense of $60.2 million associated with the leases for our corporate headquarters in Boston, Massachusetts and interest expense of $10.4 million related to the $300.0 million we borrowed in mid-2014.

Other (Expense) Income, Net

In 2015 , net other expense was $6.7 million primarily due to foreign exchange losses. In 2014 , we recorded net other income of $30.4 million primarily due to a credit of $36.7 million related to a one-time cash payment we received in 2014 from our landlord pursuant to leases for our corporate headquarters in Boston, Massachusetts. In 2013 , we recorded net other income of $6.9 million primarily related to foreign exchange gains.

Income Taxes

In 2015 , we recorded a provision for income taxes of $30.4 million , principally due to the consolidation of Parion as a VIE into our consolidated financial statements in the second quarter of 2015. In 2014 , we recorded a provision for income taxes of $7.0 million , of which approximately $3.9 million was due to the consolidation of BioAxone as a VIE into our consolidated financial statements in the fourth quarter of 2014. In 2013 , our benefit from income taxes was $122.4 million .

This benefit from income taxes was primarily due to a benefit of $127.6 million related to our impairment charge for the VX-222 intangible asset.

Discontinued Operations

In 2014, we recorded a loss from discontinued operations attributable to Vertex of $0.9 million. In 2013, we recorded income from discontinued operations of $58.6 million. Our income (losses) from discontinued operations in these periods related to gains and losses due to the deconsolidation of Alios, an intangible asset impairment charge, a benefit from income taxes related to this charge and changes in the fair value of contingent consideration we estimated Alios would receive under the collaboration agreement. For additional information regarding the Alios collaboration please refer to "Critical Accounting Policies and Estimates - Collaborations; Variable Interest Entities."

LIQUIDITY AND CAPITAL RESOURCES

As of December 31, 2015 , we had cash, cash equivalents and marketable securities of approximately $1.04 billion , which represented an increase of $26.0 million from $1.02 billion as of June 30, 2015 and a decrease of $344.6 million from approximately $1.39 billion as of December 31, 2014 .

In the second half of 2015, we maintained our cash, cash equivalents and marketable securities balance due to increased cash receipts from product sales together with $97.7 million in cash we received from issuances of common stock pursuant to our employee benefit plans, offset by cash expenditures in the second half of 2015 related to, among other things, research and development expenses, sales, general and administrative expenses and an aggregate of $105.0 million in payments, including an equity investment, in connection with entry into our collaboration agreement with CRISPR in the fourth quarter of 2015.

The decrease in cash, cash equivalents and marketable securities from December 31, 2014 to December 31, 2015 was due to cash expenditures we made during 2015 related to, among other things, research and development expenses and sales, general and administrative expenses, an $80.0 million payment to Parion in connection with entering into our collaboration agreement with Parion and an aggregate of $105.0 million in payments to CRISPR, including an equity investment, in connection with entry into our collaboration agreement with CRISPR, partially offset by cash receipts from product sales and $185.6 million in cash we received from issuances of common stock pursuant to our employee benefit plans. We also incurred $41.6 million in costs for capital expenditures including net cash flows from capital lease financing during 2015 .

Our future cash flows will be substantially dependent on product sales of KALYDECO and ORKAMBI.

Sources of Liquidity

We intend to rely on our existing cash, cash equivalents and marketable securities together with cash flows from product sales as our primary source of liquidity. We are receiving cash flows from sales of ORKAMBI in the United States and from sales of KALYDECO in both in the United States and ex-U.S. markets. We expect to begin receiving cash flows from sales of ORKAMBI in Europe beginning in the first half of 2016. Initially, we expect these cash flows will be primarily from Germany due to the time it will take to complete the reimbursement discussions in other European countries.

We borrowed $300.0 million under a credit agreement that we entered into in July 2014 and, subject to certain conditions, we may request up to an additional $200.0 million pursuant to that credit agreement. 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. Negative covenants in our credit agreement may prohibit or limit our ability to access these sources of liquidity.

Future Capital Requirements

We incur substantial operating expenses to conduct research and development activities and to operate our organization. Under the terms of our credit agreement, we are required to repay the principal amount on the $300.0 million we borrowed in July 2014 in installments of $75 million on each of October 1, 2016, January 1, 2017, April 1, 2017 and July 9, 2017. We also have substantial facility and capital lease obligations, including leases for two buildings in Boston, Massachusetts that

continue through 2028. In addition, we have entered into certain collaboration agreements with third parties that include the funding of certain research, development and commercialization efforts with the potential for future milestone and royalty payments by us upon the achievement of pre-established developmental and regulatory targets.

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

Financing Strategy

In July 2014, we borrowed $300.0 million pursuant to a credit agreement. In addition, subject to certain conditions, we may request that the lenders loan us up to an additional $200.0 million under the credit agreement. We may raise additional capital through public offerings or private placements of our securities or securing new collaborative agreements or other methods of financing. We will continue to manage our capital structure and will consider all financing opportunities, whenever they may occur, that could strengthen our long-term liquidity profile. Negative covenants in our credit agreement may prohibit our ability to obtain future financing and 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, 2015 :

	Payments Due by Period				
	2016	2017-2018	2019-2020	2021 and later	Total
	(in thousands)				
Fan Pier Leases	$ 67,206	$ 134,412	$ 145,178	$ 607,621	$ 954,417
Facility leases, excluding Fan Pier Leases	33,906	58,238	40,035	219,483	351,662
Capital lease obligations	18,773	38,394	7,808	209	65,184
Senior secured term loan	92,993	231,036	—	—	324,029
Research, development and drug supply costs	13,277	—	—	—	13,277
Other	5,839	4,201	—	7,305	17,345
Total contractual commitments and obligations	$ 231,994	$ 466,281	$ 193,021	$ 834,618	$ 1,725,914

Leases

We lease two buildings that are located at Fan Pier in Boston, Massachusetts. We commenced lease payments on these two buildings in December 2013 and the initial lease periods end in December 2028.

On December 2, 2015, we entered into a lease agreement, pursuant to which we agreed to lease approximately 170,000 square feet of office and laboratory space in a building to be built in San Diego, California. The lease will commence upon completion of the building, scheduled for the second half of 2017 and will extend for 16 years from the commencement date. The future minimum rental payments that we are obligated to pay after taking occupancy are included in "Facility leases, excluding Fan Pier Leases."

Our future minimum commitments under our Kendall Square lease are included in "Facility leases, excluding Fan Pier Leases." We have entered into three 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 $15.5 million for 2016 and $20.7 million total for 2017 and 2018 . These amounts are not offset against our obligations set forth in the table above.

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

Senior Secured Term Loan

In July 2014, we entered into a credit agreement that provides for a $300.0 million senior secured term loan. The term loan currently bears interest at 6.2% per annum and will bear interest at a rate of LIBOR plus 5.0% per annum during the third year of the term. We are required to repay principal on the term loan in quarterly installments of $75 million from October 1, 2016 through the maturity date. We include estimates for interest in "Senior secured term loan," which are equivalent to management's expectations for the probable outcome of variable interest rates that are dependent on various future events and market interest rates.

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, 2015 , we had accrued $30.6 million related to these contracts for costs incurred for services provided through December 31, 2015 , and we have approximately $197.1 million in cancelable future commitments based on existing contracts as of December 31, 2015 . 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 BioAxone, BioAxone has the potential to receive up to $90.0 million, including a license continuation fee and development and regulatory milestone payments; and commercial milestone payments as well as royalties on future product sales, if any. Pursuant to our collaboration with Parion, Parion has the potential to receive milestone and royalty payments, including up to $490.0 million in development and regulatory milestone payments for the development of VX-371 (formerly P-1037) and/or VX-551 (formerly P-1055) to treat CF. Pursuant to our collaboration with CRISPR, CRISPR has the potential to receive milestone and royalty payments, including up to $420.0 million in development, regulatory and commercial milestone payments for each of up to six targets pursuant to the collaboration. We also have royalty obligations and a remaining $13.9 million milestone payment to the CFFT that we expect to pay in 2016. 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, 2015 , we did not have any liabilities associated with uncertain tax positions. As of December 31, 2015 , 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 are based upon our consolidated financial statements prepared in accordance with generally accepted accounting principles in the United States. The preparation of these financial statements requires us to make certain estimates and assumptions that affect the reported amounts of assets and liabilities, the disclosure of contingent assets and liabilities at the date of the consolidated financial statements and the reported amounts of revenues and expenses during the reported periods. These items are monitored and analyzed by management for changes in facts and circumstances, and material changes in these estimates could occur in the future.

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

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

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

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

Revenue Recognition

Product Revenues, Net

We generate product revenues from sales in the United States and in international markets. We sell our products principally to a limited number of specialty pharmacy providers and selected regional wholesalers in North America as well as government-owned and supported customers in international markets, collectively, our customers. Our customers in North America subsequently resell our products to patients and health care providers. We contract with government agencies and various private organizations so that our products will be eligible for purchase by, or partial or full reimbursement from, such third-party payors. We recognize net product revenues from sales of our products upon delivery to our customers as long as:

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

In order to conclude that the price is fixed or determinable, we must be able to calculate our gross product revenues from our customers and reasonably estimate our net product revenues. 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. 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.

We have withdrawn INCIVEK from the market in the United States. At December 31,2015 the Company maintains an accrual of less than $1 million for government rebates for INCIVEK. There typically is no deadline by which government payors must submit claims, and as a result we are continuing to monitor this reserve. Adjustments to this reserve are reflected as either an increase or decrease to net product revenues in the period in which the adjustment is made.

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 NV, 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 NV, 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, 2015 , the remaining deferred revenue balance related to Janssen NV was not material.

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 of $412.9 million and $250.6 million related to continuing operations and discontinued operations, respectively, that related to drug candidates for the treatment of HCV infection. As of December 31, 2015 , we had $284.3 million of indefinite-lived intangible assets recorded on our balance sheet related to our VIEs.

Collaborations; Variable Interest Entities

Our collaborations require us to apply accounting policies that involve significant judgments and that have a material effect on our consolidated financial statements. Under applicable accounting guidance, as a result of the relationships established through collaboration agreements, our collaborators may be deemed to be variable interest entities, or VIEs, our licenses may result in a variable interest in collaborators as a whole and our being the primary beneficiary of VIEs. As a result, we are required to consolidate VIEs financial statements into our financial statements for the period during which we have a variable interest in the VIE and are the VIE's primary beneficiary, and if we later determine that we no longer have a variable interest or are no longer the primary beneficiary, we are required to deconsolidate the VIE. If we determine that we no longer have significant continuing involvement with a VIE, its operations and direct expenses incurred by us are reflected in our discontinued operations presentation.

In addition, each period our net loss (income) is adjusted for gains and losses in the fair value of the contingent milestone payments and royalties payable by us to our VIEs. Determining the fair value of the contingent milestone payments and royalties payable by us to VIEs requires us to make significant estimates regarding the probability and potential timing of achieving each of the milestones pursuant to the agreement, future potential net sales and appropriate discount and tax rates.

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

- Beginning in the second quarter of 2015, we are consolidating all of Parion's expenses and revenues into our consolidated statements of operations, eliminating all intercompany balances and transactions. As of December 31, 2015, our consolidated balance sheet includes Parion's balances.
- Beginning in the fourth quarter of 2014, we are consolidating all of BioAxone's expenses and revenues into our consolidated statements of operations, eliminating all intercompany balances and transactions. As of December 31, 2015, our consolidated balance sheet includes BioAxone's balances.
- As of September 30, 2014, we concluded that we no longer had significant continuing involvement with Alios due to our intent and ability to terminate the Alios Agreement, which we terminated during the fourth quarter of 2014; therefore, the operations of Alios, including collaboration expenses reimbursed by Vertex are presented as discontinued operations for the periods presented in these consolidated financial statements.
- In 2013, the deconsolidation of Alios resulted in a gain of $68.2 million attributable to Vertex. The $68.2 million gain was 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 2013, we recorded net loss (income) attributable to the Alios noncontrolling interest. This net loss (income) attributable to the Alios noncontrolling interest is included in loss from discontinued operations for 2013.

Research and Development Accruals

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

Commercial Supplies and Inventories

We began capitalizing the costs of our KALYDECO inventories on January 1, 2012 and the costs of our ORKAMBI inventories on July 1, 2014. 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.

In 2013, following periodic assessments of the recoverability of our inventories, we recorded within cost of product revenues an aggregate of $10.4 million in charges primarily related to excess and obsolete INCIVEK inventories based on our analysis of our inventory levels in relation to our commercial outlook for INCIVEK. As of December 31, 2015, all of our inventories are related to KALYDECO and ORKAMBI. Periodic assessments of the recoverability of capitalized costs involve significant estimates and judgments on the part of management.

Income Taxes

We maintain a valuation allowance on the majority of 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 $4.2 billion as of December 31, 2015 . 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, 2015 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.

Upon completion of the construction of the buildings, we evaluated the leases and determined that the leases did not meet the criteria for "sale-leaseback" treatment. Accordingly, we depreciate the asset and incur interest expense related to the financing obligation recorded on our balance sheet. We bifurcate our lease payments pursuant to the leases into (i) a portion that is allocated to the buildings and (ii) a portion that is allocated to the land on which the buildings were constructed. The portion of the lease obligations allocated to the land is treated as an operating lease. In connection with the leases for our

corporate headquarters, we incurred $60.2 million in interest expense, $13.3 million in depreciation expense and $6.5 million in operating expense in 2015. In 2016 , we expect interest expense, depreciation expense and operating expenses related to the leases for our corporate headquarters to be approximately consistent with that from 2015.

Restructuring Expenses

We have adopted several plans to restructure our facility operations for which we have incurred restructuring expenses in the three years ended December 31, 2015. In particular, in 2014, we recorded $50.9 million in costs associated with exit and disposal activities related to the relocation of our headquarters in Massachusetts from Cambridge to Boston and maintained a liability related to these activities of $6.0 million as of December 31, 2015. Our initial estimate of our liabilities for net ongoing costs associated with these facility obligations are recorded at fair value. In estimating the expenses and liabilities related to these facilities, we utilize probability-weighted discounted cash-flows of our ongoing lease obligations. In estimating the expense and liability under our lease obligations, we estimate (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. We use a credit-adjusted risk-free rate to discount the estimated cash flows.

We review our estimates and assumptions on at least a quarterly basis. We intend to continue such reviews until the termination of these facility lease obligations and will make whatever modifications we believe are necessary, based on our best judgment, to reflect any changed circumstances. Our estimates have changed in the past, and may change in the future, resulting in additional adjustments to the estimate of these liabilities. Changes to our estimate of these liabilities are recorded as additional restructuring expenses (credits). In addition, because our estimate of these liabilities includes the application of a discount rate to reflect the time-value of money, we record imputed interest costs related to these liabilities each quarter. These costs are included in restructuring expenses on our consolidated statements of operations.

Stock-based Compensation Expense

Stock-based compensation expense is determined based on the fair value of the equity award at the grant date, net of estimated forfeitures, and is adjusted each period to reflect actual forfeitures and the outcomes of certain performance conditions. For awards with performance conditions that accelerate vesting of the award, we estimate the likelihood of satisfaction of the performance conditions, which affects the period over which the expense is recognized, and recognize the expense using the accelerated attribution model. For awards with performance conditions in which the award does not vest unless the performance condition is met, we recognize expense only if we estimate that achievement of the performance condition is probable. If we conclude that vesting is probable, we recognize expense from the date that we reach this conclusion through the estimated vesting date. Since 2014, we have provided to employees who have rendered a certain number of years of service and meet certain age requirements, partial or full acceleration of vesting of their equity awards, subject to certain conditions including a notification period, upon a termination of employment other than for cause. If actual forfeitures differ significantly from our estimates, if our estimates regarding the employees who will be eligible for partial or full acceleration of their equity awards, if the likelihood of achievement of a performance conditions changes or if any of our other assumptions or estimates prove incorrect, our stock-based compensation expense, or the period over which our stock-based compensation is recognized, could be materially affected.

RECENT ACCOUNTING PRONOUNCEMENTS

Refer to Note A, “Nature of Business and Accounting Policies,” in the accompanying notes to the consolidated financial statements for a discussion of recent accounting pronouncements. There were no new accounting pronouncements adopted during 2015 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.

We have a foreign currency management program with the objective of reducing the effect of exchange rate fluctuations on our operating results and forecasted revenues and expenses denominated in foreign currencies. 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, 2015 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-48 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, 2015 . In making this assessment, it used the criteria set forth in the Internal Control—Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework)(COSO). Based on its assessment, the Company's management has concluded that, as of December 31, 2015 , 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, 2015 , 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, 2015 , based on criteria established in Internal Control—Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework) (the COSO criteria). 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, 2015 , 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, 2015 and 2014 , 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, 2015 of Vertex Pharmaceuticals Incorporated and our report dated February 16, 2016 expressed an unqualified opinion thereon.

/s/ Ernst & Young LLP

Boston, Massachusetts

February 16, 2016

ITEM 9B. OTHER INFORMATION

Not applicable.

PART III

Portions of our definitive Proxy Statement for the 2016 Annual Meeting of Shareholders, or 2016 Proxy Statement, are incorporated by reference into this Part III of our Annual Report on Form 10-K.

ITEM 10. DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE

The information regarding directors required by this Item 10 will be included in our 2016 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 2016 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 2016 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 2016 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 2016 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 2016 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 4, 2015	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	Research, Development and Commercialization Agreement, dated as of May 24, 2004, between Vertex Pharmaceuticals Incorporated and Cystic Fibrosis Foundation Therapeutics Incorporated.†		10-Q/A (Exhibit 10.2)	August 19, 2011	000-19319
10.2	Amendment No. 1 to Research, Development and Commercialization Agreement, dated as of January 6, 2006, between Vertex Pharmaceuticals Incorporated and Cystic Fibrosis Foundation Therapeutics Incorporated.†		10-K (Exhibit 10.9)	March 16, 2006	000-19319
10.3	Amendment No. 2 to Research, Development and Commercialization Agreement, dated as of March 17, 2006, between Vertex Pharmaceuticals Incorporated and Cystic Fibrosis Foundation Therapeutics Incorporated.		10-Q/A (Exhibit 10.6)	August 19, 2011	000-19319
10.4	Amendment No. 5 to Research, Development and Commercialization Agreement, effective as of April 1, 2011, between Vertex Pharmaceuticals Incorporated and Cystic Fibrosis Foundation Therapeutics Incorporated.†		10-Q (Exhibit 10.3)	August 9, 2011	000-19319
10.5	Strategic Collaboration and License Agreement, dated as of June 4, 2015, by and among Parion Sciences, Inc., Vertex Pharmaceuticals Incorporated and Vertex Pharmaceuticals (Europe) Limited.†		10-Q (Exhibit 10.2)	August 4, 2015	000-19319
10.6	Strategic Collaboration, Option and License Agreement, dated October 26, 2015, by and among CRISPR Therapeutics AG, CRISPR Therapeutics Limited, CRISPR Therapeutics, Inc., Tracr Hematology Ltd., Vertex Pharmaceuticals Incorporated and Vertex Pharmaceuticals (Europe) Limited.†	X			
Leases					
10.7	Lease, dated May 5, 2011, between Fifty Northern Avenue LLC and Vertex Pharmaceuticals Incorporated.†		10-Q (Exhibit 10.4)	August 9, 2011	000-19319

Exhibit Number	Exhibit Description	Filed with this report	Incorporated by Reference herein from—Form or Schedule	Filing Date/ Period Covered	SEC File/ Reg. Number
10.8	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
10.9	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
10.10	Lease, dated December 2, 2015, between ARE-SD Region No. 23, LLC and Vertex Pharmaceuticals Incorporated.	X			
Financing Agreements					
10.11	Credit Agreement, dated as of July 9, 2014, among Vertex Pharmaceuticals Incorporated, Macquarie US Trading LLC and the other lenders party thereto.		10-Q (Exhibit 10.2)	July 31, 2014	000-19319
10.12	2015 Amendments to Credit Agreement, dated as of July 9, 2014, among Vertex Pharmaceuticals Incorporated, Macquarie US Trading LLC and the other lenders party thereto.		10-Q (Exhibit 10.1)	October 30, 2015	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 Agreement under Amended and Restated 2006 Stock and Option Plan (granted prior to July 30, 2013).*		8-K (Exhibit 10.2)	May 15, 2006	000-19319
10.17	Form of Restricted Stock Agreement under Amended and Restated 2006 Stock and Option Plan (granted prior to July 30, 2013).*		8-K (Exhibit 10.3)	May 15, 2006	000-19319
10.18	Form of Restricted Stock Agreement (Performance Accelerated Restricted Stock) under Amended and Restated 2006 Stock and Option Plan (granted prior to July 30, 2013).*		8-K (Exhibit 10.4)	May 15, 2006	000-19319
10.19	Form of Stock Option Agreement under Amended and Restated 2006 Stock and Option Plan (granted on or after July 30, 2013).*		10-K (Exhibit 10.20)	February 13, 2015	000-19319
10.20	Form of Restricted Stock Agreement under Amended and Restated 2006 Stock and Option Plan (granted on or after July 30, 2013).*		10-K (Exhibit 10.21)	February 13, 2015	000-19319
10.21	Form of Restricted Stock Unit Agreement under Amended and Restated 2006 Stock and Option Plan (granted on or after July 30, 2013).*		10-K (Exhibit 10.22)	February 13, 2015	000-19319
10.22	Amended and Restated 2013 Stock and Option Plan.*		DEF 14A (Appendix A)	April 30, 2015	000-19319
10.23	Form of Non-Qualified Stock Option Agreement under 2013 Stock and Option Plan.*		10-K (Exhibit 10.17)	February 13, 2015	000-19319
10.24	Form of Restricted Stock Agreement under 2013 Stock and Option Plan.*		10-K (Exhibit 10.18)	February 13, 2015	000-19319
10.25	Form of Restricted Stock Unit Agreement under 2013 Stock and Option Plan (U.S.).*	X			
10.26	Form of Restricted Stock Unit Agreement under 2013 Stock and Option Plan (International).*		10-K (Exhibit 10.19)	February 13, 2015	000-19319
10.27	Non-Employee Director Deferred Compensation Plan.*	X			
10.28	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					
10.29	Agreement between Jeffrey M. Leiden and Vertex, dated December 14, 2011.*		10-K (Exhibit 10.34)	February 22, 2012	000-19319
10.30	First Amendment to Employment Agreement, dated December 10, 2014, by and between Vertex Pharmaceuticals Incorporated and Jeffrey M. Leiden.*		8-K (Exhibit 10.1)	December 15, 2014	000-19319
10.31	Employee Non-disclosure, Non-competition and Inventions Agreement between Jeffrey M. Leiden and Vertex, dated December 14, 2011.*		10-K (Exhibit 10.35)	February 22, 2012	000-19319
10.32	Employment Agreement, dated as of August 27, 2012, between Vertex Pharmaceuticals Incorporated and Stuart Arbuckle.*		10-Q (Exhibit 10.1)	November 6, 2012	000-19319
10.33	Change of Control Agreement, dated as of August 27, 2012, between Vertex Pharmaceuticals Incorporated and Stuart Arbuckle.*		10-Q (Exhibit 10.2)	November 6, 2012	000-19319

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	Employment Agreement, dated as of December 12, 2014, between Vertex Pharmaceuticals Incorporated and David Altshuler.*	X			
10.35	Change of Control Agreement, dated as of December 12, 2014, between Vertex Pharmaceuticals Incorporated and David Altshuler.*	X			
10.36	Amended and Restated Employment Agreement, dated as of November 8, 2004, between Vertex Pharmaceuticals Incorporated and Ian F. Smith.*		10-Q (Exhibit 10.13)	November 9, 2004	000-19319
10.37	Amendment No. 1 to Amended and Restated Employment Agreement between Ian F. Smith and Vertex Pharmaceuticals Incorporated, dated December 29, 2008.*		10-K (Exhibit 10.66)	February 17, 2009	000-19319
10.38	Employment Agreement, dated as of December 2, 2013, between Vertex Pharmaceuticals Incorporated and Jeffrey Chodakewicz.*		10-Q (Exhibit 10.1)	March 31, 2015	000-19319
10.39	Change of Control Agreement, dated as of December 2, 2013, between Vertex Pharmaceuticals Incorporated and Jeffrey Chodakewicz.*		10-Q (Exhibit 10.2)	March 31, 2015	000-19319
10.4	Form of Employee Non-Disclosure and Inventions Agreement.*		S-1 (Exhibit 10.4)	May 30, 1991	33-40966
10.41	Vertex Employee Compensation Plan.*	X			
10.42	Vertex Pharmaceuticals Non-Employee Board Compensation.*	X			
Subsidiaries					
21.1	Subsidiaries of Vertex Pharmaceuticals Incorporated.	X			
Consent					
23.1	Consent of Independent Registered Public Accounting Firm, Ernst & Young LLP.	X			
Certifications					
31.1	Certification of the Chief Executive Officer under Section 302 of the Sarbanes-Oxley Act of 2002.	X			
31.2	Certification of the Chief Financial Officer under Section 302 of the Sarbanes-Oxley Act of 2002.	X			
32.1	Certification of the Chief Executive Officer and the Chief Financial Officer under Section 906 of the Sarbanes-Oxley Act of 2002.	X			
101.INS	XBRL Instance	X			
101.SCH	XBRL Taxonomy Extension Schema	X			
101.CAL	XBRL Taxonomy Extension Calculation	X			
101.LAB	XBRL Taxonomy Extension Labels	X			
101.PRE	XBRL Taxonomy Extension Presentation	X			
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.

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 16, 2016 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 16, 2016
/s/ Ian F. Smith Ian F. Smith	Executive Vice President and Chief Financial Officer (Principal Financial Officer)	February 16, 2016
/s/ Paul M. Silva Paul M. Silva	Senior Vice President and Corporate Controller (Principal Accounting Officer)	February 16, 2016
/s/ Sangeeta N. Bhatia Sangeeta N. Bhatia	Director	February 16, 2016
/s/ Joshua S. Boger Joshua S. Boger	Director	February 16, 2016
/s/ Terrence C. Kearney Terrence C. Kearney	Director	February 16, 2016
/s/ Yuchun Lee Yuchun Lee	Director	February 16, 2016
/s/ Margaret G. McGlynn Margaret G. McGlynn	Director	February 16, 2016
/s/ Bruce I. Sachs Bruce I. Sachs	Director	February 16, 2016
/s/ Elaine S. Ullian Elaine S. Ullian	Director	February 16, 2016
/s/ William D. Young William D. Young	Director	February 16, 2016

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, 2015 and 2014 , 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, 2015 . 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, 2015 and 2014 , and the consolidated results of its operations and its cash flows for each of the three years in the period ended December 31, 2015 , 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, 2015 , based on the criteria established in Internal Control—Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework) and our report dated February 16, 2016 expressed an unqualified opinion thereon.

/s/ Ernst & Young LLP

Boston, Massachusetts

February 16, 2016

VERTEX PHARMACEUTICALS INCORPORATED

Consolidated Statements of Operations

(in thousands, except per share amounts)

	Year Ended December 31,		
	2015	**2014**	**2013**
Revenues:			
Product revenues, net	$ 1,000,324	$ 487,821	$ 837,645
Royalty revenues	23,959	40,919	156,592
Collaborative revenues	8,053	51,675	217,738
Total revenues	1,032,336	580,415	1,211,975
Costs and expenses:			
Cost of product revenues	117,151	39,725	88,979
Royalty expenses	7,361	21,262	41,298
Research and development expenses	995,922	855,506	882,097
Sales, general and administrative expenses	376,575	305,409	356,188
Restructuring expenses	2,206	50,925	40,521
Intangible asset impairment charges	—	—	412,900
Total costs and expenses	1,499,215	1,272,827	1,821,983
Loss from operations	(466,879)	(692,412)	(610,008)
Interest expense, net	(84,206)	(72,863)	(22,926)
Other (expense) income, net	(6,715)	30,400	6,890
Loss from continuing operations before provision for (benefit from) income taxes	(557,800)	(734,875)	(626,044)
Provision for (benefit from) income taxes	30,381	6,958	(122,422)
Loss from continuing operations	(588,181)	(741,833)	(503,622)
Loss from discontinued operations, net of tax benefit of $0, $0 and $(166,145), respectively	—	(912)	(183,928)
Net loss	(588,181)	(742,745)	(687,550)
Loss from discontinued operations attributable to noncontrolling interest	—	—	242,522
Loss attributable to noncontrolling interest	31,847	4,190	—
Net loss attributable to Vertex	$ (556,334)	$ (738,555)	$ (445,028)
Amounts attributable to Vertex:			
Loss from continuing operations	$ (556,334)	$ (737,643)	$ (503,622)
(Loss) income from discontinued operations	—	(912)	58,594
Net loss attributable to Vertex	$ (556,334)	$ (738,555)	$ (445,028)
Amounts per share attributable to Vertex common shareholders:			
Net loss from continuing operations:			
Basic	$ (2.31)	$ (3.14)	$ (2.24)
Diluted	$ (2.31)	$ (3.14)	$ (2.24)
Net (loss) income from discontinued operations:			
Basic	$ —	$ —	$ 0.26
Diluted	$ —	$ —	$ 0.26
Net loss:			
Basic	$ (2.31)	$ (3.14)	$ (1.98)
Diluted	$ (2.31)	$ (3.14)	$ (1.98)
Shares used in per share calculations:			
Basic	241,312	235,307	224,906
Diluted	241,312	235,307	224,906

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,		
	2015	**2014**	**2013**
Net loss	$ (588,181)	$ (742,745)	$ (687,550)
Changes in other comprehensive income (loss):			
Unrealized holding gains (losses) on marketable securities	249	(165)	(154)
Unrealized gains (losses) on foreign currency forward contracts, net of tax	1,767	2,034	(23)
Foreign currency translation adjustment	(1,109)	(646)	421
Total changes in other comprehensive income (loss)	907	1,223	244
Comprehensive loss	(587,274)	(741,522)	(687,306)
Comprehensive loss attributable to noncontrolling interest	31,847	4,190	—
Comprehensive loss attributable to Vertex	$ (555,427)	$ (737,332)	$ (687,306)

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,	
	2015	**2014**
Assets		
Current assets:		
Cash and cash equivalents	$ 714,768	$ 625,259
Marketable securities, available-for-sale	327,694	761,847
Restricted cash and cash equivalents (VIE)	78,910	8,418
Accounts receivable, net	177,639	75,964
Inventories	57,207	30,848
Prepaid expenses and other current assets	50,935	44,175
Total current assets	1,407,153	1,546,511
Property and equipment, net	697,715	715,812
Intangible assets	284,340	29,000
Goodwill	50,384	39,915
Note receivable	30,000	—
Restricted cash	22,083	176
Other assets	7,200	3,265
Total assets	$ 2,498,875	$ 2,334,679
Liabilities and Shareholders' Equity		
Current liabilities:		
Accounts payable	$ 74,942	$ 71,194
Accrued expenses	305,820	209,676
Deferred revenues, current portion	16,296	17,468
Accrued restructuring expense, current portion	7,894	33,107
Capital lease obligations, current portion	15,545	17,806
Senior secured term loan, current portion	71,478	14,206
Other liabilities, current portion	14,374	4,797
Total current liabilities	506,349	368,254
Deferred revenues, excluding current portion	9,714	27,808
Accrued restructuring expense, excluding current portion	7,464	12,748
Capital lease obligations, excluding current portion	42,923	39,293
Deferred tax liability	110,439	15,044
Construction financing lease obligation, excluding current portion	472,611	473,073
Senior secured term loan, excluding current portion	223,969	280,569
Other liabilities, excluding current portion	31,778	21,707
Total liabilities	1,405,247	1,238,496
Commitments and contingencies		
Shareholders' equity:		
Preferred stock, $0.01 par value; 1,000,000 shares authorized; none issued and outstanding at December 31, 2015 and 2014	—	—
Common stock, $0.01 par value; 500,000,000 and 300,000,000 shares authorized at December 31, 2015 and 2014, respectively; 246,306,818 and 241,764,398 shares issued and outstanding at December 31, 2015 and 2014, respectively	2,427	2,385
Additional paid-in capital	6,197,500	5,777,154
Accumulated other comprehensive income	1,824	917
Accumulated deficit	(5,261,784)	(4,705,450)
Total Vertex shareholders' equity	939,967	1,075,006
Noncontrolling interest	153,661	21,177
Total shareholders' equity	1,093,628	1,096,183
Total liabilities and shareholders' equity	$ 2,498,875	$ 2,334,679

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	Total Shareholders' Equity	Redeemable Noncontrolling Interest
	Shares	Amount							
Balance, December 31, 2012	217,287	$ 2,149	$ 4,519,448	$ (550)	$ (3,521,867)	$ 999,180	$ 196,672	$ 1,195,852	$ 38,530
Other comprehensive income, net of tax				244		244		244	
Net (loss) income					(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)	
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	$ —
Other comprehensive income, net of tax				1,223		1,223		1,223	
Net loss					(738,555)	(738,555)	(4,190)	(742,745)	
Issuance of common stock under benefit plans	7,975	65	274,743			274,808		274,808	
Stock-based compensation expense			178,965			178,965		178,965	
Tax benefit from equity compensation			2,160			2,160		2,160	
Noncontrolling interest upon consolidation						—	25,367	25,367	
Balance, December 31, 2014	241,764	$ 2,385	$ 5,777,154	$ 917	$ (4,705,450)	$ 1,075,006	$ 21,177	$ 1,096,183	$ —
Other comprehensive income, net of tax				907		907		907	
Net loss					(556,334)	(556,334)	(31,847)	(588,181)	
Issuance of common stock under benefit plans	4,543	42	185,234			185,276	14	185,290	
Stock-based compensation expense			235,112			235,112		235,112	
Noncontrolling interest upon consolidation							164,317	164,317	
Balance, December 31, 2015	246,307	$ 2,427	$ 6,197,500	$ 1,824	$ (5,261,784)	$ 939,967	$ 153,661	$ 1,093,628	$ —

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,		
	2015	**2014**	**2013**
Cash flows from operating activities:			
Net loss	$ (588,181)	$ (742,745)	$ (687,550)
Adjustments to reconcile net loss to net cash used in operating activities:			
Stock-based compensation expense	231,025	177,542	127,303
Depreciation and amortization expense	62,343	63,257	48,365
Deferred income taxes	3,283	281	(285,053)
Impairment of property and equipment	2,516	1,689	7,594
Excess tax benefit from share-based payment arrangements	—	(2,160)	1,252
Intangible asset impairment charges	—	—	663,500
Deconsolidation of variable interest entity	—	—	55,110
Write-downs of inventories to net realizable value	—	—	10,358
Other non-cash based compensation expense	—	—	5,860
Other non-cash items, net	9,532	—	6,742
Changes in operating assets and liabilities, excluding the effects of the acquisition and deconsolidation of variable interest entities:			
Accounts receivable, net	(104,847)	7,428	53,363
Inventories	(23,146)	(16,469)	7,142
Prepaid expenses and other assets	(9,260)	(15,771)	(12,061)
Accounts payable	(1,709)	25,048	(49,234)
Accrued expenses and other liabilities	102,746	(63,183)	34,629
Accrued restructuring expense	(30,492)	17,502	5,025
Deferred revenues	(19,242)	(25,531)	(53,011)
Net cash used in operating activities	(365,432)	(573,112)	(60,666)
Cash flows from investing activities:			
Maturities of marketable securities	1,067,443	1,557,938	2,348,295
Purchases of marketable securities	(633,041)	(1,424,172)	(2,412,418)
Payment for acquisition of variable interest entity	(80,000)	(10,000)	—
Expenditures for property and equipment	(45,302)	(51,201)	(51,393)
Investment in note receivable	(30,000)	—	—
(Increase) decrease in restricted cash and cash equivalents	(21,981)	—	31,804
Decrease in restricted cash and cash equivalents (VIE)	11,685	1,638	27,884
Decrease (increase) in other assets	52	(244)	1,698
Payments returned related to construction financing lease obligation	—	8,050	—
Payments on construction costs	—	—	(58,431)
Net cash provided by (used in) investing activities	268,856	82,009	(112,561)
Cash flows from financing activities:			
Issuances of common stock under benefit plans	185,592	274,615	265,878
Payments on construction financing lease obligation	(381)	(336)	—
Proceeds from lease financing	23,662	—	—
Payments on capital lease financing	(19,954)	(21,443)	(16,057)
Proceeds from senior secured term loan	—	294,243	—
Excess tax benefit from share-based payment arrangements	—	2,160	(1,252)
Payments to redeem secured notes	—	—	(158)
Net cash provided by financing activities	188,919	549,239	248,411
Effect of changes in exchange rates on cash	(2,834)	(2,176)	4,708
Net increase in cash and cash equivalents	89,509	55,960	79,892
Cash and cash equivalents—beginning of period	625,259	569,299	489,407
Cash and cash equivalents—end of period	$ 714,768	$ 625,259	$ 569,299

Supplemental disclosure of cash flow information:			
Cash paid for interest	$ 85,613	$ 68,963	$ 13,458
Cash paid for income taxes	$ 1,806	$ 1,210	$ 2,840
Non-cash investing and financing activities:			
Conversion of convertible senior subordinated notes (due 2015) for common stock	$ —	$ —	$ 399,842
Unamortized deferred debt issuance costs exchanged	$ —	$ —	$ 4,230
Capitalization of costs related to construction financing lease obligation	$ —	$ 25,564	$ 215,013
Assets acquired under capital lease obligations	$ —	$ 9,188	$ 50,972
Issuances of common stock exercises from employee benefit plans receivable	$ 361	$ 637	$ —

The Company has reclassified certain amounts in the years ended December 31, 2014 and 2013 between operating, investing, and financing to correct improper classifications.

The accompanying notes are an integral part of the 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 medicines for serious diseases. The Company uses precision medicine approaches with the goal of creating transformative medicines for patients in specialty markets. The Company is focused on developing and commercializing therapies for the treatment of cystic fibrosis ("CF") and advancing its research and development programs. The Company has marketed KALYDECO (ivacaftor) since it was approved in 2012 for the treatment of certain patients with CF. The Company began marketing ORKAMBI (lumacaftor in combination with ivacaftor) in the United States in 2015. In November 2015, the European Commission approved ORKAMBI, and the Company is seeking country-by-country reimbursement for ORKAMBI in Europe.

The Company's net loss attributable to Vertex for 2015 was $556.3 million , or $2.31 per share. As of December 31, 2015 , the Company had cash, cash equivalents and marketable securities of $1.04 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 ORKAMBI and 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, (ii) its wholly-owned subsidiaries and (iii) consolidated variable interest entities (VIEs). In addition, the consolidated financial statements reflect the operations of Alios BioPharma, Inc. ("Alios"), as well as direct expenses Vertex incurred as a result of the Alios Agreement, as discontinued operations. All material intercompany balances and transactions have been eliminated. The Company operates in one segment, pharmaceuticals. Please refer to Note T, "Segment Information," for enterprise-wide disclosures regarding the Company's revenues, major customers and long-lived assets by geographic area.

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, goodwill, contingent consideration, noncontrolling interest, the consolidation of VIEs and deconsolidation of a VIE, leases, the fair value of cash flow hedges and the provision for or benefit from income taxes. The Company bases its estimates on historical experience and various other assumptions, including in certain circumstances future projections, that management believes to be reasonable under the circumstances. Actual results could differ from those estimates. Changes in estimates are reflected in reported results in the period in which they become known.

Revenue Recognition

Product Revenues, Net

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

providers. The Company recognizes 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 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 and other third-party data regarding the payor mix for such product and (iv) historical experience.

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

Other Incentives: Other incentives that the Company offers include co-pay mitigation rebates provided by the Company to commercially insured patients who have coverage and who reside in states that permit co-pay mitigation programs. The Company's co-pay mitigation programs are intended to reduce each participating patient's portion of the financial responsibility for a product's purchase price to a specified dollar amount. Based upon the terms of the Company's co-pay mitigation programs, the Company estimates average co-pay mitigation amounts for each of its products in order to establish its accruals for co-pay mitigation rebates and deducts these estimated amounts from its gross product revenues at the later of the date (i) the revenues are recognized or (ii) the incentive is offered. The Company's co-pay mitigation rebates are subject to expiration.

The following table summarizes activity in each of the product revenue allowance and reserve categories for the three years ended December 31, 2015 :

	Trade Allowances	Rebates, Chargebacks and Discounts	Product Returns	Other Incentives	Total
			(in thousands)		
2015					
Beginning Balance	$ 1,463	$ 29,102	$ 4,713	$ 745	$ 36,023
Provision related to current period sales	10,890	65,781	779	3,755	81,205
Adjustments related to prior period sales	(214)	(19,410)	(993)	(235)	(20,852)
Credits/payments made	(10,050)	(30,804)	(3,271)	(2,955)	(47,080)
Ending Balance	$ 2,089	$ 44,669	$ 1,228	$ 1,310	$ 49,296
2014					
Beginning Balance	$ 1,535	$ 68,244	$ 15,799	$ 1,555	$ 87,133
Provision related to current period sales	8,468	35,713	2,478	1,347	48,006
Adjustments related to prior period sales	(43)	329	3,056	(72)	3,270
Credits/payments made	(8,497)	(75,184)	(16,620)	(2,085)	(102,386)
Ending Balance	$ 1,463	$ 29,102	$ 4,713	$ 745	$ 36,023
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

The Company adjusts its estimated rebates, chargebacks and discounts based on new information, including information regarding actual rebates, chargebacks and discounts for its products, as it becomes available. Claims by third-party payors for rebates, chargebacks and discounts frequently are submitted to the Company significantly after the related sales, potentially resulting in adjustments in the period in which the new information becomes known. In each of the periods presented, the Company's adjustments relating to prior period sales principally related to the Company's estimates for INCIVEK. During the fourth quarter of 2014, the Company withdrew INCIVEK from the market in the United States. At December 31, 2015 the Company maintains an accrual of less than $1 million for government rebates for INCIVEK.

Royalty Revenues

The Company's royalty revenues on commercial sales of INCIVO (telaprevir) by Janssen NV were based on net sales of licensed products in licensed territories as provided by Janssen NV. 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.

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

The Company evaluates amendments to its existing arrangements to determine whether they have been materially modified. In making its determination that an arrangement has been materially modified, the Company considers whether 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 evaluates the period of performance each reporting period and adjusts the period of performance on a prospective basis if there are changes to be made.

Milestone Payments: At the inception of each agreement that 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 is achieved if payment is reasonably assured. If a milestone is 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 determines whether the research and development funding would result in collaborative revenues or an offset to research and development expenses in accordance with the provisions of gross or net revenue presentation.

Concentration of Credit Risk

Financial instruments that potentially subject the Company to concentration of credit risk consist principally of money market funds and marketable securities. The Company places these investments with highly rated financial institutions, and, by policy, limits the amounts of credit exposure to any one financial institution. These amounts at times may exceed

federally insured limits. The Company also maintains a foreign currency hedging program that includes foreign currency forward contracts with several counterparties. The Company has not experienced any credit losses related to these financial instruments and does not believe it is exposed to any significant credit risk related to these instruments.

The Company also is subject to credit risk from its accounts receivable related to its product sales and collaborators. The Company evaluates the creditworthiness of each of its customers and has determined that all of its material customers are creditworthy. To date, the Company has not experienced significant losses with respect to the collection of its accounts receivable. The Company's receivables from Greece, Italy and Spain were not material at December 31, 2015, and the Company had no receivables from Portugal in 2015. The Company believes that its allowance for doubtful accounts was adequate at December 31, 2015 . Please refer to Note T, "Segment Information," for further information.

Cash and Cash Equivalents

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

Marketable Securities

The Company's marketable securities consist of investments in government-sponsored enterprise securities, corporate 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 income (loss), which is a separate component of shareholders' equity, until such gains and losses are realized. The fair value of these securities is based on quoted prices for identical or similar assets.

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

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

Accounts Receivable

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

Stock-based Compensation Expense

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

For awards with performance conditions that accelerate vesting of the award, 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. For awards with performance conditions in which the award does not vest unless the performance condition is met, the Company recognizes expense only if the Company estimates that achievement of the performance condition is probable. If the Company concludes that vesting is probable, it recognizes expense from the date it reaches this conclusion through the estimated vesting date.

Effective for equity awards granted on or after February 5, 2014, the Company provides to employees who have rendered a certain number of years' to the Company and meet certain age requirements, partial or full acceleration of vesting of these equity awards, subject to certain conditions including a notification period, upon a termination of employment other than for cause. Less than 5% of the Company's employees were eligible for partial or full acceleration of any of their equity awards as of December 31, 2015. The Company recognizes stock-based compensation expense related to these awards over a service period reflecting qualified employees eligibility for partial or full acceleration of vesting.

Research and Development Expenses

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

Research and development expenses are comprised of costs incurred by the Company in performing research and development activities, including salary and benefits; stock-based compensation expense; laboratory supplies and other direct expenses; outsourced services, including clinical trial and pharmaceutical development costs; 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 $24.5 million , $16.2 million and $19.6 million in 2015 , 2014 and 2013 , 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 shorter of the useful life of the

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

The Company capitalizes internal costs incurred to develop software for internal use during the application development stage. The Company expenses costs related to the planning and post-implementation phases of development of software for internal use as these costs are incurred. Maintenance and enhancement costs (including costs in the post-implementation stages) are expensed as incurred, unless such costs relate to substantial upgrades and enhancements to the software resulting in added functionality, in which case the costs are capitalized. Amortization of capitalized internally developed software costs is recorded in depreciation expense over the useful life of the related asset.

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

Capital Leases

The assets and liabilities associated with capital lease agreements are recorded at the present value of the minimum lease payments at the inception of the lease agreement. The assets are depreciated using the straight-line method over the shorter of the useful life of the related asset or the remaining life of the associated lease. Amortization of assets that the Company leases pursuant to a capital lease is included in depreciation expense. The Company performs an assessment of the fair value of the assets if indicators of impairment are identified during a reporting period and records the assets at the lower of the net book value or the fair value of the assets. Assets recorded under capital leases are recorded within "Property and equipment, net" and liabilities related to those assets are recorded within "Capital lease obligations, current portion" and "Capital lease obligations, excluding current portion" on the Company's consolidated balance sheets.

Income Taxes

Deferred tax assets and liabilities are recognized for the expected future tax consequences of temporary differences between the financial statement carrying amounts and the income tax bases of assets and liabilities. A valuation allowance is applied against any net deferred tax asset if, based on the available evidence, it is more likely than not that some or all of the deferred tax assets will not be realized.

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.

Assets recorded as a result of consolidating VIEs' financial condition into the Company's consolidated balance sheet do not represent additional assets that could be used to satisfy claims against the Company's general assets. The Company records the cash and cash equivalents of consolidated VIEs as restricted cash because the Company does not have control over the VIEs' cash and cash equivalents. The Company also has recorded the liabilities of its consolidated VIEs for which creditors do not have recourse to the Company's general assets outside of the VIE.

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, changes in the fair value of the contingent payments pursuant to collaborations accounted for as business combinations result in an increase or decrease in net income attributable to Vertex (or an increase or decrease 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 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.

Noncontrolling Interest

The Company records noncontrolling interest, which has historically related to consolidated VIEs, on its consolidated balance sheets. Noncontrolling interest is reflected on two separate lines if the consolidated VIE has both common shareholders and preferred shareholders that are entitled to redemption rights in certain circumstances. The Company records net loss (income) attributable to noncontrolling interest on its consolidated statements of operations, reflecting the VIEs' net loss (income) for the reporting period, adjusted for changes in the fair value of contingent milestone payments and royalties payable by the Company to the consolidated VIEs, which is evaluated each reporting period.

Deconsolidation and Discontinued Operations

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

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

Derivative Instruments, Embedded Derivatives and Hedging Activities

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

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 income (loss) as unrealized gains and losses until the forecasted underlying transaction occurs. Unrealized gains and losses on these foreign currency forward contracts are included in (i) "Prepaid expenses and other current assets" and (ii) "Other liabilities, current portion," respectively, on the Company's consolidated balance sheets. Realized gains and losses for the effective portion of such contracts are recognized in "Product revenues, net" in the consolidated statement of operations when the contract is settled with the counterparty. The Company classifies the cash flows from hedging instruments in the same category as the cash flows from the hedged items.

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

The Company assesses, both at inception and on an ongoing basis, whether the foreign currency forward contracts used in hedging transactions are highly effective in offsetting the changes in cash flows of the hedged items. The Company also assesses hedge ineffectiveness quarterly and, if determined to be ineffective, records the gain or loss related to the ineffective portion to earnings in "Other income (expense), net" in its 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 related to the cumulative translation adjustment, as the Company intends to permanently reinvest undistributed earnings in its foreign subsidiaries.

Foreign Currency Translation and Transactions

The Company primarily operates with entities that 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 income (loss), which is a separate component of shareholders' equity. Included in accumulated other comprehensive income (loss) are net unrealized losses related to foreign currency translation of $2.1 million , $1.0 million and $0.3 million at December 31, 2015 , 2014 , and 2013 , respectively. Net foreign currency exchange transaction gains or losses are included in "net loss" on the Company's consolidated statement of operations. Net transaction losses were $6.8 million and $6.4 million for 2015 and 2014 , respectively, and net transaction gains were $5.1 million in 2013 .

Net Loss Per Share Attributable to Vertex Common Shareholders

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

The Company utilizes income (loss) from continuing operations attributable to Vertex to determine whether potentially outstanding stock options and the assumed conversion of convertible notes are dilutive.

Recent Accounting Pronouncements

In 2014, the Financial Accounting Standards Board ("FASB") issued amended guidance applicable to revenue recognition that will be effective for the year ending December 31, 2018. Early adoption is permitted for the year-ending December 31, 2017. The new guidance applies a more principle based approach to recognizing revenue. The new guidance must be adopted using either a full retrospective approach for all periods presented or a modified retrospective approach. The Company is in the process of evaluating the new guidance and determining the expected effect on its consolidated financial statements.

In 2014, the FASB issued new guidance on management's responsibility in evaluating whether or not there is substantial doubt about a company's ability to continue as a going concern within one year from the date the financial statements are issued each reporting period. This new accounting guidance is effective for annual periods ending after December 15, 2016. Early adoption is permitted. The Company expects the new guidance will only effect the disclosures in its consolidated financial statements.

In 2014, the FASB issued amended guidance applicable to the presentation of financial statements and property, plant, and equipment. The amendment provides guidance for the recognition and disclosure of discontinued operations. The amendment is effective for the current fiscal year. The adoption of amended guidance did not have an effect on the Company's consolidated financial statements.

In 2015, the FASB issued amended guidance applicable to the presentation of income taxes. The amended guidance requires that all deferred tax assets and liabilities, along with any related valuation allowance, be classified as noncurrent on the balance sheet rather than being separated into current and noncurrent. This amendment represents a change in accounting principle and is effective for annual periods beginning after December 15, 2016 and interim period within those annual periods. Early adoption is permitted. The Company early adopted the amendment on a prospective basis and did not retrospectively adjust prior periods. As a result, all of the Company's deferred taxes are presented as long-term in the consolidated financial statements as of December 31, 2015.

B. Collaborative Arrangements

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 compound that targets the processing and trafficking defect of the F508del CFTR proteins discovered under the collaboration, and (ii) additional research and development activities directed at discovering new compounds targeting the processing and trafficking defect of the F508del protein.

Under the April 2011 Amendment, CFFT agreed to provide the Company with up to $75.0 million in funding over approximately five years for corrector-compound research and development activities. The Company retains the right to develop and commercialize KALYDECO (ivacaftor), ORKAMBI (lumacaftor in combination with ivacaftor), lumacaftor and VX-661. The Company recognized collaborative revenues from this collaboration of $6.5 million and $14.3 million in 2014 and 2013 , respectively. During 2015 , the Company recognized zero collaborative revenues from this collaboration.

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 first synthesized or tested during the research term that ended in 2008, including ivacaftor, lumacaftor and VX-661. The April 2011 Amendment provides for a tiered royalty in the same range on net sales of corrector compounds first synthesized or tested during the research term that ended in February 2014. In each of 2012 and 2013, CFFT earned a commercial milestone payment of $9.3 million from the Company upon achievement of certain sales levels for KALYDECO. There are no additional commercial milestone payments payable by the Company to CFFT related to sales levels for KALYDECO. In the fourth quarter of 2015, CFFT earned the first commercial milestone payment of $13.9 million from the Company upon achievement of certain sales levels of lumacaftor. The Company expects that in the first quarter of 2016, CFFT will earn the second and final commercial milestone of $13.9 million based upon achievement of certain sales levels of lumacaftor.

The Company began marketing KALYDECO in the United States and certain countries in the European Union in 2012 and began marketing ORKAMBI in the United States in 2015. The Company received approval for ORKAMBI in the European Union in 2015. The Company has royalty obligations to CFFT for ivacaftor, lumacaftor and VX-661 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 extensions. The Company has patents in the United States and European Union covering the composition-of-matter of lumacaftor that expire in 2030 and 2026, respectively, subject to potential extension. The Company has patents in the United States and European Union covering the composition-of-matter of VX-661 that expire in 2027 and 2028, respectively, subject to potential extension.

CRISPR Therapeutics AG

On October 26, 2015, the Company entered into a strategic collaboration, option and license agreement (the "CRISPR Agreement") with CRISPR Therapeutics AG and its affiliates ("CRISPR") to collaborate on the discovery and development of potential new treatments aimed at the underlying genetic causes of human diseases using CRISPR-Cas9 gene editing technology. The Company has the exclusive right to license up to six CRISPR-Cas9-based targets. In connection with the CRISPR Agreement, the Company made an upfront payment to CRISPR of $75.0 million and a $30.0 million investment in CRISPR pursuant to a convertible loan agreement that converted into preferred stock in January 2016. The Company expensed $75.0 million to research and development, and the $30.0 million investment was recorded at cost and is classified as a long-term asset on the Company's consolidated balance sheet.

The Company will fund all of the discovery activities conducted pursuant to the CRISPR Agreement. For potential hemoglobinapathy treatments, including treatments for sickle cell disease, the Company and CRISPR will share equally all research and development costs and worldwide revenues. For other targets that the Company elects to license, the Company would lead all development and global commercialization activities. For each of up to six targets that the Company elects to license, other than hemoglobinapathy targets, CRISPR has the potential to receive up to $420.0 million in development, regulatory and commercial milestones and royalties on net product sales.

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

Janssen Pharmaceutica NV

The Company has a collaboration agreement (the "Janssen HCV Agreement") with Janssen Pharmaceutica NV ("Janssen NV") for the development, manufacture and commercialization of telaprevir, which Janssen NV began marketing under the brand name INCIVO in certain of its territories in September 2011. Pursuant to the Janssen HCV Agreement, as amended, Janssen NV has a fully-paid license to manufacture and commercialize INCIVO in its territories including Europe, South America, the Middle East, Africa and Australia, subject to the payment of third-party royalties on net sales of INCIVO. In addition to the collaborative revenues, the Company recorded royalty revenues and corresponding royalty expenses related to third-party royalties that Janssen NV remains responsible for based on INCIVO net sales.

During the three years ended December 31, 2015 , the Company recognized the following revenues attributable to the Janssen HCV collaboration:

	2015	2014	2013
		(in thousands)	
Royalty revenues	$ 1,518	$ 13,481	$ 130,724
Collaborative revenues:			
Up-front and amendment payments revenues	$ —	$ —	$ 190,345
Net reimbursement for telaprevir development costs	1,946	7,104	2,793
Reimbursement for manufacturing services	—	—	10,299
Total collaborative revenues attributable to the Janssen HCV collaboration	$ 1,946	$ 7,104	$ 203,437
Total revenues attributable to the Janssen HCV collaboration	$ 3,464	$ 20,585	$ 334,161

Variable Interest Entities (VIE)

The Company has entered into several agreements pursuant to which it has licensed rights to certain drug candidates from third-party collaborators, which has resulted in the consolidation of the third parties' financial statements into the Company's consolidated financial statements as VIEs. In order to account for the fair value of the contingent milestone and royalty payments related to these collaborations under GAAP, the Company uses present-value models based on (i) assumptions regarding the probability of achieving the relevant milestones, (ii) estimates regarding the time to develop the drug candidates, (iii) estimates of future product sales and (iv) appropriate discount rates. The Company bases 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 represent a measure of credit risk and market risk associated with settling the liabilities. Significant judgment is used in determining the appropriateness of these assumptions at each reporting period. Changes in these assumptions could have a material effect on the fair value of the contingent milestone and royalty payments. The following collaborations are, or were previously, reflected in the Company's financial statements as consolidated VIEs:

Parion Sciences, Inc.

License and Collaboration Agreement

On June 4, 2015 , the Company entered into a strategic collaboration and license agreement (the "Parion Agreement") with Parion Sciences, Inc. ("Parion"). Pursuant to the agreement, the Company is collaborating with Parion to develop investigational epithelial sodium channel ("ENaC") inhibitors, including VX-371 (formerly P-1037) and VX-551 (formerly P-1055), for the potential treatment of CF and all other pulmonary diseases. The Company is leading development activities for VX-371 and VX-551 and is responsible for all costs, subject to certain exceptions, related to development and commercialization of the compounds.

Pursuant to the Parion Agreement, the Company has worldwide development and commercial rights to Parion's lead investigational ENaC inhibitors, VX-371 and VX-551, for the potential treatment of CF and all other pulmonary diseases and has the option to select additional compounds discovered in Parion's research program. Parion received an $80.0 million up-front payment and has the potential to receive up to an additional (i) $490.0 million in development and regulatory milestone payments for development of ENaC inhibitors in CF, including $360.0 million related to global filing and approval milestones, (ii) $370.0 million in development and regulatory milestones for VX-371 and VX-551 in non-CF pulmonary indications and (iii) $230.0 million in development and regulatory milestones should the Company elect to develop an additional ENaC inhibitor from Parion's research program. The Company has agreed to pay Parion tiered royalties that range from the low double digits to mid-teens as a percentage of potential sales of licensed products.

The Company may terminate the Parion Agreement upon 90 days' notice to Parion prior to any licensed product receiving marketing approval or upon 180 days' notice after a licensed product has received marketing approval. If the Company experiences a change of control prior to the initiation of the first Phase 3 clinical trial for a licensed product, Parion may terminate the Parion Agreement upon 30 days' notice, subject to the Company's right to receive specified royalties on

any subsequent commercialization of licensed products. The Parion Agreement also may be terminated by either party for a material breach by the other, subject to notice and cure provisions. Unless earlier terminated, the Parion Agreement will continue in effect until the expiration of the Company's royalty obligations, which expire on a country-by-country basis on the later of (i) the date the last-to-expire patent covering a licensed product expires or (ii) ten years after the first commercial sale in the country.

The Company determined that Parion is a VIE based on, among other factors, the significance to Parion of the ENaC inhibitors licensed to the Company pursuant to the Parion Agreement and on the Company's power to direct the activities that most significantly affect the economic performance of Parion. Accordingly, the Company consolidated Parion's financial statements beginning on June 4, 2015 . However, the Company's interests in Parion are limited to those accorded to the Company in the Parion Agreement. In particular, the Company did not acquire any equity interest in Parion, any interest in Parion's cash and cash equivalents or any control over Parion's activities that do not relate to the Parion Agreement.

Consideration for the Parion Agreement

The Company determined that the fair value of the consideration from the Company to Parion was $255.3 million as of June 4, 2015 , which consisted of (i) an $80.0 million up-front payment, (ii) the estimated fair value of the contingent research and development milestones potentially payable by the Company to Parion and (iii) the estimated fair value of potential royalty payments payable by the Company to Parion. The critical assumptions in the valuation model included probability and timing of making payments and the discount rate. The Company valued the contingent milestone and royalty payments using (a) discount rates ranging from 4.1% to 5.9% for the development milestones and (b) a discount rate of 6.6% for royalties. The consideration paid and the fair value of the contingent milestone and royalty payments payable by the Company pursuant to the Parion Agreement are set forth in the table below:

	June 4, 2015
	(in thousands)
Up-front payment	$ 80,000
Fair value of contingent milestone and royalty payments	175,340
Total	$ 255,340

Allocation of Assets and Liabilities

For the purposes of the consolidated balance sheet at June 4, 2015 , the Company allocated the total consideration, which is comprised of the up-front payment and the fair value of the contingent milestone and royalty payments, intangible assets, goodwill, deferred tax liability, net and net other assets and liabilities. The operations of Parion did not have a material effect on the consolidated financial statements of the Company and therefore no pro forma information is provided.

The Company recorded $255.3 million of intangible assets on the Company's consolidated balance sheet for Parion's in-process research and development assets. These in-process research and development assets relate to Parion's pulmonary ENaC platform, including the intellectual property related to VX-371 and VX-551, that are licensed by Parion to the Company. The difference between the fair value of the consideration and the fair value of Parion's assets (including the fair value of intangible assets) and liabilities was allocated to goodwill.

The following table summarizes the fair values of the assets and liabilities recorded on the effective date of the Parion Agreement:

	June 4, 2015
	(in thousands)
Intangible assets	$ 255,340
Goodwill	10,468
Deferred tax liability	(91,023)
Net other assets (liabilities)	(10,468)
Net assets attributable to noncontrolling interests	$ 164,317

BioAxone Biosciences, Inc.

In October 2014, the Company entered into a license and collaboration agreement (the "BioAxone Agreement") with BioAxone Biosciences, Inc. ("BioAxone"), which resulted in the consolidation of BioAxone as a VIE beginning on October 1, 2014. The Company determined that BioAxone is a VIE based on, among other factors, the significance to BioAxone of VX-210, which was licensed to the Company pursuant to the BioAxone Agreement, and on the Company's power to direct the activities that most significantly affect the economic performance of BioAxone. Accordingly, the Company consolidated BioAxone's financial statements beginning in October 2014. The Company paid BioAxone initial payments of $10.0 million in the fourth quarter of 2014.

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

Alios BioPharma, Inc.

In 2011, the Company entered into a license and collaboration agreement (the "Alios Agreement") with Alios BioPharma, Inc. ("Alios"), which was a privately-held biotechnology company, which resulted in the consolidation of Alios as a VIE through December 31, 2013. Pursuant to the Alios Agreement, the Company and Alios collaborated on the research, development and commercialization of HCV nucleotide analogues discovered by Alios through April 2014. In December 2014, the Alios Agreement terminated in accordance with its terms pursuant to a termination notice delivered by the Company in October 2014. As of September 30, 2014, the Company concluded that it no longer had significant continuing involvement with Alios due to its intent and ability to terminate the Alios Agreement, among other factors; therefore, the operations of Alios are presented as discontinued operations in these consolidated financial statements.

Aggregate VIE Financial Information

An aggregate summary of net loss attributable to noncontrolling interest related to the Company's VIEs for the three years ended December 31, 2015 was as follows:

	2015	2014	2013
		(in thousands)	
Loss attributable to noncontrolling interest before provision for income taxes	$ 6,646	$ 764	$ 283,747
Provision for (benefit from) income taxes	29,731	3,876	(166,145)
(Increase) decrease in fair value of contingent milestone and royalty payments	(4,530)	(450)	124,920
Net loss attributable to noncontrolling interest	$ 31,847	$ 4,190	$ 242,522

During the years ended December 31, 2015 and 2014 , the fair value of the contingent milestone and royalty payments related to the BioAxone Agreement increased by $0.9 million and $0.5 million , respectively. During the year ended December 31, 2015 , the fair value of the contingent milestone and royalty payments related to the Parion Agreement increased by $3.6 million . The changes in the fair value of the contingent milestone and royalty payments were primarily due to the changes in market interest rates and the time value of money. As of December 31, 2015 and 2014 , the fair value of the contingent milestone and royalty payments related to the BioAxone Agreement was $28.0 million and $27.1 million , respectively. As of December 31, 2015 , the fair value of the contingent milestone and royalty payments related to the the Parion Agreement was $179.0 million .

The following table summarizes items related to the Company's VIEs included in the Company's consolidated balance sheets as of the dates set forth in the table:

	December 31, 2015	December 31, 2014
	(in thousands)	
Restricted cash and cash equivalents (VIE)	$ 78,910	$ 8,418
Prepaid expenses and other current assets	3,138	268
Intangible assets	284,340	29,000
Goodwill	19,391	8,923
Other assets	455	42
Accounts payable	676	189
Taxes payable	24,554	3,594
Other current liabilities	7,100	297
Deferred tax liability, net	110,438	11,544
Other liabilities	300	300
Noncontrolling interest	153,661	21,177

The Company has recorded the VIEs' cash and cash equivalents as restricted cash and cash equivalents (VIE) because (i) the Company does not have any interest in or control over the VIEs' cash and cash equivalents and (ii) the Company's agreements with each VIE do not provide for the VIEs' cash and cash equivalents to be used for the development of the assets that the Company licensed from the applicable VIE. Assets recorded as a result of consolidating the Company's VIEs' financial condition into the Company's balance sheets do not represent additional assets that could be used to satisfy claims against the Company's general assets.

Outlicense Arrangements

In the ordinary course of the Company's business, the Company has entered into various agreements pursuant to which it has outlicensed rights to certain drug candidates to third-party collaborators. Although the Company does not consider any of these outlicense arrangements to be material, the most notable of these outlicense arrangements is described below. Pursuant to these outlicense arrangements, the Company's collaborators become responsible for all costs related to the continued development of such drug candidates. Depending on the terms of the arrangements, the Company's collaborators may be required to make upfront payments, milestone payments upon the achievement of certain product research and development objectives and/or pay royalties on future sales, if any, of commercial products resulting from the collaboration.

Janssen Pharmaceuticals, Inc.

In June 2014, the Company entered into an agreement (the "Janssen Influenza Agreement") with Janssen Pharmaceuticals, Inc. ("Janssen Inc."), which was amended in October 2014 to clarify certain roles and responsibilities of the parties.

Pursuant to the Janssen Influenza Agreement, Janssen Inc. has an exclusive worldwide license to develop and commercialize certain drug candidates for the treatment of influenza, including VX-787. The Company received non-refundable payments of $35.0 million from Janssen Inc. in 2014, which were recorded as collaborative revenues. The

Company has the potential to receive development, regulatory and commercial milestone payments as well as royalties on future product sales, if any.

Janssen Inc. is responsible for costs related to the development and commercialization of the compounds. The Company recorded reimbursement for these development activities of $22.8 million and $9.1 million in 2015 and 2014 , respectively. The reimbursements are recorded as a reduction to development expense in the Company's consolidated statements of operations primarily due to the fact that Janssen Inc. directs the activities and selects the suppliers associated with these activities. Janssen Inc. may terminate the Janssen Influenza Agreement, subject to certain exceptions, upon six months' notice.

C. Earnings Per Share

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 and restricted stock units that have been issued but are 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.

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

	2015	2014	2013
		(in thousands)	
Stock options	11,145	12,003	15,729
Unvested restricted stock and restricted stock units	3,024	3,091	2,165

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.

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, 2015 , 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, 2015 , 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. The fair value of the Company's foreign currency forward contracts was based on Level 2 inputs using third party pricing services. During 2015 , 2014 and 2013 , 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 (excluding VIE cash and cash equivalents) subject to fair value measurements:

	Fair Value Measurements as of December 31, 2015			
		Fair Value Hierarchy		
	Total	Level 1	Level 2	Level 3
	(in thousands)			
Financial instruments carried at fair value (asset position):				
Cash equivalents:				
Money market funds	$ 199,507	$ 199,507	$ —	$ —
Government-sponsored enterprise securities	85,994	85,994	—	—
Commercial paper	34,889	—	34,889	—
Corporate debt securities	11,533	—	11,533	—
Marketable securities:				
Government-sponsored enterprise securities	87,162	87,162	—	—
Commercial paper	141,409	—	141,409	—
Corporate debt securities	99,123	—	99,123	—
Prepaid and other current assets:				
Foreign currency forward contracts	5,161	—	5,161	—
Other assets:				
Foreign currency forward contracts	605	$ —	605	$ —
Total financial assets	$ 665,383	$ 372,663	$ 292,720	$ —
Financial instruments carried at fair value (liability position):				
Other liabilities, current portion:				
Foreign currency forward contracts	$ (769)	$ —	$ (769)	$ —
Other liabilities, excluding current portion:				
Foreign currency forward contracts	(132)	—	(132)	—
Total financial liabilities	$ (901)	$ —	$ (901)	$ —

	Fair Value Measurements as of December 31, 2014			
		Fair Value Hierarchy		
	Total	Level 1	Level 2	Level 3
	(in thousands)			
Financial instruments carried at fair value (asset position):				
Cash equivalents:				
Money market funds	$ 290,531	$ 290,531	$ —	$ —
Marketable securities:				
Government-sponsored enterprise securities	463,750	463,750	—	—
Commercial paper	51,746	—	51,746	—
Corporate debt securities	246,351	—	246,351	—
Prepaid and other current assets:				
Foreign currency forward contracts	2,011	—	2,011	—
Total	$ 1,054,389	$ 754,281	$ 300,108	$ —

VIEs had cash equivalents of $75.1 million as of December 31, 2015 that consisted of money market funds, which are valued based on Level 1 inputs. The Company's noncontrolling interest includes the fair value of the contingent payments, which are valued based on Level 3 inputs. Please refer to Note B, "Collaborative Arrangements," for further information.

As of December 31, 2015 , the fair value and carrying value of the Company's Term Loan was $295.4 million . The fair value of the Company's Term Loan was estimated based on Level 3 inputs computed using the effective interest rate of the Term Loan. The effective interest rate considers the timing and amount of estimated future interest payments as well as current market rates. Please refer to Note L, "Long Term Obligations," for further information regarding the Company's Term Loan.

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, 2015				
Cash and cash equivalents:				
Cash and money market funds	$ 582,352	$ —	$ —	$ 582,352
Government-sponsored enterprise securities	85,994	—	—	85,994
Commercial paper	34,889	—	—	34,889
Corporate debt securities	11,533	—	—	11,533
Total cash and cash equivalents	$ 714,768	$ —	$ —	$ 714,768
Marketable securities:				
Government-sponsored enterprise securities (due within 1 year)	$ 87,176	$ —	$ (14)	$ 87,162
Commercial paper (due within 1 year)	98,877	246	—	99,123
Corporate debt securities (due within 1 year)	141,515	—	(106)	141,409
Total marketable securities	327,568	246	(120)	327,694
Total cash, cash equivalents and marketable securities	$ 1,042,336	$ 246	$ (120)	$ 1,042,462
December 31, 2014				
Cash and cash equivalents:				
Cash and money market funds	$ 625,259	$ —	$ —	$ 625,259
Total cash and cash equivalents	$ 625,259	$ —	$ —	$ 625,259
Marketable securities:				
Government-sponsored enterprise securities (due within 1 year)	$ 463,788	$ 14	$ (52)	$ 463,750
Commercial paper (due within 1 year)	51,674	72	—	51,746
Corporate debt securities (due within 1 year)	196,065	2	(66)	196,001
Corporate debt securities (due after 1 year through 5 years)	50,443	—	(93)	50,350
Total marketable securities	761,970	88	(211)	761,847
Total cash, cash equivalents and marketable securities	$ 1,387,229	$ 88	$ (211)	$ 1,387,106

The Company has a limited number of marketable securities in insignificant loss positions as of December 31, 2015 , which the Company does not intend to sell and has concluded it will not be required to sell before recovery of the amortized costs for the investment at maturity. There were no charges recorded for other-than-temporary declines in fair value of marketable securities nor gross realized gains or losses recognized in 2015 , 2014 or 2013 .

F. Accumulated Other Comprehensive Income

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

	Foreign currency translation adjustment	Unrealized holding gains (losses) on marketable securities	Unrealized (losses) gains on foreign currency forward contracts, net of tax	Total
	(in thousands)			
Balance at December 31, 2012	$ (746)	$ 196	$ —	$ (550)
Other comprehensive (loss) income before reclassifications	421	(154)	(23)	244
Amounts reclassified from accumulated other comprehensive loss	—	—	—	—
Net current period other comprehensive (loss) income	421	(154)	(23)	244
Balance at December 31, 2013	$ (325)	$ 42	$ (23)	$ (306)
Other comprehensive (loss) income before reclassifications	(646)	(165)	3,591	2,780
Amounts reclassified from accumulated other comprehensive loss	—	—	(1,557)	(1,557)
Net current period other comprehensive (loss) income	(646)	(165)	2,034	1,223
Balance at December 31, 2014	$ (971)	$ (123)	$ 2,011	$ 917
Other comprehensive (loss) income before reclassifications	(1,109)	249	6,493	5,633
Amounts reclassified from accumulated other comprehensive loss	—	—	(4,726)	(4,726)
Net current period other comprehensive (loss) income	(1,109)	249	1,767	907
Balance at December 31, 2015	$ (2,080)	$ 126	$ 3,778	$ 1,824

G. Hedging

The Company maintains a hedging program intended to mitigate the effect of changes in foreign exchange rates for a portion of the Company's forecasted product revenues denominated in certain foreign currencies. The program includes foreign currency forward contracts that are designated as cash flow hedges under GAAP having contractual durations from one to eighteen months.

The Company formally documents the relationship between foreign currency forward contracts (hedging instruments) and forecasted product revenues (hedged items), as well as the Company's risk management objective and strategy for undertaking various hedging activities, which includes matching all foreign currency forward contracts that are designated as cash flow hedges to forecasted transactions. The Company also formally assesses, both at the hedge's inception and on an ongoing basis, whether the foreign currency forward contracts are highly effective in offsetting changes in cash flows of hedged items on a prospective and retrospective basis. If the Company determines that a (i) foreign currency forward contract is not highly effective as a cash flow hedge, (ii) foreign currency forward contract has ceased to be a highly effective hedge or (iii) forecasted transaction is no longer probable of occurring, the Company would discontinue hedge accounting treatment prospectively. The Company measures effectiveness based on the change in fair value of the forward contracts and the fair value of the hypothetical foreign currency forward contracts with terms that match the critical terms of the risk being hedged. As of December 31, 2015 , all hedges were determined to be highly effective and the Company had not recorded any ineffectiveness related to the hedging program.

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

Foreign Currency	As of December 31, 2015	As of December 31, 2014
	(in thousands)	
Euro	$ 103,362	$ 20,209
British pound sterling	78,756	13,515
Australian dollar	27,167	—
Total foreign currency forward contracts	$ 209,285	$ 33,724

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

As of December 31, 2015			
Assets		Liabilities	
Classification	Fair Value	Classification	Fair Value
	(in thousands)		
Prepaid and other current assets	$ 5,161	Other liabilities, current portion	$ (769)
Other assets	605	Other liabilities, excluding current portion	(132)
Total assets	$ 5,766	Total liabilities	$ (901)

As of December 31, 2014			
Assets		Liabilities	
Classification	Fair Value	Classification	Fair Value
	(in thousands)		
Prepaid and other current assets	$ 2,011	Other liabilities, current portion	$ —
Total assets	$ 2,011	Total liabilities	$ —

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

	As of December 31, 2015				
	Gross Amounts Recognized	Gross Amounts Offset	Gross Amount Presented	Gross Amount Not Offset	Legal Offset
Foreign currency forward contracts			(in thousands)		
Total assets	$ 5,766	$ —	$ 5,766	$ (901)	$ 4,865
Total liabilities	$ (901)	$ —	$ (901)	$ 901	$ —

	As of December 31, 2014				
	Gross Amounts Recognized	Gross Amounts Offset	Gross Amount Presented	Gross Amount Not Offset	Legal Offset
Foreign currency forward contracts			(in thousands)		
Total assets	$ 2,011	$ —	$ 2,011	$ —	$ 2,011

H. Inventories

Inventories consisted of the following:

	As of December 31,	
	2015	2014
	(in thousands)	
Raw materials	$ 8,696	$ 8,506
Work-in-process	40,695	20,508
Finished goods	7,816	1,834
Total	$ 57,207	$ 30,848

The Company did not record any write-offs for excess and obsolete inventories during the years ended December 31, 2015 and 2014 . In 2013 , the Company recorded within cost of product revenues $10.4 million of write-offs for excess and obsolete inventories. The write-offs for excess and obsolete inventories of $10.4 million affected the net loss attributable to Vertex per share, net of tax, by $0.05 , in 2013 .

I. Property and Equipment

Property and equipment, net consisted of the following:

	As of December 31,	
	2015	2014
	(in thousands)	
Buildings	$ 531,627	$ 531,642
Furniture and equipment	218,623	202,846
Software	124,469	113,875
Leasehold improvements	106,768	99,942
Computers	52,295	45,893
Total property and equipment, gross	1,033,782	994,198
Less: accumulated depreciation	(336,067)	(278,386)
Total property and equipment, net	$ 697,715	$ 715,812

Total property and equipment, gross, as of December 31, 2015 and 2014 , included $106.8 million and $85.6 million , respectively, for property and equipment recorded under capital leases. Accumulated depreciation, as of December 31, 2015 and 2014 , included $30.4 million and $13.1 million , respectively, for property and equipment recorded under capital leases.

As of December 31, 2015 , included in property and equipment, net were $15.4 million and $4.1 million in capitalized internally developed software costs and related amortization, respectively. As of December 31, 2014 , included in property and equipment, net were $11.2 million and $1.2 million in capitalized internally developed software costs and related amortization, respectively.

The Company recorded depreciation expense of $60.0 million , $62.3 million and $47.3 million in 2015 , 2014 and 2013 , respectively.

In 2014, in connection with the relocation of the Company’s headquarters in Massachusetts from Cambridge to Boston, the Company wrote off certain leasehold improvements that were fully depreciated and no longer utilized. There was no effect on the Company’s net property and equipment at the time of the write off because the Company had previously adjusted the useful lives of these assets to coincide with its relocation when it concluded that the relocation was probable.

J. Intangible Assets and Goodwill

Intangible Assets

As of December 31, 2015 , in-process research and development intangible assets of $284.3 million were recorded on the Company's consolidated balance sheet. The increase of $255.3 million as compared to the $29.0 million recorded as of December 31, 2014 is due to the Company's collaboration with Parion.

In June 2015, in connection with entering into the Parion Agreement, the Company recorded an in-process research and development intangible asset of $255.3 million based on the Company's estimate of the fair value of Parion's lead investigational ENaC inhibitors, including VX-371 and VX-551, that were licensed by the Company from Parion. The Company aggregated the fair value of the ENaC inhibitors into a single intangible asset because the phase, nature and risks of development as well as the amount and timing of benefits associated with the assets were similar. In October 2014, the Company recorded $29.0 million of an in-process research and development intangible asset on its consolidated balance sheet based on the Company's estimate of the fair value of VX-210, a drug candidate for patients who have spinal cord injuries that is licensed from BioAxone by the Company. The Company used discount rates of 7.1% and 7.5% in the present-value models to estimate the fair values of the ENaC inhibitors and VX-210 intangible assets, respectively. The Company also conducted an evaluation of Parion and BioAxone's other programs at the effective date of the Parion Agreement and BioAxone Agreement, respectively, and determined that market participants would not have ascribed value to those programs because of the stage of development of the assets in each program and uncertainties related to the potential development and commercialization of the programs.

In 2013, the Company determined that there were indicators that the value of the VX-222 intangible asset acquired from ViroChem in 2010 of $412.9 million reflected on its consolidated balance sheet had become impaired. 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 based on, among other things, additional data regarding VX-222 and compounds being developed by other competitors. 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.

Goodwill

As of December 31, 2015 , goodwill of $50.4 million was recorded on the Company's consolidated balance sheet. The Company allocated $10.5 million to goodwill related to the Parion collaboration during the year ended December 31, 2015 . None of the goodwill related to the Parion collaboration is expected to be deductible for income tax purposes. As of December 31, 2014 , $39.9 million was recorded on the Company's consolidated balance sheet.

K. Additional Balance Sheet Detail

Prepaid and other current assets consisted of the following:

	As of December 31,	
	2015	2014
	(in thousands)	
Prepaid expenses	$ 22,058	$ 17,569
Taxes receivable	11,651	14,093
Deferred tax asset	—	3,500
Fair value foreign currency forward contracts	5,161	2,011
Other	12,065	7,002
Total	$ 50,935	$ 44,175

Accrued expenses consisted of the following:

	As of December 31,	
	2015	2014
	(in thousands)	
Payroll and benefits	$ 87,873	$ 91,175
Research, development and commercial contract costs	55,677	38,143
Product revenue allowances	47,209	34,554
Royalty payable	60,191	12,218
Taxes payable and reserves (including VIE taxes payable)	30,953	10,038
Professional fees	7,455	7,004
Interest	4,642	5,444
Other	11,820	11,100
Total	$ 305,820	$ 209,676

Other liabilities, current portion consisted of the following:

	As of December 31,	
	2015	2014
	(in thousands)	
Deferred rent	$ 1,572	$ 4,015
Security deposits	4,000	—
Other liabilities attributable to variable interest entities	7,100	297
Other	1,702	485
Total	$ 14,374	$ 4,797

L. Long Term Obligations

Fan Pier Leases

In 2011, the Company entered into two lease agreements, pursuant to which the Company leases approximately 1.1 million square feet of office and laboratory space in two buildings (the "Buildings") at Fan Pier in Boston, Massachusetts (the "Fan Pier Leases"). The Company commenced lease payments in December 2013, and will make lease payments pursuant to the Fan Pier Leases through December 2028. The Company has an option to extend the term of the Fan Pier Leases for an additional 10 years.

Because the Company was involved in the construction project, the Company was deemed for accounting purposes to be the owner of the Buildings during the construction period and recorded project construction costs incurred by the landlord. Upon completion of the Buildings, the Company evaluated the Fan Pier Leases and determined that the Fan Pier Leases did

not meet the criteria for "sale-leaseback" treatment. Accordingly, the Company began depreciating the asset and incurring interest expense related to the financing obligation in 2013. The Company bifurcates its lease payments pursuant to the Fan Pier Leases into (i) a portion that is allocated to the Buildings and (ii) a portion that is allocated to the land on which the Buildings were constructed. The portion of the lease obligations allocated to the land is treated as an operating lease that commenced in 2011. The Company recorded interest expense of $60.2 million in each of 2015 and 2014 and of $12.4 million in 2013 . The Company recorded depreciation expense of $13.3 million , $13.4 million and $2.6 million in 2015 , 2014 and 2013 , respectively. In each of 2015 , 2014 and 2013 , the Company recorded rent expense of $6.5 million .

Property and equipment, net, included $502.3 million and $515.0 million as of December 31, 2015 and 2014 , respectively, related to construction costs for the Buildings. The carrying value of the construction financing lease obligation related to the Buildings, which excludes interest that will be imputed over the course of the Company's lease agreement for the Buildings, was $473.0 million and $473.4 million , as of December 31, 2015 and 2014 , respectively.

San Diego Lease

On December 2, 2015, the Company entered into a lease agreement for 3215 Merryfield Row, San Diego, California with ARE-SD Region No. 23, LLC. Pursuant to this agreement, the Company agreed to lease approximately 170,000 square feet of office and laboratory space in a building to be built in San Diego, California. The lease will commence upon completion of the building, scheduled for the second half of 2017, and will extend for 16 years from the commencement date. Pursuant to the lease agreement, during the initial 16-year term, the Company will pay an average of approximately $10.2 million per year in aggregate rent, exclusive of operating expenses. The Company has the option to extend the lease term for up to two additional five -year terms.

Term Loan

On July 9, 2014, the Company entered into a credit agreement with the lenders party thereto, and Macquarie US Trading LLC ("Macquarie"), as administrative agent. The credit agreement provides for a $300.0 million senior secured term loan ("Term Loan"). The credit agreement also provides that, subject to satisfaction of certain conditions, the Company may request that the lenders establish an incremental senior secured term loan facility in an aggregate amount not to exceed $200.0 million .

The Term Loan initially bore interest at a rate of 7.2% per annum, which was reduced to 6.2% per annum based on the FDA's approval of ORKAMBI. The Term Loan will bear interest at a rate of LIBOR plus 5.0% per annum during the third year of the term.

The maturity date of all loans under the facilities is July 9, 2017. Interest is payable quarterly and on the maturity date. In October 2015, the Company amended the terms of the credit agreement to provide for, among other things, a modification to the repayment schedule of the loan. As amended, the Company is required to repay principal on the Term Loan in quarterly installments of $75 million from October 1, 2016 through the maturity date.

The Company may prepay the Term Loan, in whole or in part, at any time; provided that prepayments prior to the July 9, 2016 are subject to a make-whole premium to ensure Macquarie receives approximately the present value of two years of interest payments over the life of the loan. The Company accounted for the amendment as a debt modification, as opposed to an extinguishment of debt, based on an insignificant change to the present value of the future cash flows relating to the credit agreement.

The Company's obligations under the Term Loan are unconditionally guaranteed by certain of its domestic subsidiaries. All obligations under the Term Loan, and the guarantees of those obligations, are secured, subject to certain exceptions, by substantially all of the Company's assets and the assets of all guarantors, including the pledge of all or a portion of the equity interests of certain of its subsidiaries.

The credit agreement requires that the Company maintain, on a quarterly basis, a minimum level of KALYDECO net revenues. Further, the credit agreement includes negative covenants, subject to exceptions, restricting or limiting the Company's ability and the ability of its subsidiaries to, among other things, incur additional indebtedness, grant liens, engage in certain investment, acquisition and disposition transactions, pay dividends, repurchase capital stock and enter into

transactions with affiliates. The credit agreement also contains customary representations and warranties, affirmative covenants and events of default, including payment defaults, breach of representations and warranties, covenant defaults and cross defaults. If an event of default occurs, the administrative agent would be entitled to take various actions, including the acceleration of amounts due under outstanding loans. There have been no events of default as of or during the period ended December 31, 2015 .

Based on the Company's evaluation of the Term Loan, the Company determined that the Term Loan contains several embedded derivatives. These embedded derivatives are clearly and closely related to the host instrument because they relate to the Company's credit risk; therefore, they do not require bifurcation from the host instrument, the Term Loan.

The Company incurred $5.3 million in fees paid to Macquarie that were recorded as a discount on the Term Loan and that are being recorded as additional interest expense using the effective interest method over the term of the loan in the Company's consolidated statements of operations. As of December 31, 2015 and 2014 , the unamortized discount associated with the Term Loan that was included in the senior secured term loan caption on the Company's consolidated balance sheets was $4.6 million and $5.2 million , respectively.

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.

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

During 2015, the Company's shareholders approved an amendment to the Company's Restated Articles of Organization increasing the number of authorized shares of common stock from 300,000,000 to 500,000,000 . 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, 2015 and 2014 , 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, 2015	
Title of Plan	**Group Eligible**	**Type of Award Granted**	**Awards Outstanding**	**Additional Awards Authorized for Grant**
2013 Stock and Option Plan	Employees, Non-employee Directors and Consultants	NSO, RS and RSU	5,851,040	14,124,989
2006 Stock and Option Plan	Employees, Non-employee Directors and Consultants	NSO, RS and RSU	8,274,211	—
1996 Stock and Option Plan	Employees, Non-employee Directors, Advisors and Consultants	NSO	43,664	—
		Total	14,168,915	14,124,989

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, 2015 , the stock and option plan under which the Company makes new equity awards is the Company's 2013 Plan. Under the 2013 Plan, no stock options can be awarded with an exercise price less than the fair market value on the date of grant. The Company's shareholders (i) approved an increase in the number of shares authorized for issuance pursuant to the 2013 Plan of 7,800,000 shares, plus the number of shares that remained available for issuance under the Company's 2006 Stock and Option Plan, which rolled-over into the 2013 Stock and Option Plan in 2015, (ii) approved an increase in the number of shares authorized for issuance pursuant to the 2013 Plan of 9,500,000 shares in 2014 and (iii) authorized 3,300,000 shares for issuance pursuant to the 2013 Plan in 2013.

During the three years ended December 31, 2015 , grants to current employees and directors primarily had a grant date that was the same as the date the award was approved by the Company's Board of Directors. During the three years ended December 31, 2015 , for grants to new employees and directors, the date of grant for awards was the employee's first day of employment or the date the director was elected to the Company's Board of Directors. All options awarded under the Company's stock and option plans expire not more than 10 years from the grant date.

During the three years ended December 31, 2015 , 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 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, 2015 :

	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, 2014	12,003	$ 56.81		
Granted	3,531	$ 119.09		
Exercised	(3,289)	$ 50.34		
Forfeited	(1,100)	$ 81.77		
Outstanding at December 31, 2015	11,145	$ 75.99	7.15	$ 567,531
Exercisable at December 31, 2015	5,541	$ 56.85	5.80	$ 385,214
Exercisable and Expected to Vest at December 31, 2015	10,461	$ 74.11	7.04	$ 551,593

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, 2015 , which was $126.26 based on the average of the high and low price of the Company's common stock on that date.

The total intrinsic value (the amount by which the fair market value exceeded the exercise price) of stock options exercised during 2015 , 2014 and 2013 was $252.9 million , $316.5 million and $291.6 million , respectively. The total cash received by the Company as a result of employee stock option exercises during 2015 , 2014 and 2013 was $165.6 million , $255.5 million and $246.8 million , respectively.

The following table summarizes information about stock options outstanding and exercisable at December 31, 2015 :

	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)
$18.93–$20.00	138	2.10	$ 18.93	138	$ 18.93
$20.01–$40.00	2,247	3.70	$ 34.38	2,155	$ 34.24
$40.01–$60.00	2,310	6.61	$ 48.09	1,444	$ 49.03
$60.01–$80.00	1,434	8.09	$ 75.96	557	$ 75.15
$80.01–$100.00	1,785	7.99	$ 90.28	702	$ 87.55
$100.01–$120.00	1,727	9.05	$ 109.31	294	$ 109.23
$120.01–$134.69	1,504	9.53	$ 131.04	251	$ 128.90
Total	11,145	7.15	$ 75.99	5,541	$ 56.85

The following table summarizes the restricted stock and restricted stock units activity of the Company during the year ended December 31, 2015 :

	Restricted Stock		Restricted Stock Units	
	Number of Units	Weighted-average Grant-date Fair Value	Number of Shares	Weighted-average Grant-date Fair Value
	(in thousands)	(per share)	(in thousands)	(per share)
Unvested at December 31, 2014	2,907	$ 78.18	185	$ 76.79
Granted	1,407	$ 116.63	97	$ 118.26
Vested	(1,033)	$ 68.39	(66)	$ 70.24
Cancelled	(450)	$ 91.21	(23)	$ 89.97
Unvested at December 31, 2015	2,831	$ 98.80	193	$ 98.36

The total fair value of restricted stock that vested during 2015 , 2014 and 2013 (measured on the date of vesting) was $124.0 million , $54.5 million and $50.9 million , respectively. The total fair value of restricted stock units that vested during 2015 , 2014 and 2013 (measured on the date of vesting) was $8.0 million , $2.9 million and $1.7 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. As of December 31, 2015 , there were 1,163,614 shares of common stock authorized for issuance pursuant to the ESPP.

In 2015 , the following shares were issued to employees under the ESPP:

	Year Ended December 31, 2015
	(in thousands, except per share amount)
Number of shares	233
Average price paid per share	$ 84.50

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 is based on the intrinsic value on the date of grant. Stock-based compensation, measured at the grant date based on the fair value of the award, is typically recognized as expense ratably over the requisite service period. The expense recognized over the requisite service period includes an estimate of awards that will be forfeited.

The effect of stock-based compensation expense during the three years ended December 31, 2015 was as follows:

	2015	2014	2013
	(in thousands)		
Stock-based compensation expense by line item:			
Research and development expenses	$ 152,955	$ 116,998	$ 81,183
Sales, general and administrative expenses	78,070	60,544	45,652
Total stock-based compensation expense included in costs and expenses	$ 231,025	$ 177,542	$ 126,835

The stock-based compensation expense by type of award during the three years ended December 31, 2015 was as follows:

	2015	2014	2013
		(in thousands)	
Stock-based compensation expense by type of award:			
Stock options	$ 129,276	$ 99,961	$ 84,599
Restricted stock and restricted stock units	98,811	70,678	36,479
ESPP share issuances	7,025	8,326	6,805
Less: stock-based compensation expense capitalized to inventories	(4,087)	(1,423)	(1,048)
Total stock-based compensation expense included in costs and expenses	$ 231,025	$ 177,542	$ 126,835

In 2013, the Company also recognized stock-based compensation expense recorded to noncontrolling interest (Alios), which is reflected in the Company's consolidated statements of shareholders equity and noncontrolling interest on the consolidated balance sheet and in discontinued operations attributable to noncontrolling interest as of December 31, 2014.

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

The following table sets forth the Company's unrecognized stock-based compensation expense, net of estimated forfeitures, as of December 31, 2015 , by type of award and the weighted-average period over which that expense is expected to be recognized:

	As of December 31, 2015	
	Unrecognized Expense Net of Estimated Forfeitures	Weighted-average Recognition Period
	(in thousands)	(in years)
Type of award:		
Stock options	$ 170,971	2.17
Restricted stock and restricted stock units	$ 168,742	2.59
ESPP share issuances	$ 6,232	0.65

Stock Options

The Company issues stock options with service conditions, which are generally the vesting periods of the awards. The Company uses the Black-Scholes option pricing model to estimate the fair value of stock options at the grant date. The Black-Scholes option pricing model uses the option exercise price as well as estimates and assumptions related to the expected price volatility of the Company's stock, the rate of return on risk-free investments, the expected period during which the options will be outstanding, and the expected dividend yield for the Company's stock to estimate the fair value of a stock option on the grant date. The options granted during 2015 , 2014 and 2013 had a weighted-average grant-date fair value per share of $52.16 , $39.95 and $25.79 , respectively.

The fair value of each option granted during 2015 , 2014 and 2013 was estimated on the date of grant using the Black-Scholes option pricing model with the following weighted-average assumptions:

	2015	2014	2013
Expected stock price volatility	47.29%	50.86%	46.20%
Risk-free interest rate	1.61%	1.77%	1.25%
Expected term of options (in years)	5.28	5.47	5.81
Expected annual dividends	—	—	—

The weighted-average valuation assumptions were determined as follows:

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

Restricted Stock 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, on an annual basis restricted stock and restricted stock units that vest upon the earlier of the satisfaction of (i) a performance condition or (ii) a service condition. In addition, in 2015 and 2014, the Company issued, pursuant to a retention program, restricted stock awards to certain members of senior management that will vest upon the satisfaction of both (i) a performance condition and (ii) a service condition.

Employee Stock Purchase Plan

The weighted-average fair value of each purchase right granted during 2015 , 2014 and 2013 was $37.84 , $29.59 and $21.08 , respectively. The following table reflects the weighted-average assumptions used in the Black-Scholes option pricing model for 2015 , 2014 and 2013 :

	2015	2014	2013
Expected stock price volatility	47.20%	60.32%	54.69%
Risk-free interest rate	0.40%	0.09%	0.08%
Expected term (in years)	0.72	0.75	0.74
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. Other Arrangements

Sale of HIV Protease Inhibitor Royalty Stream

In 2008, the Company sold to a third party its rights to receive royalty payments from GlaxoSmithKline plc, net of royalty amounts to be earned by and due to a third party, for a one-time cash payment of $160.0 million . These royalty payments relate to net sales of HIV protease inhibitors, which had been developed pursuant to a collaboration agreement between the Company and GlaxoSmithKline plc. As of December 31, 2015 , the Company had $26.0 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.

Other income (expense), net

In April 2014, the Company received a one-time cash payment of $36.7 million from its landlord pursuant to the Fan Pier Leases. This payment related to bonds issued pursuant to an Infrastructure Development Assistance Agreement between The Commonwealth of Massachusetts and the Company's landlord. The bonds were issued in connection with the landlord's contribution to infrastructure improvements and also were dependent upon employment levels at the Company through the bond issuance date. The Company accounted for the cash payment as a government grant as it was provided in part related to the Company's employment level in Massachusetts. Such grants are recognized in income in the period in which the conditions of the grant are met and there is reasonable assurance that the grant will be received, provided it is not subject to refund. In the second quarter of 2014, the Company recorded $36.7 million as a credit to other income (expense), net in its consolidated statements of operations because the Company's employment obligations related to these funds were satisfied as of the date of issuance of the bonds and the payment received is not subject to refund.

P. Income Taxes

The components of loss from continuing operations before provision for (benefit from) income taxes during the three years ended December 31, 2015 consisted of the following:

	2015	2014	2013
		(in thousands)	
United States	$ (272,326)	$ (645,465)	$ (10,638)
Foreign	(285,474)	(89,410)	(615,406)
Loss from continuing operations before provision for (benefit from) income taxes	$ (557,800)	$ (734,875)	$ (626,044)

The components of the provision for (benefit from) income taxes from continuing operations during the three years ended December 31, 2015 consisted of the following:

	2015	2014	2013
		(in thousands)	
Current taxes:			
United States	$ 25,623	$ 2,853	$ —
Foreign	831	2,457	1,085
State	3,629	1,366	4,080
Total current taxes	$ 30,083	$ 6,676	$ 5,165
Deferred taxes:			
United States	$ 497	$ 244	$ —
Foreign	(355)	—	(127,587)
State	156	38	—
Total deferred taxes	$ 298	$ 282	$ (127,587)
Provision for (benefit from) income taxes	$ 30,381	$ 6,958	$ (122,422)

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

	2015	2014	2013
		(in thousands)	
Loss from continuing operations before provision for (benefit from) income taxes	$ (557,800)	$ (734,875)	$ (626,044)
Expected tax provision (benefit)	(195,230)	(257,206)	(219,115)
State taxes, net of federal benefit	3,800	1,124	3,844
Foreign rate differential	47,402	39,335	79,799
Tax credits	(55,696)	(33,788)	(16,775)
Unbenefitted operating losses (gains)	226,169	241,037	(29,900)
Non-deductible expenses	5,817	18,756	9,614
Rate change	(1,224)	(1,826)	50,076
Other	(657)	(474)	35
Provision for (benefit from) income taxes	$ 30,381	$ 6,958	$ (122,422)

The foreign rate differential in the tax rate reconciliation table reflects the effect of operations in jurisdictions with tax rates that are different from the United States. As set forth in the components of loss before provision for (benefit from) income taxes, the Company had losses in foreign jurisdictions in each year presented. Due to lower foreign tax rates, particularly in the United Kingdom, the Company's tax benefit in foreign loss jurisdictions is less than the "expected" tax benefit that would have resulted from losses in these jurisdictions at corporate tax rates in the United States. The difference between the tax benefit at foreign corporate tax rates and the "expected" benefit based on corporate tax rates in the United States is reflected in the tax reconciliation table under the caption "foreign rate differential."

The unbenefitted operating losses in the tax rate reconciliation table primarily reflect a change in the valuation allowance on deferred tax assets related to the United States, United Kingdom and Switzerland. In 2015 and 2014, the valuation allowance increased primarily due to an increase in the net operating loss in the United States with no benefit due to the uncertainty in the Company's ability to use them in future periods. In the United Kingdom and Switzerland losses have been incurred that cannot be benefitted due to uncertainty in the Company's ability to use them in future periods resulting in an unfavorable effect on the tax provision.

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,	
	2015	2014
	(in thousands)	
Deferred tax assets:		
Net operating loss	$ 1,250,642	$ 996,172
Tax credit carryforwards	315,535	265,339
Intangible assets	14,673	3,174
Deferred revenues	9,341	15,771
Stock-based compensation	93,404	61,527
Inventories	5,913	13,395
Accrued expenses	27,236	37,699
Currency translation adjustment	222	—
Construction financing lease obligation	176,250	175,853
Gross deferred tax assets	1,893,216	1,568,930
Valuation allowance	(1,716,349)	(1,409,936)
Total deferred tax assets	176,867	158,994
Deferred tax liabilities:		
Property and equipment	(175,424)	(158,994)
Acquired intangibles	(110,439)	(11,544)
Unrealized gain	$ (1,088)	$ —
Net deferred tax liabilities	$ (110,084)	$ (11,544)

The Company presents its deferred tax assets and deferred tax liabilities gross on its consolidated balance sheets. As of December 31, 2015 , $110.4 million of the deferred tax liabilities are attributable to the Company's collaborations with BioAxone and Parion. As of December 31, 2014 , $11.5 million of the deferred tax liabilities are attributable to the Company's collaboration with BioAxone.

For federal income tax purposes, as of December 31, 2015 , the Company has net operating loss carryforwards of approximately $4.2 billion and tax credits of $217.5 million , which may be used to offset future federal income and tax liability, respectively. Approximately $1.1 billion 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 $1.0 billion and tax credits of $97.3 million , which may be used to offset future state income and tax liability, respectively. Approximately $195.1 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 2035. After consideration of all the evidence, both positive and negative, the Company continues to maintain a valuation allowance for the majority of the 2015 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 $306.4 million from December 31, 2014 to December 31, 2015 primarily due to an increase in net operating losses and credits.

Unrecognized tax benefits during the two years ended December 31, 2015 consisted of the following:

	2015	2014
	(in thousands)	
Unrecognized tax benefits beginning of year	$ 880	$ 2,024
Decrease for prior period positions	—	(27)
Decrease due to settlements and payments	(455)	(1,117)
Unrecognized tax benefits end of year	$ 425	$ 880

The Company had gross unrecognized tax benefits of $0.4 million and $0.9 million , respectively, as of December 31, 2015 and 2014 . At December 31, 2015 , $0.4 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, 2015 , no interest and penalties have been accrued. In 2016, it is reasonably possible that the Company will reduce the balance of its unrecognized tax benefits by approximately $0.4 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 2011 or any other major taxing jurisdiction for years before 2010, except where the Company has net operating losses or tax credit carryforwards that originate before 2010. The Company currently is under examination by Revenue Quebec for the year ended December 31, 2013 and the Internal Revenue Service, Delaware, Pennsylvania and Texas for the various periods between December 31, 2011 and December 31, 2013. No adjustments have been reported. The Company is not under examination by any other jurisdictions for any tax year. The Company concluded audits with the Canada Revenue Agency and Revenue Quebec during 2014, and Massachusetts and New York during 2015, with no material adjustments.

At December 31, 2015 , 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.

Q. Restructuring Expenses

Facility Lease Obligations

The Company has adopted several plans to restructure its facility operations for which it has incurred restructuring expenses in the three years ended December 31, 2015 . The Company's initial estimate of its liabilities for net ongoing costs associated with these facility obligations are recorded at fair value on the cease use date. In estimating the expenses and liabilities related to these facilities, the Company utilizes a probability-weighted discounted cash-flows of the Company's ongoing lease obligations. In estimating the expense and liability under its lease obligations, 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 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 these facility lease obligations, 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 these liabilities. Changes to the Company's estimate of these liabilities are recorded as additional restructuring expenses (credits). In addition, because the Company's estimate of these liabilities includes the application of a discount rate to reflect the time-value of money, the Company records imputed interest costs related to these liabilities each quarter. These costs are included in restructuring expenses on the Company's consolidated statements of operations.

2003 Kendall Restructuring

In 2003, the Company adopted a plan to restructure its operations (the "2003 Kendall Restructuring") 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 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 rentable square footage of the Kendall Square Facility related to the 2003 Kendall Restructuring currently is subleased to third parties.

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 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 Company uses a discount rate of 10% related to this restructuring activity.

The remaining lease obligations, which are associated with the 120,000 square foot portion of the Kendall Square Facility that the Company occupied and used for its operations, were recorded as rental expense in the period incurred until the Company incurred a cease use charge related to this portion of the Kendall Square Facility in the third quarter of 2014 in connection with transitioning its Massachusetts operations to Fan Pier in Boston, Massachusetts (the "Fan Pier Move Restructuring").

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 activities related to 2003 restructuring liability for 2004 through 2015 were as follows:

	2015	2014	2013	2004-2015
		(in thousands)		
Liability, beginning of the period	$ 11,596	$ 19,115	$ 23,328	$ 69,526
Cash payments	(14,625)	(17,494)	(15,255)	(211,071)
Cash received from subleases	11,089	12,912	10,670	99,709
Credit for portion of facility Vertex decided to occupy in 2005	—	—	—	(10,018)
Restructuring expense	(116)	(2,937)	372	59,798
Liability, end of the period	$ 7,944	$ 11,596	$ 19,115	$ 7,944

Fan Pier Move Restructuring

In connection with the relocation of its Massachusetts operations to Fan Pier in Boston, Massachusetts, which commenced in 2013, the Company is incurring restructuring charges related to its remaining lease obligations at its facilities in Cambridge, Massachusetts. The majority of these restructuring charges were recorded in the third quarter of 2014 upon decommissioning three facilities in Cambridge. The Company discounted the estimated cash flows related to the facilities at a discount rate of 9% . The Company will continue to incur charges through April 2018 related to the difference between the Company's estimated future cash flows related to its lease obligations, which include an estimate for sublease income to be received if applicable, and its actual cash flows. The Fan Pier Move Restructuring included lease obligations related to the 120,000 square feet of the Kendall Square Facility that the Company continued to use for its operations following its 2013 Kendall Restructuring. The remaining rentable square footage of the Kendall Square Facility related to the Fan Pier Move Restructuring was subleased to a third party in February 2015.

The activities related to the Fan Pier relocation restructuring liability for the three years ended December 31, 2015 were as follows:

	2015	2014	2013
		(in thousands)	
Liability, beginning of the period	$ 33,390	$ 797	$ —
Cash payments	(30,022)	(18,271)	(401)
Cash received from subleases	4,229	—	—
Restructuring expense	(1,633)	50,864	1,198
Liability, end of the period	$ 5,964	$ 33,390	$ 797

Other Restructuring Activities

The Company has engaged in several other restructuring activities that are unrelated to its 2003 Kendall Restructuring and the Fan Pier Move Restructuring. The most significant activity commenced in October 2013 when the Company adopted a restructuring plan that 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 CF and other research and development programs.

The activities related to the Company's other restructuring liabilities for the three years ended December 31, 2015 were as follows:

	2015	2014	2013
		(in thousands)	
Liability, beginning of the period	$ 869	$ 8,441	$ —
Cash payments	(3,374)	(10,570)	(22,916)
Asset impairments and other non-cash expense	—	—	(7,594)
Restructuring expense	3,955	2,998	38,951
Liability, end of the period	$ 1,450	$ 869	$ 8,441

R. Employee Benefits

The Company has a 401(k) retirement plan (the "Vertex 401(k) Plan") in which substantially all of its permanent U.S. employees are eligible to participate. Participants may contribute up to 60% of their annual compensation to the Vertex 401(k) Plan, subject to statutory limitations. The Company may declare discretionary matching contributions to the Vertex 401(k) Plan. 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. For the years ended December 31, 2015 , 2014 and 2013 , the Company contributed approximately $12.8 million , $12.0 million and $12.6 million to the plan, respectively. As of December 31, 2015 , 755,000 shares of common stock remained available for grant under the Vertex 401(k) Plan. In 2013 , 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
	(in thousands)
Discretionary matching contributions during the year ended December 31, 2013	$ 5,930
Shares issued during the year ended December 31, 2013	99
Shares issuable as of the year ended December 31, 2013	—

S. Commitments and Contingencies

Lease Obligations

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

The Kendall Square Lease began in January 2003 and will expire in April 2018. The Company occupied and used for its operations approximately 120,000 square feet of the Kendall Square Facility until 2014 when it moved its operations to Fan Pier. The Company has sublease arrangements in place for the remaining rentable square footage of the Kendall Square Facility, with terms that expire concurrently with the Kendall Square Lease. Please refer to Note Q, "Restructuring Expenses," for further information.

As of December 31, 2015 , future minimum commitments under the Fan Pier Leases, facility leases with terms of more than one year and contractual sublease income under the Company's subleases for the Kendall Square Facility as adjusted for a sublease executed in February 2015 were as follows:

Year	Fan Pier Leases	Kendall Square Lease	Kendall Sublease Income	Other Leases	Total Lease Commitments (Net of Sublease Income)
			(in thousands)		
2016	$ 67,206	$ 19,984	$ (15,515)	$ 13,922	$ 85,597
2017	67,206	19,984	(15,515)	15,472	87,147
2018	67,206	6,661	(5,172)	16,121	84,816
2019	72,589	—	—	20,156	92,745
2020	72,589	—	—	19,879	92,468
Thereafter	607,621	—	—	219,483	827,104
Total minimum lease payments	$ 954,417	$ 46,629	$ (36,202)	$ 305,033	$ 1,269,877

During 2015 , 2014 and 2013 , rental expense was $18.1 million , $38.9 million and $57.7 million , respectively. The majority of the Company's lease payments related to the Fan Pier Leases are recorded as interest expense because the Company is deemed for accounting purposes to be the owner of the Buildings. Please refer to Note L, "Long Term Obligations," for further information.

The Company has outstanding leases, which are accounted for as capital leases, for equipment, leasehold improvements and software licenses with terms through 2019. The capital leases bear interest at rates ranging from less than 1% to 9% per year. The following table sets forth the Company's future minimum payments due under capital leases as of December 31, 2015 :

Year	(in thousands)
2016	$ 18,773
2017	19,248
2018	19,146
2019	6,719
2020	1,089
Thereafter	209
Total payments	65,184
Less: amount representing interest	(6,716)
Present value of payments	$ 58,468

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.

Financing Arrangements

As of December 31, 2015 , the Company had irrevocable stand-by letters of credit outstanding that were issued in connection with property leases and other similar agreements totaling $21.9 million that are cash collateralized. The cash used to support these letters of credit is included in restricted cash, as of December 31, 2015 , on the Company's consolidated balance sheet.

Litigation

On May 28, 2014, a purported shareholder class action *Local No. 8 IBEW Retirement Plan & Trust 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 alleged 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 May 29, 2012, all in violation of Section 10(b) of the Securities Exchange Act of 1934, as amended, and Rule 10b-5 promulgated thereunder. The purported class consists of all persons (excluding defendants) who purchased the Company's common stock between May 7, 2012 and May 29, 2012. The plaintiffs seek unspecified monetary damages, costs and attorneys' fees as well as disgorgement of the proceeds from certain individual defendants' sales of the Company's stock. On October 8, 2014, the Court approved Local No. 8 IBEW Retirement Fund as lead plaintiff, and Scott and Scott LLP as lead counsel for the plaintiff and the putative class. The Company filed a motion to dismiss the complaint on December 8, 2014 and the plaintiffs filed their opposition to the Company's motion to dismiss on January 22, 2015. On February 23, 2015, the Company filed a reply to the plaintiffs' opposition to its motion to dismiss. The court heard oral argument on the motion to dismiss on March 6, 2015 and took the motion under advisement. On September 30, 2015, the court granted the Company's motion to dismiss. On October 15, 2015, the plaintiff filed a notice of appeal. The Company believes the claims to be without merit and intends to vigorously defend the litigation. As of December 31, 2015 , the Company has not recorded any reserves for this purported class action.

Guaranties and Indemnifications

As permitted under Massachusetts law, the Company's Articles of Organization and By-laws provide that the Company will indemnify certain of its officers and directors for certain claims asserted against them in connection with their service as an officer or director. The maximum potential amount of future payments that the Company could be required to make under these indemnification provisions is unlimited. However, the Company has purchased directors' and officers' liability insurance policies that could reduce its monetary exposure and enable it to recover a portion of any future amounts paid. No indemnification claims currently are outstanding, and the Company believes the estimated fair value of these indemnification arrangements is minimal.

The Company customarily agrees in the ordinary course of its business to indemnification provisions in agreements with clinical trial investigators and sites in its drug development programs, sponsored research agreements with academic and not-for-profit institutions, various comparable agreements involving parties performing services for the Company, and its real estate leases. The Company also customarily agrees to certain indemnification provisions in its drug discovery, development and commercialization collaboration agreements. With respect to the Company's clinical trials and sponsored research agreements, these indemnification provisions typically apply to any claim asserted against the investigator or the investigator's institution relating to personal injury or property damage, violations of law or certain breaches of the Company's contractual obligations arising out of the research or clinical testing of the Company's compounds or drug candidates. With respect to lease agreements, the indemnification provisions typically apply to claims asserted against the landlord relating to personal injury or property damage caused by the Company, to violations of law by the Company or to certain breaches of the Company's contractual obligations. The indemnification provisions appearing in the Company's collaboration agreements are similar to those for the other agreements discussed above, but in addition provide some limited indemnification for its collaborator in the event of third-party claims alleging infringement of intellectual property rights. In each of the cases above, the indemnification obligation generally survives the termination of the agreement for some extended period, although the Company believes the obligation typically has the most relevance during the contract term and for a short period of time thereafter. The maximum potential amount of future payments that the Company could be required to make under these provisions is generally unlimited. The Company has purchased insurance policies covering personal injury, property damage and general liability that reduce its exposure for indemnification and would enable it in many cases to recover all or a portion of any future amounts paid. The Company has never paid any material amounts to defend lawsuits or settle claims related to these indemnification provisions. Accordingly, the Company believes the estimated fair value of these indemnification arrangements is minimal.

Other Contingencies

The Company has certain contingent liabilities that arise in the ordinary course of its business activities. The Company accrues a reserve for contingent liabilities when it is probable that future expenditures will be made and such expenditures can be reasonably estimated. There were no material contingent liabilities accrued as of December 31, 2015 or 2014 .

T. Segment Information

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

Revenues by Product

Product revenues, net consisted of the following:

	2015	2014	2013
		(in thousands)	
KALYDECO	$ 631,674	$ 463,750	$ 371,285
ORKAMBI	350,663	—	—
INCIVEK	17,987	24,071	466,360
Total product revenues, net	$ 1,000,324	$ 487,821	$ 837,645

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.

	2015	2014	2013
		(in thousands)	
United States	$ 763,316	$ 361,074	$ 896,952
Outside of the United States			
Europe	219,596	197,611	279,557
Other	49,424	21,730	35,466
Total revenues outside of the United States	269,020	219,341	315,023
Total revenues	$ 1,032,336	$ 580,415	$ 1,211,975

In 2015 and 2014, revenues attributable to the United Kingdom were the majority of the Company's European revenues.

Significant Customers

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

	Percent of Total Gross Revenues			Percent of Gross Accounts Receivable	
	Year Ended December 31,			As of December 31,	
	2015	2014	2013	2015	2014
Walgreen Co.	20%	12%	<10%	15%	11%
CVS/Caremark	17%	<10%	<10%	17%	<10%
Accredo/Curascript	15%	<10%	<10%	16%	<10%
Bupa Home Healthcare Limited	<10%	<10%	<10%	<10%	20%
Janssen Inc.	<10%	<10%	N/A	<10%	12%
Janssen NV	<10%	<10%	22%	<10%	<10%
AmerisourceBergen Drug Corporation	<10%	<10%	21%	<10%	<10%
McKesson Corporation	<10%	<10%	21%	<10%	<10%

Property and Equipment, Net by Location

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

	As of December 31,	
	2015	2014
	(in thousands)	
United States	$ 661,421	$ 676,968
Outside of the United States		
United Kingdom	32,793	33,628
Other	3,501	5,216
Total property and equipment, net outside of the United States	36,294	38,844
Total property and equipment, net	$ 697,715	$ 715,812

U. Quarterly Financial Data (unaudited)

The following table sets forth the Company's quarterly financial data for the two years ended December 31, 2015 and have been revised to reflect discontinued operations for quarterly periods prior to the three months ended September 30, 2014.

	Three Months Ended			
	March 31, 2015	June 30, 2015	September 30, 2015	December 31, 2015
	(in thousands, except per share amounts)			
Revenues:				
Product revenues, net	$ 130,875	$ 160,388	$ 302,511	$ 406,550
Royalty revenues	6,792	5,077	5,759	6,331
Collaborative revenues	842	611	1,546	5,054
Total revenues	138,509	166,076	309,816	417,935
Costs and expenses:				
Cost of product revenues	9,381	15,409	30,269	62,092
Royalty expenses	2,926	1,451	1,691	1,293
Research and development expenses (1)	215,599	223,858	246,284	310,181
Sales, general and administrative expenses	85,860	94,394	99,772	96,549
Restructuring (income) expenses	(3,272)	2,128	1,826	1,524
Total costs and expenses	310,494	337,240	379,842	471,639
Loss from operations	(171,985)	(171,164)	(70,026)	(53,704)
Interest expense, net	(21,307)	(21,111)	(21,134)	(20,654)
Other (expense) income, net	(5,113)	1,414	(1,326)	(1,690)
Loss before provision for (benefit from) income taxes	(198,405)	(190,861)	(92,486)	(76,048)
Provision for (benefit from) income taxes	299	30,131	1,330	(1,379)
Net loss	(198,704)	(220,992)	(93,816)	(74,669)
Loss (income) attributable to noncontrolling interest	98	32,144	(1,333)	938
Net loss attributable to Vertex	$ (198,606)	$ (188,848)	$ (95,149)	$ (73,731)
Amounts per share attributable to Vertex common shareholders:				
Net loss:				
Basic and diluted	$ (0.83)	$ (0.78)	$ (0.39)	$ (0.30)
Shares used in per share calculations:				
Basic and diluted	239,493	240,757	241,969	242,987

	Three Months Ended			
	March 31, 2014	June 30, 2014	September 30, 2014	December 31, 2014
	(in thousands, except per share amounts)			
Revenues:				
Product revenues, net	$ 103,461	$ 122,319	$ 137,099	$ 124,942
Royalty revenues	10,733	13,015	8,386	8,785
Collaborative revenues (2)	4,257	3,087	33,502	10,829
Total revenues	118,451	138,421	178,987	144,556
Costs and expenses:				
Cost of product revenues	8,572	9,655	10,208	11,290
Royalty expenses	6,904	7,645	3,976	2,737
Research and development expenses	238,617	224,487	190,939	201,463
Sales, general and administrative expenses	74,212	77,446	75,224	78,527
Restructuring expenses (income) (3)	6188	(270)	40,843	4,164
Total costs and expenses	334,493	318,963	321,190	298,181
Loss from operations	(216,042)	(180,542)	(142,203)	(153,625)
Interest expense, net	(15,717)	(15,585)	(20,384)	(21,177)
Other income (expense), net (4)	451	37,731	(3,990)	(3,792)
Loss from continuing operations before provision for income taxes	(231,308)	(158,396)	(166,577)	(178,594)
Provision for income taxes	803	693	3,419	2,043
Loss from continuing operations	(232,111)	(159,089)	(169,996)	(180,637)
Loss from discontinued operations, net of tax benefit	(346)	(293)	(64)	(209)
Net loss	(232,457)	(159,382)	(170,060)	(180,846)
Loss attributable to noncontrolling interest	—	—	—	4,190
Net loss attributable to Vertex	$ (232,457)	$ (159,382)	$ (170,060)	$ (176,656)
Amounts attributable to Vertex:				
Loss from continuing operations attributable to Vertex	$ (232,111)	$ (159,089)	$ (169,996)	$ (176,447)
Loss from discontinued operations	(346)	(293)	(64)	(209)
Net loss attributable to Vertex	$ (232,457)	$ (159,382)	$ (170,060)	$ (176,656)
Amounts per share attributable to Vertex common shareholders:				
Net loss from continuing operations:				
Basic and diluted	$ (1.00)	$ (0.68)	$ (0.72)	$ (0.74)
Net loss from discontinued operations:				
Basic and diluted	$ —	$ —	$ —	$ —
Net loss:				
Basic and diluted	$ (1.00)	$ (0.68)	$ (0.72)	$ (0.74)
Shares used in per share calculations:				
Basic and diluted	232,887	233,808	236,137	238,272

1. During fourth quarter of 2015, the Company made a one-time $75.0 million upfront payment to CRISPR Therapeutics in connection with the collaboration, which was recorded as a research and development expense. See Note B, “Collaborative Arrangements,” for further information.
2. During the third quarter of 2014, the Company received a non-refundable up-front payment of $30.0 million from Janssen Inc., which was recorded as collaborative revenues. See Note B, “Collaborative Arrangements,” for further information.
3. During the third quarter of 2014, the Company recorded $40.8 million of restructuring expenses primarily related to the relocation of its corporate headquarters to Boston from Cambridge. See Note Q, “Restructuring Expenses,” for further information.
4. During the second quarter of 2014, the Company received a one-time cash payment of $36.7 million from its landlord pursuant to the Fan Pier Leases, which was recorded as other income. See Note O, “Other Arrangements,” for further information.

Exhibit 10.6

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

STRATEGIC COLLABORATION, OPTION AND LICENSE AGREEMENT

BETWEEN

VERTEX PHARMACEUTICALS INCORPORATED

VERTEX PHARMACEUTICALS (EUROPE) LIMITED

AND

CRISPR THERAPEUTICS AG

CRISPR THERAPEUTICS LIMITED

CRISPR THERAPEUTICS, INC.

TRACR HEMATOLOGY LTD.

STRATEGIC COLLABORATION, OPTION AND LICENSE AGREEMENT

This STRATEGIC COLLABORATION, OPTION AND LICENSE AGREEMENT (this " **Agreement** ") is entered into as of October 26, 2015 (the " **Effective Date** " *)* by and between, on the one hand, **VERTEX PHARMACEUTICALS INCORPORATED** , a corporation organized and existing under the laws of The Commonwealth of Massachusetts (" **Vertex Parent** "), and **VERTEX PHARMACEUTICALS (EUROPE) LIMITED,** a private limited liability company organized under the laws of England and Wales (" **Vertex UK** " and, together with Vertex Parent, " **Vertex** ") and, on the other hand, **CRISPR THERAPEUTICS AG** , a corporation organized under the laws of Switzerland (" **CRISPR AG** "), **CRISPR THERAPEUTICS, INC.,** a corporation organized under the laws of the state of Delaware (" **CRISPR Inc."), CRISPR THERAPEUTICS LIMITED** , a corporation organized under the laws of England and Wales (" **CRISPR UK** ") and **TRACR HEMATOLOGY LTD** , a UK limited company (" **Tracr"** and together with CRISPR AG, CRISPR Inc. and CRISPR UK " **CRISPR** "). Vertex and CRISPR each may be referred to herein individually as a " **Party** " or collectively as the " **Parties** ."

RECITALS

WHEREAS , CRISPR possesses certain Patents, Know-How, technology and expertise with respect to the CRISPR/Cas System (as defined below);

WHEREAS , Vertex possesses expertise in developing and commercializing human therapeutics;

WHEREAS , Vertex and CRISPR desire to enter into a strategic collaboration focused on exploring potential targets related to certain diseases and creating therapeutics using gene editing [***], including the CRISPR/Cas System, to treat such diseases; and

WHEREAS , simultaneously with the execution of this Agreement, the Parties are entering into a convertible debt instrument, pursuant to which Vertex will provide CRISPR AG with a total of $30,000,000 in funding, which funding will be converted into shares of CRISPR AG's preferred stock in accordance with the terms thereof;

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

ARTICLE 1.
DEFINITIONS

For purposes of this Agreement, the following capitalized terms will have the following meanings:

1.1. " **Acceptance** " means, with respect to an Approval Application filed for a Product, (a) in the United States, the receipt of written notice from the FDA that such Approval Application is officially " *filed* ," or (b) in the European Union, the receipt of written notice of acceptance by the EMA of such Approval Application for filing under the centralized European procedure in accordance with any feedback received from EU Regulatory Authorities; *provided that* if the centralized filing procedure is not used, then Acceptance will be determined upon the acceptance of such Approval Application by the applicable Regulatory Authority in a Major Market Country in the EU.

1.2. " **Additional Research** " has the meaning set forth in Section 2.12.

1.3. " **Additional Research Budget** " has the meaning set forth in Section 2.12.

1.4. " **Additional Research Plan** " has the meaning set forth in Section 2.12.

1.5. " **Adverse Event** " has the meaning set forth in the Applicable Law for such term (or comparable term), and will generally mean any untoward medical occurrence in a subject in any Clinical Trial who has received a Licensed Agent or Product, medical device or placebo, and which does not necessarily have a causal relationship with such Licensed Agent, Product, medical device or placebo, including any unfavorable and unintended sign (including an abnormal laboratory finding), symptom or disease temporally associated with the use of the applicable Licensed Agent or Product, whether or not related to such Licensed Agent or Product.

1.6. " **Affiliate** " means, as of any point in time and for so long as such relationship continues to exist with respect to any Person, any other Person that controls, is controlled by or is under common control with such Person. A Person will be regarded as in control of another Person if it (a) owns or controls more than 50% of the equity securities of the subject Person entitled to vote in the election of directors (or, in the case of a Person that is not a corporation, for the election of the corresponding managing authority); *provided* , *however* , that the term "Affiliate" will not include subsidiaries or other entities in which a Person owns a majority of the ordinary voting power necessary to elect a majority of the board of directors or other governing board, but is restricted from electing such majority by contract or otherwise, until such time as such restrictions are no longer in effect, or (b) possesses, directly or indirectly, the power to direct or cause the direction of the management or policies of an such Person (whether through ownership of securities or other ownership interests, by contract or otherwise).

1.7. " **Agreement** " has the meaning set forth in the Preamble.

1.8. " **Agreement Term** " means the period commencing on the Effective Date and ending on the expiration of this Agreement pursuant to Section 11.1, unless terminated earlier as provided herein.

1.9. " **Alliance Manager** " has the meaning set forth in Section 3.4.1.

1.10. " **Applicable Law** " means all applicable laws, statutes, rules, regulations and other pronouncements having the effect of law of any federal, national, multinational, state, provincial, county, city or other political subdivision, agency or other body, domestic or foreign, including any applicable rules, regulations, guidelines, or other requirements of the Regulatory Authorities that may be in effect from time to time.

1.11. " **Approval Application** " means a BLA, NDA or similar application or submission for a Product filed with a Regulatory Authority in a country or group of countries to obtain marketing approval for a biological or pharmaceutical product in that country or group of countries.

1.12. " **Audited Party** " has the meaning set forth in Section 7.9.

1.13. " **Auditing Party** " has the meaning set forth in Section 7.9.

1.14. " **Available** " has the meaning set forth in Section 1.34.

1.15. " **BLA** " means a Biological License Application that is submitted to the FDA for marketing approval for a Licensed Agent or Product pursuant to 21 C.F.R. § 601.2.

1.16. [***].

1.17. [***].

1.18. " **Breaching Party** " means the Party that is believed by the other Party to be in material breach of this Agreement.

1.19. " **Business Day** " means a Monday, Tuesday, Wednesday, Thursday or Friday that is not a day on which banking institutions in Boston, Massachusetts are authorized or obligated to close.

1.20. " **Calendar Quarter** " means the respective periods of three consecutive calendar months ending on March 31, June 30, September 30 or December 31, during the Agreement Term, or the applicable part thereof during the first or last calendar quarter of the Agreement Term.

1.21. " **Calendar Year** " means any calendar year ending on December 31, or the applicable part thereof during the first or last year of the Agreement Term.

1.22. " **cGMP** " means current Good Manufacturing Practices as specified in the United States Code of Federal Regulations, ICH Guideline Q7A, or equivalent laws, rules, or regulations of an applicable Regulatory Authority at the time of manufacture.

1.23. " **Change of Control** " means, with respect to a Party, (a) a merger or consolidation of such Party with a Third Party that results in the voting securities of such Party outstanding immediately prior thereto, or any securities into which such voting securities have been converted or exchanged, ceasing to represent more than 50% of the combined voting power of the surviving entity or the parent of the surviving entity immediately after such merger or consolidation, or (b) a transaction or series of related transactions in which a Third Party, together with its Affiliates, becomes the beneficial owner of more than 50% of the combined voting power of the outstanding securities of such Party, or (c) the sale or other transfer to a

Third Party of all or substantially all of such Party's business to which the subject matter of this Agreement relates. Notwithstanding the foregoing, with respect to CRISPR, the term "Change of Control" will not include any sale of shares of capital stock of CRISPR, in a single transaction or series of related transactions in which CRISPR issues new securities solely to institutional investors for cash or the cancellation or conversion of indebtedness or a combination thereof where such transaction(s) are conducted primarily for bona fide equity financing purposes.

1.24. " **Clinical Trial** " means a study in humans that is conducted in accordance with GCP and is designed to generate data in support of an Approval Application.

1.25. " **Collaboration Program** " means, on a Collaboration Target-by-Collaboration Target basis, a Research program dedicated to the design, optimization and Research of Licensed Agents and Products directed to such Collaboration Target pursuant to a Research Plan and, upon Vertex's exercise of the Option for a Collaboration Target, Vertex's (or with respect to any Hemoglobinopathy Target [***], the Parties') Research, Development, Manufacture and Commercialization of such Licensed Agents and Products.

1.26. " **Collaboration Program Working Group** " has the meaning set forth in Section 3.2.

1.27. " **Collaboration Target** " means a Vertex Target that Vertex has selected as the subject of a Research Plan in accordance with Section 2.3.3.

1.28. " **Combination Product** " has the meaning set forth in Section 1.117.

1.29. " **Commercialize** " or " **Commercializing** " means to market, promote, distribute, offer for sale, sell, have sold, import, export or otherwise commercialize a product, to conduct activities, other than Research, Development and Manufacturing, in preparation for the foregoing activities, including obtaining Price Approval, and to conduct post-Marketing Approval studies (including Clinical Trials). When used as a noun, "Commercialization" means any and all activities involved in Commercializing.

1.30. " **Commercially Reasonable Efforts** " means with respect to the efforts to be expended by any Person, with respect to any objective, reasonable, diligent and good faith efforts to accomplish such objective. With respect to any objective relating to the Research, Development or Commercialization of a Licensed Agent or Product, "Commercially Reasonable Efforts" means [***], taking into account, without limitation, with respect to each Licensed Agent or Product, (a) [***], (b) [***], (c) [***], (d) [***], (e) [***], (f) [***], (g) [***], (h) [***], (i) [***] and (j) [***]. "Commercially Reasonable Efforts" shall be [***].

1.31. " **Competitive Infringement** " has the meaning set forth in Section 8.6.1.

1.32. " **Competitive Program** " has the meaning set forth in Section 1.33.

1.33. " **Competitor** " means any pharmaceutical company that is conducting a research, development or commercial program for a product that is intended to (a) [***], (b) [***] or (c) [***] (each of (a)-(c), a " **Competitive Program** ").

1.34. " **Confidential Information** " means, with respect to each Party, all Know-How or other information, including proprietary information (whether or not patentable) regarding or

embodying such Party's technology, products, business information or objectives, that is communicated in any way or form by or on behalf of the Disclosing Party to the Receiving Party or its permitted recipients, prior to, on or after the Effective Date, whether or not such Know-How or other information is identified as confidential at the time of disclosure. The terms and conditions of this Agreement will be considered Confidential Information of both Parties, with both Parties deemed to be the Receiving Party of such Confidential Information. The Vertex Target List and the identity of the Collaboration Targets hereunder will be the Confidential Information of both Parties; provided, that if Vertex exercises the Option for a Collaboration Target, the identity of such Collaboration Target will be Vertex's Confidential Information and will no longer be CRISPR's Confidential Information; and provided, further, [***] Notwithstanding any provision of this Section 1.34 to the contrary, Confidential Information does not include any Know-How or information that: (a) was already known by the Receiving Party (other than under an obligation of confidentiality to the Disclosing Party) at the time of disclosure by or on behalf of the Disclosing Party; (b) was generally available to the public or otherwise part of the public domain at the time of its disclosure to the Receiving Party; (c) became generally available to the public or otherwise part of the public domain after its disclosure to the Receiving Party, other than through any act or omission of the Receiving Party in breach of its obligations under this Agreement; (d) was disclosed to the Receiving Party, other than under an obligation of confidentiality, by a Third Party who had no obligation to the Disclosing Party not to disclose such information to the Receiving Party; or (e) was independently discovered or developed by or on behalf of the Receiving Party without the use of any Confidential Information belonging to the Disclosing Party; *provided* , in connection with the foregoing exclusions from protection, that specific Confidential Information shall not be deemed to be known, generally available, in the public domain, disclosed, independently discovered or developed (individually and collectively " **Available** "), merely because broader or related information is Available, nor shall combinations of elements or principles be considered to be Available merely because individual elements thereof are Available.

1.35. " **Continuation Notice** " has the meaning set forth in Section 2.6.

1.36. " **Continuation Research** " has the meaning set forth in Section 2.6.

1.37. " **Control** " or " **Controlled** " means with respect to any Know-How or Patent or other data, information or Materials, possession of the ability by a Party or its Affiliate(s) (whether by sole or joint ownership, license or otherwise, other than pursuant to this Agreement) to grant, without violating the terms of any agreement with a Third Party, a license, access or other right in, to or under such Know-How or Patent or other data, information or Materials. Notwithstanding anything in this Agreement to the contrary, a Party will be deemed to not Control any Patents or Know-How that are owned or controlled by a Third Party described in the definition of "Change of Control," or such Third Party's Affiliates (other than an Affiliate of such Party prior to the Change of Control), (a) prior to the closing of such Change of Control, except to the extent that any such Patents or Know-How were developed prior to such Change of Control through the use of such Party's technology, or (b) after such Change of Control to the extent that such Patents or Know-How are developed or conceived by such Third Party or its Affiliates (other than such Party) after such Change of Control without using or incorporating such Party's technology.

1.38. " **Cost Report** " has the meaning set forth in Section 7.4.2.

1.39. " **Cover** ," " **Covering** " or " **Covers** " means, as to a product and Patent, that, in the absence of a license granted under, or ownership of, such Patent, the making, using, keeping, selling, offering for sale or importation of such product would infringe such Patent or, as to a pending claim included in such Patent, the making, using, selling, offering for sale or importation of such product would infringe such Patent if such pending claim were to issue in an issued patent without modification.

1.40. " **CREATE Act** " means the Cooperative Research and Technology Enhancement Act of 2004, 35 U.S.C. § 103(c)(2)-(c)(3).

1.41. " **CRISPR** " has the meaning set forth in the Preamble.

1.42. " **CRISPR Activities** " means any and all Research activities other than Vertex Activities under any Research Plan.

1.43. " **CRISPR Agreement Breach** " has the meaning set forth in Section 11.2.3(a).

1.44. " **CRISPR Background Know-How** " means any Know-How, other than Joint Program Know-How and CRISPR Program Know-How, that (a) [***] and (b) [***]. On a Collaboration Target-by-Collaboration Target basis, CRISPR Background Know-How will exclude [***]. For the avoidance of doubt, the CRISPR Background Know-How includes the Know-How claimed or disclosed in the CRISPR Platform Technology Patents.

1.45. " **CRISPR Background Patents** " means any Patent, other than a Joint Program Patent, CRISPR Program Patent or CRISPR Platform Technology Patent that (a) [***] and (b) [***]. On a Collaboration Target-by-Collaboration Target basis, CRISPR Background Patents will exclude [***].

1.46. " **CRISPR Breach Event** " has the meaning set forth in Section 11.2.3(a).

1.47. " **CRISPR Entity** " means, when used in the singular, any one of CRISPR UK, CRISPR AG, CRISPR Inc. or Tracr. " **CRISPR Entities** " means, when used in the plural, CRISPR UK, CRISPR AG, CRISPR Inc. and Tracr.

1.48. " **CRISPR Indemnified Party** " has the meaning set forth in Section 10.1.

1.49. " **CRISPR In-License Agreements** " has the meaning set forth in Section 7.6.1.

1.50. " **CRISPR Platform Technology Patents** " means all Patents that are owned, used, developed by, or licensed to CRISPR or its Affiliates, in each case to the extent Controlled by CRISPR or its Affiliates on the Effective Date or at any time during the Agreement Term, claiming [***]. For clarity, the CRISPR Platform Technology Patents (i) will not include [***] and (ii) will include all [***].

1.51. "[***] **Patent** " has the meaning set forth in Section 8.1.3(a).

1.52. " **CRISPR Program Breach** " has the meaning set forth in Section 11.2.3(a).

1.53. " **CRISPR Program Know-How** " has the meaning set forth in Section 8.1.2(a).

1.54. " **CRISPR Program Patents** " has the meaning set forth in Section 8.1.2(a).

1.55. " **CRISPR Program Technology** " has the meaning set forth in Section 8.1.2(a).

1.56. " **CRISPR Reserved Target** " means all Targets described or identified on Schedule A.

1.57. " **CRISPR/Cas System** " means a clustered regularly interspaced short palindromic repeats (CRISPR)/CRISPR-associated (Cas) protein system that comprises (a) [***] and (b) [***].

1.58. " **Development** " means, with respect to a Licensed Agent, all clinical and non-clinical research and development activities conducted after filing of an IND for such Licensed Agent, including toxicology, pharmacology test method development and stability testing, process development, formulation development, delivery system development, quality assurance and quality control development, statistical analysis, Clinical Trials (other than post-Marketing Approval Clinical Trials), regulatory affairs, pharmacovigilance, Clinical Trial regulatory activities and obtaining and maintaining Regulatory Approval. When used as a verb, "Develop" or "Developing" means to engage in Development.

1.59. " **Disclosing Party** " has the meaning set forth in Section 12.1.

1.60. " **Distracting Product** " means a product containing (a) [***] or (b) [***].

1.61. " **Distributor** " means a Third Party to whom Vertex grants a right to sell or distribute a Product, that does not make payments to Vertex that are calculated on the basis of a percentage of, or profit share on, such Third Party's sales of Products.

1.62. " **Divestiture** " means, with respect to a Distracting Product, the sale, exclusive license or other transfer by the applicable Party and its Affiliates of all of their development and commercialization rights with respect to such Distracting Product to a Third Party without the retention or reservation of any development or commercialization obligation, interest or participation rights (other than solely an economic interest or the right to enforce customary terms and conditions contained in the relevant agreements effectuating such transaction). When used as a verb, "Divest" means the to engage in a Divestiture.

1.63. " **DOJ** " has the meaning set forth in Section 4.1.2(a).

1.64. " **Effective Date** " has the meaning set forth in the Preamble.

1.65. " **EMA** " means the European Medicines Agency and any successor entity thereto.

1.66. " **Establishment of POC** " with respect to a Product, [***] that [***] (a) [***] and (b) [***].

1.67. " **European Commission** " means the European Commission or any successor entity that is responsible for granting marketing approvals authorizing the sale of pharmaceuticals in the European Union.

1.68. " **European Union** " or " **EU** " means each and every country or territory that is officially part of the European Union.

1.69. " **Exclusive License** " has the meaning set forth in Section 5.3.1.

1.70. " **Executive Officers** " means the Chief Scientific Officer of CRISPR AG, initially Sven Ante (Bill) Lundberg, and the Chief Scientific Officer of Vertex, initially David Altshuler; *provided* , that for purposes of Section 11.3.4(a), "Executive Officers" means the Chief Executive Officer of CRISPR AG, initially Rodger Novak, and the Chief Financial Officer of Vertex, initially Ian Smith.

1.71. " **FDA** " means the United States Food and Drug Administration and any successor entity thereto.

1.72. " **FD&C Act** " means the United States Federal Food, Drug, and Cosmetic Act, as amended, and the rules and regulations promulgated thereunder.

1.73. " **Field** " means the diagnosis, treatment or prevention of disease in humans or animals in [***].

1.74. " **Final Target Selection Period** " means the [***] period following the Initial Target Selection Period.

1.75. " **First Commercial Sale** " means with respect to a Product, the first sale of such Product by Vertex, its Affiliate or its Sublicensee to a Third Party resulting in Net Sales in a particular country after any required Marketing Approval for the Product has been obtained in such country.

1.76. " **Force Majeure** " means a condition, the occurrence and continuation of which is beyond the reasonable control of a Party, including an act of God, voluntary or involuntary compliance with any regulation, law or order of any government, war, civil commotion, labor strike or lock-out, epidemic, flood, failure or default of public utilities or common carriers, destruction of production facilities or materials by fire, earthquake, storm or like catastrophe.

1.77. " **Foundational Intellectual Property Rights** " means all rights, title and interest in [***]; and any worldwide patents and patent applications claiming priority thereto and all inventions covered or claimed by such patent applications (together with all provisionals, non-provisionals, substitutions, continuations, continuations-in-part, divisionals, renewals and all patents granted thereon, and all reissues, reexaminations, extensions, confirmations, revalidations, registrations and patents of addition thereof, including patent term extensions and supplementary protection certificates, international patent applications filed under the Patent Cooperation Treaty (PCT) and any foreign equivalents to any of the foregoing).

1.78. " **FTC** " has the meaning set forth in Section 4.1.2(a).

1.79. " **FTE Rate** " means, [***]; *provided* that such rates will increase or decrease on [***] over the twelve month period preceding each such January 1.

1.80. " **GAAP** " means United States generally accepted accounting principles, consistently applied.

1.81. " **GCP** " means good clinical practices, which are the then-current standards for Clinical Trials for pharmaceuticals, as set forth in the FD&C Act or other Applicable Law, and such standards of good clinical practice as are required by the Regulatory Authorities of the European Union and other organizations and governmental authorities in countries for which the applicable Licensed Agent is intended to be Developed, to the extent such standards are not less stringent than United States standards.

1.82. "[***] **Joint Program Know-How** " has the meaning set forth in Section 8.1.2(d).

1.83. "[***] **Joint Program Patents** " has the meaning set forth in Section 8.1.2(d).

1.84. "[***] **Joint Program Technology** " has the meaning set forth in Section 8.1.2(d).

1.85. "[***]" means [***], including, but not limited to, [***], and any variation thereof, in each case [***].

1.86. " **Generic Product** " means, with respect to a particular Product in a particular country, a product on the market in such country commercialized by any Third Party that is not a Sublicensee and that did not purchase such product in a chain of distribution that included any of Vertex or its Affiliates or Sublicensees, that (a) is approved by the applicable Regulatory Authority, under any then-existing laws and regulations in the applicable country pertaining to approval of generic or biosimilar biologic products, as a "generic" or "biosimilar" version of such Product, which approval uses such Product as a reference product and relies on or references pivotal safety or efficacy data in the Approval Application for such Product or (b) otherwise meets the criteria for constituting a "biosimilar" or "interchangeable" product pursuant to Section 351(k) of the Public Health Service Act (42 U.S.C. § 262(k)) or EMA Directive 2001/83/EC or any foreign equivalent thereof or successors thereto.

1.87. " **GLP** " means the then-current good laboratory practice standards promulgated or endorsed by the FDA as defined in 21 C.F.R. Part 58 or the successor thereto, or comparable regulatory standards in jurisdictions outside of the United States, to the extent such standards are not less stringent than United States standards.

1.88. " **Governmental Authority** " means any court, agency, department, authority or other instrumentality of any national, state, county, city or other political subdivision.

1.89. " **Hemoglobinopathy Target** " means a Target related to the [***].

1.90. " **HSR Act** " means the Hart-Scott-Rodino Antitrust Improvements Act of 1976, as amended, and the rules and regulations promulgated thereunder.

1.91. " **HSR Clearance Date** " means the earliest date on which the Parties have actual knowledge that all applicable waiting periods under the HSR Act with respect to the transactions contemplated hereunder have expired or have been terminated.

1.92. " **HSR Filing** " means a filing by Vertex and CRISPR with the FTC and the DOJ of a Notification and Report Form for Certain Mergers and Acquisitions (as that term is defined in the HSR Act) with respect to the matters set forth in this Agreement, together with all required documentary attachments thereto.

1.93. " **IND** " means any Investigational New Drug application, filed with the FDA pursuant to Part 312 of Title 21 of the U.S. Code of Federal Regulations, including any supplements or amendments thereto. References herein to IND will include, to the extent applicable, any comparable filings outside the United States.

1.94. " **Indemnified Party** " has the meaning set forth in Section 10.3.

1.95. " **Indemnifying Party** " has the meaning set forth in Section 10.3.

1.96. " **Initial Collaboration Targets** " means the Targets set forth on Schedule B under the heading "Initial Collaboration Targets."

1.97. " **Initial Target Selection Period** " means the first [***] of the Research Term.

1.98. **"Initiation** " or " **Initiate** " means, with respect to any Clinical Trial, dosing of the first human subject in such Clinical Trial.

1.99. " **Insolvency Event** " has the meaning set forth in Section 11.2.5.

1.100. " **Joint Development & Commercialization Agreement** " has the meaning set forth in Section 6.1.2(c).

1.101. " **Joint Program Know-How** " means [***] Joint Program Know-How, [***] Joint Program Know-How and Other Joint Program Know-How.

1.102. " **Joint Program Patents** " means [***] Joint Program Patents, [***] Joint Program Patents and Other Joint Program Patents.

1.103. " **Joint Program Technology** " means [***] Joint Program Technology, [***] Joint Program Technology and Other Joint Program Technology.

1.104. " **Joint Research Committee** " or " **JRC** " has the meaning set forth in Section 3.1.1.

1.105. " **Know-How** " means intellectual property, data, results, pre-clinical and clinical protocols and data from studies and Clinical Trials, chemical structures, chemical sequences, information, inventions, know-how, formulas, trade secrets, techniques, methods, processes, procedures and developments, whether or not patentable; *provided* that Know-How does not include Patents claiming any of the foregoing.

1.106. " **Knowledge** " means [***] of [***] after [***].

1.107. " **Liability** " has the meaning set forth in Section 10.1.

1.108. " **Licensed Agent** " means a product comprising (a) [***], where such [***], or any portion thereof is [***] or (b) [***] by such [***].

1.109. " **Licensed Know-How** " means (a) CRISPR Background Know-How, (b) CRISPR Program Know-How and (c) CRISPR's interest in the Joint Program Know-How.

1.110. " **Licensed Patents** " means (a) CRISPR Background Patents, (b) CRISPR Platform Technology Patents, (c) CRISPR Program Patents, (d) [***] Patents (until [***]) and (e) CRISPR's interest in the Joint Program Patents.

1.111. " **Licensed Technology** " means, subject to Section 5.3.2 and Section 7.6.6, any and all Licensed Patents and Licensed Know-How.

1.112. " **Major Market Country** " means any one of the following countries: [***].

1.113. " **Manufacture** " or " **Manufactured** " or " **Manufacturing** " means activities directed to making, having made, producing, manufacturing, processing, filling, finishing, packaging, labeling, quality control testing and quality assurance release, shipping or storage of a product.

1.114. " **Marketing Approval** " means, with respect to a Product in a particular jurisdiction, all approvals, licenses, registrations or authorizations necessary for the Commercialization of such Product in such jurisdiction, including, with respect to the United States, approval of an Approval Application for such Product by the FDA and with respect to the European Union, approval of an Approval Application for such Product by the European Commission.

1.115. " **Materials** " means all biological materials or chemical compounds arising out of a Party's activities under this Agreement or otherwise provided by a Party for use by the other Party to conduct activities pursuant to this Agreement, including Licensed Agents, Clinical Trial samples, cell lines, assays, viruses and vectors.

1.116. " **NDA** " means a new drug application that is submitted to the FDA for marketing approval for a Licensed Agent or Product, pursuant to 21 C.F.R. § 314.3.

1.117. " **Net Sales** " means the gross invoiced price for Products sold by Vertex, its Affiliates or Sublicensees (the " **Selling Party** ") to Third Parties, less the following deductions from such gross amounts:

(a) credits or allowances, if any are actually allowed, on account of price adjustments, recalls, claims, damaged goods, rejections or returns of items previously sold (including product returned in connection with recalls or withdrawals) and amounts written off by reason of uncollectible debt , provided that if the debt is thereafter paid, the corresponding amount shall be added to the Net Sales for the period during which it is paid ;

(b) import taxes, export taxes, excise taxes (including annual fees due under Section 9008 of the United States Patient Protection and Affordable Care Act of 2010 (Pub. L. No. 111-48)), sales taxes, value-added taxes, consumption taxes, duties or other taxes levied on, absorbed, determined or imposed with respect to such sales (excluding income or net profit taxes or franchise taxes of any kind), to the extent not reimbursed by a non-related party;

(c) insurance, customs charges, freight, shipping and other transportation costs incurred in shipping product to such non-related parties, to the extent incurred by a Selling Party and not reimbursed by a non-related party;

(d) reasonable discounts (including trade, quantity and cash discounts) actually allowed, cash and non-cash coupons, retroactive price reductions, and charge back payments and rebates granted to any non-related party (including to governmental entities or agencies, purchasers, reimbursers, customers, Distributors, wholesalers, and group purchasing organizations and managed care organizations (and other similar entities and institutions)); and

(e) rebates (or their equivalent), administrative fees, chargebacks and retroactive price adjustments and any other similar allowances granted to non-related Parties (including to Governmental Authorities, purchasers, reimbursers,

customers, Distributors, wholesalers, and managed care organizations (and other similar entities and institutions)) which effectively reduce the gross invoiced sales price of the Product.

Generally, only items that are deducted from the Selling Party's gross invoiced sales price of Product(s), as included in the Selling Party's published financial statements and that are in accordance with GAAP, applied on a consistent basis, will be deducted from such gross invoiced sales price for purposes of the calculation of Net Sales. However, compulsory payments required by federal or state governments based upon sales volume or market share of Products (but for clarity excluding taxes on the Selling Party's net income), to the extent borne by the Selling Party, will be deducted from "Net Sales" regardless of its classification in the Selling Party's published financial statements; *provided* that any such deduction will be limited to that share of such compulsory payment proportional to the share of the total sales volume or market share of the Selling Party used to compute the compulsory payment represented by applicable Net Sales of Products.

A qualifying amount may be deducted only once regardless of the number of the preceding categories that describe such amount. If a Selling Party makes any adjustment to such deductions after the associated Net Sales have been reported pursuant to this Agreement, the adjustments and payment of any royalties due will be reported with the next quarterly report. Sales between or among Vertex, its Affiliates and Sublicensees will be excluded from the computation of Net Sales if such sales are not intended for end use, but Net Sales will include the subsequent final sales to Third Parties by Vertex or any such Affiliates or Sublicensees. A Product will not be deemed to be sold if the Product is provided free of charge to a Third Party in reasonable quantities as a sample consistent with industry standard promotional and sample practices. For clarity, [***].

If a sale, transfer or other disposition with respect to Products involves consideration other than cash or is not at arm's length, then the Net Sales from such sale, transfer or other disposition will be calculated on the [***].

Solely for purposes of calculating Net Sales, if Vertex or its Affiliates or any permitted Sublicensee sells a Product in the form of a combination product containing a Licensed Agent and one or more other therapeutically or prophylactically active ingredients or delivery devices (whether combined in a single formulation or package, as applicable, or formulated separately but packaged under a single label approved by a Regulatory Authority and sold together for a single price) (a " **Combination Product** "), Net Sales of such Combination Product for the purpose of determining the payments due to CRISPR pursuant to this Agreement will be calculated by multiplying actual Net Sales of such Combination Product as determined in the first paragraph of the definition of "Net Sales" by the fraction A/(A+B) where [***]. The weighted average invoice prices referenced above will be calculated with reference to the prevailing prices during the applicable Calendar Quarter in those top selling countries that equate to [***] of Net Sales of the applicable Product in the Territory, with the prices weighted in the calculation to reflect the actual relative sales value of the Product in each of the countries to which the calculation relates. If it is not possible to determine the fraction A/(A+B) based on the criteria specified in the preceding sentence (*e.g.* , if a Product component is not sold separately), the Parties shall determine Net Sales for the Product in such Combination Product in good faith by mutual agreement [***].

1.118. "[***]" has the meaning set forth in Section 7.6.2(a).

1.119. " **Non-Breaching Party** " means the Party that believes the other Party is in material breach of this Agreement.

1.120. " **Non-Disclosing Party** " has the meaning set forth in Section 12.5.3.

1.121. " **Option** " has the meaning set forth in Section 4.1.1.

1.122. " **Option Cap** " has the meaning set forth in Section 4.1.1.

1.123. " **Option Deadline** " has the meaning set forth in Section 4.1.1.

1.124. " **Option Exercise** " means, with respect to a Collaboration Target, Vertex's exercise of an Option as provided in Section 4.1.1; *provided* , that if Vertex notifies CRISPR that an HSR Filing is required as provided, in Section 4.1.1, Option Exercise will not occur until the HSR Clearance Date.

1.125. " **Option Exercise Data Package** " means, with respect to a Collaboration Program, a data package containing the information set forth on Schedule C.

1.126. " **Other Joint Program Know-How** " has the meaning set forth in Section 8.1.2(e).

1.127. " **Other Joint Program Patents** " has the meaning set forth in Section 8.1.2(e).

1.128. " **Other Joint Program Technology** " has the meaning set forth in Section 8.1.2(e).

1.129. " **Out-of-Pocket Costs** " means, with respect to a Party, costs and expenses paid by such Party to Third Parties (or payable to Third Parties and accrued in accordance with GAAP), other than Affiliates or employees of such Party.

1.130. " **Party** " or " **Parties** " has the meaning set forth in the Preamble.

1.131. " **Patent Coordinator** " has the meaning set forth in Section 8.3.

1.132. " **Patent Costs** " means the reasonable fees and expenses paid to outside legal counsel, and filing, maintenance, disbursement and other reasonable Out-of-Pocket Costs paid to Third Parties, in connection with the Prosecution and Maintenance of Patents.

1.133. " **Patents** " means the rights and interests in and to issued patents and pending patent applications in any country, jurisdiction or region (including inventor's certificates and utility models), including all provisionals, non-provisionals, substitutions, continuations, continuations-in-part, divisionals, renewals and all patents granted thereon, and all reissues, reexaminations, extensions, confirmations, revalidations, registrations and patents of addition thereof, including patent term extensions and supplementary protection certificates, international patent applications filed under the Patent Cooperation Treaty (PCT) and any foreign equivalents to any of the foregoing.

1.134. " **Person** " means an individual, sole proprietorship, partnership, limited partnership, limited liability partnership, corporation, limited liability company, business trust, joint stock company, trust, incorporated association, joint venture or similar entity or organization, including a government or political subdivision or department or agency of a government.

1.135. " **Phase 2 Clinical Trial** " means any human Clinical Trial conducted in patients that is intended to provide preliminary evidence suggesting effectiveness of the drug, including Clinical Trials described in 21 C.F.R. §312.21(b), or, with respect to a jurisdiction other than the United States, a similar Clinical Trial.

1.136. " **Phase 3 Clinical Trial** " means, with respect to a Product, a pivotal Clinical Trial in humans performed to gain evidence with statistical significance of the efficacy of such Product in a target population, and to obtain expanded evidence of safety for such Product that is needed to evaluate the overall benefit-risk relationship of such Product, to form the basis for approval of an Approval Application by a Regulatory Authority and to provide an adequate basis for physician labeling, as described in 21 C.F.R. 312.21(c), as amended from time to time, or the corresponding regulations in jurisdictions other than the United States.

1.137. " **Price Approval** " means, in any country where a Governmental Authority authorizes reimbursement for, or approves or determines pricing for, pharmaceutical products, receipt (or, if required to make such authorization, approval or determination effective, publication) of such reimbursement authorization or pricing approval or determination.

1.138. " **Proceeding** " means an action, suit or proceeding.

1.139. " **Product** " means any pharmaceutical product, medical therapy, preparation, substance, or formulation comprising or employing, in whole or in part, a Licensed Agent. All Products comprising the same Licensed Agent(s) (and no additional Licensed Agents) will be considered the same Product under this Agreement.

1.140. "[***] **Claim** " means a claim in any Patent that [***].

1.141. " **Product Development & Commercialization Plan** " has the meaning set forth in Section 6.4.

1.142. " **Prosecution and Maintenance** " or " **Prosecute and Maintain** " means, with regard to a Patent, the preparing, filing, prosecuting and maintenance of such Patent, as well as handling re-examinations and reissues with respect to such Patent, together with the conduct of interferences, the defense of oppositions and other similar proceedings with respect to the particular Patent. For clarification, " **Prosecution and Maintenance** " or " **Prosecute and Maintain** " will not include any other enforcement actions taken with respect to a Patent.

1.143. "[***] **Patent** " has the meaning set forth in Section 8.2.2.

1.144. " **Receiving Party** " has the meaning set forth in Section 12.1.

1.145. " **Regulatory Approval** " means the technical, medical and scientific licenses, registrations, authorizations and approvals (including approvals of Approval Applications, supplements and amendments, pre- and post- approvals, and labeling approvals) of any Regulatory Authority, necessary for the Research, Development, clinical testing, commercial manufacture, distribution, marketing, promotion, offer for sale, use, import, export or sale of a pharmaceutical product in a regulatory jurisdiction, including Marketing Approval.

1.146. " **Regulatory Authority** " means, with respect to a country in the Territory, any national (*e.g.* , the FDA), supra-national (*e.g.* , the European Commission, the Council of the European Union, or the EMA), regional, state or local regulatory agency, department, bureau, commission,

council or other Governmental Authority involved in the granting of Regulatory Approvals or Price Approvals for pharmaceutical products in such country or countries.

1.147. " **Regulatory Filings** " means, collectively: (a) all INDs, Approval Applications, establishment license applications, Drug Master Files, applications for designation as an "Orphan Licensed Product(s)" under the Orphan Drug Act, for "Fast Track" status under Section 506 of the FD&C Act (21 U.S.C. § 356) or for a Special Protocol Assessment under Section 505(b)(4)(B) and (C) of the FD&C Act (21 U.S.C. § 355(b)(4)(B)) and all other similar filings (including counterparts of any of the foregoing in any country or region in the Territory); (b) any applications for Regulatory Approval or Price Approval and other applications, filings, dossiers or similar documents submitted to a Regulatory Authority in any country for the purpose of obtaining Regulatory Approval or Price Approval from that Regulatory Authority; (c) all supplements and amendments to any of the foregoing; and (d) any correspondence with Regulatory Authorities in connection with any of the foregoing.

1.148. " **Research** " means conducting research activities to discover and advance Licensed Agents and Products, including pre-clinical studies and optimization, but specifically excluding Development and Commercialization. When used as a verb, "Researching" means to engage in Research.

1.149. " **Research Budget** " has the meaning set forth in Section 2.2.

1.150. " **Research Costs** " means the costs and expenses that are actually incurred by or on behalf of CRISPR and specifically identifiable or specifically allocable to the Research activities conducted under a Research Plan (including Continuation Research) or an Additional Research Plan, including: (a) CRISPR's and its Affiliates fully absorbed internal costs with respect to such activities; and (b) all Out-of-Pocket Costs incurred by CRISPR or its Affiliates, including payments made to Third Parties with respect to such Research activities (except to the extent that such costs have been included in internal costs). CRISPR's fully absorbed internal costs will be determined at the [***]. All other costs will be determined from the books and records of CRISPR and its Affiliates maintained in accordance with GAAP.

1.151. " **Research Plan** " means each plan meeting the requirements set forth in Section 2.2 to design and optimize Licensed Agents and Products for a specified Target and to generate the data and information required to prepare the applicable Option Exercise Data Package.

1.152. " **Research Term** " has the meaning set forth in Section 2.4.

1.153. " **Residual Knowledge** " means knowledge, techniques, experience and Know-How that are (a) reflected in any Confidential Information owned or Controlled by the Disclosing Party and (b) retained in the unaided memory of any authorized representative of the Receiving Party after having access to such Confidential Information. A Person's memory will be considered to be unaided if the Person has not intentionally memorized the Confidential Information for the purpose of retaining and subsequently using or disclosing it. In no event, however, will Residual Knowledge include any knowledge, techniques, experience and Know-How to the extent (at any time, for such time) within the scope of any valid patent claim owned or Controlled by the Disclosing Party.

1.154. " **Royalty Term** " means, with respect to a Product in a country, the period commencing on the first sale of such Product in such country and ending upon the later of: (a) the expiration

of the last Valid Claim of a Licensed Patent that Covers such Product in such country; (b) [***] after the First Commercial Sale of such Product in such country; or (c) expiration of all applicable regulatory exclusivity periods, including data exclusivity, in such country with respect to such Product.

1.155. " **Safety Data Exchange Agreement** " has the meaning set forth in Section 6.6.3.

1.156. " **Selling Party** " has the meaning set forth in Section 1.117.

1.157. " **Setoff Amount** " has the meaning set forth in Section 11.3.3.

1.158. [***].

1.159. **"Shared Product** " has the meaning set forth in Section 6.1.2(a).

1.160. " **Subcontractor** " has the meaning set forth in Section 2.9.

1.161. " **Sublicense** " means, directly or indirectly, to sublicense, grant any other right with respect to, or agree not to assert, any licensed right under any Patent, Know-How or other intellectual property right. When used as a noun, "Sublicense" means any agreement to Sublicense.

1.162. " **Sublicensee** " means an Affiliate or Third Party, other than a Distributor, to whom Vertex (or a Sublicensee or Affiliate) sublicenses any of the rights granted to Vertex hereunder during the Agreement Term.

1.163. " **Substitution Cap** " has the meaning set forth in Section 2.3.2(a).

1.164. " **Target** " means a [***] the [***] of which is associated with a human disease and which is to be edited, [***] in order to treat, ameliorate or prevent such disease.

1.165. " **Target Cap** " has the meaning set forth in Section 2.3.2(a).

1.166. " **Target Selection Period** " means the Initial Target Selection Period and the Final Target Selection Period.

1.167. "[***] **Joint Program Know-How** " has the meaning set forth in Section 8.1.2(c).

1.168. "[***] **Joint Program Patents** " has the meaning set forth in Section 8.1.2(c).

1.169. "[***] **Joint Program Technology** " has the meaning set forth in Section 8.1.2(c).

1.170. " **Targeting** " means [***] a Target or the [***] thereof.

1.171. " **Territory** " means all countries of the world.

1.172. " **Third Party** " means any Person other than Vertex, CRISPR or their respective Affiliates.

1.173. " **Third Party Obligations** " means any non-financial encumbrances, obligations, restrictions, or limitations imposed by a CRISPR In-License Agreement or [***] that are required to be passed through to a sublicensee and relate to a Product or a Collaboration Target, including

field or territory restrictions, covenants, diligence obligations or limitations pertaining to enforcement of intellectual property rights.

1.174. " **United States** " or " **U.S.** " means the fifty states of the United States of America and all of its territories and possessions and the District of Columbia.

1.175. " **Valid Claim** " means a claim (a) of any issued, unexpired United States or foreign Patent, which will not, in the country of issuance, have been donated to the public, disclaimed, nor held invalid or unenforceable by a court of competent jurisdiction in an unappealed or unappealable decision, or (b) of any United States or foreign patent application, which will not, in the country in question, have been cancelled, withdrawn or abandoned. Notwithstanding the foregoing, on a country-by-country basis, a patent application pending for more than [***] years, or [***], will not be considered to have any Valid Claim for purposes of this Agreement unless and until a patent meeting the criteria set forth in clause (a) above with respect to such application issues.

1.176. " **Vertex** " has the meaning set forth in the Preamble.

1.177. " **Vertex Activities** " means, under any Research Plan, any and all Research activities that Vertex agrees to conduct and for which it is specifically designated as the responsible Party under the Research Plan.

1.178. " **Vertex Background Know-How** " means any Know-How, other than Joint Program Know-How and Vertex Program Know-How, that (a) Vertex or any of its Affiliates Control as of the Effective Date or that comes into the Control of Vertex or any of its Affiliates during the Agreement Term and (b) [***].

1.179. " **Vertex Background Patents** " means any Patent, other than a Joint Program Patent or Vertex Program Patent that (a) Vertex or any of its Affiliates Control as of the Effective Date or that comes into the Control of Vertex or any of its Affiliates during the Agreement Term and (b) [***].

1.180. " **Vertex Indemnified Party** " has the meaning set forth in Section 10.2.

1.181. " **Vertex Parent** " has the meaning set forth in the Preamble.

1.182. " **Vertex Program Know-How** " has the meaning set forth in Section 8.1.2(b).

1.183. " **Vertex Program Patents** " has the meaning set forth in Section 8.1.2(b).

1.184. " **Vertex Program Technology** " has the meaning set forth in Section 8.1.2(b).

1.185. " **Vertex Share** " has the meaning set forth in Section 7.6.4.

1.186. " **Vertex Target** " has the meaning set forth in Section 2.3.1.

1.187. " **Vertex Target List** " has the meaning set forth in Section 2.3.1.

1.188. " **Vertex Technology** " means (a) the Vertex Background Know-How, (b) the Vertex Background Patents, (c) the Vertex Program Technology, and (d) Vertex's interest in any Joint Program Technology.

1.189. " **Vertex UK** " has the meaning set forth in the Preamble.

ARTICLE 2.
RESEARCH

2.1. **Collaboration Overview** . The Parties will collaborate by performing the activities set forth in each Research Plan for the purpose of designing and optimizing Licensed Agents and Products for Vertex (or with respect to the Shared Products, for the Parties) to advance through Clinical Trials and bring to patients as commercial products in the Field.

2.2. **Research Plans** . During the Research Term CRISPR and Vertex will conduct Collaboration Programs, each under a separate Research Plan, focused on the design and optimization of Licensed Agents and Products for a specific Collaboration Target. The components of the initial Research Plans to be developed for the Collaboration Targets are attached hereto as Schedule D. Each Research Plan will be generally consistent with such initial Research Plans with respect to the scope and content thereof. The Collaboration Program Working Group will update each ongoing Research Plan and submit the updated Research Plans to the JRC for its review and approval on an as-needed basis, but in no event less than once every [***]. Each Research Plan will include (a) a description of the process and criteria to be used by the Parties to design and optimize Licensed Agents to be used in Products directed to the applicable Collaboration Target, (b) projected timelines for activities under the Research Plan, (c) a budget for activities under such Research Plan (each, a " **Research Budget** "), (d) decision points and associated criteria for the Research Plan, including, without limitation, pre-specified criteria for establishing the elements of the Option Exercise Data Package for the applicable Collaboration Target, (e) a description of which Party will be responsible for each activity under the Research Plan; *provided* that unless otherwise specified in the applicable Research Plan, each Party will be responsible for the activities for which it is listed under the heading "Responsible Party" on Schedule C, and (f) the content of an Option Exercise Data Package, and, to the extent practicable, the specific criteria for acceptance of the Option Exercise Data Package (*e.g.* , [***]).

2.3. **Target Selection** .

2.3.1. **Vertex Target List** . The Collaboration Targets will be selected from a list of Targets selected by Vertex (each such Target, a " **Vertex Target,** " and collectively, the " **Vertex Targets** " and such list, the " **Vertex Target List** "). As of the Effective Date, the initial Collaboration Targets and initial Vertex Targets are included on Schedule B.

2.3.2. **Process to Update the Vertex Target List** .

(a) Subject to Section 2.3.2(c), Vertex may [***] Targets as Vertex Targets on the Vertex Target List [***] a Target for a Vertex Target on the Vertex Target List (subject to the [***] Cap) upon written notice to CRISPR; *provided* that (i) [***], and (ii) [***] (the " **Target Cap** "). If the [***] to the Vertex Target List would cause the number of Vertex Targets on the Vertex Target List to [***] or

if Vertex is [***] during the Final Target Selection Period, such notice also will specify the Vertex Target to be [***] on the Vertex Target List by such [***] Target. Vertex shall be permitted to [***] of (A) [***] and (B) [***] ((A) or (B), as applicable, the "[***] **Cap** ").

(b) For the avoidance of doubt, (1) after the Initial Target Selection Period, Vertex may [***] Targets as Vertex Targets and (2) after the first [***] of the Final Target Selection Period Vertex may [***] Targets within the Vertex Target List, in each case, [***]. The Parties will in good faith discuss any request by Vertex during the Research Term to [***] Targets on the Vertex Target List made at any time when Vertex does not have the right to make such [***] under Section 2.3.2(a).

(c) If Vertex proposes to [***] a CRISPR Reserved Target to the Vertex Target List or [***] a CRISPR Reserved Target for a Vertex Target on the Vertex Target List pursuant to Section 2.3.2(a) above, such [***] shall not be effective, and CRISPR shall notify Vertex in writing within [***] after the date on which CRISPR receives notice of the proposed [***], that such Target is a CRISPR Reserved Target. CRISPR shall, if requested by Vertex in writing, [***] and, if CRISPR [***] that such Target is a [***] based, in whole or in part, on [***], it shall so notify Vertex. If after providing [***] Vertex will so notify CRISPR, then CRISPR will, [***]. If CRISPR [***] that such Target is a [***] under [***], Vertex may [***]. The [***] shall promptly [***]. The [***] *; provided* , that if, notwithstanding [***], CRISPR believes that a Target is a CRISPR Reserved Target under paragraph 3 of Schedule A, CRISPR may pursue [***] solely with respect to [***]. If a proposed Target is not [***] due to the provisions of this Section 2.3.2(c), such Target will not count against the Substitution Cap (if applicable) and the Vertex Target on the Vertex Target List that was to be replaced by such Target shall remain on the Vertex Target List (if applicable). If, during the Research Term, any Target excluded from the Vertex Target List pursuant to this Section 2.3.2(c) ceases to be a CRISPR Reserved Target, CRISPR will promptly notify Vertex that such Target is no longer a CRISPR Reserved Target, and, thereafter, Vertex may at its option (exercisable at any time within [***] of such notice) add such Target to the Vertex Target List, subject to the limitations set forth in this Section 2.3.2. Vertex may remove Targets from the Vertex Target List upon written notice to CRISPR and thereafter such removed Target will no longer be a Vertex Target (unless such Target is later added again as a Vertex Target in accordance with this Section 2.3.2).

2.3.3. **Collaboration Target Selection** . Vertex may elect to designate a Vertex Target as a Collaboration Target at any time during the Research Term upon written notice to CRISPR. Within [***] after the designation of a Collaboration Target, the Collaboration Program Working Group will be formed and will provide the JRC an initial draft Research Plan for such Collaboration Target. Subject to Section 3.1.3, the JRC will review such plan and agree upon a final Research Plan for such Collaboration Target. Collaboration Targets continue to be included as Vertex Targets for purposes of the Target Cap.

2.3.4. [***]. The Parties acknowledge that [***] is included as an Initial Collaboration Target [***]. During the Research Term, CRISPR will periodically disclose to Vertex any material findings generated by CRISPR in connection with CRISPR's internal research supporting the conclusion [***]. Following Vertex's receipt of such data, Vertex may elect to [***], as applicable. If any such [***] (other than [***]) is [***], (a) Vertex will [***] and (b) the Collaboration Program Working Group will prepare a Research Plan for [***] and submit such plan to the JRC for its approval as provided in Section 2.3.3.

2.4. **Research Term**. The term for the conduct of the Collaboration Programs (the " **Research Term** ") will begin on the Effective Date and will end on the earlier of (a) the date on which [***] and [***] with respect to six Collaboration Targets and (b) the [***] of the Effective Date; *provided, however,* that if any Research activities under a Research Plan (including any Continuation Research) are incomplete on such [***] (and Vertex has not [***]), the Parties will complete such activities in accordance with the applicable Research Plan, and the Research Term will be extended with respect to such Research Plan(s) for up to [***] to complete such activities or [***]; and *provided further,* that during any portion of the Research Term after the [***] of the Effective Date, the Vertex Target List will be dissolved and neither Party will have any further obligation under this Agreement (including under Section 2.13.1) with respect to any Vertex Target that was not selected as a Collaboration Target.

2.5. **Research Activities**. Following the JRC's approval of a Research Plan, each Party will use Commercially Reasonable Efforts to perform activities for which such Party is responsible under such Research Plan in accordance with the timelines set forth therein. Vertex will be responsible for carrying out all Vertex Activities under a Research Plan, and CRISPR will be responsible for carrying out all CRISPR Activities under each Research Plan. Each Party will, and will require its Affiliates and Subcontractors to, comply with all Applicable Laws in its and their conduct of the activities under a Research Plan, including where appropriate cGMP, GCP and GLP (or similar standards). No more than [***] Research Plans shall be conducted at any given time during the Initial Target Selection Period and no more than [***] Research Plans shall be conducted at any given time during the Final Target Selection Period. CRISPR will dedicate such number of FTEs as is reasonably required to perform the CRISPR Activities under the Research Plans during the Target Selection Period, which CRISPR currently anticipates will be no fewer than an average of [***] FTEs to the performance of Research Plans during the Initial Target Selection Period and no fewer than an average of [***] FTEs to the performance of Research Plans during the Final Target Selection Period.

2.6. **Option Exercise Data Package**. Within [***] after completion of activities under a Research Plan, CRISPR will provide Vertex with an Option Exercise Data Package for the relevant Collaboration Program. Following Vertex's receipt of the Option Exercise Data Package for a Collaboration Program, Vertex may exercise the Option for the relevant Collaboration Target as provided in Section 4.1; *provided* , that if, within [***] after receipt of the Option Exercise Data Package, Vertex notifies the JRC [***] that [***] with respect to [***] should be [***] of such [***] (such notice, a "[***]" and such [***]), and either (a) the requested [***] can reasonably be [***] within [***] following the initiation thereof through the use of [***] or (b) the requested [***] cannot reasonably be [***] within [***] following the initiation thereof, but the Parties mutually agree to [***], the Collaboration Program Working Group will meet and in good faith determine such amendments to the Research Plan as are required to define the activities to be conducted in connection with such Continuation Research and will submit

such amendments to the JRC for approval. Following the JRC's approval of such amendment, (i) the Parties will conduct the Continuation Research in accordance with Section 2.5, subject to any limitations or conditions that may be agreed to by the Parties in agreeing to conduct the Continuation Research under the foregoing clause (b), (ii) Vertex will fund such activities as provided in Section 2.10 and (iii) the Collaboration Program Working Group will monitor performance of such Continuation Research and meet no less than [***] (or more frequently as determined by the JRC) to discuss the status thereof. Within [***] following the completion of the Continuation Research, CRISPR will provide Vertex with a revised Option Exercise Data Package reflecting the results of the Continuation Research. CRISPR will provide to Vertex any additional Know-How or data Controlled by CRISPR relating to the applicable Collaboration Target as Vertex may reasonably request after delivery of the Option Exercise Data Package. For clarity, the preceding sentence shall not impose any obligation on CRISPR to generate additional Know-How or data.

2.7. **End of Research Term**. At the end of the Research Term, (a) neither CRISPR nor Vertex will have an obligation to perform any additional activities under any Research Plan and (b) CRISPR's obligations and Vertex's rights under this Agreement with respect to any Vertex Target that has not been designated as a Collaboration Target will terminate and the Vertex Target list will be dissolved. For clarity, the expiration of the Research Term will not affect Vertex's rights or CRISPR's obligations with respect to any Collaboration Target for which Vertex has exercised its Option as provided in Section 4.1 or for which the Option Deadline has not occurred.

2.8. **Briefing the JRC**. At each regularly scheduled meeting of the JRC, which shall be no less frequent than [***], each Party will provide detailed progress updates on activities conducted under each Research Plan along with a summary of data associated with such Research activities under such Research Plans, which updates and summaries will be provided to JRC members at least [***] in advance of any JRC meeting. The agenda for meetings of the JRC will be set by the JRC representatives. Each Collaboration Program will be reviewed by the JRC at minimum every [***].

2.9. **Subcontractors**. CRISPR may engage consultants, subcontractors, or other vendors (each, a " **Subcontractor** ") to perform any work under a Research Plan with Vertex's prior written consent; *provided* , that [***] or (b) identified on Schedule E. Vertex may engage Subcontractors to perform Vertex Activities. Each contract between a Party and a Subcontractor will be consistent with the provisions of this Agreement (including ARTICLE 8 and ARTICLE 12). Each Party will be responsible for the effective and timely management of and payment of its Subcontractors. The engagement of any Subcontractor in compliance with this Section 2.9 will not relieve the applicable Party of its obligations under this Agreement or the Research Plan. Each Party will be solely responsible for any taxes, including income, withholding, payroll, VAT, sales tax or the like, that arise from the use of a Subcontractor.

2.10. **Research Costs**. Vertex will reimburse CRISPR for Research Costs incurred by CRISPR in accordance with Section 7.4. All costs incurred by Vertex in connection with Vertex Activities will be borne solely by Vertex.

2.11. **Transfer of Materials**. To facilitate the conduct of activities under each Research Plan, each Party will provide any Materials required by the Research Plan to be transferred to the other

Party, and each Party may provide to the other Party certain other Materials. All Materials (a) will remain the sole property of the supplying Party, (b) will be used only in the fulfillment of the receiving Party's obligations or exercise of rights under this Agreement, (c) will remain solely under the control of the receiving Party, (d) will not be used or delivered by the receiving Party to or for the benefit of any Third Party (other than a permitted Subcontractor or Sublicensee) without the prior written consent of the supplying Party, and, (e) except with respect to any Materials provided by CRISPR to Vertex hereunder for use in a Clinical Trial, will not be used in research or testing involving human subjects, unless expressly agreed. Subject to Section 9.2, all Materials supplied under this Section 2.11 are supplied "as is", with no warranties of fitness for a particular purpose and must be used with prudence and appropriate caution in any experimental work, since not all of their characteristics may be known.

2.12. **Additional Research** . At any time following exercise of an Option for a Collaboration Target, Vertex may request that CRISPR provide additional Research services to Vertex, with respect to such Collaboration Target (" **Additional Research** "). Upon such request, the Parties will meet and discuss in good faith whether CRISPR is able to provide those services and a mutually-agreeable plan (the " **Additional Research Plan** "), including a timeline, and budget, which will be subject to the approval of the JRC (the " **Additional Research Budget** ") therefor; *provided* that CRISPR may, in its sole discretion, refuse to perform Additional Research. Vertex will reimburse CRISPR for Research Costs incurred in performing activities under the Additional Research Plan as provided in Section 7.4. CRISPR will provide Vertex with the results of any Additional Research promptly following the completion thereof.

2.13. **Exclusivity Covenants** .

2.13.1. [***]. Subject to Section 2.13.4(a) and Section 2.13.5, during [***], each Party agrees that, except in the performance of its obligations or exercise of its rights under this Agreement, [***] with respect to the discovery, research, development, manufacture or commercialization in the Field of (a) [***] or (b) [***]. For the avoidance of doubt, each Party's obligations under this Section 2.13.1 will terminate (i) with respect to [***] and (ii) with respect to [***].

2.13.2. [***] . Subject to Section 2.13.4(a) and Section 2.13.5, during [***], each Party agrees that, except in the performance of its obligations or exercise of its rights under this Agreement, [***] with respect to the discovery, research, development, manufacture or commercialization in the Field of (a) [***] or (b) [***]. For the avoidance of doubt, each Party's obligations under this Section 2.13.2 will terminate with respect to a [***] upon [***].

2.13.3. [***]. Subject to Section 2.13.4(a) and Section 2.13.5, commencing on the Effective Date and [***] hereunder, [***] with respect to the discovery, research, development, manufacture or commercialization in the Field of (a) [***] or (b) [***]; *provided, however* , that notwithstanding the foregoing, during such period, [***].

2.13.4. **Cystic Fibrosis** .

(a) Notwithstanding anything to the contrary contained herein, the provisions of Sections 2.13.1, 2.13.2 and 2.13.3 will not apply with respect to the discovery,

research, development, manufacture or commercialization of any product for the treatment of cystic fibrosis by Vertex or its Affiliates and Vertex and its Affiliates will not be restricted from conducting such activities.

(b) During the Agreement Term, CRISPR agrees that neither it nor any of its Affiliates will work independently or for the benefit of or with any Third Party (including the grant of any license to any Third Party) with respect to the discovery, research, development, manufacture or commercialization of any product containing (a) [***] or (b) [***], *provided* that there is [***].

2.13.5. **Delivery Technology**. Notwithstanding the provisions of Sections 2.13.1, 2.13.2, 2.13.3 and 2.13.4(b), either Party may, independently or for the benefit of or with any Third Party, discover, research, develop, manufacture or commercialize technology for use in [***].

2.13.6. **Acquisition of Distracting Product**. Notwithstanding the provisions of Sections 2.13.1, 2.13.2, 2.13.3 and 2.13.4(b), if a Party or any of its Affiliates (such Party, the " **Distracted Party** ") acquires rights to research, develop or commercialize a Distracting Product in the Field as the result of a merger, acquisition or combination with or of a Third Party other than a Change of Control (each, an " **Acquisition Transaction** ") and, on the date of the completion of such Acquisition Transaction, such Distracting Product is being researched, developed or commercialized and such activities would, but for the provisions of this Section 2.13.6, constitute a breach of Section 2.13.1, 2.13.2, 2.13.3 or 2.13.4(b), as applicable, then the Distracted Party or such Affiliate will, within [***] after the completion of such Acquisition Transaction notify the other Party of such acquisition and either:

(a) request that such Distracting Product be included in this Agreement on terms to be negotiated, in which case, the Parties will discuss the matter in good faith for a period of no less than [***] (or such longer period as may be agreed by the Parties) and, if unable to reach agreement on the terms on which such Distracting Product would be included hereunder within such period, the Distracted Party will elect to take the action specified in either clause (b) or (c) below; *provided* that the time periods specified in such clauses will be tolled for so long as the Parties are engaged in discussion under this clause (a);

(b) notify the other Party that the Distracted Party or its Affiliate will Divest its rights to such Distracting Product, in which case, within [***] after the completion of the Acquisition Transaction, the Distracted Party or its Affiliate will Divest such Distracting Product; or

(c) notify the other Party in writing that it is ceasing all such research, development and commercialization activities with respect to the Distracting Product, in which case, within [***] thereafter the Distracted Party and its Affiliates will cease all such activities.

During the discussion period under clause (a), prior to the time of Divestiture pursuant to clause (b) or prior to the termination of activities pursuant to clause (c), as applicable,

the Distracted Party and its Affiliates will use Commercially Reasonable Efforts to segregate all research, development or commercialization activities relating to the Distracting Product from Research, Development and Commercialization with respect to Licensed Agents or Products under this Agreement, including using Commercially Reasonable Efforts to ensure that (i) no personnel involved in performing the research, development or commercialization of such Distracting Product have access to non-public plans or information relating to the Research, Development or Commercialization of Products (*provided* that management personnel may review and evaluate plans and information regarding the Research, Development and Commercialization of Products in connection with portfolio decision-making) and (ii) no personnel involved in performing the Development or Commercialization of Products have access to non-public plans or information relating to the Development or Commercialization of such Distracting Product (*provided* that management personnel may review and evaluate plans and information regarding the Development and Commercialization of such Distracting Product in connection with portfolio decision-making).

2.13.7. **Change of Control** . If there is a Change of Control involving a Party (where such Party is the acquired entity), the obligations of Sections 2.13.1, 2.13.2, 2.13.3 and 2.13.4(b), as applicable, will not apply to any product containing a (a) a [***] or (b) a [***], in each case, that is Controlled by the relevant acquirer or its Affiliates that exists prior to the closing of such Change of Control; *provided* that (i) the acquired Party and the acquirer and its Affiliates existing immediately prior to the effective date of such Change of Control establish and enforce internal processes, policies, procedures and systems to segregate information relating to any such product from any Confidential Information related to the Licensed Agents and Products under this Agreement, (ii) the acquirer and its Affiliates existing immediately prior to the effective date of such Change of Control do not use, directly or indirectly, any Patents, Know-How or Confidential Information of the acquired Party (including any Patents, Know-How or Confidential Information licensed or acquired from the other Party under this Agreement) in connection with such product, and (iii) no personnel who were employees or consultants of the acquired Party or its Affiliates at any time prior to or after the Change of Control will conduct any activities relating to such product.

ARTICLE 3.
GOVERNANCE

3.1. **Joint Research Committee** .

3.1.1. **Formation** . Within 30 days after the Effective Date, the Parties will establish a joint research committee (the " **Joint Research Committee** " or " **JRC** ") to oversee and coordinate activities under this Agreement. The JRC will be comprised of [***] representatives from each Party, with one such representative to have [***]. The JRC will conduct its responsibilities hereunder in good faith and with reasonable care and diligence. The JRC will meet in person at least once each Calendar Quarter on such dates and at such times and places as agreed to by the members of the JRC. The purpose of the JRC will be to provide the members periodic updates regarding progress of activities

pursuant to this Agreement and to address the matters set forth in Section 3.1.2. Each Party will be responsible for its own expenses relating to attendance at or participation in JRC meetings.

3.1.2. **Responsibilities**. The JRC will:

(a) review and approve any initial or amended Research Plan, including the corresponding Research Budget, the planned content of an Option Exercise Data Package, and, to the extent practicable, the specific criteria for acceptance of the Option Exercise Data Package;
(b) prioritize the performance of activities under the Research Plans (including Continuation Research) for Collaboration Targets;
(c) provide comments and recommendations to each Party with respect to the conduct of activities under each Research Plan;
(d) assist in planning and facilitating the transfer of Research responsibility and activities from CRISPR to Vertex upon Option Exercise as needed;
(e) provide a forum for the Parties to discuss the objectives and progress under each Research Plan and to exchange and review scientific information and data relating to the activities being conducted under each Research Plan;
(f) during the [***], discuss the [***];
(g) during the [***], discuss the [***]; and
(h) perform such other duties as are specifically assigned to the JRC under this Agreement.

3.1.3. **Decision-Making**. The JRC members will use reasonable efforts to reach agreement on any and all matters that the JRC has the authority to decide and endeavor to reach consensus on all such matters, taking into consideration the views of each Party. If the JRC is unable to reach consensus with respect to any such matter within [***], the matter will be referred to the Executive Officers, who will use reasonable efforts to reach agreement on such matter. If such Executive Officers are unable to reach consensus with respect to such matter with [***] after such matter is first referred to such Executive Officers, then [***] will have the right to make the final decision with respect to the relevant matter; *provided that* [***] (i) will take into reasonable consideration the recommendations and concerns raised by [***], (ii) will make such decisions in good faith using reasonable business judgment, which will not be unreasonably delayed, and (iii) will not have the right to: (A) amend, modify or waive compliance with any term or condition of this Agreement; (B) make any decision that is expressly stated to require the mutual agreement of the Parties; (C) resolve any claim or dispute regarding whether or in what amount a payment is owed under this Agreement; (D) exercise its final decision-making authority in a manner that would require [***] to perform any act that [***] reasonably believes would constitute a violation of an Applicable Law; (E) make a determination that a Party is in material breach of any obligation under this Agreement or (F) amend or modify a Research Plan if such amendment or modification would require [***] to expend additional resources, whether internal or external, including capital expenditures for which [***] as provided herein.

3.1.4. **Discontinuation of the JRC**. The JRC's authority with respect to a given Collaboration Program will continue to exist until the first to occur of (a) the Parties mutually agreeing to terminate the JRC's authority with respect to such Collaboration Program and (b) the completion of all activities under the Research Plan for such Collaboration Program. The JRC will disband when it ceases to have authority over any Collaboration Program pursuant to the preceding sentence.

3.2. **Collaboration Program Working Group**. Within [***] after Vertex designates a Vertex Target as a Collaboration Target as provided in Section 2.3.3 (or with respect to the Initial Collaboration Targets, within [***] after the Effective Date), the Parties will form a working group (a " **Collaboration Program Working Group** ") comprised of an equal number of representatives from each Party having relevant expertise with respect to the given Collaboration Program. The Collaboration Program Working Group shall be chaired by a project leader from [***], whose appointment shall be subject to the reasonable approval by [***]. The Collaboration Program Working Group will create the initial Research Plan and Research Budget, the planned content of an Option Exercise Data Package, and, to the extent practicable, the specific criteria for acceptance of the Option Exercise Data Package for the applicable Collaboration Program. The Collaboration Program Working Group will also oversee and coordinate the performance of activities under the Research Plan for such Collaboration Program and perform such other activities as the JRC may delegate to the Collaboration Program Working Group from time to time. Any disputes arising out of the Collaboration Program Working Group will be escalated to the JRC for resolution.

3.3. **Other Committees**. The Parties may, by mutual agreement, form such other committees or working groups as may be necessary or desirable to facilitate the activities under this Agreement. Any dispute arising from such committees or working groups will be escalated to the JRC for resolution.

3.4. **Alliance Managers**.

3.4.1. **Appointment**. Within [***] following the Effective Date each Party will appoint (and notify the other Party of the identity of) a representative of such Party to act as its alliance manager under this Agreement (each an " **Alliance Manager** "). Each Party may replace its Alliance Manager at any time by written notice to the other Party.

3.4.2. **Specific Responsibilities**. The Alliance Managers may be, but will not be required to be, members of the JRC. The Alliance Managers will serve as the primary contact point between the Parties for the purpose of providing each Party with information regarding the other Parties' activities pursuant to this Agreement and will have the following responsibilities:

(a) schedule meetings of the JRC and circulate draft written minutes from each meeting within [***] after each such meeting;

(b) facilitate the flow of information and otherwise promoting communication, coordination and collaboration between the Parties;

(c) coordinate the various functional representatives of each Party, as appropriate, in developing and executing strategies and plans for Licensed Agents and Products;

(d) provide a single point of communication for seeking consensus both internally within the respective Party's organization and between the Parties regarding key strategy and planning issues;

(e) coordinate and facilitate budget, finance and billing activities as overseen by the JRC; and

(f) perform such other functions as requested by the JRC.

ARTICLE 4.
EXCLUSIVE OPTION

4.1. **Option** .

4.1.5. **Option and Option Deadline** . CRISPR hereby grants to Vertex and its Affiliates an exclusive option to obtain the Exclusive License with respect a maximum of six Collaboration Targets (each, an " **Option** ," and such six Collaboration Target maximum, the " **Option Cap** "). Within [***] after Vertex's receipt of an Option Exercise Data Package for the applicable Collaboration Program (the " **Option Deadline** "), Vertex will notify CRISPR as to whether or not Vertex is exercising the applicable Option; *provided,* that if, following receipt of the applicable Option Exercise Data Package, Vertex delivers a [***] to the JRC, the Option Deadline will be extended until the date that is [***] after Vertex's receipt of a revised Option Exercise Data Package reflecting the results of the Continuation Research as provided in Section 2.6. If Vertex or its designated Affiliate notifies CRISPR in writing that it wishes to exercise the applicable Option, CRISPR will, and hereby does, grant to Vertex or its designated Affiliate the Exclusive License with respect to Licensed Agents and Products directed to such Collaboration Target and, except with respect to Collaboration Targets that are [***] with respect to such Collaboration Target; *provided, however,* if Vertex determines that an HSR Filing is required to be made under the HSR Act to exercise an Option and notifies CRISPR of such determination within [***] after Vertex's receipt of the complete Option Exercise Data Package, the Parties will promptly file an HSR Filing in accordance with Section 4.1.2(a) and Vertex's election to exercise the applicable Option will not be effective (and Vertex will not be obligated to make any payment under Section 7.3.1) until the HSR Clearance Date. If Vertex fails to timely exercise an Option in accordance with this Section 4.1.1, the Option shall expire and be of no further force or effect, both Party's obligations under Section 2.13.1 shall terminate with respect to the relevant Collaboration Target, such Collaboration Target shall no longer be a Collaboration Target nor a Vertex Target and Vertex shall be deemed to have terminated the relevant Collaboration Program for purposes of ARTICLE 11 of this Agreement.

4.1.6. **HSR Compliance** .

(a) **HSR Filing** . If Vertex notifies CRISPR pursuant to Section 4.1.1 that an HSR Filing is required for Vertex to receive the Exclusive License with respect to a Collaboration Target, each of Vertex and CRISPR will, within [***] after such

notice from Vertex (or such later time as may be agreed to in writing by the Parties), file with the United States Federal Trade Commission (" **FTC** ") and the Antitrust Division of the United States Department of Justice (" **DOJ** "), any HSR Filing required with respect to the transactions contemplated hereby. The Parties will cooperate with one another to the extent necessary in the preparation of any such HSR Filing. Each Party will be responsible for its own costs and expenses (other than filing fees, which Vertex will pay) associated with any HSR Filing.

(b) **HSR Clearance** . In furtherance of obtaining clearance for an HSR Filing filed pursuant to this Section 4.1.2, CRISPR and Vertex will use their respective Commercially Reasonable Efforts to resolve as promptly as practicable any objections that may be asserted with respect to this Agreement or the transactions contemplated by this Agreement under any antitrust, competition or trade regulatory law. In connection with obtaining such HSR clearance from the FTC, the DOJ or any other governmental authority, Vertex and its Affiliates will not be required to (i) sell, divest (including through a license or a reversion of licensed or assigned rights), hold separate, transfer or dispose of any assets, operations, rights, product lines, businesses or interest therein of Vertex or any of its Affiliates (or consent to any of the foregoing actions); or (ii) litigate or otherwise formally oppose any determination (whether judicial or administrative in nature) by a governmental authority seeking to impose any of the restrictions referenced in clause (i) above.

ARTICLE 5.
LICENSE GRANTS

5.1. **Non-Exclusive Research License from CRISPR to Vertex** . Subject to the terms and conditions of this Agreement, CRISPR and, following the Subsidiary Transfer, the CRISPR Subsidiary, hereby grants Vertex UK and its Affiliates a non-exclusive, royalty-free, fully paid-up, worldwide license, with no right to grant sublicenses except to permitted Subcontractors under Section 2.9, to use the Licensed Technology solely to perform the Vertex Activities during the Research Term.

5.2. **Non-Exclusive Research and Development License from Vertex to CRISPR** . Subject to the terms and conditions of this Agreement, Vertex hereby grants to CRISPR a non-exclusive, royalty-free, fully paid-up, worldwide license, with no right to grant sublicenses except to permitted Subcontractors under Section 2.9, under the Vertex Technology solely to perform Research under the Research Plan for each Collaboration Program during the Research Term.

5.3. **License Grants to Vertex .**

5.3.1. **Development and Commercialization Licenses .** Subject to the terms and conditions of this Agreement, on a Collaboration Target-by-Collaboration Target basis, effective upon Vertex's exercise of the Option for a particular Collaboration Target in accordance with this Agreement, CRISPR and, following the Subsidiary Transfer, the CRISPR Subsidiary, grants to Vertex UK and its Affiliates an exclusive (subject to Section 6.1.2(b)), royalty-bearing, license under CRISPR's and its Affiliates' interest in the Licensed Technology

to Research, Develop, Manufacture, have Manufactured, use, keep, sell, offer for sale, import, export and Commercialize Licensed Agents and Products directed to the relevant Collaboration Target in the Field in the Territory (such license, the " **Exclusive License** "). Vertex may grant sublicenses through multiple tiers of sublicense to one or more Sublicensees of any and all rights granted to Vertex by CRISPR under the Exclusive License; *provided that* Vertex shall only be permitted to grant a Sublicense to conduct any Commercialization activities with respect to a Licensed Agent or Product [***] with CRISPR's prior written consent, such consent not to be unreasonably withheld, conditioned or delayed; and *provided* , *further* , that no such consent will be needed with respect to any Sublicense (a) granted to a Third Party to conduct Commercialization activities with respect to a Licensed Agent or Product in [***] (and not any other [***]), (b) any Sublicense granted to a Distributor or other Third Party conducting activities on Vertex's behalf or (c) any Sublicensee granted to a Third Party to Manufacture Licensed Agent or Product on Vertex's behalf. Each such Sublicense will be subject and subordinate to, and consistent with, the terms and conditions of this Agreement and will require such Sublicensee to comply with all applicable terms of this Agreement and all Third Party Obligations. Vertex shall promptly provide CRISPR with a copy of the fully executed Sublicense agreement covering any sublicense granted hereunder (which copy may be redacted to remove provisions which are not necessary to monitor compliance with this Section 5.3.1). Notwithstanding the grant of any Sublicense, Vertex shall remain primarily liable to CRISPR for the performance of all of Vertex's obligations under, and Vertex's compliance with all provisions of, this Agreement.

5.3.2. **License Conditions; Limitations** . Subject to Section 7.6, any rights and obligation hereunder, including the rights granted pursuant to any Exclusive License with respect to a Collaboration Target, are subject to and limited by any applicable Third Party Obligations to the extent the provisions of such obligations or agreements are specifically disclosed to Vertex in writing (or via electronic data room) (a) with respect to Third Party Obligations existing as of the Effective Date, prior to the Effective Date, (b) with respect to Third Party Obligations arising between the Effective Date and the delivery of the relevant Option Exercise Data Package, at the time of delivery of the Option Exercise Data Package and (c) with respect to Third Party Obligations arising after the date the applicable Exclusive License is granted hereunder, on or prior to the date on which such Third Party Obligations arise. Vertex will have the right to [***] any Third Party Patents and Know-How to which such Third Party Obligations [***] by providing CRISPR [***] (with respect to any Third Party Obligations existing at the time the relevant Option Exercise Data Package is delivered) or [***], in which case, such Third Party Patents and Know-How [***] this Agreement. If Vertex does not provide CRISPR [***] Third Party Patents and Know-How as provided above, such Third Party Patents and Know-How [***] under this Agreement and Vertex will be subject to the Third Party Obligations [***].

5.4. **Licenses to Improvements** .

5.4.1. **License to CRISPR .** Subject to the terms and conditions of this Agreement, Vertex hereby grants to CRISPR a perpetual, irrevocable, non-exclusive, royalty-free, fully paid-up, worldwide, sublicensable, license to all improvements or modifications to the CRISPR Platform Technology Patents, CRISPR Background Patents (to the extent existing on the Effective Date or otherwise claiming the CRISPR Background Know-How set forth on Schedule F), [***] or CRISPR Background Know-How set forth on Schedule F (as may be supplemented by mutual written agreement of the Parties from time to time), whether or not patentable, that arise in the course of performing activities under a Research Plan or in the course of Developing and Commercializing a Licensed Agent or Product and are Controlled by Vertex or its Affiliates to make, have made, use, sell, keep, offer for sale and import products other than Licensed Agents and Products.

5.4.2. **License to Vertex .** Subject to the terms and conditions of this Agreement, CRISPR, and, following the Subsidiary Transfer, to the extent necessary, the CRISPR Subsidiary, hereby grants to Vertex a perpetual, irrevocable, non-exclusive, royalty-free, fully paid-up, worldwide, sublicensable, license to all improvements or modifications to the Vertex Background Know-How or Vertex Background Patents, whether or not patentable, that arise in the course of performing activities under a Research Plan and are Controlled by CRISPR or its Affiliates to make, have made, use, sell, keep, offer for sale and import products other than Licensed Agents and Products.

5.5. **Technology Transfer after Option Exercise**.

5.5.1. **Transition Agreement**. Upon each exercise by Vertex of an Option, the Parties will negotiate and execute an agreement setting forth the Parties' respective obligations with respect to the transfer of data and Materials relating to the relevant Collaboration Target from CRISPR to Vertex, all in accordance with this Section 5.5.

5.5.2. **Licensed Know-How**. On a Collaboration Target-by-Collaboration Target basis, CRISPR will promptly, but no later than [***] after Vertex exercises its Option for such Collaboration Target hereunder, make available and, at Vertex's request, deliver to Vertex or one or more designated Affiliates all documented Licensed Know-How in CRISPR's possession that has not previously been provided hereunder, for use in accordance with the exercise of the applicable Exclusive License. To assist with the transfer of such Licensed Know-How, CRISPR will make its personnel reasonably available to Vertex during normal business hours to transfer such Licensed Know-How under this Section 5.5.2 and Vertex will reimburse CRISPR for the reasonable costs of such assistance at the FTE Rate within 30 days after its receipt of an invoice therefor.

5.5.3. **Transfer of Manufacturing Know-How and Materials**. Without limiting CRISPR's obligations under Section 5.5.2, within [***] following the exercise of an Option, and thereafter, promptly following Vertex's request, CRISPR will, or will cause the applicable Third Party (including any contract manufacturing organization engaged by CRISPR to Manufacture any Licensed Agent or

Product) to, transfer to Vertex (a) all Licensed Know-How that is necessary or useful to enable the Manufacture of each Licensed Agent or Product for the applicable Collaboration Target, and not previously transferred to Vertex under this Agreement, by providing copies or samples of relevant documentation, materials and other embodiments of such Licensed Know-How, and by making available its, or the applicable Third Party's, qualified technical personnel on a reasonable basis to consult with Vertex with respect to such Licensed Know-How and (b) at Vertex's request, any Materials used by CRISPR or its Affiliates or Subcontractors in the Manufacture of such Licensed Agent or Product.

5.5.4. **Transfer of Regulatory Filings and Data**. On a Collaboration Target-by-Collaboration Target basis and effective as of the date on which Vertex is granted the Exclusive License for a Collaboration Target, CRISPR will, and hereby does, assign to Vertex any and all Regulatory Filings or any other rights or permissions granted by any Regulatory Authority to Vertex related to any Licensed Agent or Product directed to such Collaboration Target, together with all Research, Development and Manufacturing data relating to such Collaboration Target, in each case, not previously assigned by CRISPR to Vertex. Further, CRISPR will take all actions and provide all assistance reasonably requested by Vertex to effect the assignments in this Section 5.5.4.

5.5.5. **Right of Reference**. Vertex hereby grants to CRISPR the right to rely upon and a right to copy, access, and otherwise use, all Adverse Event information pertaining to each Product as reasonably required in connection with the Development and Commercialization (subject to Section 2.13) of products, and Vertex shall, if requested by CRISPR, provide a signed statement that CRISPR may rely on, and the Regulatory Authority may access, in support of CRISPR's application for Regulatory Approval of such products.

5.6. **No Implied Licenses**. All rights in and to Licensed Technology not expressly licensed or assigned to Vertex under this Agreement are hereby retained by CRISPR or its Affiliates. All rights in and to any Vertex Technology not expressly licensed to CRISPR under this Agreement, are hereby retained by Vertex or its Affiliates. Except as expressly provided in this Agreement, no Party will be deemed by estoppel or implication to have granted the other Party any licenses or other right with respect to any intellectual property.

ARTICLE 6.
PROFIT/LOSS SHARING, DEVELOPMENT, MANUFACTURING AND COMMERCIALIZATION

6.1. **CRISPR Profit/Loss Sharing**.

6.1.3. **Profit/Loss Sharing**. CRISPR will jointly (with Vertex or Affiliate(s) designated by Vertex) Research, Develop and Commercialize Products containing (a) any Licensed Agent directed to a Collaboration Target that is a Hemoglobinopathy Target or (b) [***] and, in each case, for which Vertex has obtained the Exclusive License, as provided herein, unless, in each case, CRISPR exercises an Opt-Out in accordance with Schedule G.

6.1.4. **Effects of Co-Commercialization**. For each Collaboration Target set forth in clauses (a) or (b) of Section 6.1.1:

(c) each Product for the relevant Collaboration Target will be deemed a "**Shared Product**";

(d) the Exclusive License with respect to the relevant Collaboration Target will become co-exclusive (with CRISPR);

(e) within [***] after Vertex has exercised the Option to obtain the Exclusive License for such Collaboration Target, CRISPR and Vertex (or any Affiliates designated by Vertex) will enter into an agreement (the "**Joint Development & Commercialization Agreement**"), which the Parties will negotiate in good faith and which will include appropriate plans and budgets, for the joint Development and Commercialization of Shared Products (or provisions for establishing such plans) and will include (i) terms and conditions that are substantially the same as those set forth in Schedule G and (ii) other reasonable and customary provisions for transactions of this type as the Parties may agree. If the terms of this Agreement conflict with the terms of the Joint Development & Commercialization Agreement, the terms of the Joint Development & Commercialization Agreement will control with respect to the Collaboration Program that is the subject thereof and the terms of this Agreement will control with respect to all other matters; and

(f) [***].

6.2. **Responsibility**. Following an Option Exercise, Vertex will be solely responsible for all Research, Development, Manufacturing and Commercialization of Licensed Agents and Products for the relevant Collaboration Target that are performed after the date on which the Option was exercised and for all costs and expenses associated therewith, except (a) as may be otherwise provided in a Joint Development & Commercialization Agreement, (b) with respect to any incomplete activities under the relevant Research Plan or any agreed-upon Additional Research and (c) for the transfer of activities to Vertex as contemplated by Section 5.5.

6.3. **Vertex Diligence**.

6.3.3. **Development Diligence**. Except with respect to Shared Products, following Vertex's exercise of the Option for a Collaboration Target, Vertex (acting directly or through one or more Affiliates or Sublicensees) will use Commercially Reasonable Efforts to Develop, obtain Marketing Approvals for [***] in [***].

6.3.4. **Commercial Diligence**. Except with respect to Shared Products, Vertex (acting directly or through one or more Affiliates or Sublicensees) will use Commercially Reasonable Efforts to Commercialize, including seeking Price Approval on appropriate terms, [***] in [***].

6.4. **Product Development & Commercialization Plan**. On a Collaboration Program-by-Collaboration Program basis, Vertex will prepare a Development and Commercialization plan setting forth in reasonable detail (which detail shall be at least sufficient for CRISPR to evaluate

Vertex's compliance with its obligations under this Agreement) Vertex's plans for (a) the Development of each Product for the relevant Collaboration Target through Clinical Trials designed to show Establishment of POC, (b) starting after Establishment of POC, the Development of each Product through Marketing Approval and (c) starting upon Marketing Approval for a Product and continuing thereafter until the expiration of the applicable Royalty Term, Commercialization for the Product, as appropriate for the stage of the Product, including a launch plan for each Major Market Country (each, an " **Product Development & Commercialization Plan** "). If Vertex is Developing or Commercializing more than one Product directed to a Collaboration Target, the Product Development & Commercialization Plan will include the foregoing information for each such Product. Vertex will prepare the initial Product Development & Commercialization Plan for a Collaboration Program no later than [***] after Option Exercise by performing the activities set forth in each Research Plan for the relevant Collaboration Target. Once Vertex has prepared such Product Development & Commercialization Plan, Vertex will update such plan no less than [***] so that such Product Development & Commercialization Plan is an accurate reflection of Vertex's then-current plans with respect to the Development and Commercialization of the relevant Product and Vertex will provide such updates to CRISPR for its review. All Product Development & Commercialization Plans are provided solely for informational purposes, and Vertex's failure to follow a Product Development & Commercialization Plan will not constitute a breach of this Agreement. Notwithstanding the foregoing, Vertex will have no obligation under this Section 6.4 with respect to any Shared Product.

6.5. **Applicable Laws** . Each Party will, and will require its Affiliates, Sublicensees and Subcontractors to, comply with all Applicable Law in its and their Research, Development, Manufacture and Commercialization of Products, including where appropriate cGMP, GCP and GLP (or similar standards).

6.6. **Regulatory Matters; Safety Data Exchange Agreement** .

6.6.1. **Responsibilities** . Vertex or its designated Affiliates and Sublicensees will have the sole authority to prepare and file Regulatory Filings, each in its own name, and applications for Regulatory Approval and Price Approval for any and all Licensed Agents and Products directed to each Collaboration Target, and will have the sole responsibility for communicating with any Regulatory Authority both prior to and following Regulatory Approval and Price Approval, including all communications and decisions with respect to (a) pricing of Products and (b) the negotiation of Product pricing with Regulatory Authorities and other Third Parties.

6.6.2. **Ownership** . Ownership of all right, title and interest in and to any and all Regulatory Filings, Regulatory Approvals and Price Approvals directed to any Licensed Agent or any Product directed to each Collaboration Target in each country of the Territory will be held in the name of Vertex, its Affiliate, designee or Sublicensee.

6.6.3. **Pharmacovigilance** . Upon Vertex's request, the Parties will negotiate and enter into a separate safety data exchange agreement (a " **Safety Data Exchange Agreement** "). The Safety Data Exchange Agreement will set forth guidelines and procedures for the receipt, investigation, recording, review, communication,

reporting and exchange between the Parties of adverse event reports (which, for purposes of information exchange between the Parties, will include adverse events and serious adverse events, and any other information concerning the safety of any Product or Licensed Agent and, with respect to information provided by CRISPR, concerning the safety of products containing a [***] or [***]). Without limiting the foregoing, the Parties will meet to establish a safety oversight working group comprised of members of both Parties, which, except as otherwise provided in the Safety Data Exchange Agreement, will discuss processes and procedures for sharing information needed to support each Party's regulatory responsibilities and to comply with applicable regulatory pharmacovigilance requirements. Any such procedures will not be construed to restrict either Party's ability to take any action that it deems to be appropriate or required of it under the applicable regulatory requirements, if permitted by Applicable Laws. Vertex (a) will maintain a unified worldwide adverse event database for Products, and be responsible for reporting adverse events and serious adverse events to the applicable Regulatory Authorities and (b) will be responsible for all signal detection and risk management activities and will develop and approve the contents of all safety communications to Regulatory Authorities, including but not limited to expedited non-clinical and clinical safety reports and aggregate reports to health authorities, institutional review boards and ethics committees.

6.7. **Commercialization**.

6.7.1. **General**. Vertex will have sole and exclusive control over all matters relating to the Commercialization of Products, except as may be otherwise provided in a Joint Development & Commercialization Agreement.

6.7.2. **Branding**. Vertex or its designated Affiliates or Sublicensees will select and own all trademarks used in connection with the Commercialization of any and all Products. CRISPR will not use nor seek to register, anywhere in the world, any trademark that is confusingly similar to any trademark used by or on behalf of Vertex, its Affiliates or Sublicensees in connection with any Product.

6.8. **Manufacturing**. Vertex will have the exclusive right to Manufacture and supply Licensed Agents and Products itself or through one or more Affiliates or Third Parties selected by Vertex in its sole discretion. The Parties may share information relating to the Manufacture of Products, and other products to be commercialized by CRISPR, to determine whether and how to leverage their respective manufacturing efforts, but shall have no obligation hereunder to enter into an agreement with respect thereto.

ARTICLE 7.
FINANCIAL PROVISIONS

7.1. **Up-Front Fee to CRISPR AG (Switzerland)**. Within four Business Days following the Effective Date, Vertex UK will pay CRISPR AG a one-time, non-refundable, non-creditable, up-front fee of $75,000,000 payable by wire transfer of immediately available funds.

7.2. [***]. If Vertex [***], Vertex will [***] within [***] after Vertex notifies CRISPR that it is [***]. The [***] that are [***].

7.3. **Milestone Payments**.

7.3.6. Development Milestones. Subject to Section 7.3.4, Vertex will pay CRISPR the milestone payments set forth in this Section 7.3.1 with respect to each Collaboration Target [***], whether such milestone event is achieved by CRISPR, Vertex or their respective Affiliates or any Sublicensees. Each milestone payment set forth below, is payable only once per Collaboration Target, regardless of the number of Products directed to such Collaboration Target that achieve the relevant milestone event.

Milestone Number	Milestone Event	Milestone Payment
1	[***]	[***]
2	[***]	[***]
3	[***]	[***]
4	[***]	[***]
5	[***]	[***]
6	[***]	[***]
7	[***]	[***]
8	[***]	[***]
9	[***]	[***]
10	[***]	[***]
11	[***]	[***]

7.3.7. **Commercial Milestones**. Subject to Section 7.3.4, Vertex will pay CRISPR the milestone payments set forth in this Section 7.3.2 with respect to each Collaboration Target [***], whether such milestone event is achieved by Vertex or its Affiliates or any of their Sublicensees. Each milestone payment set forth below, is payable only once per Collaboration Target, regardless of the number of Products directed to such Collaboration Target that achieve the relevant milestone event or the number of times Product(s) achieve such milestone event.

Milestone Number	Milestone Event	Milestone Payment
12	[***]	[***]
13	[***]	[***]

7.3.8. **Notice; Payment; Skipped Milestones**. Vertex will provide CRISPR with written notice upon the achievement of each of the milestone events set forth in Section 7.3.1 or 7.3.2, such notice to be provided, (a) with respect to milestones under Section 7.3.1, within [***] after achievement, and (b) with respect to milestones under Section 7.3.2, [***] for the Calendar Quarter in which such milestone is first achieved. Following receipt of such notice, CRISPR will promptly invoice Vertex for the applicable milestone and Vertex

will make the appropriate milestone payment within [***] after receipt of such invoice. The milestones numbered [***] as set forth in Section 7.3.1 are intended to be successive; if a Product for a Collaboration Target is not required to undergo the event associated with any such milestone event, such skipped milestone will be deemed to have been achieved upon the achievement by such Product of the next successive milestone event. Payment for any such skipped milestone that is owed in accordance with the provisions of the foregoing sentence with respect to a given Product will be due concurrently with the payment for the next successive milestone event by such Product, it being agreed that if a Product for a Collaboration Target is not required to undergo the milestone numbered [***], the corresponding payment will be made upon the first to occur of the milestones numbered [***].

7.3.9. **Failure to Obtain Necessary Agreements .** If, at the time any milestone event under Section 7.3.1 or Section 7.3.2 is achieved, CRISPR has not obtained all necessary consents and agreements and taken all actions provided for under Section 9.3.10, [***].

7.4. **Research Costs.**

7.4.1. As soon as practicable, but in any event within [***] after the end of each [***], CRISPR will provide Vertex with a flash report estimating reimbursable Research Cost, if any, incurred by it and its Affiliates during the just-ended [***].

7.4.2. Within [***] after the end of each [***], CRISPR will submit to Vertex an itemized report of Research Costs, if any, incurred by CRISPR and its Affiliates during such [***] (the " **Cost Report** "), including reasonable supporting documentation.

7.4.3. Vertex will reimburse CRISPR for all Research Costs in accordance with the applicable Research Budget or Additional Research Budget within [***] after its receipt of the applicable Cost Report. If the Research Costs for a Research Plan or Additional Research Plan exceed the applicable Research Budget or Additional Research Budget, CRISPR may include such excess costs in the applicable Cost Report, and Vertex will reimburse such excess costs, [***].

7.4.4. Notwithstanding anything to the contrary contained herein, except as may be otherwise provided in a Joint Development & Commercialization Agreement, Vertex will not be obligated to reimburse CRISPR for any Research Costs incurred in connection with the Research of a Shared Product following Option Exercise for the relevant Collaboration Program.

7.5. **Royalties** .

7.5.4. **Royalty Rates .** Subject to Sections 7.5.2, 7.5.3 and 7.5.4, on a Product-by-Product and country-by-country basis, Vertex will pay CRISPR royalties based on the aggregate Net Sales of each Product sold by Vertex, its Affiliates or Sublicensees in the Field in the Territory during a Calendar Year at the rates set forth in the table below; *provided* , *that* Vertex will have no obligation under

this Section 7.5.1 with respect to any Shared Product. The obligation to pay royalties will be imposed only once with respect to the same unit of a Product.

Calendar Year Net Sales (in Dollars) for such Product in the Territory	Royalty Rates as a Percentage (%) of Net Sales
[***]	[***]
[***]	[***]
[***]	[***]
[***]	[***]

7.5.5. **Royalty Term .** Vertex will pay royalties to CRISPR under this Section 7.5 on a Product-by-Product and a country-by-country basis during the Royalty Term. Upon the expiration of the Royalty Term for a given Product in a given country, the Exclusive License with respect to such Product will become fully-paid, perpetual and irrevocable.

7.5.6. [***] **Generic Competition .** If one or more Generic Products with respect to a Product is marketed and sold in a given country by one or more Third Parties during any Calendar Quarter during the Royalty Term and the [***] of such Product sold during such Calendar Quarter have [***] relative to average quarterly sales ([***]) of such Product in such country during the [***] Calendar Quarters immediately prior to the Calendar Quarter during which such Generic Product(s) was first marketed and sold in such country, then the royalty rate for such Product in such country, on a Product-by-Product and country-by-country basis, will thereafter be [***] of the applicable royalty rate set forth in Section 7.5.1 for so long as such reduction in [***] persists.

7.5.7. **Third Party Licenses .** Vertex may [***] from the royalties payable to CRISPR under this Section 7.5 the following amounts: (a) [***]; (b) [***]; and (c) [***]; *provided* , *however* , that in no event will the royalties that would otherwise be payable to CRISPR, as reduced by Section 7.5.3 [***] under this Section 7.5.4; and *provided further* , that Vertex will be entitled to [***] any amounts with respect to which Vertex would have been [***] pursuant to this Section 7.5.4 but [***] in this Section 7.5.4.

7.5.8. [***] **.** If, at the time any royalties are payable pursuant to Section 7.5, [***].

7.5.9. **Royalty Reports** . During the Agreement Term, following the first sale of a Product (other than a Shared Product) giving rise to Net Sales, within [***] after the end of each Calendar Quarter, Vertex will deliver a report to CRISPR specifying on a Product-by-Product and country-by-country basis: (a) gross sales in the relevant Calendar Quarter, (b) Net Sales in the relevant Calendar Quarter, including an accounting of deductions applied to determine Net Sales; (c) a summary of the then-current exchange rate methodology then in use by

Vertex, and (d) royalties payable on such Net Sales. All royalty payments due under Section 7.5 for each Calendar Quarter will be due and payable within [***] after Vertex's delivery of the applicable report under this Section 7.5.5.

7.6. **CRISPR In-License Agreements; [***]** .

7.6.3. **CRISPR In-License Agreements .** Certain of the Licensed Technology Controlled by CRISPR or CRISPR Affiliates as of the Effective Date was in-licensed or acquired by CRISPR under the agreements with Third Party licensors or sellers listed on Schedule H (such agreements, together with each consent and agreement obtained by CRISPR pursuant to Section 9.3.10, the " **CRISPR In-License Agreements** "). Subject to Section 10.1, [***].

7.6.4. [***].

(a) Certain Licensed Technology [***] during the Term pursuant to [***]. For any [***] pursuant to which [***], CRISPR will use Commercially Reasonable Efforts to ensure that [***] with the same [***] (including the right for Vertex [***] would be [***] and [***], [***] and other potential or actual [***]. If CRISPR is [***], (a) CRISPR will so notify Vertex, and the Parties will [***] and (b) CRISPR will not [***].

(b) Notwithstanding anything to the contrary contained herein, if, following Vertex's exercise of the Option for a particular Collaboration Target, Vertex believes, in its reasonable judgment, that it may be necessary to obtain rights under any Patent having claims which Cover Licensed Agents or Products that are the subject of the Option, Vertex shall have the right to negotiate a license to such Patent.

7.6.5. [***]. Vertex shall [***] by Vertex, its Affiliates or Sublicensees. If the [***] based on the [***] across such [***] by Vertex, its Affiliates or Sublicensees. [***] with and to the extent [***].

7.6.6. [***]. Subject to Section [***], [***] arising under any [***]. [***] shall take into consideration the [***]. [***], the matter shall [***]. [***] if and when such [***].

7.6.7. [***]. If CRISPR [***] which provides [***] set forth on [***], then, [***], [***].

7.6.8. [***]. Notwithstanding the foregoing provisions of this Section 7.6, Vertex may [***] with respect to one or more [***] and, thereafter, [***].

7.7. **Payment Method; Currency** .

7.7.1. All payments under this Agreement will be paid in U.S. Dollars, by wire transfer to an account designated by CRISPR (which account CRISPR may update from time to time in writing).

7.7.2. If any amounts that are relevant to the determination of amounts to be paid under this Agreement or any calculations to be performed under this Agreement are denoted in a currency other than U.S. Dollars, then such amounts will be converted to their U.S. Dollar equivalent using Vertex's then-current standard procedures and methodology, including its then-current standard exchange rate methodology for the translation of foreign currency expenses into U.S. Dollars or, in the case of Sublicensees, such similar methodology, consistently applied.

7.8. **Withholding Tax** . Where any sum due to be paid to CRISPR hereunder is subject to any withholding or similar tax, Vertex will pay such withholding or similar tax to the appropriate Government Authority and deduct the amount paid from the amount then due CRISPR, in a timely manner and promptly transmit to CRISPR an official tax certificate or other evidence of such withholding sufficient to enable CRISPR to claim such payment of taxes. The Parties agree to cooperate with one another and use reasonable efforts to reduce or eliminate tax withholding or similar obligations in respect of royalties, milestone payments, and other payments made by Vertex to CRISPR under this Agreement. CRISPR will provide Vertex any tax forms that may be reasonably necessary in order for Vertex not to withhold tax or to withhold tax at a reduced rate under an applicable bilateral income tax treaty. Each Party will provide the other with reasonable assistance to enable the recovery, as permitted by Applicable Laws, of withholding taxes, value added taxes, or similar obligations resulting from payments made under this Agreement, such recovery to be for the benefit of the Party bearing such withholding tax or value added tax.

7.9. **Records** . During the Agreement Term, Vertex will keep and maintain accurate and complete records regarding Net Sales during the [***] preceding Calendar Years and CRISPR will keep and maintain accurate and complete records regarding the Research Cost covering the [***] preceding Calendar Years. Upon [***] prior written notice from the other Party (the " **Auditing Party** "), the Party required to maintain such records (as applicable, the " **Audited Party** ") will permit an independent certified public accounting firm of internationally recognized standing, selected by the Auditing Party and reasonably acceptable to the Audited Party, to examine the relevant books and records of the Audited Party and its Affiliates, as may be reasonably necessary to verify the royalty reports submitted by Vertex in accordance with Section 7.5.5, or Research Cost reported by CRISPR in accordance with Section 7.4, as applicable. An examination by the Auditing Party under this Section 7.9 will occur not more than [***] in any Calendar Year and will be limited to the pertinent books and records for any Calendar Year ending not more than [***] before the date of the request. The accounting firm will be provided access to such books and records at the Audited Party's facility or facilities where such books and records are normally kept and such examination will be conducted during the Audited Party's normal business hours. The Audited Party may require the accounting firm to sign a customary non-disclosure agreement before providing the accounting firm access to its facilities or records. Upon completion of the audit, the accounting firm will provide both the Auditing Party and the Audited Party a written report disclosing whether the reports submitted by Vertex, or the Research Cost reported by CRISPR, as applicable, are correct or incorrect and the specific details concerning any discrepancies. No other information will be provided to the Auditing Party. If the report or information submitted by the Audited Party results in an underpayment or overpayment, the Party owing underpaid or overpaid amount will promptly pay such amount to the other Party, and, if, as a result of such inaccurate report or information, such amount is more than [***] of the amount that was owed the Audited Party

will reimburse the Auditing Party for the reasonable expense incurred by the Auditing Party in connection with the audit.

7.10. **Late Payment**. Any payments or portions thereof due hereunder that are not paid when due will accrue interest from the date due until paid at an annual rate equal to [***] (or the maximum allowed by Applicable Law, if less).

INTELLECTUAL PROPERTY

7.11. **Ownership; Assignment**. For the avoidance of doubt, the rights and obligations of the Parties under this ARTICLE 8 are subject to and limited by any applicable Third Party Obligations to the extent the provisions of such obligations or agreements are specifically disclosed to Vertex in writing (or via electronic data room) (a) with respect to Third Party Obligations existing as of the Effective Date, prior to the Effective Date, (b) with respect to Third Party Obligations arising between the Effective Date and the delivery of the relevant Option Exercise Data Package, at the time of delivery of the Option Exercise Data Package and (c) with respect to Third Party Obligations arising after the date the applicable Exclusive License is granted hereunder, on or prior to the date on which such Third Party Obligations arise.

7.11.1. **CRISPR Technology and Vertex Technology**. As between the Parties, CRISPR will own and retain all of its rights, title and interest in and to the CRISPR Background Know-How, CRISPR Background Patents and CRISPR Platform Technology Patents and Vertex will own and retain all of its rights, title and interest in and to any Vertex Background Know-How and Vertex Background Patents, subject to any assignments, rights or licenses expressly granted by one Party to the other Party under this Agreement.

7.11.2. **Agreement Technology**.

(a) As between the Parties, CRISPR will be the sole owner of any Know-How discovered, developed, invented or created solely by CRISPR or its Affiliates or Third Parties acting on their behalf in connection with activities under this Agreement (" **CRISPR Program Know-How** ") and any Patents that cover or claim such Know-How (" **CRISPR Program Patents** " and together with the CRISPR Program Know-How, the " **CRISPR Program Technology** "), and will retain all of its rights, title and interest thereto, subject to any assignment, rights or licenses expressly granted by CRISPR to Vertex under this Agreement.

(b) As between the Parties, Vertex will be the sole owner of any Know-How discovered, developed, invented or created solely by Vertex or its Affiliates or Third Parties acting on their behalf in connection with activities under this Agreement (" **Vertex Program Know-How** ") and any Patents that cover or claim Vertex Program Know-How (" **Vertex Program Patents** " and together with the Vertex Program Know-How, the " **Vertex Program Technology** "), and will retain all of its rights, title and interest thereto, subject to any rights or licenses expressly granted by Vertex to CRISPR under this Agreement.

(c) (i) [***]: Any Know-How discovered, developed, invented or created jointly under this Agreement by both (a) Vertex, its Affiliates or Third Parties acting on Vertex's behalf and (b) CRISPR, its Affiliates or Third Parties acting on

CRISPR's behalf, while conducting activities under this Agreement, to the extent [***] ("[***] **Joint Program Know-How** "), and any Patents that [***] ("[***] **Joint Program Patents** ," and together with the [***] Joint Program Know-How, the "[***] **Joint Program Technology** "), will be owned [***], including all rights, title and interest thereto, subject to any assignment, rights or licenses expressly granted by one Party to the other Party under this Agreement. Except as expressly provided in this Agreement, [***] with respect to, or to [***] Joint Program [***], and each Party hereby [***].

(ii) [***] : All [***] Joint Program Know-How, [***] Joint Program Patents, and [***] Joint Program Technology, in each case to the extent pertaining to [***], will be [***]. Within [***], [***] will, and hereby [***], [***] or [***] designated Affiliates, [***] Joint Program Patents. [***] will take all actions and provide [***] with all [***] and will [***].

(d) Any Know-How discovered, developed, invented or created jointly under this Agreement by both (a) Vertex, its Affiliates or Third Parties acting on Vertex's behalf and (b) CRISPR, its Affiliates or Third Parties acting on CRISPR's behalf, while conducting activities under this Agreement, to the extent pertaining to [***] but not exclusively pertaining to [***] ("[***] **Joint Program Know-How** "), and any Patents that claim or cover such [***] Joint Program Know-How ("[***] **Joint Program Patents** ," and together with the [***] Joint Program Know-How, the "[***] **Joint Program Technology** "), will be [***]. [***] will, and hereby does, assign to [***] or one or more of its designated Affiliates, [***] ownership interest in all [***] Joint Program Patents. Within [***], [***]will take all actions and provide [***] with all reasonably requested assistance to effect such assignment and will execute any and all documents necessary to perfect such assignment. Any Patents [***] under this Section [***]. In addition, [***].

(e) Any Know-How discovered, developed, invented or created jointly under this Agreement by both (a) Vertex, its Affiliates or Third Parties acting on Vertex's behalf and (b) CRISPR, its Affiliates or Third Parties acting on CRISPR's behalf, while conducting activities under this Agreement, that is not [***] Joint Program Know-How or [***] Joint Program Know-How (the " **Other Joint Program Know-How** "), and any Patents that solely claim or cover such Other Joint Program Know-How (the " **Other Joint Program Patents** ," and together with the Other Joint Program Know-How, the " **Other Joint Program Technology** "), will be [***], including all rights, title and interest thereto, subject to any assignment, rights or licenses expressly granted by one Party to the other Party under this Agreement. Except as expressly provided in this Agreement, neither Party will have any obligation [***] with respect to, or to [***], Other Joint Program Technology by reason of [***] thereof, and each Party [***] the laws of any jurisdiction [***]. If such [***], each Party [***] to the [***] without [***] other Party. Notwithstanding the foregoing, if either Party [***] such Other Joint Program Technology, it shall [***] of the other Party, such [***].

(f) CRISPR will promptly disclose to Vertex in writing, and will cause its Affiliates to so disclose, the discovery, development, invention or creation of any CRISPR Program Technology under this Agreement. In addition, each Party will promptly disclose to the other Party in writing, and will cause its Affiliates to so disclose, the discovery, development, invention or creation of any Joint Program Technology under this Agreement.

7.11.3. **[***] CRISPR Product-Specific Patents to [***]** .

(d) Within [***] following the exercise of an Option by Vertex, if not previously completed by [***], CRISPR will [***], including without limitation a [***] as defined below, or as a new case to be determined by [***], consisting of [***] for the [***] that are [***] (each such [***]). Upon Vertex's exercise of an Option, all [***] will no longer be [***] and will thereafter be [***].

(e) Effective upon and following Vertex's exercise of the Option for a particular Collaboration Target, CRISPR will, and hereby does, [***] related to [***] that are [***] (whether [***]), and thereafter [***] will have [***]. CRISPR will take all actions and provide Vertex with [***] and will [***]. Any [***] under this Section 8.1.3(b) will be excluded [***] but will be included in the [***] for purposes of determining the [***].

7.11.4. **[***] CRISPR** . Effective upon [***] pursuant to Section 8.1.3, Vertex will, [***], [***] any such [***] to (a) conduct activities [***], (b) conduct [***] and (c) [***].

7.12. **Prosecution and Maintenance of Patents** . The Parties hereby agree as follows with respect to the Prosecution and Maintenance of certain Patents, for the avoidance of doubt, in each case, subject to Third Party Obligations.

7.12.1. **CRISPR Platform Technology Patents** . Anything herein to the contrary notwithstanding, and subject to Section 8.2.5, CRISPR will control and be responsible for all aspects of the Prosecution and Maintenance of the CRISPR Platform Technology Patents.

7.12.2. **CRISPR Patents .** CRISPR will control and be responsible for all aspects of the Prosecution and Maintenance of CRISPR Background Patents, CRISPR Program Patents, [***] Patents and [***] Program Patents. CRISPR will use Commercially Reasonable Efforts to Prosecute and Maintain all CRISPR Background Patents, CRISPR Program Patents, [***] Patents, other Joint Program Patents if applicable, and [***] Joint Program Patents, in each case to the extent Covering Licensed Agents or Products directed to particular Collaboration Targets using counsel reasonably acceptable to Vertex. In advance of Option Exercise for a particular Collaboration Target (*i.e* ., during the course of and in connection with each Research Plan conducted by the Parties under this Agreement), (a) CRISPR will undertake the Prosecution and Maintenance of one or more patent applications which could claim [***] Claims to the extent permitted by applicable law (each such Patent a "[***] **Patent** ") and (b) prior to the filing of any Patent application that Covers Licensed Agents or Products, the Patent Coordinators will meet and in good faith discuss the best

strategy for such filing (which, for clarity may [***] Patents). The Parties will use good faith efforts to agree on such strategy, with the goal of maximizing the value of the Parties' respective patent portfolios.

7.12.3. **Vertex Patents**. Vertex will control and be responsible for all aspects of the Prosecution and Maintenance of all Vertex Background Patents, Vertex Program Patents, [***] and [***] Joint Program Patents. Vertex will use Commercially Reasonable Efforts to Prosecute and Maintain all [***] Patents and [***] Joint Program Patents, if applicable, using counsel reasonably acceptable to CRISPR.

7.12.4. **Other Joint Program Patents**. The Parties will discuss and agree upon an allocation of responsibility for the prosecution and maintenance of the Other Joint Program Patents.

7.12.5. **Other Matters Pertaining to Prosecution and Maintenance of Patents**.

(a) Each Party will keep the other Party informed through their respective Patent Coordinators as to material developments with respect to the Prosecution and Maintenance of the CRISPR Platform Technology Patents, CRISPR Background Patents, CRISPR Program Patents, [***] Patents and Joint Program Patents for which such Party has responsibility for Prosecution and Maintenance pursuant to this Section 8.2, including by providing copies of any office actions or office action responses or other correspondence that such Party provides to or receives from any patent office, including notice of all interferences, reissues, re-examinations, or oppositions, and all patent-related filings, and by providing the other Party the timely opportunity to have reasonable input into the strategic aspects of such Prosecution and Maintenance.

(b) If, during the Agreement Term, Vertex intends to abandon patent applications for any Patent that Vertex is responsible for Prosecuting and Maintaining under Section 8.2.3 (excluding Vertex Background Patents and Vertex Program Patents that Cover technology other than Licensed Agents and Products, but including, for the avoidance of doubt, [***] Patents) in a particular country, then Vertex will so notify CRISPR of such intention at least [***] before such Patent will become abandoned, and CRISPR will have the right, but not the obligation, to assume responsibility for the Prosecution and Maintenance thereof at its own expense with counsel of its own choice.

(c) If, during the Agreement Term, CRISPR intends to abandon any CRISPR Background Patent (excluding any CRISPR Platform Technology Patents), CRISPR Program Patent, [***] Patent, [***] Joint Program Patent or Other Joint Program Patent Covering a Licensed Agent or Product that CRISPR is responsible for Prosecuting and Maintaining in a particular country, then, if Vertex's right to obtain an Exclusive License to such Patent or have such Patent assigned pursuant to Section 8.1.3, as applicable, has not expired or terminated, CRISPR will notify Vertex of such intention at least [***] before such Patent will become abandoned, and Vertex will have the right, but not the obligation, to assume responsibility for the Prosecution and Maintenance thereof at its own expense with counsel of its own choice.

7.13. **Patent Coordinators**. Each Party will appoint a patent coordinator reasonably acceptable to the other Party (each, a " **Patent Coordinator** ") to serve as such Party's primary liaison with the other Party on matters relating to the Prosecution and Maintenance and enforcement of Licensed Patents and Joint Program Patents. The Patent Coordinators will meet in person or by means of telephone or video conference at least once each Calendar Quarter during the Agreement Term. Each Party may replace its Patent Coordinator at any time by providing notice in writing to the other Party. The initial Patent Coordinators will be:

For Vertex: Kerry Flynn

For CRISPR: Tyler Dylan-Hyde

7.14. **Patent Costs**. Patent Costs arising after the Effective Date will be borne by the Parties as provided in Schedule K for the relevant period (*i.e.* , before or after Option Exercise) except as otherwise set forth in the Joint Development & Commercialization Agreement.

7.15. **Defense of Claims Brought by Third Parties**. If a Third Party initiates a Proceeding against either Party claiming a Patent owned by or licensed to such Third Party is infringed by the Research, Development, Manufacture or Commercialization of a Licensed Agent or Product, each Party that is named as a defendant in such Proceeding will have the right to defend itself in such Proceeding. The other Party will reasonably assist the defending Party in defending such Proceeding and cooperate in any such litigation at the request and expense of the defending Party. The defending Party will provide the other Party with prompt written notice of the commencement of any such Proceeding and will keep the other Party apprised of the progress of such Proceeding and will promptly furnish the other Party with a copy of each communication relating to the alleged infringement that is received by such Party. If both Parties are named as defendants in any Proceeding, both Parties may defend such Proceeding and the Parties will reasonably cooperate with respect to such defense.

7.16. **Enforcement of Patents Against Competitive Infringement**.

7.16.1. **Duty to Notify of Competitive Infringement**. If either Party learns of an infringement, unauthorized use, misappropriation or threatened infringement by a Third Party with respect to any Licensed Patents by reason of the making, using, offering to sell, selling or importing of (a) a product containing [***] or (b) the resulting [***] by such [***] (a " **Competitive Infringement** ") or any other infringement, unauthorized use, misappropriation or threatened infringement by a Third Party with respect to any CRISPR Platform Technology Patent, such Party will promptly notify the other Party in writing and will provide such other Party with available information regarding such Competitive Infringement or other infringement.

7.16.2. **Prior to License Grant**. For any Competitive Infringement with respect to a Licensed Agent or Product pertaining to a Collaboration Target that is then subject to an Option, which Competitive Infringement occurs after the Effective Date but before the date Vertex is granted the Exclusive License with respect to such Licensed Agent or Product, CRISPR will have the first right, but not the obligation, to institute, prosecute, and control a Proceeding with respect thereto, by counsel of its own choice. Vertex will have the right to engage

counsel of its own choice in connection with such Proceeding at its own expense but shall not be permitted to become party to such Proceeding unless required by Applicable Law. CRISPR will provide Vertex with prompt written notice of the commencement of any such Proceeding, and CRISPR will keep Vertex apprised of the progress of such Proceeding. Notwithstanding anything the contrary contained herein, CRISPR will at all times have the sole right to institute, prosecute, and control any Proceeding under this Section 8.6.2 to the extent involving any CRISPR Platform Technology Patents but will (a) keep Vertex reasonably apprised of the progress of such Proceeding, (b) reasonably consider Vertex's comments with respect to the conduct of such Proceeding and (c) not enter a settlement, consent judgment or other voluntary final disposition of a Proceeding that disclaims, limits the scope of, admits the invalidity or unenforceability of, or grants a license, covenant not to sue or similar immunity that has an adverse effect on Vertex's rights hereunder with respect to, a CRISPR Platform Technology Patent without Vertex's prior written consent, not to be unreasonably withheld.

7.16.3. **Following License Grant** . For any Competitive Infringement with respect to a particular Licensed Agent or Product occurring after the date Vertex is granted the Exclusive License with respect to such Licensed Agent or Product, Vertex will have the first right, but not the obligation, to institute, prosecute, and control a Proceeding with respect to such Competitive Infringement by counsel of its own choice at its own expense, and CRISPR will have the right, at its own expense, to be represented in that action by counsel of its own choice; *provided* that in such Proceeding, Vertex shall reasonably consider CRISPR's comments with respect to which Patents to seek to enforce against such infringing party, taking into consideration the overall value of the Patents Covering the relevant Licensed Agent or Product to CRISPR and its licensees. If Vertex fails to initiate a Proceeding within a period of [***] after written notice of such Competitive Infringement is first provided by a Party under Section 8.6.1, CRISPR will have the right to initiate and control a Proceeding with respect to such Competitive Infringement by counsel of its own choice, and Vertex will have the right to be represented in any such action by counsel of its own choice at its own expense; *provided,* that if Vertex notifies CRISPR during such [***] period that it is electing in good faith not to institute any Proceeding against such Competitive Infringement for strategic reasons intended to maintain the commercial value of the relevant Patent and any Licensed Agent or Product Covered thereby, CRISPR will not have the right to initiate and control any Proceeding with respect to such Competitive Infringement. Notwithstanding anything to the contrary contained herein, CRISPR will at all times have the sole right to institute, prosecute, and control any Proceeding under this Section 8.6.3 to the extent involving any CRISPR Platform Technology Patents but will (a) keep Vertex reasonably apprised of the progress of such Proceeding, (b) reasonably consider Vertex's comments with respect to the conduct of such Proceeding and (c) not enter a settlement, consent judgment or other voluntary final disposition of a Proceeding that disclaims, limits the scope of, admits the invalidity or unenforceability of, or grants a license, covenant not to sue or similar immunity that has an adverse effect on Vertex's rights hereunder with respect to, a CRISPR

Platform Technology Patent without Vertex's prior written consent, not to be unreasonably withheld.

7.16.4. **Joinder** .

(a) If a Party initiates a Proceeding in accordance with this Section 8.6 or Section 8.7 the other Party agrees to be joined as a party plaintiff where necessary and to give the first Party reasonable assistance and authority to file and prosecute the Proceeding. Subject to Section 8.6.5, the costs and expenses of each Party incurred pursuant to this Section 8.6.4 will be borne by the Party initiating such Proceeding. CRISPR agrees to use Commercially Reasonable efforts to cause Third Parties to be joined as a party plaintiff where necessary.

(b) If one Party initiates a Proceeding in accordance with this Section 8.6, the other Party may join such Proceeding as a party plaintiff where necessary for such other Party to seek lost profits with respect to such infringement.

7.16.5. **Share of Recoveries** . Any damages or other monetary awards recovered with respect to a Proceeding brought pursuant to this Section 8.6 will be shared as follows:

(a) the amount of such recovery will first [***]; then

(b) any remaining proceeds constituting direct or actual damages for acts of infringement occurring prior to the date Vertex is granted the Exclusive License with respect to the relevant Licensed Agent or Product [***];

(c) any remaining proceeds constituting direct or actual damages for acts of infringement occurring after the date Vertex is granted the Exclusive License with respect to the relevant Licensed Agent or Product [***]; and

(d) any remaining proceeds constituting punitive or treble damages will be allocated between the Parties as follows: [***].

Notwithstanding the foregoing, any Out-of Pocket Costs incurred in connection with a Proceeding with respect to a Shared Product shall be included in the Other-Out-of-Pocket Costs (as defined in Schedule G) and the proceeds of such proceeding shall be deemed Net Sales for purposes of determining the Net Profit or Net Loss (each, as defined in Schedule G).

7.16.6. **Settlement** . Notwithstanding anything to the contrary under this ARTICLE 8, neither Party may enter a settlement, consent judgment or other voluntary final disposition of a suit under this ARTICLE 8 that disclaims, limits the scope of, admits the invalidity or unenforceability of, or grants a license, covenant not to sue or similar immunity under a Patent Controlled by the other Party or its Affiliates without first obtaining the written consent of the Party that Controls the relevant Patent; *provided* that the foregoing limitation shall not apply to CRISPR's rights with respect to the CRISPR Platform Technology Patents (subject to the restriction set forth in Sections 8.6.2 and 8.6.3).

7.17. **Other Infringement**.

7.17.1. **Joint Program Patents**. With respect to the infringement of a Joint Program Patent that is not a Competitive Infringement, the Parties will cooperate in good faith to bring suit together against such infringing party or the Parties may decide to permit one Party to solely bring suit. Any damages or other monetary awards recovered with respect to a Proceeding brought pursuant to this Section 8.7.1 will be shared as follows: (a) the amount of such recovery [***]; then (b) any remaining proceeds will be allocated as follows: (i) [***]; and (ii) [***].

7.17.2. **Patents Solely Owned by CRISPR**. CRISPR will retain all rights to pursue an infringement of any Patent solely owned by CRISPR that is not a Competitive Infringement and CRISPR will retain all recoveries with respect thereto.

7.17.3. **Patents Solely Owned by Vertex.** Vertex will retain all rights to pursue an infringement of any Patent solely owned by Vertex and Vertex will retain all recoveries with respect thereto.

7.18. **Patent Listing**. Following Vertex's exercise of the Option for a Collaboration Target, Vertex will have the sole right, but not the obligation, to submit to all applicable Regulatory Authorities patent information pertaining to each applicable Product pursuant to 21 U.S.C. § 355(b)(1)(G) (or any amendment or successor statute thereto), any similar statutory or regulatory requirement enacted in the future regarding biologic products, or any similar statutory or regulatory requirement in any non-U.S. country or other regulatory jurisdiction; *provided* that Vertex shall not be permitted to provide any such information with respect to CRISPR Platform Technology Patents without CRISPR's prior written consent.

7.19. **CREATE Act**. Notwithstanding anything to the contrary in this ARTICLE 8, neither Party will have the right to make an election under the CREATE Act when exercising its rights under this ARTICLE 8 without the prior written consent of the other Party, which will not be unreasonably withheld, conditioned or delayed. With respect to any such permitted election, the Parties will use reasonable efforts to cooperate and coordinate their activities with respect to any submissions, filings or other activities in support thereof. The Parties acknowledge and agree that this Agreement is a "joint research agreement" as defined in the CREATE Act.

7.20. **Additional Right and Exceptions**. Notwithstanding any provision of this ARTICLE 8, CRISPR retains the sole right to Prosecute and Maintain CRISPR Platform Technology Patents and to control any enforcement of CRISPR Platform Technology Patents, subject to the restrictions set forth in Sections 8.6.2 and 8.6.3.

7.21. **Patent Term Extension**. The Parties will cooperate with each other in obtaining patent term restoration in any country in the Territory under any statute or regulation equivalent or similar to 35 U.S.C. § 156, where applicable to a Product. After the date Vertex is granted the Exclusive License with respect to a Product, [***] Vertex Background Patents, [***] Patents, Vertex Program Patents, [***] Joint Program Patents, Joint Program Patents and [***] Joint Program Patents [***]. CRISPR will abide by Vertex's determination and cooperate, as reasonably requested by Vertex, in connection with the foregoing (including by providing appropriate information and executing appropriate documents).

7.22. **Recording**. If Vertex deems it necessary or desirable to register or record this Agreement or evidence of this Agreement with any patent office or other appropriate Governmental Authority in one or more jurisdictions in the Territory, CRISPR will reasonably cooperate to execute and deliver to Vertex any documents accurately reflecting or evidencing this Agreement that are necessary or desirable, in Vertex's reasonable judgment, to complete such registration or recordation. Vertex will reimburse CRISPR for all reasonable Out-of-Pocket Costs, including attorneys' fees, incurred by CRISPR in complying with the provisions of this Section 8.12.

ARTICLE 8.
REPRESENTATIONS AND WARRANTIES

8.1. **Representations and Warranties of Vertex**. Vertex hereby represents and warrants to CRISPR, as of the Effective Date, that:

8.1.5. each of Vertex Parent and Vertex UK are duly organized, validly existing and in good standing under the laws of the jurisdiction of its incorporation or organization and has full corporate power and authority to enter into this Agreement and to carry out the provisions hereof;

8.1.6. each of Vertex Parent and Vertex UK (a) has the requisite power and authority and the legal right to enter into this Agreement and to perform its obligations hereunder and (b) has taken all requisite action on its part to authorize the execution and delivery of this Agreement and the performance of its obligations hereunder;

8.1.7. each of Vertex Parent and Vertex UK has the requisite resources and expertise to perform its obligations hereunder;

8.1.8. this Agreement has been duly executed and delivered on behalf of each of Vertex Parent and Vertex UK, and constitutes a legal, valid and binding obligation, enforceable against each of Vertex Parent and Vertex UK in accordance with the terms hereof;

8.1.9. the execution, delivery and performance of this Agreement by each of Vertex Parent and Vertex UK will not constitute a default under or conflict with any agreement, instrument or understanding, oral or written, to which either entity is a party or by which either entity is bound, or violate any law or regulation of any court, governmental body or administrative or other agency having jurisdiction over Vertex Parent or Vertex UK; and

8.1.10. each of Vertex Parent and Vertex UK has obtained all necessary consents, approvals and authorizations of all Governmental Authorities and other Persons or entities required to be obtained by it in connection with the execution and delivery of this Agreement.

8.2. **Representations and Warranties of CRISPR**. Each of the CRISPR Entities, jointly and severally, hereby represents and warrants to Vertex, as of the Effective Date, that, except as otherwise set forth on Schedule L:

8.2.10. Each of CRISPR AG, CRISPR Inc., CRISPR UK and Tracr are duly organized, validly existing and in good standing under the laws of the jurisdiction of its incorporation or organization and has full corporate power and authority to enter into this Agreement and to carry out the provisions hereof;

8.2.11. Each of CRISPR AG, CRISPR Inc., CRISPR UK and Tracr (a) has the requisite power and authority and the legal right to enter into this Agreement and to perform its obligations hereunder and (b) has taken all requisite action on its part to authorize the execution and delivery of this Agreement and the performance of its obligations hereunder;

8.2.12. [***], each of CRISPR AG, CRISPR Inc., CRISPR UK and Tracr has the requisite resources and expertise to perform its obligations hereunder;

8.2.13. this Agreement has been duly executed and delivered on behalf of CRISPR, and constitutes a legal, valid and binding obligation, enforceable against it in accordance with the terms hereof;

8.2.14. the execution, delivery and performance of this Agreement by CRISPR will not constitute a default under or conflict with any agreement, instrument or understanding, oral or written, to which it is a party or by which it is bound, or violate any law or regulation of any court, governmental body or administrative or other agency having jurisdiction over it;

8.2.15. CRISPR has obtained all necessary consents, approvals and authorizations of all Governmental Authorities and other Persons or entities required to be obtained by CRISPR in connection with the execution and delivery of this Agreement;

8.2.16. the Licensed Technology constitutes all of the Patents and Know-How Controlled by CRISPR that are necessary to Research, Develop, Manufacture or Commercialize Licensed Agents and Products contemplated under the Collaboration Programs in the Field;

8.2.17. CRISPR is the sole and exclusive owner or exclusive licensee of the [***], all of which are free and clear of any liens, charges and encumbrances, and, as of the Effective Date, neither any license granted by CRISPR to any Third Party, nor any license granted by any Third Party to CRISPR conflicts with the license grants to Vertex hereunder (or the Exclusive License to be granted to Vertex upon Option Exercise) and CRISPR is entitled to grant all rights and licenses (or sublicenses, as the case may be) under such Patents it purports to grant to Vertex under this Agreement and the Exclusive Licenses to be granted to Vertex upon Option Exercise;

8.2.18. Schedule L sets forth a true, correct and complete list of all CRISPR Platform Technology Patents and CRISPR Background Patents as of the Effective Date and indicates (a) whether each such Patent is a [***] or a [***] and (b) whether such Patent is owned by CRISPR or licensed by CRISPR from a Third Party and if so, identifies the licensor or sublicensor from which the Patent is licensed;

8.2.19. CRISPR has independently developed all Licensed Technology or otherwise has a valid right to use, and to permit Vertex, Vertex's Affiliates and Vertex's Sublicensees to use, the Licensed Technology for all permitted purposes under this Agreement;

8.2.20. the CRISPR Background Know-How is free and clear of liens, charges or encumbrances other than licenses granted to Third Parties that are not inconsistent with the rights and licenses granted to Vertex hereunder;

8.2.21. the CRISPR Platform Technology Patents and CRISPR Background Patents, are, or, upon issuance, will be, valid and enforceable patents and no Third Party [***], (a) is infringing any such Patents or (b) has challenged the extent, validity or enforceability of such Patents (including by way of example through the institution or written threat of institution of interference, nullity or similar invalidity proceedings before the United States Patent and Trademark Office or any analogous foreign Governmental Authority);

8.2.22. it has complied with all Applicable Laws, including any disclosure requirements of the United States Patent and Trademark Office or any analogous foreign Governmental Authority, in connection with the Prosecution and Maintenance of the CRISPR Platform Technology Patents and CRISPR Background Patents and has timely paid all filing and renewal fees payable with respect to any such Patents for which it controls Prosecution and Maintenance;

8.2.23. it has obtained assignments from the inventors of all inventorship rights relating to the [***] and [***] that it owns, and all such assignments of inventorship rights relating to such Patents are valid and enforceable;

8.2.24. except for the CRISPR In-License Agreements, there is no agreement between CRISPR (or any of its Affiliates) and any Third Party pursuant to which CRISPR has acquired Control of any of the Licensed Technology, and no Third Party has any right, title or interest in or to, or any license under, any of the Licensed Technology. All CRISPR In-License Agreements are in full force and effect and have not been modified or amended (except for amendments provided to Vertex prior to the Effective Date). Neither CRISPR nor, [***], the Third Party licensor in a CRISPR In-License Agreement is in default with respect to a material obligation under such CRISPR In-License Agreement, and neither such party has claimed or has grounds upon which to claim that the other party is in default with respect to a material obligation under, any CRISPR In-License Agreement;

8.2.25. CRISPR and its Affiliates have taken commercially reasonable measures consistent with industry practices to protect the secrecy, confidentiality and value of all CRISPR Background Know-How that constitutes trade secrets under Applicable Law (including requiring all employees, consultants and independent contractors to execute binding and enforceable agreements requiring all such employees, consultants and independent contractors to maintain the confidentiality of such CRISPR Background Know-How) and, [***], such CRISPR Background Know-How has not been used, disclosed to or discovered by any Third Party except pursuant to such confidentiality

agreements and there has not been a breach by any party to such confidentiality agreements;

8.2.26. no Licensed Technology is subject to any funding agreement with any government or governmental agency;

8.2.27. [***], the Research, Development, Manufacture, use, sale, offer for sale, supply or importation by CRISPR or Vertex (or their respective Affiliates or Sublicensees) of a Licensed Agent or Product does not and will not infringe any issued patent of any Third Party or, if and when issued, any claim within any patent application of any Third Party;

8.2.28. there are no judgments or settlements against or owed by CRISPR [***], [***], pending or threatened claims or litigation, in either case relating to the Licensed Technology;

8.2.29. there is no action, claim, demand, suit, proceeding, arbitration, grievance, citation, summons, subpoena, inquiry or investigation of any nature, civil, criminal, regulatory or otherwise, in law or in equity, pending [***], [***], threatened against CRISPR, any of its Affiliates or any Third Party, in each case in connection with the Licensed Technology or relating to the transactions contemplated by this Agreement; and

8.2.30. CRISPR has not employed (and, [***], has not used a contractor or consultant that has employed) any Person debarred by the FDA (or subject to a similar sanction of EMA or foreign equivalent), or any Person that is the subject of an FDA debarment investigation or proceeding (or similar proceeding of EMA or foreign equivalent), in any capacity in connection with this Agreement.

8.3. **CRISPR Covenants**. Each of the CRISPR Entities, jointly and severally, hereby covenants to Vertex that, except as expressly permitted under this Agreement:

8.3.5. CRISPR will maintain and not breach any CRISPR In-License Agreements [***] that provide a grant of rights from such Third Party to CRISPR that are Controlled by CRISPR and are licensed or may become subject to a license from CRISPR to Vertex for a Licensed Agent or Product under this Agreement;

8.3.6. CRISPR will promptly notify Vertex of any material breach by one or more CRISPR Entities or a Third Party of any CRISPR In-License Agreements or [***] that provides a grant of rights from such Third Party to one or more CRISPR Entities and are licensed or may become subject to a license from CRISPR to Vertex to conduct Vertex Activities or for a Licensed Agent or Product under this Agreement, and in the event of a breach by [***], will [***]. CRISPR will [***] as soon as possible, but in no event later than the date on which [***];

8.3.7. it will not amend, modify or terminate any CRISPR In-License Agreement or [***] in a manner that would have an adverse effect on Vertex's rights hereunder without first obtaining Vertex's written consent, which consent may be withheld in Vertex's sole discretion;

8.3.8. it will not enter into any new agreement or other obligation with any Third Party, or amend an existing agreement with a Third Party, in each case that adversely restricts, limits or encumbers the rights granted to Vertex under this Agreement or the additional rights or licenses Vertex would acquire upon Option Exercise;

8.3.9. it will not, and will cause its Affiliates not to (a) license, sell, assign or otherwise transfer to any Person any Licensed Technology (or agree to do any of the foregoing), except as provided in Section 8.1.3 or except as will not adversely restrict, limit or encumber the rights granted to Vertex under this Agreement or the additional rights or licenses Vertex would acquire upon Option Exercise, or (b) incur or permit to exist, with respect to any Licensed Technology, any lien, encumbrance, charge, security interest, mortgage, liability, grant of license to Third Parties or other restriction (including in connection with any indebtedness);

8.3.10. it will use Commercially Reasonable Efforts to obtain and maintain the requisite resources and expertise to perform its obligations hereunder;

8.3.11. all employees and Subcontractors of CRISPR performing Research or Development activities hereunder on behalf of CRISPR will be obligated to assign to CRISPR all right, title and interest in and to any inventions developed by them, whether or not patentable, or, solely with respect to Subcontractors, grant exclusive license rights to CRISPR with a right to grant sublicenses through multiple tiers;

8.3.12. it will not engage, in any capacity in connection with this Agreement any Person who either has been debarred by the FDA, is the subject of a conviction described in Section 306 of the FD&C Act or is subject to any such similar sanction;

8.3.13. CRISPR will inform Vertex in writing promptly if it or any Person engaged by CRISPR or any of its Affiliates who is performing services under this Agreement or any ancillary agreements is debarred or is the subject of a conviction described in Section 306 of the FD&C Act, or if any action, suit, claim, investigation or legal or administrative proceeding is pending or, to CRISPR's Knowledge, is threatened, relating to the debarment or conviction of CRISPR, any of its Affiliates or any such Person performing services hereunder or thereunder;

8.3.14. Within [***] after the Effective Date, [***] will take all actions necessary (including, without limitation, [***] to ensure [***], effective [***], which actions may include, without limitation, [***] and executing all documents necessary in connection therewith.

8.3.15. CRISPR shall use Commercially Reasonable Efforts (A) to, within [***] of the Effective Date, [***] directly or indirectly [***] that [***], that have [***] and that [***] and other intellectual property rights or (B) shall otherwise work together [***]. To the extent [***] execute such documents as are necessary to [***] and (ii) CRISPR shall [***] and the [***] shall be [***].

8.4. **Vertex Covenants** . Vertex hereby covenants to CRISPR that, except as expressly permitted under this Agreement:

8.4.10. it will use Commercially Reasonable Efforts to obtain and maintain the requisite resources and expertise to perform its obligations hereunder;

8.4.11. Vertex will not engage, in any capacity in connection with this Agreement any Person who either has been debarred by the FDA, is the subject of a conviction described in Section 306 of the FD&C Act or is subject to any such similar sanction; and

8.4.12. Vertex will inform CRISPR in writing promptly if it or any Person engaged by Vertex or any of its Affiliates who is performing services under this Agreement or any ancillary agreements is debarred or is the subject of a conviction described in Section 306 of the FD&C Act, or if any action, suit, claim, investigation or legal or administrative proceeding is pending or, [***], is threatened, relating to the debarment or conviction of CRISPR, any of its Affiliates or any such Person performing services hereunder or thereunder.

8.5. **Disclaimer** . Except as otherwise expressly set forth in this Agreement, neither Party nor its Affiliates makes any representation or extends any warranty of any kind, either express or implied, including any warranty of merchantability or fitness for a particular purpose. Vertex and CRISPR understand that each Product is the subject of ongoing Research and Development and that neither Party can assure the safety, usefulness or commercial or technical viability of any Product.

ARTICLE 9.
INDEMNIFICATION; INSURANCE

9.1. **Indemnification by Vertex** . Vertex will indemnify, defend and hold harmless CRISPR, each of its Affiliates, and each of its and its Affiliates' employees, officers, directors and agents (each, an " **CRISPR Indemnified Party** ") from and against any and all liability, loss, damage, expense (including reasonable attorneys' fees and expenses) and cost (collectively, a " **Liability** ") that the CRISPR Indemnified Party may be required to pay to one or more Third Parties to the extent resulting from or arising out of:

9.1.31. any claims of any nature arising out of the Research, Development, Manufacture, Commercialization or use of any Licensed Agent or Product by, on behalf of, or under the authority of, Vertex (other than by any CRISPR Indemnified Party), other than (a) claims by Third Parties relating to misappropriation of trade secrets or other intellectual property rights arising out of the exercise of rights under the Licensed Know-How, or (b) claims for which CRISPR is required to indemnify Vertex pursuant to Section 10.2; or

9.1.32. the material breach by Vertex of any of its representations, warranties or covenants set forth in this Agreement, except to the extent caused by the negligence or intentional acts of CRISPR or any CRISPR Indemnified Party.

9.2. **Indemnification by CRISPR** . Each CRISPR Entity will jointly and severally indemnify, defend and hold harmless Vertex, its Affiliates, Sublicensees, distributors and each of its and their respective employees, officers, directors and agents (each, a " **Vertex Indemnified Party** ") from and against any and all Liabilities that the Vertex Indemnified Party may be required to pay to one or more Third Parties to the extent resulting from or arising out of:

9.2.16. the material breach by CRISPR (or any CRISPR Entity(ies)) of any of its representations, warranties or covenants set forth in this Agreement, except to the extent caused by the negligence or intentional acts of Vertex or any Vertex Indemnified Party; or

9.2.17. any claims of any nature arising out of the Research activities performed by CRISPR (or any CRISPR Entity(ies)) with respect to any Licensed Agent or Product prior to the Effective Date or during the Research Term, other than claims for which Vertex is required to indemnify CRISPR pursuant to Section 10.1.

9.3. **Procedure**. Each Party will notify the other Party in writing if it becomes aware of a claim for which indemnification may be sought hereunder. In case any proceeding (including any governmental investigation) will be instituted involving any Party in respect of which indemnity may be sought pursuant to this ARTICLE 10, such Party (the " **Indemnified Party** ") will give prompt written notice of the indemnity claim to the other Party (the " **Indemnifying Party** ") and provide a copy to the Indemnifying Party of any complaint, summons or other written or verbal notice that the Indemnified Party receives in connection with any such claim. An Indemnified Party's failure to deliver written notice will relieve the Indemnifying Party of liability to the Indemnified Party under this ARTICLE 10 only to the extent such delay is prejudicial to the Indemnifying Party's ability to defend such claim. Provided that the Indemnifying Party is not contesting the indemnity obligation, the Indemnified Party will permit the Indemnifying Party to control any litigation relating to such claim and the disposition of such claim by negotiated settlement or otherwise and any failure to contest prior to assuming control will be deemed to be an admission of the obligation to indemnify. The Indemnifying Party will act reasonably and in good faith with respect to all matters relating to such claim and will not settle or otherwise resolve such claim without the Indemnified Party's prior written consent which will not be withheld, delayed or conditioned unreasonably other than settlements only involving the payment of monetary awards for which the Indemnifying Party will be fully-responsible. The Indemnified Party will cooperate with the Indemnifying Party in such Party's defense of any claim for which indemnity is sought under this Agreement, at the Indemnifying Party's sole cost and expense.

9.4. **Insurance**. Each Party will maintain, at its cost, reasonable insurance against liability and other risks associated with its activities contemplated by this Agreement and will furnish to the other Party evidence of such insurance upon request. Notwithstanding the foregoing, Vertex may self-insure to the extent that it self-insures for its other activities.

9.5. **Limitation of Consequential Damages**. Except for (a) claims of a Third Party that are subject to indemnification under this ARTICLE 10, (b) claims arising out of a Party's willful misconduct, or (c) a Party's breach of Section 2.13 or ARTICLE 12, neither Party nor any of its Affiliates will be liable to the other Party or its Affiliates for any incidental, consequential, special, punitive or other indirect damages or lost or imputed profits or royalties, lost data or cost of procurement of substitute goods or services, whether liability is asserted in contract, tort (including negligence and strict product liability), indemnity or contribution, and irrespective of whether that Party or any representative of that Party has been advised of, or otherwise might have anticipated the possibility of, any such loss or damage.

ARTICLE 10.
TERM; TERMINATION

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

10.1.18. on a country-by-country and Product-by-Product basis, on the date of expiration of all payment obligations under this Agreement with respect to such Product in such country;

10.1.19. in its entirety upon the expiration of all payment obligations under this Agreement with respect to all Products in all countries pursuant to Section 11.1.1; and

10.1.20. in its entirety upon expiration of all Options if Vertex has not exercised any Option as provided in Section 4.1.1.

10.2. **Termination of the Agreement**.

10.2.13. **Vertex's Termination for Convenience**. Vertex will be entitled to terminate this Agreement as a whole, or terminate this Agreement in part with respect to a particular Collaboration Program, for convenience by providing CRISPR 90 days' written notice of such termination; *provided, however* , that if any termination under this Section 11.2.1 applies to a Product for which Vertex has received Marketing Approval, Vertex will provide CRISPR no less than 270 days' notice of such termination.

10.2.14. **Termination Due to Failure to Obtain HSR Clearance**. If the Parties make an HSR Filing with respect to a Collaboration Target under Section 4.1.2 and the HSR Clearance Date has not occurred on or prior to [***] after the effective date of the latest HSR Filing made by the Parties with respect to a Collaboration Target, this Agreement will terminate solely with respect to the applicable Collaboration Program at the election of either Party immediately upon notice to the other Party, if (a) the FTC or the DOJ has instituted (or threatened to institute) any action, suit or proceeding including seeking, threatening to seek or obtaining a preliminary injunction under the HSR Act against Vertex and CRISPR to enjoin or otherwise prohibit the transactions contemplated by this Agreement related to such proposed Collaboration Program, or (b) the Parties have not resolved any and all objections of the FTC and DOJ as contemplated by Section 4.1.2(b). Notwithstanding the foregoing, this Section 11.2.2 will not apply if an HSR Filing is not required for Vertex to receive the Exclusive License with respect to a Collaboration Target. If this Agreement is terminated pursuant to this Section 11.2.2 with respect to a particular Collaboration Target, such Collaboration Target will not count towards the Option Cap. If, following termination of this Agreement with respect to a Collaboration Target under this Section 11.2.2, CRISPR or any of its Affiliates or sublicensees Commercializes a Product for the relevant Collaboration Target, [***] of (i) [***] and (ii) [***].

[***]. The terms of Sections 1.117, 7.5.2, 7.5.5, 7.7, 7.8, 7.9 and 7.10 will apply with respect [***], *mutatis mutandis* .

10.2.15. **Termination for Material Breach** .

(c) **Vertex's Right to Terminate** . If CRISPR (or any CRISPR Entity(ies)) is in material breach of this Agreement, then Vertex may deliver notice of such material breach to CRISPR. If the breach is curable, CRISPR will have [***] from the receipt of such notice to cure such breach. If either CRISPR fails to cure such breach within such [***] period or the breach is not subject to cure (a " **CRISPR Breach Event** "), Vertex may either (i) terminate this Agreement (A) if such breach relates solely relates to a particular Collaboration Program, with respect to the Collaboration Program affected by such breach (a " **CRISPR Program Breach** ") or (B) if such breach relates to multiple Collaboration Programs or this Agreement as a whole (a " **CRISPR Agreement Breach** "), in its entirety, by providing written notice to CRISPR or (ii) elect to exercise the alternate remedy provisions set forth in Section 11.3 (in lieu of termination).

(d) **CRISPR's Right to Terminate.**

(i) If Vertex is in material breach of this Agreement, then CRISPR may deliver notice of such material breach to Vertex. If the breach is curable, Vertex will have [***] following receipt of such notice to cure such breach (except to the extent such breach involves the failure to make a payment when due, which breach must be cured within [***] following receipt of such notice). If Vertex fails to cure such breach within the [***] or [***] period, as applicable, or the breach is not subject to cure, CRISPR in its sole discretion may terminate this Agreement (i) if such breach relates solely relates to a particular Collaboration Program, with respect to the Collaboration Program affected by such breach or (ii) if such breach relates to multiple Collaboration Programs or this Agreement as a whole, in its entirety, by providing written notice to Vertex.

(ii) If Vertex (A) commences or actively and voluntarily participates in any action or proceeding (including any patent opposition or re-examination proceeding), or otherwise asserts any claim, challenging or denying the validity or enforceability of any claim of any Patent that is licensed to Vertex under this Agreement or (B) actively and voluntarily assists any other Person in bringing or prosecuting any action or proceeding (including any patent opposition or re-examination proceeding) challenging or denying the validity or enforceability of any claim of any Patent that is licensed to Vertex under this Agreement (each of (A) and (B), a " **Patent Challenge** "), then, to the extent permitted by Applicable Law, CRISPR shall have the right, in its sole discretion, to give notice to Vertex that CRISPR may terminate the license(s) granted under such Patent to Vertex [***] following such notice, and, unless Vertex withdraws or causes to be withdrawn all such challenge(s) (or in the case of *ex-parte* proceedings, multi-party proceedings, or other Patent Challenges that Vertex does not have the power to unilaterally withdraw or cause to be withdrawn), Vertex

ceases assisting any other party to such Patent Challenge and, to the extent Vertex is a party to such Patent Challenge, it withdraws from such Patent Challenge within such [***] period, CRISPR shall have the right to terminate this Agreement by providing written notice thereof to Vertex. The foregoing right to terminate shall not apply with respect to any Patent Challenge where the Patent Challenge is made in defense of an assertion of the relevant Patent that is first brought by CRISPR against Vertex. For the avoidance of doubt, any participation by Vertex or its employees in any claim, challenge or proceeding in response to a subpoena or as required under a pre-existing agreement between Vertex's employee(s) or consultant(s) and their prior employer(s) shall not constitute active and voluntary participation or assistance and shall not give rise to CRISPR's right to terminate any license hereunder.

10.2.16. **Disputes Regarding Material Breach** . Notwithstanding the foregoing, if the Breaching Party in Section 11.2.3 disputes in good faith the existence, materiality, or failure to cure of any such breach that is not a payment breach, and provides notice to the Non-Breaching Party of such dispute within the relevant cure period, the Non-Breaching Party will not have the right to terminate this Agreement in accordance with Section 11.2.3, or the right to exercise the alternative remedy provisions of 11.3, as applicable, unless and until the relevant dispute has been resolved. It is understood and acknowledged that during the pendency of such dispute, all the terms and conditions of this Agreement will remain in effect and the Parties will continue to perform all of their respective obligations hereunder.

10.2.17. **Termination for Insolvency** . If CRISPR (or any CRISPR Entity(ies)) makes an assignment for the benefit of creditors, appoints or suffers appointment of a receiver or trustee over all or substantially all of its property, files a petition under any bankruptcy or insolvency act or has any such petition filed against it that is not discharged within [***] of the filing thereof (each, an " **Insolvency Event** "), then Vertex may terminate this Agreement in its entirety effective immediately upon written notice to CRISPR. If Vertex terminates this Agreement pursuant to this Section 11.2.5:

(a) All rights and licenses now or hereafter granted by CRISPR to Vertex under or pursuant to this Agreement, including, for the avoidance of doubt, any Exclusive Licenses are, for all purposes of Section 365(n) of the U.S. Bankruptcy Code, licenses of rights to "intellectual property" as defined in the U.S. Bankruptcy Code. Upon the occurrence of any Insolvency Event with respect to CRISPR (or any CRISPR Entity(ies)), CRISPR agrees that Vertex, as licensee of such rights under this Agreement, will retain and may fully exercise all of its rights and elections under the U.S. Bankruptcy Code. CRISPR will, during the term of this Agreement, create and maintain current copies or, if not amenable to copying, detailed descriptions or other appropriate embodiments, to the extent feasible, of all intellectual property licensed under this Agreement. Each Party acknowledges and agrees that "embodiments" of intellectual property within the meaning of Section 365(n) include laboratory notebooks, cell lines, product samples and inventory, research studies and data, all Regulatory Approvals (and

all applications for Regulatory Approval) and rights of reference therein, the Licensed Technology and all information related to the Licensed Technology. If (x) a case under the U.S. Bankruptcy Code is commenced by or against CRISPR (or any CRISPR Entity(ies)), (y) this Agreement is rejected as provided in the U.S. Bankruptcy Code, and (z) Vertex elects to retain its rights hereunder as provided in Section 365(n) of the U.S. Bankruptcy Code, CRISPR (in any capacity, including debtor-in-possession) and its successors and assigns (including a trustee) will:

(i) provide to Vertex all such intellectual property (including all embodiments thereof) held by CRISPR and such successors and assigns, or otherwise available to them, immediately upon Vertex's written request. Whenever CRISPR or any of its successors or assigns provides to Vertex any of the intellectual property licensed hereunder (or any embodiment thereof) pursuant to this Section 11.2.5(a)(i), Vertex will have the right to perform CRISPR's obligations hereunder with respect to such intellectual property, but neither such provision nor such performance by Vertex will release CRISPR from liability resulting from rejection of the license or the failure to perform such obligations; and

(ii) not interfere with Vertex's rights under this Agreement, or any agreement supplemental hereto, to such intellectual property (including such embodiments), including any right to obtain such intellectual property (or such embodiments) from another entity, to the extent provided in Section 365(n) of the U.S. Bankruptcy Code.

(b) All rights, powers and remedies of Vertex provided herein are in addition to and not in substitution for any and all other rights, powers and remedies now or hereafter existing at law or in equity (including the U.S. Bankruptcy Code) in the event of the commencement of a case under the U.S. Bankruptcy Code with respect to CRISPR. The Parties agree that they intend the following rights to extend to the maximum extent permitted by Applicable Law, and to be enforceable under U.S. Bankruptcy Code Section 365(n):

(i) the right of access to any intellectual property rights (including all embodiments thereof) of CRISPR, or any Third Party with whom CRISPR contracts to perform an obligation of CRISPR under this Agreement, and, in the case of any such Third Party, which is necessary for the Manufacture, use, sale, import or export of Licensed Agents; and

(ii) the right to contract directly with any Third Party to complete the contracted work.

10.3. **Alternative Remedies to Termination** .

10.3.9. **Prior to Option Exercise** . If a CRISPR Breach Event occurs prior to Vertex exercising its Option with respect to a particular Collaboration Target, Vertex may elect the alternative remedy provisions of this Section 11.3.1 with respect to each Collaboration Target for which it has not yet exercised the Option and

that is subject to such CRISPR Breach Event (in the case of a CRISPR Program Breach), or all such Collaboration Targets (in the case of a CRISPR Agreement Breach), by providing written notice of such election to CRISPR, in which case, this Agreement will continue in full force and effect with the following modifications with respect to each Collaboration Target for which Vertex elects to exercise its rights under this Section 11.3.1. If Vertex exercises its rights under this Section 11.3.1, such exercise shall be Vertex's sole remedy in connection with such CRISPR Breach Event; Vertex shall have no other rights hereunder or at law or in equity with respect to the relevant CRISPR Breach Event; and CRISPR shall have no obligation to cure such CRISPR Breach Event.

(a) if CRISPR has not completed the activities for which it is responsible under the applicable Research Plan, [***], in which case, [***], If [***] for such activities, CRISPR will [***] and Vertex will [***] as provided herein;

(b) Vertex's obligations under [***] will not apply with respect to the applicable Collaboration Target;

(c) CRISPR will provide to Vertex [***] and [***] in [***] under the relevant [***] in an efficient and orderly manner;

(d) in the event that Vertex subsequently elects to obtain the Exclusive License with respect to any such Collaboration Target, such election shall be regarded as an Option pursuant to Section 4.1.1 (subject to the Option Cap), provided that [***].

10.3.10. **After Option Exercise**. If a CRISPR Breach Event occurs after Vertex exercises its Option with respect to a particular Collaboration Target, Vertex may elect the alternative remedy provisions of this Section 11.3.2 with respect to any Collaboration Target for which it has exercised the Option and that is subject to such CRISPR Breach Event (in the case of a CRISPR Program Breach), or all such Collaboration Targets (in the case of a CRISPR Agreement Breach), by providing written notice of such election to CRISPR, in which case, this Agreement will continue in full force and effect with the following modifications with respect to each Collaboration Target for which Vertex elects to exercise its rights under this Section 11.3.2, each at Vertex's election. If Vertex exercises its rights under this Section 11.3.2, such exercise shall be Vertex's sole remedy in connection with such CRISPR Breach Event; Vertex shall have no other rights hereunder or at law or in equity with respect to the relevant CRISPR Breach Event; and CRISPR shall have no obligation to cure such CRISPR Breach Event.

(a) CRISPR's right to [***];

(b) Vertex may [***] required or permitted [***] established pursuant to this Agreement in connection with the [***]; *provided, however,* Vertex will not have the right to: (i) [***] of this Agreement; (ii) [***] of the Parties, (iii) [***] under this Agreement; (iv) exercise its [***] would constitute a violation of an Applicable Law; (v) make a determination [***] under this Agreement or (vi)

require [***], whether internal or external, including capital expenditures for which [***] as provided herein; and

(c) to the extent CRISPR is then conducting Additional Research, Vertex may, but will not be obligated to, assume responsibility for such Additional Research, in which case, Vertex's obligation to fund such activities as provided in Section 7.4 will terminate. If Vertex does not elect to assume responsibility for such activities, CRISPR will continue to perform such activities and Vertex will continue to reimburse CRISPR for Research Costs arising out of such activities as provided herein.

10.3.11. [***]. If (a) CRISPR (or any CRISPR Entity(ies)) commits a breach or series of breaches of this Agreement, (b) Vertex incurs at least [***] in aggregate losses, damages and expenses as a result of such breach or breaches, (c) Vertex does not terminate this Agreement in its entirety or with respect to a Collaboration Target or Product due to such breach or breaches, and (d) Vertex has not exercised its rights under Section 11.3.1 or 11.3.2, as applicable, with respect to such breach or breaches, then, in addition to any other remedies Vertex may have under this Agreement, at law or in equity or otherwise, [***]. [***] Vertex will provide CRISPR with a written certificate, signed by Vertex's Chief Financial Officer, certifying [***]. Notwithstanding the foregoing, if CRISPR notifies Vertex in writing that it disputes Vertex's assertion that CRISPR (or any CRISPR Entity(ies)) is in breach of this Agreement [***], then (a) Vertex will initiate the dispute resolution process set forth in Section 11.3.4, and (b) pending the Parties' agreement regarding the appropriate [***] or a determination by the mediator [***] in accordance with Section 11.3.4(b), Vertex will [***]. If the Parties cannot settle their dispute by mutual agreement, then, in accordance with Section 11.3.4(b), the mediator will determine (1) [***], (2) [***] and (3) if [***], in which case Vertex [***].

10.3.12. [***] **Dispute Resolution**.

(a) **Escalation**. If Vertex has exercised its [***] rights under Section 11.3.3, and there is a dispute regarding whether CRISPR is in breach of this Agreement [***], either Party may make a written request that [***] be referred for resolution to Executive Officers of each Party (or their designees). Within [***] after such request, the Executive Officers of each Party (or their designees) will meet in person at a mutually acceptable time and location or by means of telephone or video conference to negotiate a settlement of a [***]. Each Party may elect to have such Party's JRC representatives participate in such meeting, if desired, *provided* that it provides the other Party with reasonable advance notice of such intent so as to enable the other Party to have its JRC representatives also participate in such meeting, if desired. In the event that the Executive Officers of each Party (or their designees) fail to resolve the [***] within such [***] the [***] will be referred to mediation under Section 11.3.4(b).

(b) **Mediation**. If a [***] cannot be resolved pursuant to Section 11.3.4(a), the Parties agree to try in good faith to resolve any such [***] by non-binding mediation administered by JAMS End Dispute in accordance with its

commercial mediation rules. The mediation will be conducted by a single mediator appointed by agreement of the Parties who will have previous financial experience in the pharmaceutical industry, or failing such agreement by JAMS End Dispute in accordance with its commercial mediation rules. Unless otherwise mutually agreed upon by the Parties, the mediation proceedings will be conducted in Boston, Massachusetts. The Parties agree that [***] the cost of the mediation, including filing and hearing fees, and the cost of the mediator(s). Each Party will bear its own attorneys' fees and associated costs and expenses. If the Parties are unable to resolve a [***] pursuant to such mediation, then at the completion of such mediation the mediator will decide the following issues, which decision will be binding on the Parties pending final resolution of the [***] by a court of competent jurisdiction:

(i) Whether the [***] by Vertex pursuant to Section 11.3.3 exceeds the mediator's objective good faith estimate of [***]; and

(ii) What amount (if any) may Vertex [***] under Section 11.3.3 , which [***].

(c) **Mediator Resolution** .

(i) If the mediator determines that [***] by Vertex pursuant to Section 11.3.3 [***], the Parties will promptly cause [***] as provided for in Section 7.10. The Parties will promptly cause [***].

(ii) If the mediator determines that Vertex may [***] under Section 11.3.3 , Vertex may [***].

(iii) The decisions rendered by mediator with respect to [***] will be binding on the Parties pending resolution of the [***] by the agreement of the Parties or by a court of competent jurisdiction in accordance with this Agreement.

10.4. **Consequences of Expiration or Termination of the Agreement** .

10.4.3. **In General** . If this Agreement expires or is terminated by a Party in accordance with this ARTICLE 11 at any time and for any reason, the following terms will apply to any Product in any country that is the subject of such expiration or termination:

(c) The Parties will return (or destroy, as directed by the other Party) all data, files, records and other materials containing or comprising the other Party's Confidential Information, except to the extent such Confidential Information is subject to a license or similar grant of rights that survives such termination or is necessary or useful to conduct activities for a surviving Collaboration Program or Product or country. Notwithstanding the foregoing, the Parties will be permitted to retain one copy of such data, files, records, and other materials for archival and legal compliance purposes.

(d) Termination or expiration of this Agreement for any reason will be without prejudice to any rights or financial compensation that will have accrued to the benefit of a Party prior to such termination or expiration. Such termination or expiration will not relieve a Party from obligations that are expressly indicated to survive the termination or expiration of this Agreement.

(e) The following provisions of this Agreement will survive any expiration or termination of this Agreement: Article 1 (Definitions), Section 5.3 (License Grants to Vertex) (solely in the event of expiration, not termination) Section 5.4 (Licenses to Improvements), Section 5.6 (No Implied Licenses), Article 7 (Financial Provisions), solely to the extent of accrued obligation as contemplated by Section 11.4.1(b), Section 8.1.1 (Ownership; Assignment – CRISPR Technology and Vertex Technology), 8.1.2 (Ownership; Assignment – Agreement Technology), Sections 8.5-8.6 (with respect to proceedings to the extent relating to events occurring prior to the effective date of termination) 8.6.4 (Joinder), Article 10 (Indemnification; Insurance), Section 11.2.5 (Public Announcements; Publications), Section 11.4 (Consequences of Expiration or Termination of the Agreement), Sections 12.1, 12.2, 12.3, 12.4 and 12.6 (Confidentiality) and Article 13 (Miscellaneous)."

10.4.4. **Termination Before License Grant**. If this Agreement expires or is terminated, in whole or in part with respect to a Collaboration Target, by a Party in accordance with this ARTICLE 11 before Vertex has been granted an Exclusive License for a particular Collaboration Target, then, in addition to the terms set forth in Section 11.4.1, the following terms will apply to each Collaboration Target that is the subject of such expiration or termination:

(a) Vertex's Option under Section 4.1 will expire and CRISPR will be free to Research, Develop, Manufacture and Commercialize the applicable Licensed Agents or Products in the applicable counties on its own or with a Third Party;

(b) except with respect to (i) any termination by Vertex under Section 11.2.3(a) or (ii) any expiration or termination with respect to a Collaboration Target that is associated with [***], effective upon such termination, Vertex hereby grants to CRISPR a non-exclusive, royalty-free, irrevocable, perpetual, worldwide license, which CRISPR may sublicense through multiple tiers, under all Vertex Program Technology Controlled by Vertex or its Affiliates (A) generated under the applicable Collaboration Program or (B) used in such terminated Collaboration Program to Develop, Manufacture and Commercialize Licensed Agents and Products directed to the relevant Collaboration Target; *provided* , that if the grant of such license to CRISPR with respect to any Know-How or Patent included in the Vertex Program Technology or CRISPR's exercise of such license would [***] or would require compliance with any provision of any license between Vertex and a Third Party, Vertex will so notify CRISPR and such Know-How or Patent will only be included in the foregoing license if, following receipt of such notice, [***] and comply with any such provision; and

(c) except as explicitly set forth in Section 11.4.1, Vertex will have no further rights and CRISPR will have no further obligations with respect to each terminated Collaboration Target.

10.4.5. **Termination After License Grant** . If this Agreement is terminated, in whole or in part with respect to a Product or Collaboration Target, by a Party in accordance with this ARTICLE 11 (but not if this Agreement expires in accordance with its terms) after Vertex has been granted an Exclusive License for a particular Collaboration Target, then, in addition to the terms set forth in Section 11.4.1, the following terms will apply to any Product or Collaboration Target that is the subject of such termination:

(c) except as set forth in Section 11.4.3(f), the applicable licenses granted by CRISPR to Vertex under this Agreement will terminate and Vertex and its Affiliates will cease all Research, Development, Manufacture and Commercialization activities with respect to the applicable Products;

(d) Vertex will assign back to the CRISPR Entity designated by CRISPR AG any Patents assigned to Vertex under Section 8.1.3 that relate to the applicable Collaboration Target to the extent that such Patents do not also relate to a Collaboration Target for which Vertex is maintaining the Exclusive License;

(e) except with respect to (i) any termination by Vertex under Section 11.2.3(a) or (ii) any expiration or termination with respect to a Collaboration Target that is associated with [***], Vertex shall, as promptly as practicable, transfer to the CRISPR Entity designated by CRISPR AG or such CRISPR Entity's designee possession and ownership of all Regulatory Approvals solely relating to the Development, Manufacture or Commercialization of any terminated Product or Collaboration Target within such terminated Collaboration Program;

(f) except as explicitly set forth in Section 11.4.1, Vertex will have no further rights and CRISPR will have no further obligations with respect to the terminated Products and Collaboration Target(s);

(g) except with respect to (i) any termination by Vertex under Section 11.2.3(a) or (ii) any termination with respect to a Collaboration Target that is associated with [***], and subject to Section 11.4.3(f), effective upon such termination, Vertex hereby grants to CRISPR a non-exclusive, royalty-free, irrevocable, perpetual, worldwide license, which CRISPR may sublicense through multiple tiers, under all Vertex Program Technology Controlled by Vertex or its Affiliates and (A) generated under the applicable Collaboration Program or (B) used in such terminated Collaboration Program to Develop, Manufacture and Commercialize Licensed Agents and Products directed to the relevant Collaboration Target; *provided* , that if the grant of such license to CRISPR with respect to any Know-How or Patent included in the Vertex Program Technology or CRISPR's exercise of such license would [***] or would require compliance with any provision of any license between Vertex and a Third Party, Vertex will so notify CRISPR and such Know-How or Patent will only be included in the foregoing license

if, following receipt of such notice, [***] and comply with any such provision; and

(h) any permitted Sublicense of Vertex will, at the Sublicensee's option, survive such termination; *provided* that the Sublicensee is not in material breach of any of its obligations under such Sublicense. In order to effect this provision, at the request of the Sublicensee, CRISPR will enter into a direct license with the Sublicensee on substantially the same terms as this Agreement (taking into account the scope of the licensee granted under such Sublicense); *provided* that CRISPR will not be required to undertake obligations in addition to those required by this Agreement, and that CRISPR's rights under such direct license will be consistent with its rights under this Agreement, taking into account the scope of the license granted under such direct license. Any such Sublicense would continue to include rights to any Patent assigned to CRISPR pursuant to Section 11.4.3(b) to the extent such rights were included in such Sublicense prior to termination and the license to CRISPR set forth in Section 11.4.3(e), if applicable, would not include rights to any Patent Controlled by Vertex to the extent such license would conflict with any rights granted to the relevant Sublicensee under such Patent.

ARTICLE 11.
CONFIDENTIALITY

11.1. **Confidentiality**. Except to the extent expressly authorized by this Agreement or otherwise agreed in writing, the Parties agree that, during the Agreement Term and for [***] thereafter, each Party (the " **Receiving Party** ") receiving any Confidential Information of the other Party (the " **Disclosing Party** ") hereunder will: (a) keep the Disclosing Party's Confidential Information confidential; (b) not publish, or allow to be published, and will not otherwise disclose, or permit the disclosure of, the Disclosing Party's Confidential Information in any manner not expressly authorized pursuant to the terms of this Agreement; and (c) not use, or permit to be used, the Disclosing Party's Confidential Information for any purpose other than as expressly authorized pursuant to the terms of this Agreement. Without limiting the generality of the foregoing, to the extent that Vertex provides to CRISPR (or any CRISPR Entity(ies)) any Confidential Information owned by any Third Party, CRISPR will handle such Confidential Information in accordance with the terms and conditions of this ARTICLE 12 applicable to a Receiving Party.

11.2. **Authorized Disclosure**. Notwithstanding the foregoing provisions of Section 12.1, each Party may disclose Confidential Information belonging to the other Party to the extent such disclosure is reasonably necessary to:

11.2.13. file or prosecute patent applications as contemplated by this Agreement;

11.2.14. prosecute or defend litigation;

11.2.15. exercise its rights and perform its obligations hereunder; or

11.2.16. comply with Applicable Law.

If a Party deems it reasonably necessary to disclose Confidential Information belonging to the other Party pursuant to this Section 12.2, the Disclosing Party will to the extent possible give reasonable advance written notice of such disclosure to the other Party and take reasonable measures to ensure confidential treatment of such information. In addition to the foregoing, [***] may disclose [***] Confidential Information to Third Parties as reasonably required to facilitate the actual or potential Research, Development, Manufacture or Commercialization of [***] or Products; *provided* that such disclosure is covered by terms of confidentiality and non-use similar to those set forth herein.

Notwithstanding anything to the contrary contained herein, in no event may [***] disclose [***] Confidential Information to any Third Party (including any of CRISPR's investors, collaborators or licensees) engaged in the research, development, manufacture or commercialization of pharmaceutical products.

11.3. **SEC Filings and Other Disclosures**. Either Party may disclose the terms of this Agreement (i) to the extent required to comply with Applicable Law, including the rules and regulations promulgated by the United States Securities and Exchange Commission or any equivalent governmental agency in any country in the Territory; *provided* , that such Party will reasonably consider the comments of the other Party regarding confidential treatment sought for such disclosure and (ii) to its advisors (including financial advisors, attorneys and accountants), actual or potential acquisition partners, financing sources or investors and underwriters on a need to know basis; *provided* that such disclosure is covered by terms of confidentiality similar to those set forth herein (which may include professional ethical obligations).

11.4. **Residual Knowledge Exception**. Notwithstanding any provision of this Agreement to the contrary, Confidential Information will not include Residual Knowledge. Any use made by the Receiving Party of Residual Knowledge is on an "as is, where is" basis, with all faults and all representations and warranties disclaimed and at its sole risk.

11.5. **Public Announcements; Publications**.

11.5.1. **Coordination**. CRISPR and Vertex will, from time to time and at the request of the other Party, discuss the general information content relating to this Agreement that may be publicly disclosed; *provided* , *however* , that [***] will have no obligation to consult with [***] with respect to any scientific publication or public announcement concerning [***] Research, Development, Manufacture, Commercialization or use of any [***] or Product (except as otherwise expressly set forth in Section 12.5.3).

11.5.2. **Announcements**. The Parties will jointly issue a press release, in the form attached hereto as Schedule M, regarding the signing of this Agreement on a date to be determined by Vertex within [***] following the Effective Date. Except as set forth in the preceding sentence and as may be expressly permitted under Section 12.3, or as required to comply with Applicable Law (including the rules and regulations promulgated by the United States Securities and Exchange Commission or any equivalent governmental agency in any country in the Territory), neither Party will make any public announcement regarding this Agreement without the prior written approval of the other Party. For the sake of clarity, nothing in this Agreement will prevent [***] from making any scientific publication or public announcement concerning [***] Research, Development, Manufacture or Commercialization activities with respect to any

[***] or Product under this Agreement; *provided* , *however* , that, except as permitted under Section 12.2, [***] will not disclose any of [***] Confidential Information in any such publication or announcement without obtaining CRISPR's prior written consent to do so.

11.5.3. **Publications** . During the Agreement Term, each Party will submit to the other Party (the " **Non-Disclosing Party** ") for review and approval any proposed academic, scientific and medical publication or public presentation related to any Licensed Agent or Product or any activities conducted pursuant to any Research Plan. In each such instance, such review and approval will be conducted for the purposes of preserving the value of the Licensed Technology and the Vertex Technology, the rights granted to Vertex hereunder and determining whether any portion of the proposed publication or presentation containing the Non-Disclosing Party's Confidential Information should be modified or deleted. Written copies of such proposed publication or presentation required to be submitted hereunder will be submitted to the Non-Disclosing Party no later than [***] before submission for publication or presentation (or five Business Days in advance in the case of an abstract). The Non-Disclosing Party will provide its comments with respect to such publications and presentations within [***] of its receipt of such written copy (or [***] in the case of an abstract). The review period may be extended for an additional [***] if the Non-Disclosing Party reasonably requests such extension including for the preparation and filing of patent applications. Notwithstanding anything to the contrary, the Non-Disclosing Party may require that the other Party redact the Non-Disclosing Party's Confidential Information from any such proposed publication or presentation. CRISPR and Vertex will each comply with standard academic practice regarding authorship of scientific publications and recognition of contribution of other parties in any publication. Notwithstanding the foregoing, Vertex's obligation to submit any publication to CRISPR for review and approval under this Section 12.5.3 will not apply to any publication made with respect to a Collaboration Program following Vertex's exercise of the applicable Option that does not contain CRISPR's Confidential Information or disclose any non-public information included in the Licensed Technology; *provided* , that where reasonably possible, Vertex will provide CRISPR with an advance copy of such publication if such publication is [***].

11.6. **Vertex Information Rights** .

11.6.1. If Vertex determines in good faith that CRISPR (or any CRISPR Entity(ies)) is an entity that is subject to financial consolidation with Vertex for the purposes of its quarterly and annual financial statements (or otherwise requires such information in order to comply with GAAP), CRISPR will make available to Vertex:

(d) as soon as practicable, but in any event within [***] after the end of each Calendar Quarter (i) an unaudited balance sheet as of the end of such Calendar Quarter, (ii) unaudited statements of income and cash flows for such Calendar Quarter, (iii) an unaudited statement of stockholders' equity for such period, and (iv) a detailed trial balance as of the end of such Calendar Quarter, all

prepared in accordance with GAAP (except that such financial statements may (x) be subject to year-end audit adjustments and (y) not contain all notes thereto that may be required in accordance with GAAP) and thereafter will promptly provide such other information as Vertex may reasonably request;

(e) as soon as practicable, but in any event within [***] after the end of each Calendar Year (i) an audited balance sheet as of the end of such Calendar Year, (ii) audited statements of income and cash flows for such Calendar Year, (iii) an audited statement of stockholders' equity for such Calendar Year and (iv) a detailed trial balance as of the end of such Calendar Year, together with related footnotes all prepared in accordance with GAAP and audited and certified by a nationally recognized independent public accounting firm; and

(f) on or prior to December 31 of each Calendar Year (other than the Calendar Year ending December 31, 2015),, such [***] as of [***] of such year as prepared by [***].

ARTICLE 12.
MISCELLANEOUS

12.1. **Assignment**. Neither this Agreement nor any interest hereunder will be assignable by either Party without the prior written consent of the other Party, except as follows: (a) Vertex, and subject to Section 13.2, CRISPR, may, subject to the terms of this Agreement, assign its rights and obligations under this Agreement by way of sale of itself or the sale of the portion of such Party's business to which this Agreement relates, through merger, sale of assets or sale of stock or ownership interest; *provided* that such sale is not primarily for the benefit of its creditors; and *provided further* that no CRISPR Entity may assign its rights and obligations hereunder unless all CRISPR Entities are assigning their rights and obligations hereunder to the same Third Party; and (b) either Party may assign its rights and obligations under this Agreement to any of its Affiliates; *provided* that such Party will remain liable for all of its rights and obligations under this Agreement. An assigning Party will promptly notify the other Party of any assignment or transfer under the provisions of this Section 13.1. This Agreement will be binding upon the successors and permitted assigns of the Parties and the name of a Party appearing herein will be deemed to include the names of such Party's successors and permitted assigns to the extent necessary to carry out the intent of this Agreement. Any assignment not in accordance with this Section 13.1 will be void.

12.2. **Change of Control of CRISPR**.

12.2.6. **Notification**. CRISPR will notify Vertex in writing promptly (and in any event within [***] Business Days) following the execution of a definitive agreement by any CRISPR Entity, its Affiliates or its equity holders that could reasonably be expected to result in a Change of Control of any CRISPR Entity.

12.2.7. **Effects of Change of Control of CRISPR**. If during the Agreement Term any CRISPR Entity undergoes a Change of Control to a Competitor, then upon the effective date of such Change of Control (a) Vertex's obligation to provide CRISPR [***] will terminate and (b) Vertex will [***] with respect to the [***].

12.3. **Force Majeure**. Each Party will be excused from the performance of its obligations under this Agreement to the extent that such performance is prevented by Force Majeure and the nonperforming Party promptly provides notice of the prevention to the other Party. Such excuse will be continued so long as the condition constituting force majeure continues and the nonperforming Party uses Commercially Reasonable Efforts to remove the condition.

12.4. **Representation by Legal Counsel**. Each Party hereto represents that it has been represented by legal counsel in connection with this Agreement and acknowledges that it has participated in the drafting hereof. In interpreting and applying the terms and provisions of this Agreement, the Parties agree that no presumption will exist or be implied against the Party that drafted such terms and provisions.

12.5. **Notices**. All notices which are required or permitted hereunder will be in writing and sufficient if delivered personally or sent by nationally-recognized overnight courier, addressed as follows:

If to Vertex:

Vertex Pharmaceuticals Incorporated
Attn: Business Development
50 Northern Avenue
Boston, Massachusetts 02110

with a copy to:

Vertex Pharmaceuticals Incorporated
Attn: Corporate Legal
50 Northern Avenue
Boston, Massachusetts 02110

and:

Ropes & Gray LLP
Attn: Marc A. Rubenstein
Prudential Tower
800 Boylston Street
Boston, Massachusetts 02199-3600

If to CRISPR:

CRISPR Therapeutics Ltd.
Attn: Chief Legal Officer
85 Tottenham Court Road
London W1T 4TQ
United Kingdom

with a copy to:

Goodwin Procter LLP
Attn: Christopher Denn
53 State Street

Boston, Massachusetts 02109

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

12.6. **Amendment**. No amendment, modification or supplement of any provision of this Agreement will be valid or effective unless made in writing and signed by a duly authorized officer of each of Vertex Parent, Vertex UK and CRISPR AG, CRISPR Inc., CRISPR UK and Tracr.

12.7. **Waiver**. No provision of this Agreement will be waived by any act, omission or knowledge of a Party or its agents or employees except by an instrument in writing expressly waiving such provision and signed by a duly authorized officer of the waiving Party. The waiver by either of Vertex or CRISPR of any breach of any provision hereof by the other Party will not be construed to be a waiver of any succeeding breach of such provision or a waiver of the provision itself. Written waiver of any provision of this Agreement by of any one of the CRISPR Entities in accordance with this Section 13.7 shall be binding upon each of CRISPR UK, CRISPR AG, CRISPR Inc. and Tracr.

12.8. **Severability**. If any clause or portion thereof in this Agreement is for any reason held to be invalid, illegal or unenforceable, the same will not affect any other portion of this Agreement, as it is the intent of the Parties that this Agreement will be construed in such fashion as to maintain its existence, validity and enforceability to the greatest extent possible. In any such event, this Agreement will be construed as if such clause of portion thereof had never been contained in this Agreement, and there will be deemed substituted therefor such provision as will most nearly carry out the intent of the Parties as expressed in this Agreement to the fullest extent permitted by Applicable Law.

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

12.10. **Export Control**. This Agreement is made subject to any restrictions concerning the export of products or technical information from the United States of America or other countries that may be imposed upon or related to CRISPR or Vertex from time to time. Each Party agrees that it will not export, directly or indirectly, any technical information acquired from the other Party under this Agreement or any products using such technical information to a location or in a manner that at the time of export requires an export license or other governmental approval, without first obtaining the written consent to do so from the appropriate Governmental Authority.

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

12.12. **Entire Agreement**. This Agreement constitutes and contains the complete, final and exclusive understanding and agreement of the Parties and cancels and supersedes any and all prior negotiations, correspondence, understandings and agreements, whether oral or written, between the Parties respecting the subject matter hereof and thereof, including that certain Confidentiality Agreement between Vertex Parent and CRISPR dated May 6, 2015, which is hereby superseded and replaced in its entirety as of the Effective Date, and any Confidential Information disclosed by the Parties under such agreement will be treated in accordance with the provisions of ARTICLE 12.

12.13. **Independent Contractors**. Both Parties are independent contractors under this Agreement. Nothing herein contained will be deemed to create an employment, agency, joint venture or partnership relationship between the Parties hereto or any of their agents or employees, or any other legal arrangement that would impose liability upon one Party for the act or failure to act of the other Party. Neither Party will have any express or implied power to enter into any contracts or commitments or to incur any liabilities in the name of, or on behalf of, the other Party, or to bind the other Party in any respect whatsoever.

12.14. **Interpretation**. Except where the context expressly requires otherwise, (a) the use of any gender herein will be deemed to encompass references to either or both genders, and the use of the singular will be deemed to include the plural (and vice versa), (b) the words "include," "includes" and "including" will be deemed to be followed by the phrase "without limitation," (c) the word "will" will be construed to have the same meaning and effect as the word "shall," (d) any definition of or reference to any agreement, instrument or other document herein will be construed as referring to such agreement, instrument or other document as from time to time amended, supplemented or otherwise modified (subject to any restrictions on such amendments, supplements or modifications set forth herein), (e) any reference herein to any Person will be construed to include the Person's successors and assigns, (f) the words "herein," "hereof" and "hereunder," and words of similar import, will be construed to refer to this Agreement in its entirety and not to any particular provision hereof, (g) all references herein to Sections, Schedules or Exhibits will be construed to refer to Sections, Schedules or Exhibits of this Agreement, and references to this Agreement include all Schedules and Exhibits hereto, (h) the word "notice" will mean notice in writing (whether or not specifically stated) and will include notices, consents, approvals and other written communications contemplated under this Agreement, (i) provisions that require that a Party, the Parties or any committee hereunder "agree," "consent" or "approve" or the like will require that such agreement, consent or approval be specific and in writing, whether by written agreement, letter, approved minutes or otherwise (but excluding e-mail and instant messaging), (j) references to any specific law, rule or regulation, or article, section or other division thereof, will be deemed to include the then-current amendments thereto or any replacement or successor law, rule or regulation thereof, (k) any definition of or reference to any agreement, instrument or other document herein will be construed as referring to such agreement, instrument or other document as from time to time amended, supplemented or otherwise modified (subject to any restrictions on such amendments, supplements or modifications set forth herein), and (l) the term "or" will be interpreted in the inclusive sense commonly associated with the term "and/or."

12.15. **No Third Party Rights or Obligations**. No provision of this Agreement will be deemed or construed in any way to result in the creation of any rights or obligations in any Person not a Party to this Agreement.

12.16. **Further Actions**. Each Party agrees to execute, acknowledge and deliver such further instruments, and to do all such other acts, as may be necessary or appropriate in order to carry out the purposes and intent of this Agreement.

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

12.18. **CRISPR Entities**. Notwithstanding anything to the contrary in this Agreement:

12.18.1. CRISPR UK, CRISPR AG, CRISPR Inc. and Tracr shall be jointly and severally liable to Vertex for all obligations of CRISPR under this Agreement;

12.18.2. Breach or violation of any representation, warranty covenant or other obligation of CRISPR under this Agreement may result from, be caused by or arise from the act or omission of any one or more of the CRISPR Entities;

12.18.3. Any particular right or interest of CRISPR under this Agreement shall only be exercisable once by the first CRISPR Entity to exercise such right or interest hereunder on behalf of CRISPR (*i.e* ., Vertex shall not be liable to more than one CRISPR Entity with respect to any particular right or interest of CRISPR hereunder, including, without limitation, any payment obligations of Vertex hereunder); and

12.18.4. Any consent or approval of CRISPR permitted or required under this Agreement by any one of CRISPR UK, CRISPR AG, CRISPR Inc. or Tracr shall be binding upon all of the CRISPR Entities.

[SIGNATURE PAGE FOLLOWS]

* - * - * - *

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

VERTEX PHARMACEUTICALS INCORPORATED	**CRISPR THERAPEUTICS AG**
By: /s/ Ian Smith	By: /s/ Rodger Novak
Name: Ian Smith	Name: Rodger Novak
Title: Chief Financial Officer	Title: CEO
VERTEX PHARMACEUTICALS (EUROPE) LIMITED	**CRISPR THERAPEUTICS LIMITED**
By: /s/ Ian Smith	By: /s/ Rodger Novak
Name: Ian Smith	Name: Rodger Novak
Title: Director	Title: CEO

Schedule A

CRISPR Reserved Targets

Following are the CRISPR Reserved Targets:

1. The following Targets:

    a. [***]
    b. [***]
    c. [***]
    d. [***]
    e. [***]
    f. [***]
    g. [***]
    h. [***]
    i. [***]
    j. [***]

2. All Targets that are, [***] (a) [***] or (b) [***] or (c) [***].

3. All Targets that are, at the time Vertex has proposed to add such a Target to the Vertex Target List, [***].

4. All Targets that are, at the time Vertex has proposed to add such a Target to the Vertex Target List, Targets that are [***].

All Targets that are, at the time Vertex has proposed to add such a Target to the Vertex Target List, Targets that are [***].

Schedule B

Initial Vertex Targets

1) **CFTR (cystic fibrosis transmembrane conductance regulator)**
2) [***]
3) [***]
4) [***]
5) [***]
6) [***]
7) [***]
8) [***]
9) [***]
10) [***]
11) [***]
12) [***]
13) [***]

Initial Collaboration Targets

1) **CFTR (cystic fibrosis transmembrane conductance regulator)**
2) [***]
   [***]

Schedule C

Option Exercise Data Package

- Option Exercise Data Package. All data for the Option Exercise Data Package is pre-specified by the Collaboration Program Working Group and is reviewed and endorsed by the JRC.
- The responsibilities below would be specified on a program by program basis and endorsed by the JRC ahead of beginning any Research Plan.
- Upon completion of the work, the data for each item is presented to the JRC and compared to the pre-specification. The JRC endorses the interpretation that the data are or are not consistent with the pre-specification.

Item	Party Responsible for Generating Item/Data
[***]	CRISPR & Vertex
[***]	CRISPR
[***]	CRISPR
[***]	CRISPR and Vertex
[***]	Vertex and CRISPR
[***]	Vertex
[***]	Vertex
[***]	CRISPR

Schedule D

Initial Research Plan Components

The following are key elements for the Research Plans. A full Research Plan will be created by the Collaboration Program Working Group utilizing these elements in accordance with Section 2.2. The provisions will be approved by the JRC in accordance with ARTICLE 3.

Target Name	Description	
Work Plan Items	Listing of all items required to complete the work plan. This should include all of the items in Schedule C	Listing of responsible parties for each of the work items.
Key milestones	Listing of key waypoints on the way to a transition agreement.	Listing of key dates for each of the milestones.
Budget	Out of Pocket Spend – CRISPR FTE – CRISPR FTE – Vertex	Listing of dollar amounts
Key pieces of data and required values	Listing of key pieces of data expected in the Option Exercise Data Package. This is a critical element and will have to be carefully considered. E.g. for a [***] etc. are other possible values. These will be highly Target specific.	Minimum acceptable values for each of these data. These should be prospective and objective wherever possible.
Key dependencies	List key dependencies on various elements.	
Assumptions	List project assumptions.	
Risks	Listing of key risks, probabilities and impacts	Describe mitigation/ contingency/ avoidance plan

Schedule E

Subcontractors

SCHEDULE E

Schedule F

CRISPR Background Know-How
(as of 26 October 2015)

Confidential Materials omitted and filed separately with the Securities and Exchange Commission. A total of 1 page was omitted. [***]

SCHEDULE F

Schedule G

Terms of Joint Development & Commercialization Agreement

ARTICLE 1.

DEFINITIONS.

1.1. " **Audited Party** " has the meaning set forth in Section 7.6.

1.2. " **Auditing Party** " has the meaning set forth in Section 7.6.

1.3. " **Baseball Arbitration** " means "baseball" style arbitration in accordance with the arbitration procedure set forth on Schedule I of the Agreement.

1.4. " **Commercialization Budget** " has the meaning set forth in Section 5.1.

1.5. " **Commercialization Costs** " means the sum of the following costs and expenses incurred by the Parties or their respective Affiliates, in Commercializing the Shared Products (and related Manufacturing activities) in the Territory, in each case, to the extent incurred in accordance with the Commercialization Plan and Commercialization Budget:

(a) Expenses incurred in connection with the [***] ;

(b) Expenses incurred to conduct [***] ;

(c) [***] representing the [***] as defined in the [***] , in each case, to the extent directly attributable to [***] ;

(d) Expenses identifiable to the [***] , in each case, to the extent incurred specifically with respect [***] ;

(e) Expenses incurred in connection with the [***];

(f) Expenses directly associated with [***] , in each case, that are incurred with respect to a [***];

(g) [***];

(h) Expenses reasonably necessary and identifiable to the [***] with respect to: [***] ;

(i) [***]; and

(j) any other Expenses approved by the JCC and included in the Commercialization Budget that are not otherwise included in any other Commercialization Cost category.

Commercialization Costs will exclude [***] .

1.6. " **Commercialization Plan** " has the meaning set forth in Section 5.1.

1.7. " **Development Budget** " has the meaning set forth in Section 3.1.

1.8. " **Development Costs** " means the sum of the following costs and expenses incurred by the Parties and their respective Affiliates in Developing the Shared Product (and related

Manufacturing activities) in the Territory, in each case, to the extent incurred in accordance with the Global Development Plan and the Development Budget, including:

(a) Expenses incurred in [***];

(b) [***];

(c) [***] incurred in connection with [***];

(d) Expenses associated with [***], to the extent incurred with respect to [***];

(e) Expenses incurred in connection with [***], including the Parties' [***];

(f) Expenses associated with [***]; and

(g) any other Expenses incurred for [***] and included in the [***] .

Development Costs will exclude [***].

1.9. " **Expenses** " means Out-of-Pocket Costs and FTE Costs.

1.10. " **FTE Costs** " means the product of (a) the number of FTEs (proportionately, on a per-FTE basis) used by a Party or its Affiliates in directly performing activities assigned to such Party under and in accordance with the Global Development Plan, Commercialization Plan or Medical Affairs Plan, as applicable, and (b) the FTE Rate.

1.11. " **FTE** " means one employee full-time for one year or more than one person working the equivalent of a full-time person, working directly on performing activities under the Global Development Plan, Medical Affairs Plan or Commercialization Plan, as applicable, where "full-time" is considered [***] hours for one Calendar Year. No additional payment will be made with respect to any individual who works more than [***] hours per Calendar Year and any individual who devotes less than [***] hours per Calendar Year will be treated as an FTE on a pro rata basis based upon the actual number of hours worked divided by [***] .

1.12. " **Global Development Plan** " has the meaning set forth in Section 3.1.

1.13. " **Global Branding Strategy** " has the meaning set forth in Section 5.2.2.

1.14. " **JCC** " has the meaning set forth in Section 2.1.

1.15. " **JDC** " has the meaning set forth in Section 2.1.

1.16. " **JSC** " has the meaning set forth in Section 2.1.

1.17. " **Lead Commercialization Party** " has the meaning set forth in Section 5.1.

1.18. " **Licensed Vertex Know-How** " means (a) [***] , that (i) [***] and (ii) [***], (b) [***] and (c) [***] .

1.19. " **Licensed Vertex Background Patents** " means (a) [***] that (i) [***] and (ii) [***] , (b) [***] and (c) the [***] .

1.20. " **Manufacturing Costs** " means the costs of Manufacturing Shared Product, which (a) to the extent such Shared Product is Manufactured by a Party or its Affiliates, [***] and (b) to the extent such Shared Product is Manufactured by a Third Party in an arms-length transaction, [***] .

SCHEDULE G

1.21. " **Manufacturing Working Group** " has the meaning set forth in Section 6.1.

1.22. " **Medical Affairs Activities** " means responding to external inquiries or complaints, the planning for and conduct of investigator sponsored Clinical Trials not included in the Global Development Plan, medical education, speaker programs, advisory boards, thought leader activities, educational grants and fellowships, local country government affairs, Phase 3b Clinical Trials, phase IV/post-Regulatory Approval Clinical Trials, generating health economics and outcomes research data from patient reported outcomes, prospective observational studies and retrospective observational studies, and economic models and reimbursement dossiers, deployment of MSLs, medical affairs clinical trial management, doctors in field (other than MSLs), scientific publications and medical communications.

1.23. " **Medical Affairs Budget** " has the meaning set forth in ARTICLE 4.

1.24. " **Medical Affairs Costs** " means all Expenses incurred by the Parties in connection with the conduct of Medical Affairs Activities in accordance with the Medical Affairs Plan and the Medical Affairs Budget;

1.25. " **Medical Affairs Plan** " has the meaning set forth in ARTICLE 4.

1.26. " **MSL** " means medical science liaisons.

1.27. " **Net Loss** " means, for a given period, Net Sales (including deemed Net Sales under Section 8.6.5 of the Agreement) in the Territory less Program Expenses, where the result is a negative number.

1.28. " **Net Profit** " means, for a given period, Net Sales (including deemed Net Sales under Section 8.6.5 of the Agreement) in the Territory less Program Expenses, where the result is a positive number.

1.29. " **Opt-Out Royalty** " has the meaning set forth in Section 11.4.

1.30. " **Other Out-of-Pocket Costs** " means:

(a)Expenses associated with [***] pursuant to the [***] ;

(b)[***] ;

(c)[***], in each case, that are [***] ; and

(d)Expenses incurred in connection with the [***] .

1.31. " **Patent Costs** " means all Expenses reasonably allocated to the Shared Products for the prosecution, maintenance and enforcement of Patents that Cover the Shared Products.

1.32. " **Pharmacovigilance Agreement** " has the meaning set forth in Section 8.1.

1.33. " **Program Expenses** " means Development Costs, Commercialization Costs, Medical Affairs Costs, Patent Costs and Other Out-of-Pocket Costs.

1.34. " **Project Leader** " has the meaning set forth in Section 3.1.

1.35. " **Project Team** " has the meaning set forth in Section 3.1.

1.36. " **Reconciliation Report** " has the meaning set forth in Section 7.4.

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1.37. " **Subcontract** " has the meaning set forth in ARTICLE 9.

1.38. " **Subcontractor** " has the meaning set forth in ARTICLE 9.

1.39. " **Summary Statement** " has the meaning set forth in Section 7.3.

1.40. " **Trademark** " means all trademarks, service marks, trade names, brand names, sub-brand names, trade dress rights, product configuration rights, certification marks, collective marks, logos, taglines, slogans, designs or business symbols and all words, names, symbols, colors, shapes, designations or any combination thereof that function as an identifier of source or origin or quality, whether or not registered, and all statutory and common law rights therein, and all registrations and applications therefor, together with all goodwill associated with, or symbolized by, any of the foregoing.

ARTICLE 2.
GOVERNANCE.

2.1. **Committees** . Within [***] after execution of the Joint Development & Commercialization Agreement, the Parties will establish a joint steering committee (the " **JSC** ") to provide high-level oversight and decision-making regarding the activities of the Parties under the Joint Development & Commercialization Agreement. The JSC's responsibilities will include (a) reviewing and overseeing the overall global Development, Manufacture and Commercialization of the Shared Products in the Field, (b) overseeing the JDC, JCC and any other committees and working groups established with respect to the Shared Product and resolving matters on which the JDC, JCC or such committees and working groups are unable to reach consensus and (c) performing such other functions as may be established in the Joint Development & Commercialization Agreement. The JSC will oversee a joint development committee (the " **JDC** ") and a joint commercialization committee (the " **JCC** ") and such other committees and working groups as the JSC may determine are appropriate from time to time.

2.2. **Decision-Making** . The JSC, JDC, JCC and all other committees and working groups [***] with the goal being to maximize the chance of successfully developing and commercializing a [***] in a manner consistent with Applicable Laws and the Joint Development & Commercialization Agreement. Disputes arising out of the JDC, JCC or any other committee or working group will be escalated to the JSC for resolution. Disputes arising at the JSC will be referred to senior executives of each Party for resolution. whereupon the Parties' senior executives will meet in person if requested by either such senior executive and attempt in good faith to resolve such dispute by negotiation and consultation for a [***] period following such referral. If the senior executives do not resolve such dispute within such [***] period, such dispute shall be submitted to [***] .

ARTICLE 3.
DEVELOPMENT.

3.1. **Global Development Plan** . The JDC will oversee the Development of Shared Products by the Parties in the Field in the Territory. Each Shared Product will be Developed in accordance with a global development plan (the " **Global Development Plan** "). The Global Development Plan will include a plan for the Development of the Shared Product in the

Territory through Regulatory Approval, including a regulatory strategy, high-level study design criteria, an allocation of responsibilities between the Parties, timelines and a budget for activities conducted under the Global Development Plan (the " **Development Budget** "). The JDC will update the Global Development Plan [***] (or more frequently as needed) and submit it to the JSC for approval. The Parties will establish a project team (the " **Project Team** ") to oversee and coordinate activities under the Global Development Plan. The Project Team be formed with an experienced team leader (" **Project Leader** "), and the composition of the Project Team will be determined by the Project Leader based on available personnel from each Party across functions. The Project Team will conduct its responsibilities under the Global Development Plan in good faith and with reasonable care and diligence. The Project Team will provide the JDC with periodic updates regarding the progress of activities pursuant to the Global Development Plan.

3.2. **Development Activities.**

3.2.1. **Regulatory Matters** . Regulatory activities will be jointly carried out by the Project Team under the guidance of the JDC. All Regulatory Filings and Regulatory Approvals that relate to Shared Products shall be filed by and held in the name of [***] or its relevant Affiliates. [***] shall use Commercially Reasonable Efforts, in consultation with [***] to seek to obtain and maintain Regulatory Approval for the Shared Product in the Field. [***] will oversee, monitor and manage all regulatory interactions, communications and filings with, and submissions to, Regulatory Authorities with respect to the Shared Products. [***] , in consultation with [***] , will control all regulatory activities with respect to the Shared Products, including determining the labeling strategy and the content of submissions; *provided* that [***] may review and comment on such strategies and submissions. Vertex will prepare all regulatory submissions and provide [***] with advance drafts of any material documents or other material correspondence pertaining to the Shared Products, including any proposed labeling, that [***] plans to submit to any Regulatory Authority. [***] may provide comments regarding such documents and other correspondence prior to their submission, which comments [***] will consider in good faith. [***] will provide [***] with copies of all material submissions it makes to, and all material correspondence it receives from, a Regulatory Authority pertaining to a Regulatory Approval of a Shared Product within [***] after receipt. [***] will provide [***] with reasonable advance notice of any meeting or teleconference with any Regulatory Authority with respect to the Shared Products. Subject to Applicable Law, [***] will have the right to participate as an observer in all material meetings, conferences and discussions by [***] with Regulatory Authorities pertaining to Development of the Shared Products or Regulatory Approval of the Shared Products.

3.2.2. **Clinical Trials** . The JDC will allocate responsibility between the Parties for the conduct of Clinical Trials and the various other Development activities addressed in the Global Development Plan. [***] will have final decision-making authority with respect to the protocol for any Clinical Trial conducted under the Global Development Plan and the statistical analysis plan for any such Clinical Trial.

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The Party that has responsibility for conducting the Clinical Trial will have the responsibility for the packaging and labeling of clinical drug supplies, unless otherwise agreed by the Parties.

3.2.3. **Independent Activities** . The Joint Development & Commercialization Agreement will include a mechanism for each Party to propose additional Clinical Trials for inclusion in the Global Development Plan. If the other Party does not agree to include such additional Clinical Trial in the Global Development Plan, the requesting Party may conduct such Clinical Trial at its sole expense (*i.e.* such expenses will not be included as Development Costs); *provided* that neither Party may conduct any Clinical Trial that [***] . The non-requesting Party will not have the right to use the data resulting from such Clinical Trial in a substantive manner as the basis for obtaining new or expanded Regulatory Approval for a Product in the Field or for commercial purposes for a Product in the Field unless and until such Party reimburses the requesting Party for [***] of the Development Costs..

3.3 **Diligence.** Each Party will use Commercially Reasonable Efforts to execute and to perform, or cause to be performed, the activities assigned to it in the Global Development Plan, and to cooperate with the other Party in carrying out the Global Development Plan in accordance with the timelines therein. Each Party and its Affiliates will conduct its Development activities in good scientific manner and in compliance with Applicable Law. Notwithstanding anything to the contrary contained herein, a Party or its Affiliates will not be obligated to undertake or continue any Development activities with respect to the Shared Products if such Party (or any of its Affiliates) reasonably determines that performance of such Development activity would violate Applicable Law or infringe or misappropriate a Third Party's intellectual property.

ARTICLE 4.
MEDICAL AFFAIRS ACTIVITIES.

The Parties, acting through the JSC, will develop and agree upon a global medical affairs plan for the Shared Product that describes the Medical Affairs Activities to be conducted in the Territory, key tactics and strategies for implementing those activities, the relative responsibilities of the Parties and the associated budget for such activities (such plan, the " **Medical Affairs Plan** " and such budget, the " **Medical Affairs Budget** "). CRISPR will lead and manage Medical Affairs Activities in the United States and Vertex will lead and manage Medical Affairs Activities outside of the United States, in each case, in accordance with the Medical Affairs Plan. The number of MSLs to be deployed in each jurisdiction will be determined by the JSC at least [***] prior to potential launch.

ARTICLE 5.
COMMERCIALIZATION.

5.1. **Commercialization Plan** . The JCC will oversee the Commercialization of Shared Products by the Parties in the Field in the Territory. No later than [***] prior to the anticipated launch of the Shared Product in the first country in the Territory, the JCC will develop and submit to the JSC for approval, a Commercialization plan (the " **Commercialization Plan** ") that

sets forth the Commercialization activities to be undertaken by the Parties with respect to the Commercialization of the Shared Product in the Territory. The Commercialization Plan may include activities on a region-by-region or country-by-country basis, as determined by the JCC. The JCC will update the Commercialization Plan on [***] (or more frequently as needed) and submit it to the JSC for approval. The Commercialization Plan will include (a) the Global Branding Strategy, (b) a marketing strategy, (c) a communications strategy that includes plans for public relations, conferences and exhibitions and other external meetings, internal meetings and communications, publications and symposia, internet activities and core brand package, (d) a high level operating plan for the implementation of such strategies on [***] , including information related to Shared Product positioning, core messages to be communicated and pricing strategies, (e) a detailing strategy, (f) a pricing strategy, (g) all other material activities to be conducted in connection with the Commercialization of the Shared Product in the Field in the Territory and (h) a budget for activities conducted under the Commercialization Plan (the " **Commercialization Budget** "). The Commercialization Plan will include a meaningful role for both Parties. In allocating responsibilities between the Parties, the JCC will take into consideration each Party's expertise, capabilities, staffing and available resources to take on such activities, as well as the Parties' intention to provide CRISPR an opportunity to build and expand its expertise, capabilities, staffing and available resources in connection with performing Commercialization activities allocated to it. CRISPR shall be the Commercializing lead for Shared Products in the United States and Vertex shall be the Commercializing lead for Shared Products outside of the United States. The Commercializing lead, with respect to the United States or outside of the United States, respectively, shall be referred to herein as the "Lead Commercialization Party" for such jurisdiction (as applicable, the " **Lead Commercialization Party** " Unless otherwise specified in the Commercialization Plan, the Parties will jointly be responsible for conducting all Commercialization activities outside of the United States, such activities to be determined by the JSC.

5.2. **Commercialization Activities** .

5.2.1. **Training** . The Parties will jointly prepare training programs and materials for employees and sales representatives with respect to the Shared Product, with the goal of ensuring compliance with all Applicable Laws and each Party's compliance policies. Each Party will be solely responsible for training its employees and sales representatives in accordance with such training program.

5.2.2. **Global Branding Strategy** . The JCC will develop a global branding strategy for Shared Products in the Territory, including, with respect to each Shared Product, a life cycle plan, brand vision, positioning, key messaging, concept and imagery, Trademarks (including name and logos), brand public relations and supporting market research (the " **Global Branding Strategy** ") and submit such strategy to the JSC for approval.

5.2.3. **Trademarks** . The JCC will select a product Trademark for each Shared Product throughout the world consistent with the Global Branding Strategy. Each Shared Product will be promoted and sold in the Territory under the applicable Trademarks.

SCHEDULE G

5.2.4. **Marketing** . The JCC will agree upon a marketing strategy for the Shared Product, including Shared Product positioning, messaging, appearance and launch sequencing, consistent with the Global Branding Strategy. Marketing activities and responsibilities for each Party will be determined by the JCC.

5.2.5. **Managed Markets and Market Access** . The JCC will agree upon a strategy for the managed markets and market access for the Shared Product, including, without limitation, payer strategy and account management. Such activities and responsibilities for each Party will be determined by the JCC.

5.2.6. **Pricing** . The JCC will establish a global pricing strategy for the Shared Product (including list price, targeted net pricing, sales-weighted average discounts and rebates, the approach to pricing with different types of accounts and plans, types of discounts and rebates) in the Territory. The responsibility of each Party regarding the implementation of such global pricing strategy, including negotiating pricing and reimbursement with governments and private payers will be determined by the JCC.

5.2.7. **Field Sales** . The Parties will jointly promote the Shared Product (including performing sales calls) in the Territory in accordance with the Commercialization Plan. CRISPR will lead and manage the promotion of the Shared Product in the United States. Vertex will have the right provide [***] of the FTES with respect to the Shared Product in the United States. Vertex will lead and manage promotion of the Shared Product outside of the United States and CRISPR will have the right to provide [***] of the FTES with respect to the Shared Product in the Major Market Countries (outside of United States). CRISPR and Vertex will each ensure that its and its Affiliates' sales representatives do not make any representation, statement, warranty or guaranty with respect to the Shared Product that is not consistent with the applicable current package insert of prescribing information or other documentation accompanying or describing a Shared Product, including mutually approved limited warranty and disclaimers, if any. CRISPR and Vertex will each ensure that its and its Affiliates' sales representatives do not make any statements, claims or undertakings to any person with whom they discuss or promote the Shared Products that are not consistent with, or provide or use any labeling, literature or other materials other than those promotional materials currently approved for use by the JCC.

5.2.8. **Distribution and Patient Services** . The Parties will jointly be responsible for distribution and patient services for the Shared Product in the Territory, including contracting with applicable service providers, such activities to be determined by the JCC [***] prior to launch of the Shared Product.

5.2.9. **Booking Sales; Distribution** . CRISPR will invoice, sell and book all sales of Shared Products in the United States and be responsible for warehousing and distributing such Shared Products in the United States. Vertex will invoice, sell and book all sales of Shared Products outside of the United States and be responsible for warehousing and distributing such Shared Products outside of the United States.

SCHEDULE G

5.3. **Diligence** . Each Party will use Commercially Reasonable Efforts to execute and to perform, or cause to be performed, the activities assigned to it under the Commercialization Plan. Each Party and its Affiliates will conduct its Commercialization activities in compliance with Applicable Law. Notwithstanding anything to the contrary contained herein, a Party or its Affiliates will not be obligated to undertake or continue any Commercialization activities with respect to the Shared Products if such Party (or any of its Affiliates) reasonably determines that performance of such Commercialization activity would violate Applicable Law or infringe or misappropriate a Third Party's intellectual property.

ARTICLE 6.
MANUFACTURING.

6.1. **Quality Agreement** . The Parties will meet to negotiate in good faith and agree on quality analysis and control criteria for the Manufacture of the Shared Product within [***] after the effective date of the Joint Development & Commercialization Agreement. The agreed upon criteria will be set forth in a quality agreement containing mutually agreed terms and conditions that are customary for agreements of this type.

6.2. **Working Group** . The Parties will establish a manufacturing working group (the " **Manufacturing Working Group** ") to oversee matters relating to the Manufacture of the Shared Product. The Manufacturing Working Group will report to the JDC for Development-related Manufacturing matters and will report to the JCC for Commercialization-related Manufacturing matters. The Manufacturing Working Group's responsibilities will include: (a) developing plans to transfer Manufacturing-related Know-How between the Parties as needed to facilitate the Manufacture of the Shared Product; (b) establishing standards applicable to each Party's Manufacturing activities and reviewing each Party's performance against such standards; conducting technical reviews, and (c) sharing planning and budgeting information with the JDC and JCC.

6.3. **Responsibility** . The Parties will share responsibility for Manufacturing clinical supplies of Shared Product as determined by the Manufacturing Working Group. Unless otherwise agreed by the Parties, Vertex will be responsible for Manufacturing commercial supplies of Shared Product.

ARTICLE 7.
ALLOCATION OF NET PROFIT AND NET LOSS.

7.1. **Allocation** . Each Party will be entitled to 50% of the Net Profits or will bear 50% of the Net Loss, as applicable, during the term of the Joint Development & Commercialization Agreement. If either Party elects to Opt-Out (as defined below), the other Party shall pay royalties in accordance with Section 11.4.

7.2. **Calculation** . Net Profit or Net Loss will be calculated for each Calendar Quarter by determining the [***] and subtracting [***].

7.3. **Payment of Expenses; Summary Statements** . Subject to reconciliation as provided in Section 7.4, the Party initially incurring Program Expenses will be responsible for and pay for all such Program Expenses so incurred. Each Party will maintain the books and records referred to in Section 7.6 and will accrue all Program Expenses and Net Sales) in accordance

with the terms and conditions hereof and in accordance with GAAP. Within [***] after the end of each [***] , each Party will submit to the other a non-binding, good faith estimate of the Program Expenses accrued and Net Sales during the just-ended [***] . Within [***] after the end of each [***] , each Party will submit to the other a written report reflecting the accrual of Program Expenses and Net Sales during the just-ended [***] , except that each Party's submission for the last month of such [***] will be a good faith estimate and not actual amounts (each, a " **Summary Statement** "). Each Summary Statement (after the initial Summary Statement) will reflect an adjustment for the actual amount of the previous [***] as needed. Any reporting and reconciliation of variances between estimated and actual costs and expenses may be delayed by a [***] as reasonably necessary in light of a Party's internal reporting procedures. The Parties' respective Summary Statements will serve as the basis of the Reconciliation Reports prepared by the Parties pursuant to Section 7.4. Upon the request of either Party from time to time, the Parties' respective finance departments, coordinated by the JDC, or JCC, as appropriate, will discuss any questions or issues arising from the Summary Statements, including the basis for the accrual of specific Program Expenses.

7.4. **Reconciliation** . Vertex will prepare a reconciliation report, as soon as practicable after the receipt of CRISPR's Summary Statement, but in any event within [***] after the end of each [***] , accompanied by reasonable supporting documents and calculations sufficient to support each Party's financial reporting obligations, independent auditor requirements and obligations under the Sarbanes-Oxley Act, which reconciles the amounts accrued and reported in each Party's Summary Statement during such [***] and the share of the Net Profits and Net Losses to be allocated to each of the Parties for such [***] in accordance with Section 7.1 (such report, the " **Reconciliation Report** "). Payment to reconcile Net Profit or Net Loss shall be made by the owing Party to the other Party within [***] after such Reconciliation Report is complete.

7.5. **Cost Overruns** . If a Party's aggregate Development Costs, Medical Affairs Costs or Commercialization Costs in any Calendar Year are likely to exceed or exceed those set forth in the Development Budget, Medical Affairs Budget or Commercialization Budget, as applicable, for all of its activities under the Development Plan, Medical Affairs Plan or Commercialization Plan, as applicable, in such Calendar Year by up to [***] of the aggregate amount set forth in the Development Budget, Medical Affairs Budget or Commercialization Budget, as applicable, such Party will provide the other Party with an explanation for such excess costs and expenses, and such excess costs and expenses will be included in the Development Costs, Medical Affairs Cost or Commercialization Costs, as applicable, and shared by the Parties as provided herein. To the extent a Party's aggregate Development Costs, Medical Affairs Costs or Commercialization Costs, as applicable, exceed those set forth in the Development Budget, Medical Affairs Budget or Commercialization Budget, as applicable, by more than [***] , unless otherwise agreed by the Parties, such Expenses will not be shared by the Parties and the Party incurring such Expenses will be solely responsible for such Expenses.

7.6. **Books and Records** . Each Party will keep and maintain accurate and complete records regarding Program Expenses and Net Sales, during the [***] preceding Calendar Years. Upon [***] prior written notice from the other Party (the " **Auditing Party** "), the Party

required to maintain such records (as applicable, the " **Audited Party** ") will permit an independent certified public accounting firm of internationally recognized standing, selected by the Auditing Party and reasonably acceptable to the Audited Party, to examine the relevant books and records of the Audited Party and its Affiliates, as may be reasonably necessary to verify the Summary Statements and Reconciliation Reports. An examination by the Auditing Party under this Section 7.6 will occur not more than [***] in any Calendar Year and will be limited to the pertinent books and records for any Calendar Year ending not more than [***] before the date of the request. The accounting firm will be provided access to such books and records at the Audited Party's facility or facilities where such books and records are normally kept and such examination will be conducted during the Audited Party's normal business hours. The Audited Party may require the accounting firm to sign a customary non-disclosure agreement before providing the accounting firm access to its facilities or records. Upon completion of the audit, the accounting firm will provide both the Auditing Party and the Audited Party a written report disclosing whether the applicable Summary Statements and Reconciliation Reports are correct or incorrect and the specific details concerning any discrepancies. No other information will be provided to the Auditing Party. If the report or information submitted by the Audited Party results in an underpayment or overpayment, the Party owing underpaid or overpaid amount will promptly pay such amount to the other Party, and, if, as a result of such inaccurate report or information, such amount is more than [***] of the amount that was owed the Audited Party will reimburse the Auditing Party for the reasonable expense incurred by the Auditing Party in connection with the audit.

ARTICLE 8.
ADVERSE EVENTS.

8.1. **Pharmacovigilance Agreement** . The Parties will meet to negotiate in good faith and agree on processes and procedures for sharing safety information within [***] after the effective date of the Joint Development & Commercialization Agreement. The agreed upon processes and procedures will be set forth in a pharmacovigilance agreement (the " **Pharmacovigilance Agreement** ") containing mutually agreed terms and conditions that are customary for agreements of this type. The Pharmacovigilance Agreement will include provisions establishing a joint safety oversight working group to oversee the conduct of the Parties' activities under the Pharmacovigilance Agreement and to coordinate the Parties' interactions with respect to pharmacovigilance activities.

8.2. **Global Safety Database** . The JCC will establish pharmacovigilance and safety strategy for the Shared Product. Pursuant to such strategy, Vertex will establish the global safety database for such Shared Product. Vertex will maintain a global database of safety information including, but not limited to, adverse events and pregnancy reports for such Shared Product, which will be used for regulatory reporting and responses to safety queries from Regulatory Authorities by both Parties. CRISPR will, and will cause its Affiliates to, transfer all adverse events information in its or their possession or control to the global safety database within a mutually agreed period of time that provides Vertex with sufficient time to enter all of the data and to obtain validation of the database.

8.3. **Risk Management and Signal Detection Activities** . Vertex shall be primarily responsible for all signal detection and risk management activities for Shared Products. These signal detection activities shall include, but are not limited to, proactive review and evaluation of all safety information from the Global Safety Database (including by way of example, Individual Case Safety Reports, aggregate safety information, literature reports, and non-clinical data).

ARTICLE 9.
SUBCONTRACTING

Each Party may subcontract the performance of any activities undertaken by such Party in accordance with the Global Development Plan, Medical Affairs Plan or Commercialization Plan to one or more Third Parties (each such Third Party, a " **Subcontractor** ") pursuant to a written agreement (a " **Subcontract** "). Notwithstanding the foregoing, if either Party desires to subcontract any such activities, it will first discuss the matter with the other Party and reasonably consider using the other Party for such subcontracted activities, taking into account the capabilities of the other Party and potential impact on costs, as a potential alternative to subcontracting such activities to a Third Party. If, following such discussion a Party still desires to subcontract the performance of any such activity to one or more Third Parties, it may proceed to do so; *provided* , that prior to entering into any Subcontract which the subcontracting Party reasonably anticipates will entail payments to the Subcontractor in excess of [***] with respect to subcontracted activities under the Joint Development & Commercialization Agreement, the subcontracting Party will obtain the JSC's approval, not to be unreasonably withheld, of use of the proposed Subcontractor to conduct the activities proposed to be subcontracted prior to execution of the applicable Subcontract.

ARTICLE 10.
LICENSES; IP

10.1. **License Grants** . Vertex will grant CRISPR a co-exclusive (with Vertex) license under Vertex's and its Affiliates' interest in the Licensed Vertex Know-How and Licensed Vertex Patents, with the right to Sublicense through multiple tiers (subject to Section 10.2), to Research, Develop, Manufacture, have Manufactured, use, keep, sell, offer for sale, import, export and Commercialize Shared Products in the Field in the Territory. Additionally, the license rights granted by CRISPR to Vertex under Section 5.3.1 of the Agreement will be modified to be co-exclusive (with CRISPR) for Shared Products in the Territory.

10.2. **Sublicensing** . Subject to the rights granted or retained by the Parties under the Joint Development & Collaboration Agreement, either Party may Sublicense (through multiple tiers) to its Affiliates or Third Parties any and all rights granted to it by the other Party or retained by such Party with respect to the Research, Development, Manufacture and Commercialization of the Shared Products; *provided* , that neither Party may grant any such Sublicense in a Major Market Country without the prior written consent of the other Party; and *provided* , *further* , that if either Party intends to Sublicense any such rights in any country, it will discuss the matter with the Other Party and in good faith consider using the Other Party to conduct any sublicensed activities. If a Party grants any such Sublicense it will

remain responsible for its obligations under the Joint Development & Commercialization Agreement and will be responsible for the performance of the relevant sublicensee.

10.3. [***] . If a Party believes, in its reasonable judgment, that it may be necessary to obtain rights under any [***] in order to Research, Develop, Manufacture or Commercialize a Shared Product in the Field, such Party will promptly notify the other Party and the Parties will discuss such matter in good faith. Unless otherwise agreed, [***] will have the first right to enter into a license with the relevant Third Party to acquire rights to the [***] . If the Parties are unable to agree on whether any Know-How or Patents are [***] , the Party that believes such rights are necessary may enter into a license with the relevant Third Party; *provided* , that [***] unless and until the other Party agrees, or as determined by arbitration or other dispute resolution mechanisms to [***] .

10.4. **Trademarks** . The Lead Commercialization Party will own and retain all rights to Trademarks for Shared Products in their respective jurisdiction, and all goodwill associated with or attached thereto arising out of the use thereof by the Parties, their Affiliates and Sublicensees will inure to the benefit of such Lead Commercialization Party. Each non-Lead Commercialization Party, on behalf of itself and its Affiliates, will assign to the Lead Commercialization Party or its relevant Affiliate all right, title and interest in and to such Shared Product Trademarks and goodwill in the relevant jurisdiction. The non-Lead Commercialization Party will not contest, oppose or challenge the Lead Commercialization Party's ownership of such Shared Product Trademarks in the relevant jurisdiction. The Lead Commercialization Party will own rights to any Internet domain names incorporating any Trademark for the Shared Product, or any variation or part of any such Trademark, as its URL address or any part of such address in the applicable jurisdiction. The Lead Commercialization Party will use Commercially Reasonable Efforts to register, maintain and enforce the Trademarks for the Shared Product in the relevant jurisdiction.

ARTICLE 11.
TERM; TERMINATION.

11.1. **Term.** The term of the Joint Development & Commercialization Agreement will commence on the execution of the Joint Development & Commercialization Agreement and continue in full force and effect until there is no longer a Global Development Plan or Commercialization Plan contemplating Development or Commercialization of a Shared Product in the Territory, unless earlier terminated as provided below.

11.2. **Termination Generally** . The provisions of Sections 11.2.1, 11.2.3, 11.2.4 and 11.2.5 of the Agreement will apply to the Joint Development & Commercialization Agreement, *mutatis mutandis.*

11.3. **Alternative Remedies** . The alternative remedy provisions of Section 11.3 of the Agreement will not apply to Hemoglobinopathy Targets or [***] or to the Joint Development & Commercialization Agreement.

11.4. **Opt-Out.** After [***] for a Shared Product directed to a particular Collaboration Target, either Party may opt out of the Joint Development & Commercialization Agreement for all Shared Products directed to such Collaboration Target upon [***] notice to the other Party (" **Opt-Out** "). The other Party shall pay such opting out Party royalties (" **Opt-Out**

Royalties ") in accordance with this Section 11.4 and the terms of Sections 7.5.2, 7.5.3, 7.5.4 and 7.5.5 of the Strategic Collaboration Option and License Agreement shall apply to such royalties, *mutatis mutandis* . The applicable royalty rates shall be determined in accordance with the table set forth below based on the timing of the Opt-out Notice. Upon the other Party's receipt of such notice, all rights and obligations under the Joint Development & Commercialization Agreement with respect to Shared Products directed to such Collaboration Target shall terminate. If the opting out Party is CRISPR, such Shared Product(s) shall be deemed Product(s) directed to a Collaboration Target other than a Hemoglobinopathy Target [***] under the Strategic Collaboration, Option and License Agreement, and the terms and conditions of such agreement shall apply with respect to all Products directed to the opted out Collaboration Target; provided, that in lieu of the royalty rates payable under Section 7.5.1 of such agreement Vertex shall pay royalties at the rates set forth in this Section 11.4. If the opting out Party is Vertex, the Parties shall negotiate in good faith a termination agreement for all Products directed to such opted out Collaboration Target, including, without limitation, reasonable diligence obligations and obligations of CRISPR for sharing of information regarding such Products with Vertex, which obligations will be substantially similar to the obligations imposed by Vertex under the Joint Development & Commercialization Agreement. For the avoidance of doubt, the allocation of Net Profits and Net Loss pursuant to Section 7.1 shall terminate upon the Opt-Out.

Timing of Opt Out	**Net Sales (in Dollars) for such Shared Products in the Territory**	**Opt-Out Royalty Rates as a Percentage (%) of Net Sales of such Shared Products**
[***]	[***]	[***]
	[***]	[***]
	[***]	[***]
	[***]	[***]
[***]	[***]	[***]
	[***]	[***]
	[***]	[***]
	[***]	[***]

SCHEDULE G

ARTICLE 12.
INDEMNITY

The Joint Development & Commercialization Agreement will include commercially reasonable indemnity provisions, which will include (but not be limited to) an obligation for each Party to indemnify the other Party from, against and in respect of any and all Liability incurred or suffered by the other Party to the extent resulting from: (a) any breach of, or inaccuracy in, any representation or warranty made by the indemnifying Party, or any breach or violation by the indemnifying Party of any covenant or agreement in the Joint Development & Commercialization Agreement; or (b) the negligence or intentional misconduct of, or violation of Applicable Law (including off-label promotion) by, the indemnifying Party, any of its Affiliates or Sublicensees, or any of their respective directors, officers, employees and agents, in performing its obligations or exercising its rights under the Joint Development & Commercialization Agreement.

SCHEDULE G

Schedule H

CRISPR In-License Agreements

Confidential Materials omitted and filed separately with the Securities and Exchange Commission. A total of 1 page was omitted.
[***]

SCHEDULE H

Schedule I

Baseball Arbitration Procedures

Selection of Baseball Expert and Submission of Positions. The Parties will select and agree upon a mutually acceptable independent Third Party expert who is neutral, disinterested and impartial, and has the experience specified in Schedule G for the applicable dispute (the "Baseball Expert"). If the Parties are unable to mutually agree upon a Baseball Expert within [***] following the delivery of the request for Baseball Arbitration, then upon request by either Party, the Baseball Expert will be an arbitrator appointed by Judicial and Mediation Services ("JAMS"), which arbitrator need not have the above-described experience. Once the Baseball Expert has been selected, each Party will within [***] following selection of the Baseball Expert provide the Baseball Expert and the other Party with a written report setting forth its position with respect to the substance of the dispute and may submit a revised or updated report and position to the Baseball Expert within [***] of receiving the other Party's report. If so requested by the Baseball Expert, each Party will make oral submissions to the Baseball Expert based on such Party's written report, and each Party will have the right to be present during any such oral submissions.

JAMS Supervision. In the event the Baseball Expert is a JAMS arbitrator selected by JAMS as provided in this Schedule I, the matter will be conducted as a binding arbitration in accordance with JAMS procedures, as modified by this Schedule I (including that the arbitrator will adopt as his or her decision the position of one Party or the other, as described below). In such event, the arbitrator may retain a Third Party expert with the same experience specified in Schedule F for the Baseball Expert to assist in rendering such decision, and the expenses of any such expert will be shared by the Parties as costs of the arbitration as provided in this Schedule I.

Determination by the Baseball Expert. The Baseball Expert will, no later than [***] after the last submission of the written reports and, if any, oral submissions, select one of the Party's positions as his or her final decision, and will not have the authority to modify either Party's position or render any substantive decision other than to so select the position of either Party as set forth in their respective written report (as initially submitted, or as revised in accordance with this Schedule I, as applicable). The decision of the Baseball Expert will be the sole, exclusive and binding remedy between them regarding the dispute submitted to such Baseball Expert.

Location; Costs. Unless otherwise mutually agreed upon by the Parties, the in-person portion (if any) of such proceedings will be conducted in Boston, Massachusetts. [***].

Timetable for Completion in [***] **.** The Parties will use, and will direct the Baseball Expert to use, commercially reasonable efforts to resolve a dispute within [***] after the selection of the Baseball Expert, or if resolution within [***] is not reasonably achievable, as determined by the Baseball Expert, then as soon thereafter as is reasonably practicable.

Schedule J

Identified Third Party IP

U.S. Patent No.	U.S. Patent Application No.	Filing Data
[***]	[***]	[***]
[***]	[***]	[***]
[***]	[***]	[***]
[***]	[***]	[***]
[***]	[***]	[***]
[***]	[***]	[***]
[***]	[***]	[***]
[***]	[***]	[***]
[***]	[***]	[***]
[***]	[***]	[***]

Schedule K

Patent Costs

	Prior to Option Exercise	After Option Exercise
CRISPR Platform Technology Patents	[***]	[***]
CRISPR Background Patents	[***]	[***]
CRISPR Program Patent	[***]	[***]
[***] Patents	[***]	[***]
[***] Patents	[***]	[***]
[***] Joint Program Patents	[***]	[***]
Other Joint Program Patent	[***]	[***]
[***] Joint Program Patents	[***]	[***]

***** Either Party may decline to pay its share of costs for Prosecuting and Maintaining any Other Joint Program Patents in a particular country or particular countries, in which case, the declining Party will, and will cause its Affiliates to, assign to the other Party (or, if such assignment is not possible, grant a fully-paid exclusive license in) all of their rights, titles and interests in and to such Other Joint Program Patents.

Schedule L

CRISPR Disclosures

Confidential Materials omitted and filed separately with the Securities and Exchange Commission. A total of 6 pages were omitted. [***]

Schedule M

Press Release

SCHEDULE M

Vertex and CRISPR Therapeutics Establish Collaboration to Use CRISPR- Cas9 Gene Editing Technology to Discover and Develop New Treatments for Genetic Diseases

-Gene editing technology to be used to discover treatments to address the mutations and genes known to cause and contribute to cystic fibrosis-

-Vertex and CRISPR to utilize gene editing approach to discover treatments for genetic diseases, including sickle cell disease-

-Companies establish four-year research collaboration; CRISPR to receive $105 million up- front payment, of which $30 million is an equity investment, with potential for additional milestones and royalty payments-

BOSTON AND CAMBRIDGE, MASS – October XX, 2015 - Vertex Pharmaceuticals Incorporated (Nasdaq: VRTX) and CRISPR Therapeutics today announced that the two companies have entered into a strategic research collaboration focused on the use of CRISPR's gene editing technology, known as CRISPR-Cas9, to discover and develop potential new treatments aimed at the underlying genetic causes of human disease. The collaboration will evaluate the use of CRISPR-Cas9 across multiple diseases where targets have been validated through human genetics. Vertex and CRISPR will focus their initial gene editing research on discovering treatments to address the mutations and genes known to cause and contribute to cystic fibrosis and sickle cell disease. Vertex and CRISPR will also evaluate a specified number of other genetic targets as part of the collaboration. Vertex will have exclusive rights to license up to six new CRISPR-Cas9-based treatments that emerge from the collaboration. As part of the collaboration, Vertex made an up-front commitment of $105 million to CRISPR, including $75 million in cash and a $30 million equity investment. CRISPR is also eligible to receive future development, regulatory and sales milestones and royalty payments on future sales.

"CRISPR-Cas9 is an important scientific and technological breakthrough that holds significant promise for the future discovery of potentially transformative treatments for many genetic diseases," said David Altshuler, M.D., Ph.D., Vertex's Executive Vice President, Global Research and Chief Scientific Officer. "As a company founded on innovative science, we're

excited to begin this collaboration with CRISPR, as it puts us at the forefront of what we believe may be a fundamental change in the future treatment of disease -- using gene editing technologies to address the underlying genetic causes of many diseases."

"Vertex has a track record of developing innovative medicines for cystic fibrosis and other serious diseases, making them a great partner to accelerate the therapeutic promise of gene editing," said Rodger Novak, M.D., Chief Executive Officer of CRISPR Therapeutics. "For CRISPR, this collaboration validates the potential for gene editing in human therapeutics and provides important financial support for continued investment in our platform and proprietary pipeline of programs."

About the Collaboration

Under the terms of the collaboration, Vertex and CRISPR will jointly use the CRISPR-Cas9 technology to discover and develop potential new treatments that correct defects in specific gene targets known to cause or contribute to particular diseases. The initial focus of the collaboration will be on the use of CRISPR-Cas9 to potentially correct the mutations in the cystic fibrosis transmembrane conductance regulator (CFTR) gene known to result in the defective protein that causes CF and to edit other genes that contribute to the disease. Additionally, the companies will seek to discover and develop gene-based treatments for hemoglobinopathies, including sickle cell disease. Additional discovery efforts focused on a specified number of other genetic targets will also be conducted under the collaboration. Discovery activities will be conducted primarily by CRISPR, and the related expenses will be fully funded by Vertex. Vertex has the option to an exclusive license for up to six gene-based treatments that emerge from the four-year research collaboration. Vertex will fund 100 percent of the development expenses of licensed treatments. For each of the up to six treatments in-licensed for development, Vertex will pay future development, regulatory and sales milestones of up to $420 million as well as royalty payments on future sales.

Vertex and CRISPR will collaborate on the research, development and commercialization of treatments for hemoglobinopathies that emerge from the collaboration. Specifically for hemoglobinopathies, including treatments for sickle cell disease, Vertex and CRISPR will equally share all research and development costs and sales, with CRISPR Therapeutics leading commercialization efforts in the U.S. For all other diseases, Vertex will lead all development and global commercialization activities.

Vertex will pay CRISPR $75 million in cash as part of its up-front commitment. Vertex will also provide a $30 million investment in CRISPR, which is a private company. The investment will

provide Vertex with an ownership stake in CRISPR. The collaboration also provides Vertex with an observer seat on the CRISPR Board of Directors, which will be filled by Dr. Altshuler.

About Gene Editing with CRISPR-Cas9

"CRISPR" refers to Clustered Regularly Interspaced Short Palindromic Repeats that occur in the genome of certain bacteria, from which the system was discovered. Cas9 is a CRISPR- associated endonuclease (an enzyme) known to act as the "molecular scissors" that cut and edit, or correct, disease-associated DNA in a cell. A guide RNA directs the Cas9 molecular scissors to the exact site of the disease-associated mutation. Once the molecular scissors make a cut in the DNA, additional cellular mechanisms and exogenously added DNA will use the cell's own machinery and other elements to specifically 'repair' the DNA. This technology may offer the ability to directly modify or correct the underlying disease-associated changes in the human genome for the potential treatment of a large number of both rare and common diseases.

Emmanuelle Charpentier, Ph.D., one of CRISPR Therapeutics' scientific founders , co-invented the CRISPR-Cas9 technology and is the recipient of multiple prestigious awards in recognition of the potential contribution that the CRISPR-Cas9 technology may have on global health. The other scientific co-founders of CRISPR are Craig Mello, Ph.D., Chad Cowan, Ph.D., Matthew Porteus, M.D., Ph.D., and Daniel Anderson, Ph.D.

About Vertex

Vertex is a global biotechnology company that aims to discover, develop and commercialize innovative medicines so people with serious diseases can lead better lives. In addition to our clinical development programs focused on cystic fibrosis, Vertex has more than a dozen ongoing research programs aimed at other serious and life-threatening diseases.

Founded in 1989 in Cambridge, Mass., Vertex today has research and development sites and commercial offices in the United States, Europe, Canada and Australia. For five years in a row, *Science* magazine has named Vertex one of its Top Employers in the life sciences. For
additional information and the latest updates from the company, please visit www.vrtx.co m .

About CRISPR Therapeutics

The mission of CRISPR Therapeutics is to develop transformative gene-based medicines for patients with serious diseases. Our therapeutic approach aims to cure diseases at the molecular level using the breakthrough gene editing technology called CRISPR-Cas9. With our multi- disciplinary team of world-renowned academics, drug developers and clinicians, we are uniquely positioned to translate CRISPR-Cas9 technology into human therapeutics. We have licensed the foundational CRISPR-Cas9 patent estate for human therapeutic use from our scientific founder, Dr. Emmanuelle Charpentier. We are headquartered in Basel, Switzerland, our R&D operations are in Cambridge, Massachusetts and we have corporate offices in London, United Kingdom. www.crisprtx.com

Special Note Regarding Forward-looking Statements
This press release contains forward-looking statements as defined in the Private Securities Litigation Reform Act of 1995, including, without limitation, Dr. Altshuler's statements in the second paragraph of the press release, Dr. Novak's statements in the third paragraph of the press release and the information provided regarding the future development of treatments for genetic diseases using the CRISPR-Cas9 technology. While Vertex believes the forward-looking statements contained in this press release are accurate, these forward-looking statements represent the company's beliefs only as of the date of this press release and there are a number of factors that could cause actual events or results to differ materially from those indicated by such forward-looking statements. Those risks and uncertainties include, among other things, that data may not support further development of the gene-based treatments subject to the collaboration due to safety, efficacy or other reasons, and other risks listed under Risk Factors in Vertex's annual report and quarterly reports filed with the Securities and Exchange Commission and available through the company's website at www.vrtx.com. Vertex disclaims any obligation to update the information contained in this press release as new information becomes available.

(VRTX-GEN)

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LEASE AGREEMENT

THIS LEASE AGREEMENT (this " **Lease** ") is made this 2nd day of December, 2015, between **ARE-SD REGION NO. 23, LLC** , a Delaware limited liability company (" **Landlord** "), and **VERTEX PHARMACEUTICALS INCORPORATED** , a Massachusetts corporation (" **Tenant** ").

Building: That to be constructed Building to be known as 3215 Merryfield Row, San Diego, California.

Premises: The Building, containing approximately 170,523 rentable square feet, including the subterranean parking garage located in the Building, all as shown on **Exhibit A** .

Project: The real property on which the Building in which the Premises are located, consisting of approximately 4.5 acres, together with all improvements thereon and appurtenances thereto as described on **Exhibit B** .

Base Rent:

Months 1* – 12:	$0 per rsf of the Premises per month
Months 13 – 60:	$4.50 per rsf of the Premises per month
Months 61 – 72:	$4.84 per rsf of the Premises per month
Months 73 – 84:	$4.98 per rsf of the Premises per month
Months 85 – 96:	$5.13 per rsf of the Premises per month
Months 97 – 108:	$5.29 per rsf of the Premises per month
Months 109 – 120:	$5.44 per rsf of the Premises per month
Months 121 – 132:	$5.61 per rsf of the Premises per month
Months 133 – 144:	$5.77 per rsf of the Premises per month
Months 145 – 156:	$5.95 per rsf of the Premises per month
Months 157 – 168:	$6.12 per rsf of the Premises per month
Months 169 – 180:	$6.30 per rsf of the Premises per month
Months 181 – 192:	$6.49 per rsf of the Premises per month

*Month 1 is the month in which the Rent Commencement Date occurs.

Rentable Area of Premises: 170,523 sq. ft.

Rentable Area of Building: 170,523 sq. ft.

Rentable Area of Project: Approximately 230,523 sq. ft., subject to adjustment as provided for in Section 5 hereof.

Tenant's Share of Operating Expenses of Building: 100%

Building's Share of Operating Expenses of Project: 73.97%, subject to adjustment as provided for in Section 5 hereof.

Security Deposit: None

Target Commencement Date: December 1, 2016

Base Term: Beginning on the Commencement Date and ending 192 months from the first day of the first full month following the Rent Commencement Date.

Permitted Use: Research and development laboratory, related office and other related uses consistent with the character of the Project and otherwise in compliance with the provisions of Section 7 hereof.

Address for Rent Payment: c/o Alexandria Real Estate Equities, Inc. Dept LA 23447 Pasadena, CA 91185-3447

Landlord's Notice Address: 385 E. Colorado Boulevard, Suite 299 Pasadena, CA 91101 Attention: Corporate Secretary

Tenant's Notice Address Prior to Rent Commencement Date: 50 Northern Avenue Boston, MA 02210 Attention: Lease Administrator

Tenant's Notice Address After the Rent Commencement Date: 50 Northern Avenue Boston, MA 02210 Attention: Lease Administrator

With a copy to Tenant's attorney below with respect to notices of Default (and, as a courtesy only, Landlord shall endeavor to deliver notices relating to the Right of First Refusal and the Extension Right to Tenant's attorney but Landlord's failure to deliver such notices to Tenant's attorney shall in no event constitute a default by Landlord or a failure by Landlord to deliver the applicable notice to Tenant):

Bowditch & Dewey LLP
175 Crossing Boulevard
Framingham, MA 01702
Attention: Paul C. Bauer

The following Exhibits and Addenda are attached hereto and incorporated herein by this reference:

[X] **EXHIBIT A** - PREMISES DESCRIPTION	[X] **EXHIBIT B** - DESCRIPTION OF PROJECT
[X] **EXHIBIT C** - WORK LETTER	[X] **EXHIBIT D** - COMMENCEMENT DATE
[X] **EXHIBIT E** - RULES AND REGULATIONS	[X] **EXHIBIT F** - TENANT'S PERSONAL PROPERTY
[X] **EXHIBIT G** - EV PARKING STATIONS	[X] **EXHIBIT H** - SITE PLAN
[X] **EXHIBIT I** - VERTEX AREA	[X] **EXHIBIT J** - INTENTIONALLY OMITTED
[X] **EXHIBIT K** - SIGNAGE	[X] **EXHIBIT L** - MAINTENANCE OBLIGATIONS

1. **Lease of Premises** . Upon and subject to all of the terms and conditions hereof, Landlord hereby leases the Premises to Tenant and Tenant hereby leases the Premises from Landlord. The portions of the Project which are for the non-exclusive use of tenants of the Project are collectively referred to herein as the " **Common Areas** ." The Common Areas shall include, but not be limited to, all common driveways, sidewalks, parking areas, walkways and benches located at the Project. Landlord reserves the right to modify Common Areas, provided that such modifications do not materially reduce the Common Area or materially adversely affect Tenant's use of the Premises for the Permitted Use. From and after the Rent Commencement Date through the expiration of the Term, Tenant shall have access to the Building and the Premises 24 hours a day, 7 days a week, except in the case of emergencies, as the result of Legal Requirements, the performance by Landlord of any installation, maintenance or repairs, or any other temporary interruptions, and otherwise subject to the terms of this Lease. The site plan attached as **Exhibit H** reflects the site plan currently planned by Landlord for the Project which site plan remains subject to change by Landlord, provided that material changes to the Building shall be subject to Tenant's prior written approval, which shall not be unreasonably withheld, conditioned or delayed. In addition, Tenant shall have the exclusive right to use the areas outside the Building shown as Vertex areas on **Exhibit I** attached hereto (including, without limitation, the central plant, loading dock area, emergency generator yard, storage sheds, cooling tower, chiller room and trash enclosure and the courtyard/meadow area located on the east side of the Building facing the canyons) (collectively, " **Exclusive Use Areas** ").

2. **Delivery; Acceptance of Premises; Commencement Date** . Landlord shall use reasonable efforts to deliver the Premises to Tenant on or before the Target Commencement Date (as such date may be extended to the extent of Tenant Delays and/or Force Majeure (as hereinafter defined) delays (provided that in no event may Force Majeure delays exceed 9 months) on a day-for-day basis) with the

Cold Shell in Tenant Improvement Work Readiness Condition (" **Delivery** " or " **Deliver** ") so that Tenant may commence construction of the Tenant's Work in the Building. The date on which Landlord Delivers the Premises to Tenant shall constitute the " **Landlord Delivery Date** ". If Landlord fails to timely Deliver the Premises, Landlord shall not be liable to Tenant for any loss or damage resulting therefrom, except as provided in the immediately following sentence, and this Lease shall not be void or voidable except as provided herein. If the Landlord Delivery Date does not occur (i) within 60 days after the Target Commencement Date (as such date may be extended to the extent of Tenant Delays and Force Majeure delays (provided that in no event may Force Majeure delays exceed 9 months) on a day-for day basis) (as extended, the " **Adjusted Target Commencement Date** ") the Abatement Period (as defined in Section 3 below) shall be extended by one additional day for each day after the Adjusted Target Commencement Date that Landlord fails to Deliver the Premises to Tenant, and (ii) within 120 days after the Adjusted Target Commencement Date, the Abatement Period shall thereafter be extended by two days for each day after the date that is 120 days after the Adjusted Target Commencement Date that Landlord fails to Deliver the Premises. As used herein, the terms " **Landlord's Work** ," " **Cold Shell** ," " **Tenant's Work** ," " **Tenant Delay** " and " **Tenant Improvement Work Readiness Condition** " shall have the meanings set forth for such terms in the Work Letter.

The " **Commencement Date** " shall be the earlier of (i) the Landlord Delivery Date, and (ii) the date Landlord could have Delivered the Premises but for Tenant Delays. The " **Rent Commencement Date** " shall be the date that is 10 months after the Commencement Date. If substantial completion of the Tenant's Work is delayed due to Landlord Delays (as defined in the Work Letter) or Force Majeure (provided that in no event may Force Majeure delays exceed 4.5 months) beyond the scheduled Rent Commencement Date as calculated in the immediately preceding sentence, the Rent Commencement Date shall be extended to the extent of such Landlord Delays and/or Force Majeure (provided that in no event may Force Majeure delays exceed 4.5 months) on a day-for-day basis. Upon request of either party, Landlord and Tenant shall execute and deliver a written acknowledgment of the Commencement Date, the Rent Commencement Date and the expiration date of the Term when such are established in the form of the "Acknowledgement of Commencement Date" attached to this Lease as **Exhibit D** ; provided , however , the failure of either party to execute and deliver such acknowledgment shall not affect either party's rights hereunder. The " **Term** " of this Lease shall be the Base Term, as defined above on the first page of this Lease and any Extension Terms which Tenant may elect pursuant to Section 40 hereof.

Tenant acknowledges and agrees that (i) Landlord's obligation to develop the Building as contemplated in this Lease is subject to Landlord entering into a lease termination agreement with The Scripps Research Institute, an existing tenant in a building located at the Project as of the date of this Lease, for an early termination of its lease at the Project on terms and conditions acceptable to Landlord in its sole and absolute discretion (the " **Lease Termination Agreement** "), and (ii) the effectiveness of this Lease shall be subject to Landlord entering into the Lease Termination Agreement on or before March 25, 2016 (which March 25, 2016 date shall not be extended due to Force Majeure) (the " **Condition Precedent** "). If the Condition Precedent is not satisfied by the date set forth above, this Lease shall automatically terminate in its entirety and none of the provisions of this Lease shall have any force or effect. If this Lease terminates pursuant to the immediately preceding sentence, neither Landlord nor Tenant shall have any further rights, duties or obligations under this Lease.

Tenant acknowledges and agrees that (i) Landlord does not currently have the required governmental entitlements necessary for the development of the Building or the Project as contemplated in this Lease (collectively, the " **Approvals** "), (ii) Landlord shall have no obligation to commence the construction of the Building prior to obtaining such Approvals (and the expiration of any challenge periods), (iii) Landlord's obligation to develop the Building as contemplated in this Lease is subject to Landlord's ability to obtain, on terms and conditions acceptable to Landlord in its reasonable discretion, all of the Approvals, and (iv) Landlord shall have the sole right to determine all matters related to the Approvals. Landlord shall use good faith reasonable efforts to obtain the Approvals, provided such Approvals are on terms acceptable to Landlord, in its reasonable discretion. If, notwithstanding Landlord's good faith reasonable efforts, Landlord is unable to obtain a building permit for Landlord's Work from the City of San Diego (the " **Building Permit** ") on or

before April 1, 2017, and Tenant has not otherwise elected to terminate this Lease pursuant to this Section 2 , this Lease may be terminated by Landlord or Tenant by written notice to the other and, if so terminated, neither Landlord nor Tenant shall have any further rights, duties or obligations under this Lease, except with respect to provisions which expressly survive the termination of this Lease. Notwithstanding the foregoing, if Landlord obtains the Building Permit prior to the exercise by Landlord or Tenant of the foregoing termination right, then such termination right shall expire and be of no further force or effect. Tenant agrees that, upon reasonable advance written request from Landlord, to make a senior level executive of Tenant (Vice President or higher) available to attend meetings with Landlord and the City of San Diego, to support Landlord in its efforts to obtain on an expedited basis the necessary governmental approvals (including, without limitation, the Approvals) to construct the Building as contemplated in this Lease.

If Landlord does not complete the demolition of the 3215 Merryfield building existing as of the date of this Lease by December 1, 2016 (as such date may be extended to the extent of Tenant Delays and Force Majeure delays (provided that in no event may Force Majeure delays exceed 6 months) on a day-for day basis) (as extended, the " **Target Demolition Completion Date** ") and so long as Tenant delivers, on or before the date that is 30 days prior to the Target Demolition Completion Date, written notice to Landlord of its intention to terminate this Lease for Landlord's failure to complete such demolition (an " **Intention Notice** ") on or before the Target Demolition Completion Date, this Lease may be terminated by Tenant by written notice to Landlord, and if so terminated by Tenant, neither Landlord nor Tenant shall have any further rights, duties or obligations under this Lease, except with respect to provisions which expressly survive termination of this Lease. If Tenant does not (1) timely deliver an Intention Notice, and (2) elect to terminate this Lease by delivery of written notice pursuant to the immediately preceding sentence within 10 business days of the Target Demolition Completion Date, such right to terminate this Lease shall be waived and this Lease shall remain in full force and effect. If the Landlord Delivery Date does not occur by May 1, 2017 (as such date may be extended to the extent of Tenant Delays and Force Majeure delays (provided that in no event may Force Majeure delays exceed 6 months) (as extended, the " **Outside Landlord Delivery Date** "), this Lease may be terminated by Tenant by written notice to Landlord, and if so terminated by Tenant, neither Landlord nor Tenant shall have any further rights, duties or obligations under this Lease, except with respect to provisions which expressly survive termination of this Lease. If Tenant does not elect to terminate this Lease pursuant to the immediately preceding sentence within 10 business days following the Outside Landlord Delivery Date, such right to terminate this Lease shall be waived and this Lease, and any applicable extension of the Abatement Period, shall remain in full force and effect. Notwithstanding anything to the contrary contained in this Lease and for the avoidance of any doubt, the termination rights set forth in this Section 2 shall terminate on the Commencement Date; provided, however that such termination of Tenant's termination rights shall in no event affect or be deemed a forfeiture of any extension of the Abatement Period to which Tenant may be entitled pursuant to this Section 2 .

Except as set forth in the Work Letter: (i) Tenant shall accept the Premises in their condition as of the Commencement Date, subject to all applicable Legal Requirements (as defined in Section 7 hereof); and (ii) Landlord shall otherwise have no obligation for any defects in the Premises. Tenant shall have the right to access the Project and the Premises prior to the Landlord Delivery Date for design purposes and Tenant shall have 24 hour per day, 7 day per week access to the Building on and after the Landlord Delivery Date for construction of the Tenant's Work in accordance with the terms of the Work Letter; provided, however, that all such access is coordinated with Landlord, and Tenant complies with this Lease and all other reasonable restrictions and conditions Landlord may impose during such periods of access. Any access to the Premises by Tenant before the Commencement Date shall be subject to all of the terms and conditions of this Lease, excluding the obligation to pay Base Rent and Operating Expenses.

Except as otherwise expressly provided for in this Lease, Tenant agrees and acknowledges that neither Landlord nor any agent of Landlord has made any representation or warranty with respect to the suitability of the Premises or the Project for the conduct of Tenant's business, and Tenant waives any implied warranty that the Premises or the Project are suitable for the Permitted Use.

3. **Rent** .

(a) **Base Rent** . Tenant shall pay to Landlord in advance, without demand, abatement, deduction or set-off, monthly installments of Base Rent on or before the first day of each calendar month during the Term hereof after the Rent Commencement Date, in lawful money of the United States of America, at the office of Landlord for payment of Rent set forth above, or to such other person or at such other place as Landlord may from time to time designate in writing. Payments of Base Rent for any fractional calendar month shall be prorated. The obligation of Tenant to pay Base Rent and other sums to Landlord and the obligations of Landlord under this Lease are independent obligations. Tenant shall have no right at any time to abate, reduce, or set-off any Rent (as defined in Section 5) due hereunder except for any abatement as may be expressly provided in this Lease.

Notwithstanding anything to the contrary contained in this Lease, so long as no Default has occurred under this Lease, for the period commencing on the Rent Commencement Date through the last day of the 12 th month after the Rent Commencement Date (the " **Abatement Period** "), as such Abatement Period may be extended pursuant to the first paragraph of Section 2 , Tenant shall not be required to pay Base Rent for the Premises.

(b) **Additional Rent** . In addition to Base Rent, Tenant agrees to pay to Landlord as additional rent (" **Additional Rent** "): (i) commencing on the Rent Commencement Date, Tenant's Share of "Operating Expenses" (as defined in Section 5), and (ii) any and all other amounts Tenant assumes or agrees to pay under the provisions of this Lease, including, without limitation, any and all other sums that may become due by reason of any default of Tenant or failure to comply with the agreements, terms, covenants and conditions of this Lease to be performed by Tenant, after any applicable notice and cure period.

4. **Base Rent Adjustments** . Base Rent shall be increased during the Base Term pursuant to the schedule set forth on Page 1 of this Lease.

5. **Operating Expense Payments** . Commencing on the Rent Commencement Date, Tenant shall be responsible for Tenant's Share of Operating Expenses during the Term. Landlord shall deliver to Tenant a written estimate of Operating Expenses for each calendar year during the Term (the " **Annual Estimate** "), which may be reasonably revised by Landlord from time to time during such calendar year. Commencing on the Rent Commencement Date and continuing thereafter on the first day of each month during the Term, Tenant shall pay Landlord an amount equal to 1/12th of Tenant's Share of the Annual Estimate. Payments for any fractional calendar month shall be prorated.

The term " **Operating Expenses** " means all costs and expenses of any kind or description whatsoever incurred or accrued each calendar year by Landlord with respect to the Building (including the Building's Share of Operating Expenses for the Project) (including, without duplication, Taxes (as defined in Section 9), capital repairs, replacements and improvements amortized on a straight line basis over the useful life of such capital items as reasonably determined taking into consideration all relevant factors (e.g., the 24 hour operation of the Building Systems, where applicable), and the costs of Landlord's third party property manager (not to exceed 2.0% of Base Rent) or, if there is no third party property manager, administration rent in the amount of 2.0% of Base Rent (provided that during the Abatement Period, Tenant shall nonetheless be required to pay administration rent each month equal to the amount of administration rent that Tenant would have been required to pay in the absence of there being an Abatement Period). " **Operating Expenses for the Project** " means all costs and expenses of any kind or description incurred or accrued each calendar year by Landlord with respect to the Project which are not specific to the Building or any other building located in the Project. Operating Expenses and Operating Expenses for the Project shall not include:

(a) the original construction costs of the Project including, but not limited to Landlord's Work, and renovation prior to the date of this Lease and costs of correcting defects in such original construction or renovation;

(b) capital expenditures for expansion of the Project;

(c) interest, principal payments of Mortgage (as defined in Section 27) debts of Landlord, financing costs and amortization of funds borrowed by Landlord, whether secured or unsecured, and all payments of base rent (but not taxes or operating expenses) directly associated with the Project under any ground lease or other underlying lease of all or any portion of the Project;

(d) depreciation of the Project (except for capital improvements, the cost of which are includable in Operating Expenses);

(e) advertising, promotional, legal and space planning expenses and leasing commissions and other costs and expenses incurred in procuring and leasing space to tenants for the Project, including any leasing office maintained in the Project, free rent, moving expenses and construction allowances for tenants;

(f) legal and other expenses incurred in the negotiation or enforcement of leases;

(g) completing, fixturing, improving, renovating, painting, redecorating or other work, which Landlord pays for or performs for other tenants within their premises, and costs of correcting defects in such work;

(h) costs for which Landlord is entitled to be reimbursed by other tenants of the Project or Taxes to be paid directly by Tenant or other tenants of the Project, whether or not actually paid;

(i) salaries, wages, benefits and other compensation paid to officers and employees of Landlord who (x) do not have day to day responsibility for the operating, managing or servicing of the Building or the Project or (y) are above the level of senior vice president, provided that the expense of any personnel not dedicated exclusively to the Building or the Project shall be equitably prorated to reflect time spent on operating, managing or otherwise servicing the Building or the Project vis-a-vis time spent on matters unrelated to operating, managing or otherwise servicing the Building or the Project;

(j) general organizational, administrative and overhead costs relating to maintaining Landlord's existence, either as a corporation, partnership, or other entity, including general corporate, legal and accounting expenses;

(k) costs (including attorneys' fees, accountant fees, and costs of settlement, judgments and payments in lieu thereof) incurred in connection with negotiations or disputes with tenants, other occupants, or prospective tenants, and costs and expenses, including legal fees, incurred in connection with negotiations or disputes with employees, consultants, management agents, leasing agents, purchasers or mortgagees of the Project;

(l) costs incurred by Landlord due to the violation by Landlord, its employees, agents or contractors or any tenant of the terms and conditions of any lease of space in the Project or any Legal Requirement (as defined in Section 7);

(m) penalties, fines or interest incurred as a result of Landlord's inability or failure to make payment of its obligations in a timely manner (other than as a result of any late payments by Tenant to Landlord) including, but not limited to, Taxes and/or to file any tax or informational returns when due, or from Landlord's failure to make any payment of Taxes required to be made by Landlord hereunder before delinquency;

(n) overhead and profit increment paid to Landlord or to subsidiaries or affiliates of Landlord for goods and/or services in or to the Project to the extent the same exceeds the costs of such goods and/or services rendered by unaffiliated third parties on a competitive basis;

(o) costs of Landlord's charitable or political contributions, or of fine art maintained at the Project;

(p) costs in connection with services (including electricity), items or other benefits of a type which are not standard for the Project and which are not available to Tenant without specific charges therefor, but which are provided to another tenant or occupant of the Project, whether or not such other tenant or occupant is specifically charged therefor by Landlord;

(q) all transaction costs incurred in the actual or contemplated sale or refinancing of the Project or an interest in the Project;

(r) net income taxes of Landlord or the owner of any interest in the Project, franchise, capital stock, gift, estate or inheritance taxes or any federal, state or local documentary taxes imposed against the Project or any portion thereof or interest therein;

(s) costs actually reimbursed to Landlord under any warranty carried by Landlord for the Project, which warranties Landlord shall, as part of Operating Expenses, use commercially reasonable efforts to enforce, provided, that if Tenant pays for such a cost as part of Operating Expenses and Landlord actually receives reimbursement for such cost under its warranty in a subsequent year, Tenant shall receive a credit against Operating Expenses in the year in which such reimbursement is received by Landlord in an amount equal to its pro rata share of the amount of the reimbursement for such cost received by Landlord under its warranty, not to exceed the amount actually paid by Tenant;

(t) any expenses otherwise includable within Operating Expenses to the extent actually reimbursed by insurance (or would have been reimbursed by insurance required to be carried by Landlord pursuant to Section 17), which policies Landlord shall, as part of Operating Expenses, use commercially reasonable efforts to enforce, provided, that if Tenant pays for such expense as part of Operating Expenses and Landlord actually receives reimbursement for such expense from Landlord's insurance in a subsequent year, Tenant shall receive a credit against Operating Expenses in the year in which such reimbursement is received by Landlord in an amount equal to its pro rata share of the amount of the reimbursement for such expense received by Landlord from its insurance, not to exceed the amount actually paid by Tenant;

(u) costs occasioned by condemnation;

(v) costs and expenses resulting from the adjudicated gross negligence or willful misconduct of Landlord;

(w) the cost of any "tap fees" or the one-time lump sum sewer or water connection fees for the Building payable in connection with the initial construction of the Building;

(x) any costs incurred to remove, study, test or remediate Hazardous Materials in or about the Building or the Project (provided, however, that the foregoing is in no event intended to limit Tenant's obligations under Section 28 or Section 30 of this Lease);

(y) except for the Amenities Fee (as defined in Section 40(a)), the costs, whether operating, maintenance, capital or otherwise, relating to The Alexandria and/or the Amenities, as such terms are defined in Section 41 (not including the cost of any ancillary services or items payable by Tenant in connection with its use of The Alexandria and/or the Amenities). For the avoidance of any doubt, Tenant shall be obligated to pay for all services and items payable by Tenant pursuant to Section 41 , the Standard Use Agreements and any other agreements executed by Tenant in connection with the use of the Amenities;

(z) reserves for repairs, maintenance and replacements;

(aa) rentals of equipment ordinarily considered to be of a capital nature (such as elevators and HVAC systems) except if such equipment is reasonably and customarily leased either temporarily or

permanently in the operation of Class A office and laboratory buildings in the Torrey Pines area of San Diego; provided, however, that in no event shall any specific piece of equipment that is part of the original construction of the Building be leased as part of such original construction of the Building and passed through as part of Operating Expenses (but, for the avoidance of any doubt any replacement of such equipment may be leased by Landlord and the cost thereof, to the extent such leasing costs do not exceed the capital costs of comparable purchased equipment amortized as set forth herein, passed through as part of Operating Expenses unless such cost is expressly required to be excluded as provided for in this clause (aa));

(bb) property management fees other than as specifically permitted above;

(cc) salaries, wages or other compensation paid to employees of any third party property management organization being paid a fee by Landlord for its services where such services are covered by a management fee;

(dd) costs of insurance deductibles in excess of deductibles that Tenant can demonstrate are "commercially reasonable deductible" amounts reasonably consistent with the amounts carried by owners of comparable projects in the Torrey Pines area of San Diego; provided , however , that deductibles in excess of $100,000 shall be amortized on a straight-line basis with interest at 8% per annum over the greater of ten (10) years or the then remaining Base Term of this Lease (exclusive of any extension of the Base Term, provided that if the greater period is 10 years and thereafter Tenant extends the Base Term of this Lease, then amortization shall continue during the Term, as extended, to the extent necessary to achieve a 10 year amortization from the date such payments commenced), and, for each year (or partial year) during such amortization period (including any extension of the Base Term), Operating Expenses shall include the amortized portion of such deductible allocable to such year (or partial year);

(ee) to the extent that Tenant does not lease space in the Spectrum 3 Building, costs incurred with respect to Common Areas located within and serving only tenants of the Spectrum 3 Building;

(ff) the cost of environmental testing conducted by Landlord pursuant to Section 30(d) which Landlord is prohibited from passing through to Tenant pursuant to Section 30(d) ;

(gg) the original construction costs of the Spectrum 3 Building and costs of correcting defects in such original construction of the Spectrum 3 Building;

(hh) the costs of improvements, maintenance, repairs or replacements to be made to the Spectrum 3 Building or any portion thereof; and

(ii) any expenses otherwise includable within Operating Expenses to the extent actually reimbursed by persons other than tenants of the Project under leases for space in the Project.

Notwithstanding anything to the contrary contained herein, commencing on the Rent Commencement Date, all costs and expenses of any kind incurred by Landlord or Tenant (including, without limitation, for operations, maintenance, repairs and/or replacements) with respect to the Exclusive Use Areas shall be fully allocable to the Building and Tenant shall be responsible for 100% of all such costs and expenses (except to the extent such costs are excluded from Operating Expenses pursuant to this Section 5). Tenant shall not be responsible for maintenance costs and expenses incurred by Landlord or any other tenant of the Project with respect to areas of the Project which may be designated by Landlord as exclusive use areas serving only the Spectrum 3 Building or areas of the Project that are materially inaccessible to Tenant, except to the extent caused by Tenant or any Tenant Party.

Within 90 days after the end of each calendar year (or such longer period as may be reasonably required not to exceed 180 days after the end of the calendar year), Landlord shall furnish to Tenant a statement (an " **Annual Statement** ") showing in reasonable detail: (a) the total and Tenant's Share of actual Operating Expenses for the previous calendar year, and (b) the total of Tenant's payments in respect of

Operating Expenses for such year. If Tenant's Share of actual Operating Expenses for such year exceeds Tenant's payments of Operating Expenses for such year, the excess shall be due and payable by Tenant as Rent within 30 days after delivery of such Annual Statement to Tenant. If Tenant's payments of Operating Expenses for such year exceed Tenant's Share of actual Operating Expenses for such year Landlord shall pay the excess to Tenant within 30 days after delivery of such Annual Statement, except that after the expiration, or earlier termination of the Term or if Tenant is delinquent in its obligation to pay Rent, Landlord shall pay the excess to Tenant after deducting all other amounts due Landlord. Landlord's and Tenant's obligations to pay any overpayments or deficiencies due pursuant to this paragraph shall survive the expiration or earlier termination of this Lease. Following November 30 th of each calendar year, Tenant shall not be responsible for the payment of items of Operating Expenses not reflected in the Annual Statement delivered by Landlord for the prior calendar year, except for Taxes for which Tenant is responsible under this Lease and/or any costs for which Landlord is billed after November 30 th of the calendar year in which the Annual Statement is delivered.

The Annual Statement shall be final and binding upon Tenant unless Tenant, within 180 days after Tenant's receipt thereof (or, with respect to any item for which Tenant is responsible under such Annual Statement for which Tenant is billed following Landlord's delivery of such Annual Statement to Tenant, within 180 days after Tenant's receipt of such bill), shall contest any item therein by giving written notice to Landlord, specifying each item contested and the reason therefor. If, during such applicable 180 day period, Tenant reasonably and in good faith questions or contests the accuracy of Landlord's statement of Tenant's Share of Operating Expenses, Landlord will provide Tenant (or a representative designated by Tenant by written notice to Landlord) with access to Landlord's books and records relating to the operation of the Project and such information reasonably necessary to evaluate the Operating Expenses (the " **Expense Information** "). If after Tenant's review of such Expense Information, Landlord and Tenant cannot agree upon the amount of Tenant's Share of Operating Expenses, then Tenant shall have the right to have an independent regionally or nationally recognized real estate company that provides operating expense auditing services selected by Tenant and approved by Landlord (which approval shall not be unreasonably withheld or delayed), working pursuant to a fee arrangement other than a contingent fee (at Tenant's sole cost and expense, except as otherwise expressly provided in this paragraph), audit and/or review the Expense Information for the year in question (the " **Independent Review** "). The results of any such Independent Review shall be binding on Landlord and Tenant. If the Independent Review shows that the payments actually made by Tenant with respect to Operating Expenses for the calendar year in question exceeded Tenant's Share of Operating Expenses for such calendar year, Landlord shall at Landlord's option either (i) credit the excess amount to the next succeeding installments of estimated Operating Expenses or (ii) pay the excess to Tenant within 30 days after delivery of such statement, except that after the expiration or earlier termination of this Lease or if Tenant is delinquent in its obligation to pay Rent, Landlord shall pay the excess to Tenant after deducting all other amounts due Landlord. If the Independent Review shows that Tenant's payments with respect to Operating Expenses for such calendar year were less than Tenant's Share of Operating Expenses for the calendar year, Tenant shall pay the deficiency to Landlord within 30 days after delivery of such statement. If the Independent Review shows that Tenant has overpaid with respect to Operating Expenses by more than 4% then Landlord shall reimburse Tenant for all costs incurred by Tenant for the Independent Review. Operating Expenses for the calendar years in which Tenant's obligation to share therein begins and ends shall be prorated.

Landlord and Tenant agree that the rentable square footage of the Premises and the Building set forth on page 1 of this Lease shall be the rentable square footage of the Premises and the Building during the Term of this Lease and shall not be subject to re-measurement unless expressly agreed to in writing by the parties (e.g., in connection with a Change Order (as defined in the Work Letter)).

Upon the substantial completion of the Spectrum 3 Building, Landlord shall determine the rentable square footage of the Spectrum 3 Building in accordance with either (i) ANSI/BOMA Z65.3-2009 for the Gross Areas of Building, if the Spectrum 3 Building will be a single tenant building, or (ii) the BOMA 2010 Standard Methods of Measurement for multi-tenant buildings, if the Spectrum 3 Building will be leased to multiple tenants. Once the rentable square footage of the Spectrum 3 Building has been determined pursuant

to the immediately preceding sentence, Landlord shall notify Tenant in writing of the rentable square footage of the Spectrum 3 Building. If the Rentable Area of Project (based on the rentable square footage of the Spectrum 3 Building plus the Rentable Area of the Building) deviates from the amount reflected in the definition of " **Rentable Area of Project** " on page 1 of this Lease, then this Lease shall be amended so as to (i) reflect the Rentable Area of Project (based on the rentable square footage of the Spectrum 3 Building plus the Rentable Area of the Building) and (ii) appropriately adjust the amount set forth in the definition of " **Building's Share of Operating Expenses of Project** " which was calculated based on the Rentable Area of Project set forth on page 1 of this Lease.

" **Tenant's Share** " shall be the percentage set forth on the first page of this Lease as Tenant's Share as reasonably adjusted by Landlord for changes in the physical size of the Premises or the Project occurring thereafter. For the avoidance of any doubt, Tenant shall pay as part of Operating Expenses the Building's Share of Operating Expenses of Project for those Operating Expenses which are not specific to the Building or the Spectrum 3 Building. Base Rent, Tenant's Share of Operating Expenses and all other amounts payable by Tenant to Landlord hereunder are collectively referred to herein as " **Rent** ."

6. **Intentionally Omitted** .

7. **Use** . The Premises shall be used solely for the Permitted Use set forth in the basic lease provisions on page 1 of this Lease, and in compliance with all laws, orders, judgments, ordinances, regulations, codes, directives, permits, licenses, covenants and restrictions now or hereafter applicable to the Premises, and to the use and occupancy thereof, including, without limitation, the Americans With Disabilities Act, 42 U.S.C. § 12101, et seq. (together with the regulations promulgated pursuant thereto, " **ADA** ") (collectively, " **Legal Requirements** " and each, a " **Legal Requirement** "). Tenant shall, upon 5 days' written notice from Landlord, discontinue any use of the Premises which is declared by any Governmental Authority (as defined in Section 9) having jurisdiction to be a violation of a Legal Requirement. Tenant will not use or permit the Premises to be used for any purpose or in any manner that would void Tenant's or Landlord's insurance or cause the disallowance of any sprinkler credits. Tenant shall reimburse Landlord promptly upon demand for any additional premium charged for any such insurance policy by reason of Tenant's failure to comply with the provisions of this Section or otherwise caused by Tenant's use and/or occupancy of the Premises (other than for general office and non-hazardous laboratory purposes). Tenant will use the Premises in compliance with this Lease and will not commit or permit waste, overload the floor or structure of the Premises, subject the Premises to use that would damage the Premises (other than ordinary wear and tear) or unreasonably obstruct or unreasonably interfere with the rights of Landlord or other tenants or occupants of the Project, including conducting or giving notice of any auction, liquidation, or going out of business sale on the Premises, or use or allow the Premises to be used for any unlawful purpose. Tenant shall cause any equipment or machinery to be installed in the Premises so as to reasonably prevent sounds or vibrations from the Premises from extending into Common Areas located outside the Building, or other improved space in the Project. Tenant shall not place any machinery or equipment which would overload the floor in or upon the Premises.

Landlord shall be responsible, at Landlord's cost and not as part of Operating Expenses, for the compliance of the Common Areas of the Project (located outside the Building) and Landlord's Work with Legal Requirements as of Shell Substantial Completion (as defined in the Work Letter). If, following the Shell Substantial Completion, the Common Areas of the Project and/or Landlord's Work are determined not to be in compliance with Legal Requirements as of the Shell Substantial Completion, Landlord shall, within a reasonable period following such determination, perform, at Landlord's sole cost and expense and not as part of Operating Expenses, the alterations or improvements to the Common Areas of the Project or Landlord's Work, as applicable, required to cause the Common Areas of the Project and Landlord's Work to be in compliance with Legal Requirements as of Shell Substantial Completion. Following the Commencement Date, Landlord shall, as an Operating Expense (to the extent such Legal Requirement is generally applicable to similar buildings in the area in which the Project is located) and at Tenant's expense (to the extent such Legal Requirement is triggered by reason of Tenant's, as compared to other tenants of the Project, specific use of the Premises or Tenant's Alterations) make any alterations or modifications to the Common Areas or

the exterior of the Building that are required by Legal Requirements. Except as provided in the 2 immediately preceding sentences, Tenant, at its sole expense, shall make any alterations or modifications to the interior or the exterior of the Premises or the Project that are required by Legal Requirements (including, without limitation, compliance of the Premises with the ADA) related to Tenant's use or occupancy of the Premises. Notwithstanding any other provision herein to the contrary, Tenant shall be responsible for any and all demands, claims, liabilities, losses, costs, expenses, actions, causes of action, damages or judgments, and all reasonable expenses incurred in investigating or resisting the same (including, without limitation, reasonable attorneys' fees, charges and disbursements and costs of suit) (collectively, " **Claims** ") arising out of or in connection with Legal Requirements related to Tenant's particular use or occupancy of the Premises or Tenant's Alterations. For purposes of Section 1938 of the California Civil Code, as of the date of this Lease, the Project has not been inspected by a certified access specialist.

8. **Holding Over** . If, with Landlord's express written consent, Tenant retains possession of the Premises after the termination of the Term, (i) unless otherwise agreed in such written consent, such possession shall be subject to immediate termination by Landlord at any time, (ii) all of the other terms and provisions of this Lease (including, without limitation, the adjustment of Base Rent pursuant to Section 4 hereof) shall remain in full force and effect (excluding any expansion or renewal option or other similar right or option) during such holdover period, (iii) Tenant shall continue to pay Base Rent in the amount payable upon the date of the expiration or earlier termination of this Lease or such other amount as Landlord may indicate, in Landlord's sole and absolute discretion, in such written consent, and (iv) all other payments shall continue under the terms of this Lease. If Tenant remains in possession of the Premises after the expiration or earlier termination of the Term without the express written consent of Landlord, (A) Tenant shall become a tenant at sufferance upon the terms of this Lease except that the monthly Base Rent shall be equal to 150% of Base Rent in effect during the last 30 days of the Term, and (B) Tenant shall be responsible for all damages suffered by Landlord resulting from or occasioned by Tenant's holding over, including consequential damages. Notwithstanding the foregoing, if Tenant notifies Landlord in writing no less than 90 days prior to the expiration or earlier termination of the Term of Tenant's intention to hold over, then (w) Tenant shall become a tenant at sufferance upon the terms of this Lease except that the monthly Base Rent shall (1) for the first 30 days of the holdover period, be equal to 125% of Base Rent in effect during the last 30 days of the Term, and (2) thereafter, commencing on the 31 st day of such holdover period, be equal to 150% of Base Rent in effect during the last 30 days of the Term, (x) for the first 30 days of such holdover period, Tenant shall not be responsible for any damages suffered by Landlord resulting from or occasioned by Tenant's holding over, (y) for the period commencing on the 31 st day through the 90 th day of such holdover period, Tenant shall only be responsible for any direct damages suffered by Landlord resulting from or occasioned by Tenant's holding over, and (z) following the 90 th day of such holdover period, Tenant shall be responsible for all damages suffered by Landlord resulting from or occasioned by Tenant's holding over, including consequential damages. No holding over by Tenant, whether with or without consent of Landlord, shall operate to extend this Lease except as otherwise expressly provided, and this Section 8 shall not be construed as consent for Tenant to retain possession of the Premises. Acceptance by Landlord of Rent after the expiration of the Term or earlier termination of this Lease shall not result in a renewal or reinstatement of this Lease.

9. **Taxes** . Landlord shall pay, as part of Operating Expenses, all taxes, levies, fees, assessments and governmental charges of any kind, existing as of the Commencement Date or thereafter enacted (collectively referred to as " **Taxes** "), imposed by any federal, state, regional, municipal, local or other governmental authority or agency, including, without limitation, quasi-public agencies (collectively, " **Governmental Authority** ") during the Term, including, without limitation, all Taxes: (i) imposed on or measured by or based, in whole or in part, on rent payable to (or gross receipts received by) Landlord under this Lease and/or from the rental by Landlord of the Project or any portion thereof, or (ii) based on the square footage, assessed value or other measure or evaluation of any kind of the Premises or the Project, or (iii) assessed or imposed by or on the operation or maintenance of any portion of the Premises or the Project, including parking, or (iv) assessed or imposed by, or at the direction of, or resulting from Legal Requirements, or interpretations thereof, promulgated by any Governmental Authority, or (v) imposed as a license or other fee, charge, tax, or assessment on Landlord's business or occupation of leasing space in the Project. Landlord

may, at Landlord's sole discretion or as otherwise reasonably agreed upon by Landlord and Tenant, contest by appropriate legal proceedings the amount, validity, or application of any Taxes or liens securing Taxes. Any written request received by Landlord from Tenant requesting that Landlord contest Taxes shall be considered by Landlord in good faith and Landlord's approval of such request shall not be unreasonably withheld, conditioned or delayed. If Landlord agrees to contest Taxes pursuant to a request from Tenant, the reasonable costs and expenses in connection with such contest of Taxes shall be borne by Tenant. Notwithstanding anything to the contrary herein, Landlord shall only charge Tenant for assessments as if those assessments were paid by Landlord over the longest possible term which Landlord is permitted to pay for the applicable assessments without additional charge other than interest, if any, provided under the terms of the underlying assessments. If Landlord secures an abatement or refund of Taxes for the Project for a period during the Term, Tenant shall receive Tenant's Share of such abatement or refund (i.e., the net amount after paying all reasonable costs and expenses of security the abatement or refund, including reasonably attorneys' fees) as a credit to be applied by Landlord against Operating Expenses next coming due (or, if no further Operating Expenses are due from Tenant under this Lease and Tenant is not in Default under this Lease, by a cash payment to Tenant). Taxes shall not include any net income taxes, or any capital, stock, succession, transfer, franchise, gift, estate or inheritance taxes imposed on Landlord except to the extent such taxes are in substitution for any Taxes payable hereunder, nor shall Taxes include any late payments, penalties or fines (except to the extent such late penalties, penalties or fines are incurred as a result of Tenant's timely failure to pay Tenant's Share of Taxes as required under this Lease). Taxes shall also not include any items to the extent otherwise included in Operating Expenses, costs incurred by Landlord with respect to the original development and construction of the Building, Taxes accruing with respect to the Building (and the development of the Building) prior to the Rent Commencement Date, costs incurred with respect to the original development and construction of Spectrum 3 Building, reserves for future taxes, or any development fee (whether payable on a one-time or annual basis) imposed on Landlord specifically as a condition for the issuance of the development permit for the Building (e.g., fees for transit, housing, schools, open space, child care, arts programs, traffic mitigations measures, environmental impact reports and traffic studies; provided, however, that Tenant shall be required to comply with any traffic demand management plans applicable to the Project and the costs thereof shall be included as part of Operating Expenses). If any such Tax is levied or assessed directly against Tenant, then Tenant shall be responsible for and shall pay the same at such times and in such manner as the taxing authority shall require. Tenant shall pay, prior to delinquency, any and all Taxes levied or assessed against any personal property or trade fixtures placed by Tenant in the Premises, whether levied or assessed against Landlord or Tenant. If any Taxes on Tenant's personal property or trade fixtures are levied against Landlord or Landlord's property, or if the assessed valuation of the Project is increased by a value attributable to improvements in or alterations to the Premises, whether owned by Landlord or Tenant and whether or not affixed to the real property so as to become a part thereof, higher than the base valuation on which Landlord from time-to-time allocates Taxes to all tenants in the Project, Landlord shall have the right, but not the obligation, to pay such Taxes. Landlord's determination of any excess assessed valuation shall be binding and conclusive, absent manifest error. The amount of any such payment by Landlord shall constitute Additional Rent due from Tenant to Landlord within 30 days following demand.

10. **Parking** . Subject to all matters of record, Force Majeure, a Taking (as defined in Section 19 below) and the exercise by Landlord of its rights hereunder, Tenant shall have the right, at no additional cost to Tenant during the Base Term, to use 400 parking spaces at the Project, subject to Landlord's reasonable rules and regulations. Tenant shall have the exclusive right to use all of the parking spaces located in the subterranean parking garage under the Building, which shall be applied against the total number of parking spaces made available for Tenant's use pursuant to the immediately preceding sentence. Tenant shall have the right to install, subject to compliance with Legal Requirements, a roll down door at the main entrance of the subterranean parking garage to control access to the subterranean parking garage via the use of Building access cards. The balance of the parking spaces available for Tenant's use shall be located in the portions of surface parking lot located on and serving the Project designated for non-reserved parking in common with other tenants of the Project. Tenant will use reasonable efforts to cause the parking spaces located in the subterranean parking garage to be fully occupied before using parking spaces in the surface parking lot located on and serving the Project. Landlord shall in no event grant rights to other tenants

of the Project to use more parking spaces in the surface parking lot than, together with the spaces allocated to Tenant pursuant to this Section 10 , are available for use by tenants of the Project in the surface parking lot. Notwithstanding anything to the contrary contained herein, Landlord has the right, during periods of lower demand for parking by Tenant (e.g., after regular business hours) and following written notice to Tenant, to use the surface parking lots serving the Project on a temporary and occasional basis for invitees of The Alexandria. The terms of **Exhibit G** attached hereto shall apply with respect to any installation by Tenant of electric vehicle car charging stations at the Project. The plan attached as **Exhibit A** reflects the subterranean parking at the Building currently contemplated by Landlord. Landlord shall not reduce the number of parking spaces in the subterranean parking garage shown on such plan unless required to do so in connection with the Approvals and only after obtaining Tenant's written consent thereto, which consent shall not be unreasonably withheld, conditioned or delayed. Tenant shall not reduce the number of parking spaces in the subterranean parking garage as shown on the plan without Landlord's written consent thereto, which consent shall not be unreasonably withheld, conditioned or delayed.

11. **Utilities, Services** . To the extent that Tenant may do so, Tenant shall contract directly with utility providers for all water, electricity, gas (if applicable), sewer and other utilities, and refuse and trash collection (" **Utilities** ") required by Tenant for the Premises following the Rent Commencement Date and continuing during the Term. Landlord shall cooperate with Tenant, at no cost to Landlord, in making such arrangement with the Utility providers. If billed directly to Tenant, Tenant shall pay directly to such Utility providers prior to delinquency for all such Utilities furnished to Tenant or the Project during the Term and shall pay for all maintenance charges for Utilities, and any storm sewer charges or other similar charges for Utilities imposed by any Governmental Authority or Utility provider, and any taxes, penalties, surcharges or similar charges thereon. To the extent that any Utilities, maintenance charges for Utilities, any storm sewer charges or other similar charges for Utilities imposed by any Governmental Authority or Utility provider, or any taxes, penalties, surcharges or similar charges are paid for by Landlord, Tenant shall reimburse Landlord for such costs as Operating Expenses. Except as otherwise expressly provided in this Lease, no interruption or failure of Utilities, from any cause whatsoever other than Landlord's gross negligence or willful misconduct, shall result in eviction or constructive eviction of Tenant, termination of this Lease or the abatement of Rent. Tenant shall be responsible for obtaining and paying for its own janitorial services for the Premises.

Notwithstanding anything to the contrary set forth herein, if (i) a stoppage of an Essential Service (as defined below) to the Premises shall occur and such stoppage is due solely to the gross negligence or willful misconduct of Landlord and not due in any part to any act or omission on the part of Tenant or any Tenant Party or any matter beyond Landlord's reasonable control (any such stoppage of an Essential Service being hereinafter referred to as a " **Service Interruption** "), and (ii) such Service Interruption continues for more than 5 consecutive business days after Landlord shall have received written notice thereof from Tenant, and (iii) as a result of such Service Interruption, the conduct of Tenant's normal operations in the Premises are materially and adversely affected, then there shall be an abatement of one day's Base Rent and Operating Expenses for each day during which such Service Interruption continues after such 5 business day period; provided, however, that if any part of the Premises is reasonably useable for Tenant's normal business operations or if Tenant conducts all or any part of its operations in any portion of the Premises notwithstanding such Service Interruption, then the amount of each daily abatement of Base Rent and Operating Expenses shall only be proportionate to the nature and extent of the interruption of Tenant's normal operations or ability to use the Premises. Except for the self-help rights provided for in Section 31 below, the rights granted to Tenant under this paragraph shall be Tenant's sole and exclusive remedy resulting from a Service Interruption, and Landlord shall not otherwise be liable for any loss or damage suffered or sustained by Tenant resulting from any failure or cessation of services. For purposes hereof, the term " **Essential Services** " shall mean the following services: gas, water, sewer and electricity, but in each case only to the extent that Landlord has an obligation to provide same to Tenant under this Lease.

12. **Alterations and Tenant's Property** . The Tenant's Work shall be governed by the Work Letter and not this Section 12 . Any alterations, additions, or improvements made to the Premises by or on behalf of Tenant, including additional locks or bolts of any kind or nature upon any doors or windows in the Premises, but excluding the installation, removal or realignment of furniture systems (other than removal of

furniture systems owned or paid for by Landlord) not involving any modifications to the structure or connections (other than by ordinary plugs or jacks) to Building Systems (as defined in Section 13) (" **Alterations** ") shall be subject to Landlord's prior written consent, which may be given or withheld in Landlord's sole discretion if any such Alteration materially, adversely affects the structure or Building Systems and shall not be otherwise unreasonably withheld, conditioned or delayed. Notwithstanding the foregoing, Tenant may construct non-structural Alterations in the Premises without advance notice to Landlord if the cost of such work does not exceed $250,000 per project (" **No Notice Alterations** "). Upon written request from Landlord not more than once each calendar year, Tenant shall provide "as built" plans for any No Notice Alterations constructed by Tenant in the Premises. Notwithstanding the foregoing, Tenant shall be required to request Landlord's prior written approval with respect to any Alteration that would constitute a No Notice Alteration if such No Notice Alteration would materially diminish the value of any existing leasehold improvements (e.g., converting any laboratory space to office space). If Landlord approves any Alterations, Landlord may impose such conditions on Tenant in connection with the commencement, performance and completion of such Alterations as Landlord may deem appropriate in Landlord's reasonable discretion. Any request for approval shall be in writing, delivered not less than 15 days in advance of any proposed construction, and accompanied by plans, specifications, bid proposals, work contracts and such other information concerning the nature and cost of the alterations as may be reasonably requested by Landlord, including the identities and mailing addresses of all persons performing work or supplying materials. Landlord's right to review plans and specifications and to monitor construction shall be solely for its own benefit, and Landlord shall have no duty to ensure that such plans and specifications or construction comply with applicable Legal Requirements. Tenant shall cause, at its sole cost and expense, all Alterations to comply with insurance requirements and with Legal Requirements and shall implement at its sole cost and expense any alteration or modification required by Legal Requirements as a result of any Alterations. Tenant shall pay to Landlord, as Additional Rent, on demand an amount equal to the out-of-pocket cost incurred by Landlord in connection with any Alteration to cover Landlord's overhead and expenses for plan review, coordination, scheduling and supervision. Before Tenant begins any Alteration, Landlord may post on and about the Premises notices of non-responsibility pursuant to applicable law. Tenant shall reimburse Landlord for, and indemnify and hold Landlord harmless from, any expense incurred by Landlord by reason of faulty work or inadequate cleanup done by Tenant or its contractors.

Tenant shall cause the completion of all Alterations work free and clear of liens, and shall provide (and cause each contractor or subcontractor to provide) certificates of insurance for workers' compensation and other coverage in amounts and from an insurance company reasonably satisfactory to Landlord protecting Landlord against liability for personal injury or property damage during construction. Upon completion of any Alterations, Tenant shall deliver to Landlord: (i) sworn statements setting forth the names of all contractors and subcontractors who did the work and final lien waivers from all such contractors and subcontractors; and (ii) "as built" plans for any such Alteration.

Except for Removable Installations (as hereinafter defined), all Installations (as hereinafter defined) shall be and shall remain the property of Landlord during the Term and following the expiration or earlier termination of the Term, shall not be removed by Tenant at any time during the Term, and shall remain upon and be surrendered with the Premises as a part thereof. Notwithstanding the foregoing, if Tenant requests in writing at the time Tenant requests approval of any Installation that Landlord determine whether or not Landlord will require removal of an Installation at the expiration or earlier termination of the Term, Landlord shall, within 10 business days after such request, notify Tenant of its determination. If Landlord by such determination requires that Tenant remove such Installation upon the expiration or earlier termination of the Term, Tenant shall do so in accordance with the immediately succeeding sentence. Upon the expiration or earlier termination of the Term, Tenant shall remove (i) all wires, cables or similar equipment which Tenant has installed in the Premises or in the risers or plenums of the Building other than those installed as part of the Tenant's Work, (ii) any Installations for which Landlord has given Tenant timely notice of removal in accordance with the immediately preceding sentence, and (iii) all of Tenant's Property (as hereinafter defined), and Tenant shall restore and repair any damage caused by or occasioned as a result of such removal, including, without limitation, capping off all such connections behind the walls of the Premises and repairing any holes. During any restoration period beyond the expiration or earlier termination of the Term, Tenant

shall pay Rent to Landlord as provided herein as if said space were otherwise occupied by Tenant. If Landlord is requested by Tenant or any lender, lessor or other person or entity claiming an interest in any of Tenant's Property to waive any lien Landlord may have against any of Tenant's Property, and Landlord consents to such waiver, then Landlord shall be entitled to be paid as administrative rent a fee of $1,000 per occurrence for its time and effort in preparing and negotiating such a waiver of lien.

For purposes of this Lease, (x) " **Removable Installations** " means any items listed on **Exhibit F** attached hereto and any items agreed by Landlord in writing to be included on **Exhibit F** in the future, (y) " **Tenant's Property** " means Removable Installations and, other than Installations, any trade fixtures, personal property or equipment of Tenant that may be removed provided that after such removal and repair of any damage caused by such removal there is no remaining material damage to the Premises and such removal and repair does not adversely affect the operation of any Building Systems or the operations of any laboratory spaces within the Premises, and (z) " **Installations** " means all installed or affixed property of any kind paid for with the TI Fund, all Alterations, all fixtures, and all partitions, hardware, built-in machinery, built-in casework and cabinets and other similar additions, equipment, property and improvements built into the Premises so as to become an integral part of the Premises, including, without limitation, fume hoods which penetrate the roof or plenum area, installed cage washers, built-in cold rooms, built-in warm rooms, walk-in cold rooms, walk-in warm rooms, deionized water systems, HVAC, chillers, built-in plumbing, electrical and mechanical equipment and systems, and any installed power generator and transfer switch.

13. **Landlord's Repairs** . Landlord, as an Operating Expense, shall maintain all of the structural (including the roof and exterior walls), exterior, parking (including the subterranean garage) and other Common Areas of the Project, including HVAC, plumbing, fire sprinklers, elevators and all other building systems serving the Premises and other portions of the Project (" **Building Systems** "), in good repair, reasonable wear and tear and uninsured losses and damages caused by Tenant, or by any of Tenant's assignees, sublessees, licensees, agents, servants, employees, invitees and contractors (or any of Tenant's assignees, sublessees and/or licensees respective agents, servants, employees, invitees and contractors) (each, a " **Tenant Party** " and collectively, " **Tenant Parties** ") excluded. Losses and damages caused by Tenant or any Tenant Party shall be repaired by Landlord, to the extent not covered by insurance, at Tenant's sole cost and expense. Landlord reserves the right to stop Building Systems services when reasonably necessary (i) by reason of accident or emergency, or (ii) after delivery of written notice to Tenant and reasonable efforts to coordinate with Tenant to minimize disruption to Tenant's operations, for planned repairs, alterations or improvements, which are, in the judgment of Landlord, desirable or necessary to be made, until said repairs, alterations or improvements shall have been completed. Landlord shall have no responsibility or liability for failure to supply Building Systems services during any such period of interruption; provided , however , that Landlord shall, except in case of emergency, provide Tenant 5 days advance notice of any planned stoppage of Building Systems services for routine maintenance, repairs, alterations or improvements. Tenant shall promptly give Landlord written notice of any repair required by Landlord pursuant to this Section of which Tenant is aware, after which Landlord shall make a commercially reasonable effort to effect such repair. Landlord shall not be liable for any failure to make any repairs or to perform any maintenance unless such failure shall persist for an unreasonable time after Tenant's written notice of the need for such repairs or maintenance. Tenant waives its rights under any state or local law to terminate this Lease or, except for the self-help rights provided for in Section 31 below, to make such repairs at Landlord's expense and agrees that the parties' respective rights with respect to such matters shall be solely as set forth herein. Repairs required as the result of fire, earthquake, flood, vandalism, war, or similar cause of damage or destruction shall be controlled by Section 18 .

Tenant shall have the self-help rights provided for in Section 31 .

Notwithstanding anything to the contrary contained in this Lease, as of the Rent Commencement Date, the maintenance and repair obligations for the Building shall be allocated between Landlord and Tenant as set forth on **Exhibit L** attached hereto. The maintenance obligations allocated to Tenant pursuant to **Exhibit L** (the " **Tenant Maintenance Obligations** ") shall be performed by Tenant at Tenant's sole cost and expense. The Tenant Maintenance Obligations shall include the procurement and maintenance of contracts,

in form and substance reasonably satisfactory to Landlord, with copies to Landlord upon Landlord's written request, for and with contractors reasonably acceptable to Landlord specializing and experienced in the respective Tenant Maintenance Obligations. If Landlord does not object to a contract provided by Tenant to Landlord for approval within 5 business days after Landlord's receipt of such contract from Tenant, such contract shall be deemed approved. Notwithstanding anything to the contrary contained herein, the scope of work of any such contracts entered into by Tenant pursuant to this paragraph shall, at a minimum, comply with manufacturer's recommended maintenance procedures for the optimal performance of the applicable equipment. Landlord shall, notwithstanding anything to the contrary contained in this Lease, have no obligation to perform any Tenant Maintenance Obligations. The Tenant Maintenance Obligations shall not include the right or obligation on the part of Tenant to make any structural and/or capital repairs or improvements to the Project, and Landlord shall, during any period that Tenant is responsible for the Tenant Maintenance Obligations, continue to be responsible, as part of Operating Expenses, for capital repairs and replacements required to be made to the Project. If Tenant fails to maintain any portion of the Building for which Tenant is responsible as part of the Tenant Maintenance Obligations in a manner reasonably acceptable to Landlord within the requirements of this Lease, Landlord shall have the right, but not the obligation, to provide Tenant with written notice thereof and to assume the Tenant Maintenance Obligations if Tenant does not cure Tenant's failure within 30 days after receipt of such notice.

14. **Tenant's Repairs** . Subject to Section 13 hereof, Tenant, at its expense, shall repair, replace and maintain in good condition all portions of the Premises, including, without limitation, entries, doors, ceilings, interior windows, interior walls, and the interior side of demising walls. Such repair and replacement may include capital expenditures and repairs whose benefit may extend beyond the Term. Should Tenant fail to make any such repair or replacement or fail to maintain the Premises, Landlord shall give Tenant notice of such failure. If Tenant fails to commence cure of such failure within 30 days of Landlord's notice, and thereafter diligently prosecute such cure to completion, Landlord may perform such work and shall be reimbursed by Tenant within 30 days after demand therefor; provided, however, that if such failure by Tenant creates or could create an emergency, Landlord may immediately commence cure of such failure and shall thereafter be entitled to recover the costs of such cure from Tenant. Subject to Sections 17 and 18 , Tenant shall bear the full uninsured cost of any repair or replacement to any part of the Project that results from damage caused by Tenant or any Tenant Party and any repair that benefits only the Premises.

15. **Mechanic's Liens** . Tenant shall discharge, by bond or otherwise, any mechanic's lien filed against the Premises or against the Project for work claimed to have been done for, or materials claimed to have been furnished to, Tenant within 15 business days after the filing thereof, at Tenant's sole cost and shall otherwise keep the Premises and the Project free from any liens arising out of work performed, materials furnished or obligations incurred by Tenant. Should Tenant fail to discharge any lien described herein, Landlord shall have the right, but not the obligation, to pay such claim or post a bond or otherwise provide security to eliminate the lien as a claim against title to the Project and the cost thereof shall be immediately due from Tenant as Additional Rent. If Tenant shall lease or finance the acquisition of office equipment, furnishings, or other personal property of a removable nature utilized by Tenant in the operation of Tenant's business, Tenant warrants that any Uniform Commercial Code Financing Statement filed as a matter of public record by any lessor or creditor of Tenant will upon its face or by exhibit thereto indicate that such Financing Statement is applicable only to removable personal property of Tenant located within the Premises. In no event shall the address of the Project be furnished on the statement without qualifying language as to applicability of the lien only to removable personal property, located in an identified suite held by Tenant.

16. **Indemnification** . Tenant hereby indemnifies and agrees to defend, save and hold Landlord harmless from and against any and all Claims for injury or death to persons or damage to property occurring within or about the Premises, arising directly or indirectly out of use or occupancy of the Premises or a breach or default by Tenant in the performance of any of its obligations hereunder, except to the extent caused by the willful misconduct or negligence of Landlord. Landlord shall not be liable to Tenant for, and Tenant assumes all risk of damage to, personal property (including, without limitation, loss of records kept within the Premises). Tenant further waives any and all Claims for injury to Tenant's business or loss of income relating to any such damage or destruction of personal property (including, without limitation, any loss of

records). Landlord shall not be liable for any damages arising from any act, omission or neglect of any tenant in the Project or of any other third party.

Subject to all of the other provisions of this Lease including, without limitation, the waivers provided for in Section 17 , Landlord hereby indemnifies and agrees to defend, save and hold Tenant harmless from and against any and all third party Claims for injury or death to persons or damage to property occurring at the Project (outside of the Premises) to the extent caused by the willful misconduct or negligence of Landlord.

Notwithstanding any contrary provision of this Lease, neither party shall be liable to the other party for any consequential damages arising under this Lease; provided that this sentence shall not apply to Landlord's damages (x) as expressly provided for in Section 8 , and/or (y) in connection with Tenant's obligations as more fully set forth in Section 30 . In no event shall the foregoing limit the damages to which Landlord is entitled under Section 21(c)(ii)(A)-(D) .

17. **Insurance** . Landlord shall maintain all risk property and, if applicable, sprinkler damage insurance covering the full replacement cost of the Project. Landlord shall further procure and maintain (i) commercial general liability insurance with a single loss limit of not less than $2,000,000 for bodily injury and property damage with respect to the Project, and (ii) earthquake coverage (provided that such earthquake coverage may, at Landlord's option, be included in a blanket policy and may be sublimited). Landlord may, but is not obligated to, maintain such other insurance and additional coverages as it may deem reasonably necessary, including, but not limited to, flood, environmental hazard, loss or failure of building equipment, errors and omissions, rental loss during the period of repair or rebuilding, workers' compensation insurance and fidelity bonds for employees employed to perform services and insurance for any improvements installed by Tenant or which are in addition to the standard improvements customarily furnished by Landlord without regard to whether or not such are made a part of the Project. All such insurance shall be included as part of the Operating Expenses. The Project may be included in a blanket policy (in which case the cost of such insurance allocable to the Project will be reasonably determined by Landlord based upon the insurer's cost calculations). At least 60% of the all risk capacity insurers under such blanket policy shall have a rating of not less than policyholder rating of A- and financial category rating of at least Class IX in "Best's Insurance Guide". Tenant shall also reimburse Landlord for any increased premiums or additional insurance which Landlord reasonably deems necessary as a result of the particular use of the Premises by Tenant or any Tenant Parties.

Tenant, at its sole cost and expense, shall maintain during the Term: all risk property insurance with business interruption and extra expense coverage, covering the full replacement cost of all property and improvements installed or placed in the Premises by Tenant at Tenant's expense; workers' compensation insurance with no less than the minimum limits required by law; employer's liability insurance with such limits as required by law; and commercial general liability insurance, with a minimum limit of not less than $5,000,000 per occurrence for bodily injury and property damage with respect to the Premises. The commercial general liability insurance policy shall name Alexandria Real Estate Equities, Inc., and Landlord, its officers, directors, employees, managers, agents, invitees and contractors (each a " **Landlord Party** " and collectively, " **Landlord Parties** "), as additional insureds; insure on an occurrence and not a claims-made basis; be issued by insurance companies which have a rating of not less than policyholder rating of A- and financial category rating of at least Class IX in "Best's Insurance Guide"; shall not be cancelable for nonpayment of premium unless 10 days prior written notice shall have been given to Landlord from the insurer; not contain a hostile fire exclusion; contain a contractual liability endorsement; and provide primary coverage to Landlord (any policy issued to Landlord providing duplicate or similar coverage shall be deemed excess over Tenant's policies). Certificates of insurance showing the limits of coverage required hereunder and showing Landlord as an additional insured shall be delivered to Landlord by Tenant prior to (i) the earlier to occur of (x) the Commencement Date, or (y) the date that Tenant accesses the Premises under this Lease, and (ii) each renewal of said insurance. Tenant's policy may be a "blanket policy" with an aggregate per location endorsement which specifically provides that the amount of insurance shall not be prejudiced by other losses covered by the policy. Tenant shall, at least 5 days prior to the expiration of such policies, furnish Landlord with renewal certificates.

In each instance where insurance is to name Landlord as an additional insured, Tenant shall upon written request of Landlord also designate and furnish certificates so evidencing Landlord as additional insured to: (i) any lender of Landlord holding a security interest in the Project or any portion thereof, (ii) the landlord under any lease wherein Landlord is tenant of the real property on which the Project is located, if the interest of Landlord is or shall become that of a tenant under a ground or other underlying lease rather than that of a fee owner, and/or (iii) any management company retained by Landlord to manage the Project.

Notwithstanding anything in this Section 17 to the contrary, for so long as Tenant can provide Landlord with reasonably acceptable evidence that Tenant is maintaining an equity market cap of not less than $15,000,000,000, Tenant may self-insure for the insurance required by Tenant to be maintained pursuant to this Section 17 . With respect to Tenant's self-insurance, Landlord and Tenant agree as follows: (a) that Tenant's self-insurance shall be treated as actual insurance and that such self-insurance shall be the primary coverage for every risk for which Tenant is liable or responsible hereunder; (b) the waiver of subrogation provisions set forth in this Lease shall apply to Tenant's self-insurance as though Tenant were maintaining the insurance required under this Lease, (c) Tenant shall bear the entire cost of the defense of any claim for which it is responsible under the terms of this Lease including, without limitation, the defense of Landlord, and (d) Tenant shall use its own funds to pay any claim or indemnity or replace any property or otherwise provide the funding which would have been available from insurance proceeds but for Tenant's election to self-insure. If Tenant elects to self-insure, Landlord shall be considered to be covered by the same insurance terms, including, but not limited to, insuring grants, exclusions, conditions and limits, by which it would have been covered had insurance covering such risk been in effect. Notwithstanding anything to the contrary contained in this Lease, Tenant hereby releases Landlord from any liability for loss or damage caused by Landlord and/or any Landlord Party against which Tenant has elected to self-insure but which Tenant would otherwise be required to insure against under this Lease and in no event shall Landlord be liable for any loss or damage which Landlord would not otherwise be responsible but for Tenant's election to self insure. The right to self-insure shall only apply to Vertex Pharmaceuticals Incorporated.

The property insurance obtained by Landlord and Tenant shall include a waiver of subrogation by the insurers and all rights based upon an assignment from its insured, against Landlord or Tenant, and their respective officers, directors, employees, managers, agents, invitees and contractors (" **Related Parties** "), in connection with any loss or damage thereby insured against. Neither party nor its respective Related Parties shall be liable to the other for loss or damage caused by any risk insured against under property insurance required to be maintained hereunder, and each party waives any claims against the other party, and its respective Related Parties, for such loss or damage. The failure of a party to insure its property shall not void this waiver. Landlord and its respective Related Parties shall not be liable for, and Tenant hereby waives all claims against such parties for, business interruption and losses occasioned thereby sustained by Tenant or any person claiming through Tenant resulting from any accident or occurrence in or upon the Premises or the Project from any cause whatsoever. If the foregoing waivers shall contravene any law with respect to exculpatory agreements, the liability of Landlord or Tenant shall be deemed not released but shall be secondary to the other's insurer.

Landlord may require insurance policy limits described in this Section 17 to be raised to conform with requirements of Landlord's lender and/or insurance consultants; provided, however, that the increased amount of coverage is consistent with coverage amounts then being required by institutional owners of Class A buildings in the Torrey Pines area of San Diego other than Landlord and affiliates of Landlord.

18. **Restoration** . If, at any time during the Term, the Premises are damaged or destroyed by a fire or other casualty, Landlord shall notify Tenant within 60 days after discovery of such damage as to the amount of time Landlord reasonably estimates it will take to restore the Premises, as applicable (the " **Restoration Period** "). If the Restoration Period is estimated to exceed 12 months (the " **Maximum Restoration Period** "), or if Landlord reasonably determines such casualty to be an uninsured casualty, Landlord may, in such notice, elect to terminate this Lease as of the date that is 75 days after the date of discovery of such damage or destruction; provided, however , that notwithstanding Landlord's election to restore, Tenant may elect to terminate this Lease by written notice to Landlord delivered within 15 business

days of receipt of a notice from Landlord estimating a Restoration Period for the Premises longer than the Maximum Restoration Period. Unless either Landlord or Tenant so elects to terminate this Lease, Landlord shall, subject to receipt of sufficient insurance proceeds other than any shortfall resulting from Landlord's failure to maintain the insurance required to be maintained by Landlord pursuant to Section 17 (with any deductible to be treated as an Operating Expense subject to and in accordance with Section 5), use good faith efforts to promptly restore the Premises (excluding the improvements installed by Tenant or by Landlord and paid for by Tenant), subject to delays arising from the collection of insurance proceeds, from Force Majeure events or as needed to obtain any license, clearance or other authorization of any kind required to enter into and restore the Premises issued by any Governmental Authority having jurisdiction over the use, storage, handling, treatment, generation, release, disposal, removal or remediation of Hazardous Materials (as defined in Section 30) in, on or about the Premises (collectively referred to herein as " **Hazardous Materials Clearances** "); provided , however , that if repair or restoration of the Premises is not substantially complete as of the end of the Maximum Restoration Period or, if longer, the Restoration Period, Landlord may, in its sole and absolute discretion, by written notice to Tenant delivered within 15 business days of the expiration of the Maximum Restoration Period or, if longer, the Restoration Period elect not to proceed with such repair and restoration, or Tenant may by written notice to Landlord delivered within 15 business days of the expiration of the Maximum Restoration Period or, if longer, the Restoration Period, elect to terminate this Lease, in which event Landlord shall be relieved of its obligation to make such repairs or restoration and this Lease shall terminate as of the date that is 75 days after the later of: (i) discovery of such damage or destruction, or (ii) the date all required Hazardous Materials Clearances are obtained.

Tenant, at its expense, shall promptly perform, subject to delays arising from the collection of insurance proceeds, from Force Majeure (as defined in Section 34) events or to obtain Hazardous Material Clearances, all repairs or restoration not required to be done by Landlord and shall promptly re-enter the Premises and commence doing business in accordance with this Lease. Notwithstanding the foregoing, either Landlord or Tenant may terminate this Lease upon written notice to the other if the Premises are damaged during the last year of the Term and Landlord reasonably estimates that it will take more than 2 months to repair such damage; provided, however, that such notice is delivered within 10 business days after the date that Landlord provides Tenant with written notice of the estimated Restoration Period. Notwithstanding anything to the contrary contained herein, Landlord shall also have the right to terminate this Lease if Landlord maintains the insurance required to be maintained by Landlord under this Lease, but insurance proceeds are not available for such restoration. Rent shall be equitably and proportionately abated from the date of discovery of the damage or destruction until occupancy of the Premises is legally permitted, in the proportion to which the area of the Premises, if any, which is not usable by Tenant bears to the total area of the Premises; provided, however, that if Tenant fails to obtain any Hazardous Materials Clearances required in order for Landlord to access the Premises (or any portion thereof) or for Landlord to perform repair or reconstruction activities within 60 days after the date of discovery of the damage or destruction, then Tenant shall not be entitled to any abatement following such initial 60 day period and shall be required to pay Rent for the Premises during any period following such initial 60 day period that Landlord's access to the Premises (or any portion thereof) or Landlord's repair or reconstruction activities are delayed in any way solely as a result of Tenant's failure to obtain any Hazardous Materials Clearances. Such abatement shall be the sole remedy of Tenant, and except as provided in this Section 18 , Tenant waives any right to terminate the Lease by reason of damage or casualty loss.

The provisions of this Lease, including this Section 18 , constitute an express agreement between Landlord and Tenant with respect to any and all damage to, or destruction of, all or any part of the Premises, or any other portion of the Project, and any statute or regulation which is now or may hereafter be in effect shall have no application to this Lease or any damage or destruction to all or any part of the Premises or any other portion of the Project, the parties hereto expressly agreeing that this Section 18 sets forth their entire understanding and agreement with respect to such matters.

19. **Condemnation** . If the whole or any material part of the Premises or the Project is taken for any public or quasi-public use under governmental law, ordinance, or regulation, or by right of eminent domain, or by private purchase in lieu thereof (a " **Taking** " or " **Taken** "), and the Taking would in Landlord's

reasonable judgment, materially interfere with or impair Landlord's ownership or operation of the Project or would in the reasonable judgment of Landlord and Tenant either prevent or materially interfere with Tenant's use of the Premises (as resolved, if the parties are unable to agree, by arbitration by a single arbitrator with the qualifications and experience appropriate to resolve the matter and appointed pursuant to and acting in accordance with the rules of the American Arbitration Association), then upon written notice by Landlord or Tenant to the other this Lease shall terminate and Rent shall be apportioned as of said date. If part of the Premises shall be Taken, and this Lease is not terminated as provided above, Landlord shall promptly restore the Premises and the Project as nearly as is commercially reasonable under the circumstances to their condition prior to such partial Taking and the rentable square footage of the Building, the rentable square footage of the Premises, Tenant's Share of Operating Expenses and the Rent payable hereunder during the unexpired Term shall be reduced to such extent as may be fair and reasonable under the circumstances. Upon any such Taking, Landlord shall be entitled to receive the entire price or award from any such Taking without any payment to Tenant, and Tenant hereby assigns to Landlord Tenant's interest, if any, in such award. Tenant shall have the right, to the extent that same shall not diminish Landlord's award, to make a separate claim against the condemning authority (but not Landlord) for such compensation as may be separately awarded or recoverable by Tenant for moving expenses and damage to Tenant's trade fixtures, if a separate award for such items is made to Tenant. Tenant hereby waives any and all rights it might otherwise have pursuant to any provision of state law to terminate this Lease upon a partial Taking of the Premises or the Project.

20. **Events of Default** . Each of the following events shall be a default (" **Default** ") by Tenant under this Lease:

(a) **Payment Defaults** . Tenant shall fail to pay any installment of Rent or any other payment hereunder when due; provided, however, that Landlord will give Tenant written notice and an opportunity to cure any failure to pay Rent within 5 days of any such notice not more than twice in any 12 month period and Tenant agrees that such notice shall be in lieu of and not in addition to, or shall be deemed to be, any notice required by law.

(b) **Insurance** . Any insurance required to be maintained by Tenant pursuant to this Lease shall be canceled or terminated or shall expire or shall be reduced or materially changed, or Landlord shall receive a notice of nonrenewal of any such insurance and Tenant shall fail to obtain replacement insurance before the expiration of the current coverage.

(c) **Abandonment** . Tenant shall abandon the Premises. Tenant shall not be deemed to have abandoned the Premises if (i) Tenant provides Landlord with advance notice prior to vacating and, at the time of or during a reasonable time after vacating the Premises, Tenant completes Tenant's obligations with respect to the Surrender Plan in compliance with Section 28 , (ii) Tenant has made reasonable arrangements reasonably acceptable to Landlord for the security of the Premises for the balance of the Term, and (iii) Tenant continues during the balance of the Term to satisfy all of its obligations under the Lease as they come due.

(d) **Improper Transfer** . Tenant shall assign, sublease or otherwise transfer all or any portion of Tenant's interest in this Lease or the Premises except as expressly permitted herein, or Tenant's interest in this Lease shall be attached, executed upon, or otherwise judicially seized and such action is not released within 90 days of the action.

(e) **Liens** . Tenant shall fail to discharge or otherwise obtain the release of any lien placed upon the Premises in violation of this Lease within 15 business days after any such lien is filed against the Premises.

(f) **Insolvency Events** . Tenant or any guarantor or surety of Tenant's obligations hereunder shall: (A) make a general assignment for the benefit of creditors; (B) commence any case, proceeding or other action seeking to have an order for relief entered on its behalf as a debtor or to adjudicate it a bankrupt or insolvent, or seeking reorganization, arrangement, adjustment, liquidation, dissolution or composition of

it or its debts or seeking appointment of a receiver, trustee, custodian or other similar official for it or for all or of any substantial part of its property (collectively a " **Proceeding for Relief** "); (C) become the subject of any Proceeding for Relief which is not dismissed within 90 days of its filing or entry; or (D) be dissolved or otherwise fail to maintain its legal existence (if Tenant, guarantor or surety is a corporation, partnership or other entity).

(g) **Estoppel Certificate or Subordination Agreement** . Tenant fails to execute any document required from Tenant under Sections 23 or 27 within 10 days after a second notice requesting such document.

(h) **Other Defaults** . Tenant shall fail to comply with any provision of this Lease other than those specifically referred to in this Section 20 , and, except as otherwise expressly provided herein, such failure shall continue for a period of 30 days after written notice thereof from Landlord to Tenant.

Any notice given under Section 20(h) hereof shall: (i) specify the alleged default, (ii) demand that Tenant cure such default, (iii) be in lieu of, and not in addition to, or shall be deemed to be, any notice required under any provision of applicable law, and (iv) not be deemed a forfeiture or a termination of this Lease unless Landlord elects otherwise in such notice; provided that if the nature of Tenant's default pursuant to Section 20(h) is such that it cannot be cured by the payment of money and reasonably requires more than 30 days to cure, then Tenant shall not be deemed to be in default if Tenant commences such cure within said 30 day period and thereafter diligently prosecutes the same to completion; provided , however , that such cure shall be completed no later than 90 days from the date of Landlord's notice.

21. **Landlord's Remedies** .

(a) **Payment By Landlord; Interest** . Upon a Default by Tenant hereunder, Landlord may, without waiving or releasing any obligation of Tenant hereunder, make such payment or perform such act. All sums so paid or incurred by Landlord, together with interest thereon, from the date such sums were paid or incurred, at the annual rate equal to 12% per annum or the highest rate permitted by law (the " **Default Rate** "), whichever is less, shall be payable to Landlord on demand as Additional Rent. Nothing herein shall be construed to create or impose a duty on Landlord to mitigate any damages resulting from Tenant's Default hereunder.

(b) **Late Payment Rent** . Late payment by Tenant to Landlord of Rent and other sums due will cause Landlord to incur costs not contemplated by this Lease, the exact amount of which will be extremely difficult and impracticable to ascertain. Such costs include, but are not limited to, processing and accounting charges and late charges which may be imposed on Landlord under any Mortgage covering the Premises. Therefore, if any installment of Rent due from Tenant is not received by Landlord within 5 days after the date such payment is due, Tenant shall pay to Landlord an additional sum equal to 6% of the overdue Rent as a late charge. Notwithstanding the foregoing, before assessing a late charge the first time in any calendar year, Landlord shall provide Tenant written notice of the delinquency and will waive the right if Tenant pays such delinquency within 5 days thereafter. The parties agree that this late charge represents a fair and reasonable estimate of the costs Landlord will incur by reason of late payment by Tenant. In addition to the late charge, Rent not paid when due shall bear interest at the Default Rate from the 5th day after the date due until paid.

(c) **Remedies** . Upon the occurrence of a Default, Landlord, at its option, without further notice or demand to Tenant, shall have in addition to all other rights and remedies provided in this Lease, at law or in equity, the option to pursue any one or more of the following remedies, each and all of which shall be cumulative and nonexclusive, without any notice or demand whatsoever.

(i) Terminate this Lease, or at Landlord's option, Tenant's right to possession only, in which event Tenant shall immediately surrender the Premises to Landlord, and if Tenant fails to do so, Landlord may, without prejudice to any other remedy which it may have for possession or arrearages in rent, enter upon and take possession of the Premises and expel or remove Tenant

and any other person who may be occupying the Premises or any part thereof, without being liable for prosecution or any claim or damages therefor;

(ii) Upon any termination of this Lease, whether pursuant to the foregoing Section 21(c)(i) or otherwise, due to a Default by Tenant, Landlord may recover from Tenant the following:

(A) The worth at the time of award of any unpaid rent which has been earned at the time of such termination; plus

(B) The worth at the time of award of the amount by which the unpaid rent which would have been earned after termination until the time of award exceeds the amount of such rental loss that Tenant proves could have been reasonably avoided; plus

(C) The worth at the time of award of the amount by which the unpaid rent for the balance of the Term after the time of award exceeds the amount of such rental loss that Tenant proves could have been reasonably avoided; and

(D) Any other amount necessary to compensate Landlord for all the detriment proximately caused by Tenant's failure to perform its obligations under this Lease or which in the ordinary course of things would be likely to result therefrom, specifically including, but not limited to, brokerage commissions and advertising expenses incurred, expenses of remodeling the Premises or any portion thereof for a new tenant, whether for the same or a different use, and any special concessions made to obtain a new tenant.

The term " **rent** " as used in this Section 21 shall be deemed to be and to mean all sums of every nature required to be paid by Tenant pursuant to the terms of this Lease, whether to Landlord or to others. As used in Sections 21(c)(ii)(A) and (B) , above, the " **worth at the time of award** " shall be computed by allowing interest at the Default Rate. As used in Section 21(c)(ii)(C) above, the " **worth at the time of award** " shall be computed by discounting such amount at the discount rate of the Federal Reserve Bank of San Francisco at the time of award plus 1%.

(iii) Landlord may continue this Lease in effect after Tenant's Default and recover rent as it becomes due (Landlord and Tenant hereby agreeing that Tenant has the right to sublet or assign hereunder, subject only to reasonable limitations). Accordingly, if Landlord does not elect to terminate this Lease following a Default by Tenant, Landlord may, from time to time, without terminating this Lease, enforce all of its rights and remedies hereunder, including the right to recover all Rent as it becomes due.

(iv) If Landlord elects to terminate this Lease following a Default by Tenant, Landlord shall have the right, subject to the terms of any agreements of subordination or nondisturbance entered into by Landlord, to terminate any and all subleases, licenses, concessions or other consensual arrangements for possession entered into by Tenant and affecting the Premises or may, in Landlord's sole discretion, succeed to Tenant's interest in such subleases, licenses, concessions or arrangements. Upon Landlord's election to succeed to Tenant's interest in any such subleases, licenses, concessions or arrangements, Tenant shall, as of the date of notice by Landlord of such election, have no further right to or interest in the rent or other consideration receivable thereunder.

(v) Independent of the exercise of any other remedy of Landlord hereunder or under applicable law, Landlord may conduct an environmental test of the Premises as generally described in Section 30(d) hereof, at Tenant's expense.

(d) **Effect of Exercise** . Exercise by Landlord of any remedies hereunder or otherwise available shall not be deemed to be an acceptance of surrender of the Premises and/or a termination of this Lease by Landlord, it being understood that such surrender and/or termination can be effected only by the express

written agreement of Landlord and Tenant. Any law, usage, or custom to the contrary notwithstanding, Landlord shall have the right at all times to enforce the provisions of this Lease in strict accordance with the terms hereof; and the failure of Landlord at any time to enforce its rights under this Lease strictly in accordance with same shall not be construed as having created a custom in any way or manner contrary to the specific terms, provisions, and covenants of this Lease or as having modified the same and shall not be deemed a waiver of Landlord's right to enforce one or more of its rights in connection with any subsequent default. A receipt by Landlord of Rent or other payment with knowledge of the breach of any covenant hereof shall not be deemed a waiver of such breach, and no waiver by Landlord of any provision of this Lease shall be deemed to have been made unless expressed in writing and signed by Landlord. To the greatest extent permitted by law, Tenant waives the service of notice of Landlord's intention to re-enter, re-take or otherwise obtain possession of the Premises as provided in any statute, or to institute legal proceedings to that end, and also waives all right of redemption in case Tenant shall be dispossessed by a judgment or by warrant of any court or judge. Any reletting of the Premises or any portion thereof shall be on such terms and conditions as Landlord in its sole discretion may determine. Landlord shall not be liable for, nor shall Tenant's obligations hereunder be diminished because of, Landlord's failure to relet the Premises or collect rent due in respect of such reletting or otherwise to mitigate any damages arising by reason of Tenant's Default. Landlord shall, however, use commercially reasonable efforts to mitigate the damages arising by reason of the termination of this Lease as a result of a Default by Tenant; provided, however, that in no event shall mitigation require Landlord to consider, among other things, (i) any tenant which does not satisfy Landlord's then current underwriting criteria, in the exercise of Landlord's sole and absolute discretion, for comparable size premises, (ii) subdividing the Premises unless Landlord elects in its sole and absolute discretion to do so, (iii) any change in use of the Premises or any alterations which would lessen the value of the leasehold improvements, (iv) granting any tenant improvement allowances, free rent or other lease concessions, or (v) accepting any tenant if Landlord would have the right to reject such tenant if such tenant were a proposed assignee or sublessee of Tenant including, without limitation, considering the factors described in Section 22(b) .

22. **Assignment and Subletting** .

(a) **General Prohibition** . Without Landlord's prior written consent subject to and on the conditions described in this Section 22 , Tenant shall not, directly or indirectly, voluntarily or by operation of law, assign this Lease or sublease the Premises or any part thereof or mortgage, pledge, or hypothecate its leasehold interest or grant any concession or license within the Premises, and any attempt to do any of the foregoing shall be void and of no effect. If Tenant is a corporation, partnership or limited liability company, the shares or other ownership interests thereof which are not actively traded upon a stock exchange or in the over-the-counter market, a transfer or series of transfers whereby 50% or more of the issued and outstanding shares or other ownership interests of such corporation, partnership or limited liability company are, or voting control is, transferred (but excepting transfers upon deaths of individual owners) from a person or persons or entity or entities which were owners thereof at time of execution of this Lease to persons or entities who were not owners of shares or other ownership interests of the corporation, partnership or limited liability company at time of execution of this Lease, shall be deemed an assignment of this Lease requiring the consent of Landlord as provided in this Section 22 .

(b) **Permitted Transfers** . If Tenant desires to assign, sublease, hypothecate or otherwise transfer this Lease or sublet the Premises other than pursuant to a Permitted Assignment (as defined below), then at least 15 days, but not more than 60 days, before the date Tenant desires the assignment or sublease to be effective (the " **Assignment Date** "), Tenant shall give Landlord a notice (the " **Assignment Notice** ") containing such information about the proposed assignee or sublessee, including the proposed use of the Premises and any Hazardous Materials proposed to be used, stored handled, treated, generated in or released or disposed of from the Premises, the Assignment Date, any relationship between Tenant and the proposed assignee or sublessee, and all material terms and conditions of the proposed assignment or sublease, including a copy of any proposed assignment or sublease in its final form, and such other information as Landlord may deem reasonably necessary or appropriate to its consideration whether to grant its consent. Landlord shall, by giving written notice to Tenant within 15 days after receipt of the Assignment Notice, either:

(i) grant such consent (provided that Landlord shall further be entitled to a copy of the final signed form of sublease prior to the effective date of any such subletting to confirm that it conforms to the draft previously provided by Tenant), (ii) refuse such consent, in its reasonable discretion; or (iii) as to an assignment of the entire Lease for the remainder of the Term, terminate this Lease as of the Assignment Date (an " **Assignment Termination** "). Among other reasons, it shall be reasonable for Landlord to withhold its consent in any of these instances: (1) the proposed assignee or subtenant is a governmental agency; (2) in Landlord's reasonable judgment, the use of the Premises by the proposed assignee or subtenant would entail any alterations that would materially lessen the value of the leasehold improvements in the Premises, or would require materially increased services by Landlord; (3) the use of the Premises by the proposed assignee or subtenant would not be consistent with the uses in general of laboratory tenants in Class A buildings in the Torrey Pines area of San Diego; (4) in Landlord's reasonable judgment, the proposed assignee or subtenant lacks the creditworthiness to support the financial obligations it will incur under the proposed assignment or sublease; (5) in Landlord's reasonable judgment, the character, reputation, or business of the proposed assignee or subtenant is materially detrimental to the Project; (6) Landlord has received from any prior landlord to the proposed assignee or subtenant a materially negative report concerning such prior landlord's experience with the proposed assignee or subtenant; (7) Landlord has experienced previous defaults by or is in litigation with the proposed assignee or subtenant; (8) the use of the Premises by the proposed assignee or subtenant will violate any applicable Legal Requirement; or (9) until all of the rentable square footage of the Spectrum 3 Building has been leased at least once, the proposed assignee or subtenant is an entity with whom Landlord is then actively negotiating to lease space in the Project. If Landlord delivers notice of its election to exercise an Assignment Termination, Tenant shall have the right to withdraw such Assignment Notice by written notice to Landlord of such election within 5 business days after Landlord's notice electing to exercise the Assignment Termination. If Tenant withdraws such Assignment Notice, this Lease shall continue in full force and effect. If Tenant does not withdraw such Assignment Notice, this Lease, and the term and estate herein granted, shall terminate as of the Assignment Date. No failure of Landlord to exercise any such option to terminate this Lease, or to deliver a timely notice in response to the Assignment Notice, shall be deemed to be Landlord's consent to the proposed assignment, sublease or other transfer. Tenant shall pay to Landlord a fee equal to One Thousand Five Hundred Dollars ($1,500) in connection with its consideration of any Assignment Notice and/or its preparation or review of any consent documents. Notwithstanding the foregoing, Landlord's consent to an assignment of this Lease or a subletting of any portion of the Premises to any entity controlling, controlled by or under common control with Tenant (a " **Control Permitted Assignment** ") shall not be required, provided that Landlord shall have the right to approve the form of any such sublease or assignment. In addition, Tenant shall have the right to assign this Lease, upon 30 days prior written notice to Landlord but without obtaining Landlord's prior written consent, to a corporation or other entity which is a successor-in-interest to Tenant, by way of merger, consolidation or corporate reorganization, or by the purchase of all or substantially all of the assets or the ownership interests of Tenant provided that (i) such merger or consolidation, or such acquisition or assumption, as the case may be, is for a good business purpose and not principally for the purpose of transferring the Lease, and (ii) the net worth (the excess of total "assets" over total "liabilities" using the definitions of "assets" and "liabilities" promulgated under generally accepted accounting principles (" **GAAP** ")) of the assignee is not less than the greater of the net worth (as determined above and as evidenced by a certification from the Chief Financial Officer of such assignee) of Tenant as of (A) the Commencement Date, or (B) as of the date of the assignment, and (iii) such assignee shall agree in writing to assume all of the terms, covenants and conditions of this Lease (a " **Corporate Permitted Assignment** "). Control Permitted Assignments and Corporate Permitted Assignments are hereinafter referred to as " **Permitted Assignments** ."

(c) **Additional Conditions** . As a condition to any such assignment or subletting, whether or not Landlord's consent is required, Landlord may require:

(i) that any assignee or subtenant agree, in writing at the time of such assignment or subletting, that if Landlord gives such party notice that Tenant is in default under this Lease, such party shall thereafter make all payments otherwise due Tenant directly to Landlord, which payments will be received by Landlord without any liability except to credit such payment against those due under the Lease, and any such third party shall agree to attorn to Landlord or its successors and

assigns should this Lease be terminated for any reason; provided , however , in no event shall Landlord or its successors or assigns be obligated to accept such attornment; and

(ii) A list of Hazardous Materials, certified by the proposed assignee or sublessee to be true and correct, which the proposed assignee or sublessee intends to use, store, handle, treat, generate in or release or dispose of from the Premises, together with copies of all documents relating to such use, storage, handling, treatment, generation, release or disposal of Hazardous Materials by the proposed assignee or subtenant in the Premises or on the Project, prior to the proposed assignment or subletting, including, without limitation: permits; approvals and reports; storage and management plans; plans relating to the installation of any storage tanks to be installed at the Project (provided, said installation of tanks shall only be permitted after Landlord has given its written consent to do so, which consent shall not be unreasonably withheld, conditioned or delayed); and all closure plans or any other documents required by any and all federal, state and local Governmental Authorities for any storage tanks installed in, on or under the Project for the closure of any such tanks. Neither Tenant nor any such proposed assignee or subtenant is required, however, to provide Landlord with any portion(s) of such documents containing information of a proprietary nature which, in and of themselves, do not contain a reference to any Hazardous Materials or hazardous activities.

(d) **No Release of Tenant, Sharing of Excess Rents** . Notwithstanding any assignment or subletting, Tenant and any guarantor or surety of Tenant's obligations under this Lease shall at all times remain fully and primarily responsible and liable for the payment of Rent and for compliance with all of Tenant's other obligations under this Lease. Except in connection with any Permitted Assignment, if the Rent due and payable by a sublessee or assignee (or a combination of the rental payable under such sublease or assignment plus any bonus or other consideration therefor or incident thereto in any form) exceeds the sum of the rental payable under this Lease, in the case of a sublease as allocated to the space subject to the sublease, (excluding however, any Rent payable under this Section) plus the actual and reasonable brokerage fees, legal costs, lease concessions and any design or construction fees directly related to and required pursuant to the terms of any such sublease (with all such amounts amortized over the term of the sublease or, in the case of an assignment, the then-remaining term of the Lease) (" **Excess Rent** "), then Tenant shall be bound and obligated to pay Landlord as Additional Rent hereunder 50% of such Excess Rent within 10 days following receipt thereof by Tenant. If Tenant shall sublet the Premises or any part thereof, Tenant hereby immediately and irrevocably assigns to Landlord, as security for Tenant's obligations under this Lease, all rent from any such subletting, and Landlord as assignee for Tenant, or a receiver for Tenant appointed on Landlord's application, may collect such rent and apply it toward Tenant's obligations under this Lease; except that, until the occurrence of a Default, Tenant shall have the right to collect such rent.

(e) **No Waiver** . The consent by Landlord to an assignment or subletting shall not relieve Tenant or any assignees of this Lease or any sublessees of the Premises from obtaining the consent of Landlord to any further assignment or subletting nor shall it release Tenant or any assignee or sublessee of Tenant from full and primary liability under the Lease. The acceptance of Rent hereunder, or the acceptance of performance of any other term, covenant, or condition thereof, from any other person or entity shall not be deemed to be a waiver of any of the provisions of this Lease or a consent to any subletting, assignment or other transfer of the Premises.

(f) **Intentionally Omitted** .

23. **Estoppel Certificate** . Tenant shall, within 10 business days of written notice from Landlord, execute, acknowledge and deliver a statement in writing in any form reasonably requested by a proposed lender or purchaser, (i) certifying that this Lease is unmodified and in full force and effect (or, if modified, stating the nature of such modification and certifying that this Lease as so modified is in full force and effect) and the dates to which the rental and other charges are paid in advance, if any, (ii) acknowledging that there are not any uncured defaults on the part of Landlord hereunder, or specifying such defaults if any are claimed, and (iii) setting forth such further information with respect to the status of this Lease or the Premises as may

be reasonably requested by a prospective bona fide third party purchaser or encumbrancer. Any such statement may be relied upon by any prospective purchaser or encumbrancer of all or any portion of the real property of which the Premises are a part. Tenant's failure to deliver such statement within 10 days after Landlord's delivery to Tenant of a second written request therefor, shall be conclusive upon Tenant that the Lease is in full force and effect and without modification except as may be represented by Landlord in any certificate prepared by Landlord and delivered to Tenant for execution.

Landlord shall, within 10 business days of written notice from Tenant, execute an estoppel certificate (which may include good faith and factually correct comments by Landlord) to Tenant's bona fide third party lender, an assignee pursuant to a Permitted Assignment, or an approved subtenant or assignee: (i) certifying that this Lease is unmodified and in full force and effect (or, if modified, stating the nature of such modification and certifying that this Lease as so modified is in full force and effect) and the dates to which the rental and other charges are paid in advanced, if any, (ii) acknowledging that there are not, to Landlord's actual knowledge, Defaults on the part of Tenant hereunder, or specifying such Defaults if any are claimed and (iii) setting forth such further information with respect to the status of this Lease or the Premises as may be reasonably requested thereon.

24. **Quiet Enjoyment** . So long as Tenant is not in Default under this Lease, Tenant shall, subject to the terms of this Lease, at all times during the Term, have peaceful and quiet enjoyment of the Premises against any person claiming by, through or under Landlord.

25. **Prorations** . All prorations required or permitted to be made hereunder shall be made on the basis of a 360 day year and 30 day months.

26. **Rules and Regulations** . Tenant shall, at all times during the Term, comply with the rules and regulations attached hereto, and with reasonable, non-discriminatory, new written rules and regulations from time to time established by Landlord covering the use of the Premises or the Project. Any new rules and regulations imposed by Landlord pursuant to this Section 26 shall not (i) materially adversely affect Tenant's parking, access to or use of the Premises for the Permitted Use, (ii) materially increase Tenant's financial obligations to Landlord under this Lease in a manner not otherwise contemplated by the other provisions of this Lease, and/or (iii) materially adversely affect Tenant's rights or obligations under this Lease. The current rules and regulations are attached hereto as **Exhibit E** . If there is any conflict between said rules and regulations (including any later promulgated rules and regulations) and other provisions of this Lease, the terms and provisions of this Lease shall control. Landlord shall not have any liability or obligation for the breach of any rules or regulations by other tenants in the Project and Landlord shall not enforce such rules and regulations in a discriminatory manner among tenants in the Project.

27. **Subordination** . This Lease and Tenant's interest and rights hereunder are hereby made and shall be subject and subordinate at all times to the lien of any Mortgage now existing or hereafter created on or against the Project or the Premises, and all amendments, restatements, renewals, modifications, consolidations, refinancing, assignments and extensions thereof, without the necessity of any further instrument or act on the part of Tenant; provided , however that so long as there is no Default hereunder, Tenant's rights set forth in this Lease including its rights to use, occupy and possess the Premises shall not be disturbed by the Holder of any such Mortgage. Tenant agrees, at the election of the Holder of any such Mortgage, to attorn to any such Holder. Tenant agrees upon demand to execute, acknowledge and deliver such instruments, confirming such subordination, and such instruments of attornment as shall be requested by any such Holder, provided any such instruments contain appropriate non-disturbance provisions assuring Tenant's quiet enjoyment of the Premises as set forth in Section 24 hereof. Notwithstanding the foregoing, any such Holder may at any time subordinate its Mortgage to this Lease, without Tenant's consent, by notice in writing to Tenant, and thereupon this Lease shall be deemed prior to such Mortgage without regard to their respective dates of execution, delivery or recording and in that event such Holder shall have the same rights with respect to this Lease as though this Lease had been executed prior to the execution, delivery and recording of such Mortgage and had been assigned to such Holder. The term " **Mortgage** " whenever used in this Lease shall be deemed to include deeds of trust, security assignments and any other

encumbrances, and any reference to the " **Holder** " of a Mortgage shall be deemed to include the beneficiary under a deed of trust. As of the date of this Lease, there is no existing Mortgage encumbering the Project.

28. **Surrender** . Upon the expiration of the Term or earlier termination of Tenant's right of possession, Tenant shall surrender the Premises to Landlord in the same condition as received, subject to any Alterations or Installations permitted by Landlord to remain in the Premises, free of Hazardous Materials brought upon, kept, used, stored, handled, treated, generated in, or released or disposed of from, the Premises by any person other than a Landlord Party during the Term or any holding over (collectively, " **Tenant HazMat Operations** ") and released of all Hazardous Materials Clearances, if any, broom clean, ordinary wear and tear and casualty loss and condemnation covered by Sections 18 and 19 excepted. At least 3 months prior to the surrender of the Premises, Tenant shall deliver to Landlord a narrative description of the actions proposed (or required by any Governmental Authority) to be taken by Tenant in order to surrender the Premises (including any Installations permitted by Landlord to remain in the Premises) at the expiration or earlier termination of the Term, free from any residual impact from the Tenant HazMat Operations and otherwise released for unrestricted use and occupancy (the " **Surrender Plan** "). Such Surrender Plan shall be accompanied by a current listing of (i) all Hazardous Materials licenses and permits held by or on behalf of any Tenant Party with respect to the Premises, and (ii) all Hazardous Materials used, stored, handled, treated, generated, released or disposed of from the Premises, and shall be subject to the review and reasonable approval of Landlord's environmental consultant. In connection with the review and approval of the Surrender Plan, upon the request of Landlord, Tenant shall deliver to Landlord or its consultant such additional non-proprietary information concerning Tenant HazMat Operations as Landlord shall reasonably request. On or before such surrender, Tenant shall deliver to Landlord evidence that the approved Surrender Plan shall have been satisfactorily completed and Landlord shall have the right, subject to reimbursement at Tenant's expense as set forth below, to cause Landlord's environmental consultant to inspect the Premises and perform such additional procedures as may be deemed reasonably necessary to confirm that the Premises are, as of the effective date of such surrender or early termination of the Lease, free from any residual impact from Tenant HazMat Operations. Tenant shall reimburse Landlord, as Additional Rent, for the reasonable, actual out-of pocket expense incurred by Landlord for Landlord's environmental consultant to review and approve the Surrender Plan and to visit the Premises and verify satisfactory completion of the same, which cost shall not exceed $5,000. Landlord shall have the unrestricted right to deliver such Surrender Plan and any report by Landlord's environmental consultant with respect to the surrender of the Premises to third parties.

If Tenant shall fail to prepare or submit a Surrender Plan approved by Landlord, or if Tenant shall fail to complete the approved Surrender Plan, or if such Surrender Plan, whether or not approved by Landlord, shall fail to adequately address any residual effect of Tenant HazMat Operations in, on or about the Premises, Landlord shall have the right to take such actions as Landlord may deem reasonable or appropriate to assure that the Premises and the Project are surrendered free from any residual impact from Tenant HazMat Operations, the reasonable cost of which actions shall be reimbursed by Tenant as Additional Rent, without regard to the limitation set forth in the first paragraph of this Section 28 .

Tenant shall immediately return to Landlord all keys and/or access cards to parking, the Project, restrooms or all or any portion of the Premises furnished to or otherwise procured by Tenant. If any such access card or key is lost, Tenant shall pay to Landlord, at Landlord's election, either the cost of replacing such lost access card or key or the cost of reprogramming the access security system in which such access card was used or changing the lock or locks opened by such lost key. Any Tenant's Property, Alterations and property not so removed by Tenant as permitted or required herein shall be deemed abandoned and may be stored, removed, and disposed of by Landlord at Tenant's expense, and Tenant waives all claims against Landlord for any damages resulting from Landlord's retention and/or disposition of such property. All obligations of Tenant hereunder not fully performed as of the termination of the Term, including the obligations of Tenant under Section 30 hereof, shall survive the expiration or earlier termination of the Term, including, without limitation, indemnity obligations, payment obligations with respect to Rent and obligations concerning the condition and repair of the Premises.

29. **Waiver of Jury Trial** . TO THE EXTENT PERMITTED BY LAW, TENANT AND LANDLORD WAIVE ANY RIGHT TO TRIAL BY JURY OR TO HAVE A JURY PARTICIPATE IN RESOLVING ANY DISPUTE, WHETHER SOUNDING IN CONTRACT, TORT, OR OTHERWISE, BETWEEN LANDLORD AND TENANT ARISING OUT OF THIS LEASE OR ANY OTHER INSTRUMENT, DOCUMENT, OR AGREEMENT EXECUTED OR DELIVERED IN CONNECTION HEREWITH OR THE TRANSACTIONS RELATED HERETO.

30. **Environmental Requirements** .

(a) **Prohibition/Compliance/Indemnity** . Tenant shall not cause or permit any Hazardous Materials (as hereinafter defined) to be brought upon, kept, used, stored, handled, treated, generated in or about, or released or disposed of from, the Premises or the Project by Tenant or any Tenant Party in violation of applicable Environmental Requirements (as hereinafter defined). Subject to the provisions of the last sentence of this Section 30(a) , if Tenant breaches the obligation stated in the preceding sentence, or if the presence of Hazardous Materials in the Premises during the Term or any holding over results in contamination of the Premises, the Project or any adjacent property or if contamination of the Premises, the Project or any adjacent property by Hazardous Materials brought into, kept, used, stored, handled, treated, generated in, or released or disposed of from, the Premises by anyone other than Landlord and Landlord's employees, agents and contractors otherwise occurs during the Term or any holding over, Tenant hereby indemnifies and shall defend and hold Landlord, its officers, directors, employees, agents and contractors harmless from any and all actions (including, without limitation, remedial or enforcement actions of any kind, administrative or judicial proceedings, and orders or judgments arising out of or resulting therefrom), costs, claims, damages (including, without limitation, punitive damages and damages based upon diminution in value of the Premises or the Project, or the loss of, or restriction on, use of the Premises or any portion of the Project), expenses (including, without limitation, attorneys', consultants' and experts' fees, court costs and amounts paid in settlement of any claims or actions), fines, forfeitures or other civil, administrative or criminal penalties, injunctive or other relief (whether or not based upon personal injury, property damage, or contamination of, or adverse effects upon, the environment, water tables or natural resources), liabilities or losses (collectively, " **Environmental Claims** ") which arise during or after the Term as a result of such contamination. This indemnification of Landlord by Tenant includes, without limitation, costs incurred in connection with any investigation of site conditions or any cleanup, treatment, remedial, removal, or restoration work required by any federal, state or local Governmental Authority because of Hazardous Materials present in the air, soil or ground water above, on, or under the Premises. Without limiting the foregoing, if the presence of any Hazardous Materials on the Premises, the Building, the Project or any adjacent property caused or permitted by Tenant or any Tenant Party results in any contamination of the Premises, the Building, the Project or any adjacent property, Tenant shall promptly take all actions at its sole expense and in accordance with applicable Environmental Requirements as are necessary to return the Premises, the Building, the Project or any adjacent property to the condition existing prior to the time of such contamination, provided that Landlord's approval of such action shall first be obtained, which approval shall not unreasonably be withheld so long as such actions would not potentially have any material adverse long-term or short-term effect on the Premises, the Building or the Project. Tenant acknowledges having received a copy of Landlord's Phase I environmental site assessment report with respect to the Project. Notwithstanding anything to the contrary contained in Section 28 or this Section 30 , Tenant shall not be responsible for, and the indemnification and hold harmless obligation set forth in this paragraph shall not apply to (i) contamination in the Premises which Tenant can reasonably establish existed in the Premises immediately prior to the Commencement Date, (ii) the presence of any Hazardous Materials in the Premises which Tenant can reasonably establish migrated from outside of the Premises into the Premises, or (iii) contamination caused by Landlord or any Landlord's employees, agents and contractors, unless in any case, the presence of such Hazardous Materials (x) is the result of a breach by Tenant of any of its obligations under this Lease, or (y) was caused, contributed to or exacerbated by Tenant or any Tenant Party.

(b) **Business** . Landlord acknowledges that it is not the intent of this Section 30 to prohibit Tenant from using the Premises for the Permitted Use. Tenant may operate its business according to prudent industry practices so long as the use or presence of Hazardous Materials is strictly and properly monitored

according to all then applicable Environmental Requirements. As a material inducement to Landlord to allow Tenant to use Hazardous Materials in connection with its business, Tenant agrees to deliver to Landlord prior to the Commencement Date a list identifying each type of Hazardous Materials to be brought upon, kept, used, stored, handled, treated, generated on, or released or disposed of from, the Premises and setting forth any and all governmental approvals or permits required in connection with the presence, use, storage, handling, treatment, generation, release or disposal of such Hazardous Materials on or from the Premises (" **Hazardous Materials List** "). Tenant shall maintain a current and up to date Hazardous Materials List at the Premises and with applicable Governmental Authorities. Tenant shall deliver to Landlord an updated Hazardous Materials List at any time that Tenant is required to deliver a Hazardous Materials List to any Governmental Authority (e.g., the fire department) in connection with its use or occupancy of the Premises. Tenant shall deliver to Landlord true and correct copies of the following documents (the " **Haz Mat Documents** ") relating to the use, storage, handling, treatment, generation, release or disposal of Hazardous Materials prior to the Commencement Date, or if unavailable at that time, concurrent with the receipt from or submission to a Governmental Authority: permits; approvals; reports and correspondence; storage and management plans, notice of violations of any Legal Requirements; plans relating to the installation of any storage tanks to be installed at the Project (provided, said installation of tanks shall only be permitted after Landlord has given Tenant its written consent to do so, which consent may not be unreasonably withheld, conditioned or delayed); all closure plans or any other documents required by any and all federal, state and local Governmental Authorities for any storage tanks installed in, on or under the Project for the closure of any such tanks; and a Surrender Plan (to the extent surrender in accordance with Section 28 cannot be accomplished in 3 months). Tenant is not required, however, to provide Landlord with any portion(s) of the Haz Mat Documents containing information of a proprietary nature which, in and of themselves, do not contain a reference to any Hazardous Materials or hazardous activities. It is not the intent of this Section to provide Landlord with information which could be detrimental to Tenant's business should such information become possessed by Tenant's competitors.

(c) **Intentionally Omitted** .

(d) **Testing** . Landlord shall have the right to conduct annual tests of the Premises to determine whether any contamination of the Premises or the Project has occurred as a result of Tenant's use. Tenant shall be required to pay the cost of such annual test of the Premises if there is violation of this Section 30 ; provided, however, that if Tenant conducts its own tests of the Premises using third party contractors and test procedures acceptable to Landlord which tests are certified to Landlord, Landlord shall accept such tests in lieu of the annual tests to be paid for by Tenant, if applicable. In addition to the annual tests Landlord may conduct pursuant to this Section 30(d) , Landlord may conduct additional tests at the expiration or earlier termination of the Term to determine if contamination has occurred as a result of Tenant's use of the Premises. In connection with such testing, upon the request of Landlord, Tenant shall deliver to Landlord or its consultant such non-proprietary information concerning the use of Hazardous Materials in or about the Premises by Tenant or any Tenant Party. If contamination has occurred (not including Hazardous Materials residue that would typically be removed upon the decommissioning of the Premises) for which Tenant is liable under this Section 30 , Tenant shall pay the costs to conduct such tests. If no such contamination is found, Landlord shall pay the costs of such tests (which shall not constitute an Operating Expense). Landlord shall provide Tenant with a copy of all third party, non-confidential reports and tests of the Premises made by or on behalf of Landlord during the Term without representation or warranty and subject to a confidentiality agreement. Tenant shall, at its sole cost and expense, promptly and satisfactorily remediate any contamination for which Tenant is liable under this Section 30 identified by such testing in accordance with all Environmental Requirements. Landlord's receipt of or satisfaction with any environmental assessment in no way waives any rights which Landlord may have against Tenant.

(e) **Control Areas** . Tenant shall be entitled to use 100% of the Hazardous Materials inventory within any control area or zone located within the Building, as designated by the applicable building code, for chemical use or storage. If Tenant does not lease all of the Spectrum 3 Building (as defined below), Tenant shall be allowed to utilize up to its pro rata share of the Hazardous Materials inventory within any control area or zone (located within Tenant's premises in the Spectrum 3 Building), as designated by the

applicable building code, for chemical use or storage. As used in the preceding sentence, Tenant's pro rata share of any control areas or zones located within Tenant's premises in the Spectrum 3 Building shall be determined based on the rentable square footage that Tenant leases within the applicable control area or zone. For purposes of example only, if a control area or zone contains 10,000 rentable square feet and 2,000 rentable square feet of a tenant's premises are located within such control area or zone (while such premises as a whole contains 5,000 rentable square feet), the applicable tenant's pro rata share of such control area would be 20%.

(f) **Underground Tanks** . In no event shall Tenant have the right to install or use any underground storage tanks storing Hazardous Materials at the Project. The term "underground storage tank" as used in this Lease shall not include above-ground storage tanks located in the subterranean parking garage and/or the mechanical/service yard.

(g) **Tenant's Obligations** . Each party's obligations under this Section 30 shall survive the expiration or earlier termination of the Lease. During any period of time after the expiration or earlier termination of this Lease required by Tenant or Landlord to complete the removal from the Premises of any Hazardous Materials for which Tenant is responsible under this Lease (including, without limitation, the release and termination of any licenses or permits restricting the use of the Premises and the completion of the approved Surrender Plan), Tenant shall continue to pay the full Rent in accordance with this Lease for any portion of the Premises not relet by Landlord in Landlord's sole discretion, which Rent shall be prorated daily.

(h) **Definitions** . As used herein, the term " **Environmental Requirements** " means all applicable present and future statutes, regulations, ordinances, rules, codes, judgments, orders or other similar enactments of any Governmental Authority regulating or relating to environmental conditions on, under, or about the Premises or the Project, or the environment, including without limitation, the following: the Comprehensive Environmental Response, Compensation and Liability Act; the Resource Conservation and Recovery Act; and all state and local counterparts thereto, and any regulations or policies promulgated or issued thereunder. As used herein, the term " **Hazardous Materials** " means and includes any substance, material, waste, pollutant, or contaminant listed or defined as hazardous or toxic, or regulated by reason of its impact or potential impact on humans, animals and/or the environment under any Environmental Requirements, asbestos and petroleum, including crude oil or any fraction thereof, natural gas liquids, liquefied natural gas, or synthetic gas usable for fuel (or mixtures of natural gas and such synthetic gas). As defined in Environmental Requirements, Tenant is and shall be deemed to be the " **operator** " of Tenant's " **facility** " and the " **owner** " of all Hazardous Materials brought on the Premises by Tenant or any Tenant Party, and the wastes, by-products, or residues generated, resulting, or produced therefrom.

31. **Tenant's Remedies/Limitation of Liability** .

(a) **Generally** . Landlord shall not be in default hereunder unless Landlord fails to perform any of its obligations hereunder within 30 days after written notice from Tenant specifying such failure (unless such performance will, due to the nature of the obligation, require a period of time in excess of 30 days, then after such period of time as is reasonably necessary). Upon any default by Landlord, Tenant shall give notice by registered or certified mail to any Holder of a Mortgage covering the Premises and to any landlord of any lease of property in or on which the Premises are located and Tenant shall offer such Holder and/or landlord a reasonable opportunity to cure the default, including time to obtain possession of the Project by power of sale or a judicial action if such should prove necessary to effect a cure; provided Landlord shall have furnished to Tenant in writing the names and addresses of all such persons who are to receive such notices. All obligations of Landlord hereunder shall be construed as covenants, not conditions; and, except as may be otherwise expressly provided in this Lease, Tenant may not terminate this Lease for breach of Landlord's obligations hereunder.

All obligations of Landlord under this Lease will be binding upon Landlord only during the period of its ownership of the Premises and not thereafter. The term " **Landlord** " in this Lease shall mean only the

owner for the time being of the Premises. Upon the transfer by such owner of its interest in the Premises, such owner shall thereupon be released and discharged from all obligations of Landlord thereafter accruing, but such obligations shall be binding during the Term upon each new owner for the duration of such owner's ownership.

(b) **Tenant's Self-Help Remedy** . If Landlord is in default of any of its obligations to maintain and repair the Premises (other than as a result of a casualty, which shall be governed solely by the provisions of Section 18 of this Lease) (collectively referred to in this Section 31(b) as " **repairs** "), then notwithstanding anything to the contrary contained in this Lease, Tenant may, provided that it does not materially adversely affect any Building Systems affecting other tenants of the Project or materially adversely affect the Building structure , perform such repairs subject to the following terms and conditions:

(i) Tenant shall deliver written notice to Landlord and any Holder whose name and address has previously been furnished to Tenant in writing (the " **Self-Help Notice** ") of Tenant's intention to perform such repairs, which Self-Help Notice shall state in bold-faced all capital letters: "FAILURE TO PERFORM SUCH WORK IN TEN (10) DAYS SHALL RESULT IN TENANT'S EXERCISE OF SELF-HELP". If neither Landlord nor lender commences to cure Landlord's failure to perform such repairs within 10 days after receipt of the Self-Help Notice, then Tenant may take such action as is reasonably necessary to perform such repairs;

(ii) All repairs performed by Tenant or its agents pursuant to this Section 31(b) must be performed in a good and workmanlike manner in compliance with applicable Legal Requirements and, to the extent possible, using contractors then under contract to perform maintenance at the Project whose names have been provided to Tenant by Landlord or whose names are otherwise reasonably known to Tenant, and shall not void any warranties or guaranties on the Premises or the Project;

(iii) In the event Landlord's failure relates to repairs that are bona fide emergency repairs (i.e., necessary to prevent or remediate a material and imminent threat to the health or safety of persons or necessary to prevent a material adverse affect on Tenant's business operations), then notwithstanding the provisions of Section 31(b)(i) above, the Self-Help Notice shall be in the form and shall be given in such amount of time as is reasonable in the circumstances, and if Landlord or lender fails to respond within a time as is reasonable in the circumstances, Tenant may cause such emergency repairs to be made pursuant to the requirements set forth herein; and

(iv) Landlord shall reimburse Tenant for Tenant's reasonable out-of-pocket third party costs of the performance of the repairs that are incurred under the terms of this Section 31(b) (the " **Reimbursement Amount** ") within 30 days after Tenant's submission to Landlord of Tenant's bill therefor, which bill shall be accompanied by receipted, itemized invoices (with reasonable supporting documentation) and conditional lien releases from all contractors, subcontractors, materialmen and suppliers that performed the work or provided the material or services reflected in the bill), provided, however, in no event shall such emergency repairs exceed what is required to end the pending emergency (it being understood and agreed by Landlord that in the case of an emergency, depending upon the circumstances, overtime and/or premium time labor charges may be reasonable). Tenant shall provide unconditional lien waivers to Landlord in connection with all such bills paid within 10 days after Landlord's payment of Tenant's bill. In the event Landlord fails to pay all or any portion of the Reimbursement Amount due Tenant under this Section 31(b) within 30 days after receipt of Tenant's bill therefore, together with the invoices therefor, supporting documentation and the conditional lien releases required by this Section 31(b)(iv) , along with written notice to Landlord stating in bold-faced, all capital letters that: "FAILURE TO REIMBURSE WITHIN THIRTY (30) DAYS SHALL RESULT IN TENANT'S EXERCISE OF OFFSET RIGHTS", Tenant may offset such delinquent amount against up to 20% of the monthly Base Rent due from Tenant until Tenant has been reimbursed in full, provided that Tenant shall provide Landlord with unconditional lien waivers in connection with the work relating to such amounts within 10 days of the date on which the amount

has been fully paid or so offset, or as soon thereafter as reasonably practicable. Notwithstanding the foregoing, if Landlord delivers to Tenant a good faith written objection notice within 10 business days after receipt of Tenant's notice of intent to offset, setting forth with reasonable particularity Landlord's reasons for its claim that Landlord is not required to pay Tenant all or any specified portion of the Reimbursement Amount, then Tenant shall not be entitled to offset the disputed portion of the Reimbursement Amount. If Landlord and Tenant are not able to reach agreement with respect to the disputed matters within 10 business days after Tenant's receipt of such notice from Landlord, the parties shall submit such dispute to arbitration conducted by the American Arbitration Association in San Diego in accordance with the "Expedited Procedures" of its Commercial Arbitration Rules. Unless the parties otherwise agree, the arbitrator must be a retired judge of the Superior Court of the State of California. All costs associated with arbitration shall be awarded to the prevailing party as determined by the arbitrator. Nothing contained in this Section 31(b) is intended to preclude or limit Landlord from passing through as part of Operating Expenses any Reimbursement Amount to the extent Landlord is otherwise not precluded under Section 5 from passing through such cost as part of Operating Expenses.

Notwithstanding anything to the contrary contained herein, the self-help remedies provided for in this Section 31 shall in no event apply to Landlord's Work and Tenant shall have no right to perform any portion of or complete the construction of Landlord's Work.

32. **Inspection and Access** . Landlord and its agents, representatives, and contractors may enter the Premises at any reasonable time to inspect the Premises and to make such repairs as may be required or permitted pursuant to this Lease. Landlord and Landlord's representatives may enter the Premises during business hours on not less than 2 business days advance written notice (except in the case of emergencies in which case Landlord shall provide such notice as is reasonable under the circumstances and such entry may be at any time) for the purpose of effecting any such repairs, inspecting the Premises, showing the Premises to prospective purchasers and, during the last year of the Term, to prospective tenants. Landlord shall use reasonable efforts to coordinate with Tenant to schedule any such entry and activity in order to minimize interruption of Tenant's operations at the Premises. Landlord may erect a suitable sign on the Building stating the Premises within the Building are available to let during the last year of the Term or that the Project is available for sale. Landlord shall not erect any signs on the Building in connection with the availability of space available to let in the Spectrum 3 Building. Landlord may grant easements, make public dedications, designate Common Areas and create restrictions on or about the Project outside the Building, provided that no such easement, dedication, designation or restriction materially adversely affects Tenant's use or occupancy of the Premises for the Permitted Use or materially adversely affects Tenant's rights with respect to the Exclusive Use Areas (other than on a temporary basis). At Landlord's request, Tenant shall execute such instruments as may be necessary for such easements, dedications or restrictions. Tenant shall at all times, except in the case of emergencies, have the right to escort Landlord or its agents, representatives, contractors or guests while the same are in the Premises, provided such escort does not materially and adversely affect Landlord's access rights hereunder. During Landlord's access of the Premises, Landlord shall use reasonable efforts to comply with Tenant's reasonable security requirements; provided, however, that Tenant has notified Landlord of such security requirements prior to Landlord's entry into the Premises. Landlord shall use reasonable efforts to comply with Tenant's written protocol with respect to entering restricted portions of the Premises; provided, however, that a copy of the same has previously been provided to Landlord. Tenant shall have the right to designate (on plans provided by Tenant to Landlord, which may be reasonably updated by Tenant from time to time upon notice to Landlord) certain areas of the Premises as limited access areas required to protect the health of persons or security of confidential and proprietary information, which limited access areas shall not be entered into by Landlord or Landlord's representatives without a Tenant representative, except in the case of an emergency or as otherwise reasonably necessary.

Subject to the terms of this Section 32 , Landlord may from time to time during the Term, during regular business hours and/or otherwise at times mutually acceptable to Landlord and Tenant, conduct third

party tours of certain portions of the Premises reasonably agreed upon in advance by Landlord and Tenant (" **Tours** ") which Tours may be held with not less than 1 business day's advance notice.

33. **Security** . Landlord shall develop jointly with Tenant, subject to Tenant's approval, which approval shall not be unreasonably withheld, conditioned or delayed, a commercially reasonable security plan (the " **Security Plan** ") for the exterior perimeter and Common Areas of the Project. Landlord shall provide (or cause to be provided) security to the Project in accordance with the Security Plan, the cost of which shall constitute an Operating Expense. Notwithstanding anything to the contrary contained in Section 5 , prior to the commencement of construction of the Spectrum 3 Building by Landlord, Tenant shall, as part of Operating Expenses, be responsible for all costs and expenses incurred by Landlord with respect to the provision of security to the Project. Notwithstanding the fact that Landlord provides (or causes to be provided) security services at the Project at any time during the Term, Landlord shall not be deemed to owe Tenant, or any person claiming by, through or under Tenant, any special duty or standard of care as a result of Landlord's provision of such security services and in no event shall Landlord be responsible for the efficacy of such security measures. Tenant acknowledges and agrees that security devices and services, if any, while intended to deter crime may not in given instances prevent theft or other criminal acts and that Landlord is not providing any security services with respect to the Premises. Tenant agrees that Landlord shall not be liable to Tenant for, and Tenant waives any claim against Landlord with respect to, any loss by theft or any other damage suffered or incurred by Tenant in connection with any unauthorized entry into the Premises or any other breach of security with respect to the Premises. Tenant shall be solely responsible for the personal safety of Tenant's officers, employees, agents, contractors, guests and invitees while any such person is in, on or about the Premises and/or the Project. Tenant shall at Tenant's cost obtain insurance coverage to the extent Tenant desires protection against such criminal acts.

Subject to the terms of this Lease, including, without limitation, Tenant's compliance with Section 12 , Tenant, at Tenant's sole cost and expense, shall have the right to install and maintain a security and card access system including cameras inside and outside the Premises (including, as may be coordinated with Landlord as provided below, the Common Areas) (" **Tenant's Security System** "), subject to the following conditions: (i) Tenant's plans and specifications for the proposed location of Tenant's Security System and Tenant's protocol for the operation of Tenant's Security System shall be subject to Landlord's prior written approval, which approval will not be unreasonably withheld; provided, however, that Tenant shall coordinate the installation and operation of Tenant's Security System with Landlord to assure that Tenant's Security System may be compatible with the Building's systems and equipment and Tenant does not violate the reasonable privacy rights of any other occupants of the Project; (ii) Landlord shall be provided with keys, codes and/or access cards, as applicable, and means of immediate access to fully exercise all of its entry rights under the Lease with respect to the Premises; and (iii) Tenant shall be solely responsible, at Tenant's sole cost and expense, for the monitoring, operation and removal of Tenant's Security System. Upon the expiration or earlier termination of this Lease, Tenant shall remove Tenant's Security System. All costs and expenses associated with the removal of Tenant's Security System and the repair of any damage to the Premises and the Building resulting from the installation and/or removal of same shall be borne solely by Tenant. Notwithstanding anything to the contrary contained herein, Landlord shall not be directly or indirectly liable to Tenant, any Tenant Parties or any other person and Tenant hereby waives any and all claims against and releases Landlord from any and all claims arising as a consequence of or related to Tenant's Security System, or the failure thereof.

34. **Force Majeure** . Except for the payment of Rent or as otherwise specifically excluded or limited in this Lease, neither Landlord nor Tenant shall be held responsible or liable for delays in the performance of its obligations hereunder when caused by, related to, or arising out of acts of God, catastrophic weather, national, regional, or local disasters, calamities, or catastrophes, material delay in issuance or revocation of permits beyond the time periods customarily required by the City for such issuance or revocation, as applicable, enemy or hostile governmental action, terrorism, insurrection, riots, civil disturbance or commotion, fire or other casualty (" **Force Majeure** "). In the event that either party is delayed from performing any obligation hereunder as a result of Force Majeure, such party shall promptly give notice to the other

party of the delay in question, specifying in such notice the nature of the delay and such party's good faith estimate of the length of the delay in question.

35. **Brokers** . Landlord and Tenant each represents and warrants that it has not dealt with any broker, agent or other person (collectively, " **Broker** ") in connection with this transaction and that no Broker brought about this transaction, other than DTZ. Landlord and Tenant each hereby agree to indemnify and hold the other harmless from and against any claims by any Broker, other than the broker, if any named in this Section 35 , claiming a commission or other form of compensation by virtue of having dealt with Tenant or Landlord, as applicable, with regard to this leasing transaction. Landlord shall be responsible for all commissions due to DTZ arising out of the execution of this Lease in accordance with the terms of a separate written agreement between DTZ and Landlord.

36. **Limitation on Landlord's Liability** . NOTWITHSTANDING ANYTHING SET FORTH HEREIN OR IN ANY OTHER AGREEMENT BETWEEN LANDLORD AND TENANT TO THE CONTRARY: (A) LANDLORD SHALL NOT BE LIABLE TO TENANT OR ANY OTHER PERSON FOR (AND TENANT AND EACH SUCH OTHER PERSON ASSUME ALL RISK OF) LOSS, DAMAGE OR INJURY, WHETHER ACTUAL OR CONSEQUENTIAL TO: TENANT'S PERSONAL PROPERTY OF EVERY KIND AND DESCRIPTION, INCLUDING, WITHOUT LIMITATION TRADE FIXTURES, EQUIPMENT, INVENTORY, SCIENTIFIC RESEARCH, SCIENTIFIC EXPERIMENTS, LABORATORY ANIMALS, PRODUCT, SPECIMENS, SAMPLES, AND/OR SCIENTIFIC, BUSINESS, ACCOUNTING AND OTHER RECORDS OF EVERY KIND AND DESCRIPTION KEPT AT THE PREMISES AND ANY AND ALL INCOME DERIVED OR DERIVABLE THEREFROM; (B) THERE SHALL BE NO PERSONAL RECOURSE TO LANDLORD FOR ANY ACT OR OCCURRENCE IN, ON OR ABOUT THE PREMISES OR ARISING IN ANY WAY UNDER THIS LEASE OR ANY OTHER AGREEMENT BETWEEN LANDLORD AND TENANT WITH RESPECT TO THE SUBJECT MATTER HEREOF AND ANY LIABILITY OF LANDLORD HEREUNDER SHALL BE STRICTLY LIMITED SOLELY TO LANDLORD'S INTEREST IN THE PROJECT OR ANY PROCEEDS FROM SALE OR CONDEMNATION THEREOF AND ANY INSURANCE PROCEEDS PAYABLE IN RESPECT OF LANDLORD'S INTEREST IN THE PROJECT OR IN CONNECTION WITH ANY SUCH LOSS; AND (C) IN NO EVENT SHALL ANY PERSONAL LIABILITY BE ASSERTED AGAINST LANDLORD IN CONNECTION WITH THIS LEASE NOR SHALL ANY RECOURSE BE HAD TO ANY OTHER PROPERTY OR ASSETS OF LANDLORD OR ANY OF LANDLORD'S OFFICERS, DIRECTORS, EMPLOYEES, AGENTS OR CONTRACTORS. UNDER NO CIRCUMSTANCES SHALL LANDLORD OR ANY OF LANDLORD'S OFFICERS, DIRECTORS, EMPLOYEES, AGENTS OR CONTRACTORS BE LIABLE FOR INJURY TO TENANT'S BUSINESS OR FOR ANY LOSS OF INCOME OR PROFIT THEREFROM.

37. **Severability** . If any clause or provision of this Lease is illegal, invalid or unenforceable under present or future laws, then and in that event, it is the intention of the parties hereto that the remainder of this Lease shall not be affected thereby. It is also the intention of the parties to this Lease that in lieu of each clause or provision of this Lease that is illegal, invalid or unenforceable, there be added, as a part of this Lease, a clause or provision as similar in effect to such illegal, invalid or unenforceable clause or provision as shall be legal, valid and enforceable.

38. **Signs; Exterior Appearance** . Tenant shall not, without the prior written consent of Landlord, which may be granted or withheld in Landlord's sole discretion: (i) attach any awnings, exterior lights, decorations, balloons, flags, pennants, banners, painting or other projection to any outside wall of the Building, (ii) use any curtains, blinds, shades or screens other than Landlord's standard window coverings, (iii) coat or otherwise sunscreen the interior or exterior of any windows, (iv) attach any items to the windows with tape or any other adhesive substance, or (v) place any items of any type which can be viewed from the exterior of the Premises in violation of applicable Legal Requirements. Tenant shall not place any furniture or other items in the window line on the street facing side of the Building that is not professional in appearance.

Tenant shall have the exclusive right to display, at Tenant's cost and expense, one or more signs bearing Tenant's name and/or logo at the top of the Building (collectively, the " **Building Signs** ") in a location selected by Tenant and reasonably acceptable to Landlord if not shown on **Exhibit K** attached hereto. Subject

to applicable Legal Requirements, the parties anticipate the Building Signs will total 100 square feet. Notwithstanding the foregoing, Tenant acknowledges and agrees that the Building Signs including, without limitation, the size, color and type, shall be subject to Landlord's prior written approval, which shall not be unreasonably withheld, conditioned or delayed, shall be consistent with Landlord's signage program at the Project and shall be subject to any and all other required approvals and applicable Legal Requirements. Tenant shall be responsible, at Tenant's sole cost and expense, for the maintenance of the Building Signs, for the removal of the Building Signs at the expiration or earlier termination of this Lease and for the repair of all damage resulting from such removal. The Building Signs shall be personal to Vertex Pharmaceuticals Incorporated, except that such right may be assigned in connection with any Permitted Assignment.

Tenant shall, at Tenant's sole cost and expense, have the non-exclusive right to install a sign bearing Tenant's name on the Monument Sign serving the Project (the " **Monument Sign** "), as reflected on **Exhibit K** attached hereto. Tenant acknowledges and agrees that Tenant's signage on the Monument Sign including, without limitation, the location, size, color and type shall be subject to Landlord's prior written approval, which shall not be unreasonably withheld, conditioned or delayed, shall be subject to and consistent with Landlord's signage program at the Project and shall be subject to any and all other required approvals and applicable Legal Requirements. Tenant shall be responsible, at Tenant's sole cost and expense, for the maintenance of Tenant's signage on the Monument Sign, for the removal of Tenant's signage from the Monument Sign at the expiration or earlier termination of this Lease and for the repair of all damage resulting from such removal. The Monument Sign shall be personal to Vertex Pharmaceuticals Incorporated, except that such right may be assigned in connection with any Permitted Assignment. Tenant has elected option A reflected on **Exhibit K** with respect to the Monument Sign.

39. **Right to Expand** .

(a) **Expansion in the Project** . Subject to Landlord's obtaining all required Approvals (subject to the third paragraph of Section 2 above), Landlord shall, within 24 months after the Rent Commencement Date, construct a second building at the Project containing approximately 40,000-60,000 rentable square feet of rentable space (the " **Spectrum 3 Building** "). Landlord shall, in the exercise of its sole and absolute discretion, make the decisions as to all matters regarding the Spectrum 3 Building including, without limitation, the size thereof. Tenant acknowledges that, if Landlord so elects in its sole and absolute discretion, all or a portion of the Spectrum 3 Building may consist of small suites (e.g., a science hotel). So long as Tenant is then leasing not less than 75% of the Premises, then, subject to the terms of this Section 39 , the first time that Landlord intends to accept a written proposal (the " **Pending Deal** ") to lease all or a portion of the ROFR Space (as hereinafter defined) to a third party, Landlord shall deliver to Tenant written notice (the " **Pending Deal Notice** ") of the existence and the material terms of such Pending Deal. For purposes of this Section 39(a) , " **ROFR Space** " shall mean any space in the Spectrum 3 Building. Tenant shall be entitled to exercise its right under this Section 39(a) only with respect to the entire ROFR Space described in such Pending Deal Notice (the " **Identified Space** "). Within 10 business days after Tenant's receipt of the Pending Deal Notice, Tenant shall deliver to Landlord written notice (the " **Space Acceptance Notice** ") if Tenant elects to lease the Identified Space. Tenant's right to receive the Pending Deal Notice and election to lease or not lease the Identified Space pursuant to this Section 39(a) is hereinafter referred to as the " **Right of Refusal** ." If Tenant elects to lease the Identified Space by delivering the Space Acceptance Notice within the required 10 business day period, Tenant shall be deemed to agree to lease the Identified Space on the same general terms and conditions as this Lease except that the terms of the Lease shall be modified to reflect the terms of the Pending Deal Notice for the rental of the Identified Space, provided, however, that (i) if the term of the lease with respect to the Identified Space would pursuant to the Pending Deal expire prior to the term of the Lease with respect to the then-existing Premises, then the term of the Lease with respect to the Identified Space shall be modified to be co-terminous with the Term of this Lease with respect to the then-existing Premises, and (ii) if the term of the lease with respect to the Identified Space is modified to be co-terminous with the term of the then-existing Premises pursuant to sub-section (i), then the economic terms set forth in the Pending Deal Notice shall be equitably adjusted to account for such extension of the term with respect to the Identified Space, provided that such adjustment of the economic terms shall be no less favorable to Landlord on an annual basis than the economic terms set forth in the Pending Deal (and with market rate

annual increases in base rent for the Identified Space for that portion of the lease term for the Identified Space beyond the term provided for in the Pending Deal), as reasonably determined by Landlord and Tenant. If the term of the lease with respect to the Identified Space would pursuant to the Pending Deal expire after the term of this Lease with respect to the then-existing Premises, then the term of the lease with respect to the Identified Space shall be as provided in the Pending Deal (and, for the avoidance of any doubt, no adjustment shall be made to the term of this Lease for the then-existing Premises). Notwithstanding anything to the contrary contained herein, in no event shall the Work Letter or the TI Allowance (as defined in the Work Letter) apply to the Identified Space, as the terms and conditions of the Pending Deal Notice (as may be equitably adjusted by Landlord), including any tenant improvement allowance provided for in the Pending Deal Notice, shall apply. If Tenant fails to deliver a Space Acceptance Notice to Landlord within the required 10 business day period, Tenant shall be deemed to have waived its rights under this Section 39(a) to lease the Identified Space identified in the applicable Pending Deal Notice, and Landlord shall have the right to lease such Identified Space to the third party subject to the Pending Deal (or an affiliate of such third party) (" **Pending Deal Party** "). Tenant's Right of First Refusal with respect to such Identified Space shall be restored if Landlord fails to enter into an agreement to lease the Identified Space to the Pending Deal Party within 6 months after Landlord's deliver of the Pending Deal Notice to Tenant. Tenant's Right of First Refusal shall exist with respect to each portion of the Spectrum 3 Building until such portion of the Spectrum 3 Building has been subject to a Pending Deal. For the avoidance of any doubt, Tenant shall in no event be entitled to a second Pending Deal Notice with respect to any space in the Spectrum 3 Building once Landlord has entered into a lease with a Pending Deal Party with respect to such space in the Spectrum 3 Building.

If Tenant leases a portion of the Spectrum 3 Building and a portion of the Spectrum 3 Building is leased to a third party, the following Lease provisions shall also apply to Tenant's leasing of the Identified Space (and in the event of any conflict between the provisions of this paragraph and the other provisions of the this Lease with respect to the leasing of the Identified Space, the provisions of this paragraph shall govern): (i) Tenant shall not, without the prior written consent of Landlord, which consent shall not be unreasonably withheld, conditioned or delayed, use the Identified Space in any manner which will require ventilation, air exchange, heating, gas, steam, electricity or water beyond the existing capacity of the Spectrum 3 Building as proportionately allocated to the Identified Space based upon Tenant's share of the Spectrum 3 Building as usually furnished for the Permitted Use, (ii) Tenant's Alterations affecting the structure of the Spectrum 3 Building or the Building Systems serving the Spectrum 3 Building shall require Landlord's consent which consent may be given or withheld in Landlord's sole discretion, (iii) Landlord may equitably increase, in Landlord's reasonable discretion, Tenant's share of Operating Expenses for any item of expense or cost reimbursable by Tenant that relates to a repair, replacement, or service that benefits only the Identified Space or only a portion of the Spectrum 3 Building that includes the Identified Space or that varies with occupancy or use. Also, so long as Tenant leases any portion of the Spectrum 3 Building, Section 5(hh) shall be deleted in its entirety.

(b) **Amended Lease** . If: (i) Tenant fails to timely deliver a Space Acceptance Notice, or (ii) after the expiration of a period of 20 days from the date Landlord delivers to Tenant a lease amendment or lease agreement for the Identified Space no lease amendment or lease agreement for the Identified Space acceptable to both parties each in their reasonable discretion has been executed and delivered by Tenant to Landlord, Tenant shall be deemed to have waived its right to lease the Identified Space subject to the applicable Pending Deal, subject to terms of Section 39(a) .

(c) **Exceptions** . Notwithstanding the above, the Right of First Refusal shall, at Landlord's option, not be in effect and may not be exercised by Tenant:

(i) during any period of time that Tenant is in Default under any provision of the Lease; or

(ii) if Tenant has been in Default under any provision of the Lease 3 or more times, whether or not the Defaults are cured, during the 12 month period prior to the date on which Tenant seeks to exercise the Right of First Refusal.

(d) **Termination** . The Right of First Refusal shall, at Landlord's option, terminate and be of no further force or effect even after Tenant's due and timely exercise of the Right of First Refusal, if, after such exercise, but prior to the commencement date of the lease of such Right of First Refusal, (i) Tenant fails to timely cure any default by Tenant under the Lease; or (ii) Tenant has Defaulted 3 or more times during the period from the date of the exercise of the Right of First Refusal to the date of the commencement of the lease of the Identified Space, whether or not such Defaults are cured.

(e) **Subordinate** . Tenant hereby acknowledges and agrees that, notwithstanding anything to the contrary contained in this Lease, Tenant's Right of First Refusal shall be subject and subordinate to any expansion rights granted in the Spectrum 3 Building to any Pending Deal Party with whom Landlord enters into a lease for space in the Spectrum 3 Building.

(f) **Rights Personal** . The Right of First Refusal is personal to Vertex Pharmaceuticals Incorporated and is not assignable without Landlord's consent, which may be granted or withheld in Landlord's sole discretion separate and apart from any consent by Landlord to an assignment of Tenant's interest in the Lease, except that it may be assigned in connection with any Permitted Assignment of this Lease.

(g) **No Extensions** . The period of time within which the Right of First Refusal may be exercised shall not be extended or enlarged by reason of Tenant's inability to exercise the Right of First Refusal.

40. **Right to Extend Term** . Tenant shall have the right to extend the Term of the Lease upon the following terms and conditions:

(a) **Extension Rights** . Tenant shall have 2 consecutive rights (each, an " **Extension Right** ") to extend the term of this Lease for 5 years each (each, an " **Extension Term** ") on the same terms and conditions as this Lease (other than with respect to Base Rent and the Work Letter) by giving Landlord written notice of its election to exercise each Extension Right at least 12 months prior to the expiration of the Base Term of the Lease or the expiration of the prior Extension Term.

Upon the commencement of any Extension Term, Base Rent shall be payable at the Market Rate (as defined below). As used herein, " **Market Rate** " shall mean the rate (including, if applicable, periodic (but no more frequently than annual) increases) that comparable landlords of comparable buildings have accepted in current transactions from non-equity (i.e., not being offered equity in the buildings) and nonaffiliated tenants of similar financial strength for space of comparable size, quality (including all Tenant's Work, Alterations and other improvements) and floor height in Class A laboratory/office buildings in the Torrey Pines area of San Diego for a comparable term, with the determination of the Market Rate to take into account all relevant factors, including tenant inducements, views, signage rights, covered parking, available amenities other than the Amenities, age of the Building, age of mechanical systems serving the Premises, leasing commissions, allowances or concessions, if any. In addition, there may be a market rent for the parking rights provided hereunder if tenants of comparable buildings in the Torrey Pines area of San Diego are then customarily paying fees for parking rights granted under their leases and provided further that in the event that there is a market rent for parking rights, Base Rent shall exclude any consideration as to parking rights. Also, on the first day of each month during each Extension Term, Tenant shall also be required to pay an amenities fee in connection with the Amenities (the " **Amenities Fee** "). The Amenities Fee payable on the commencement date of the first year of the Extension Term shall be an amount calculated as follows: $0.18 per rentable square foot of the Premises per month escalated on each date that Base Rent is adjusted pursuant to the schedule set forth on page 1 of this Lease and on the commencement date of the Extension Term by multiplying the amount payable immediately before such adjustment date and commencement date, as applicable, by 2.9% (for example, on the first day of the 61 st month of the Base Term, the $0.18 per rentable square foot of the Premises per month would be escalated by 2.9% to $0.18522 per rentable square foot of the Premises per month and on the first day of the 73 rd month of the Base Term, the $0.18522 per rentable square foot of the Premises per month would be escalated to $0.19 per rentable square foot of the Premises per month, and so on). The Amenities Fee shall continue to increase through the first Extension Term by 2.9% on each annual anniversary of the commencement date of the first Extension Term and, if

Tenant elects to exercise its second Extension Term, the Amenities Fee shall increase on the commencement date of the second Extension Term and on each annual anniversary of the commencement date of the second Extension Term by 2.9%.

If, on or before the date which is 270 days prior to the expiration of the Base Term of this Lease or the expiration of the prior Extension Term (as applicable), Tenant has not agreed with Landlord's determination of the Market Rate and the rent escalations during the applicable Extension Term after negotiating in good faith, Tenant shall be deemed to have elected arbitration as described in Section 40(b) . If Tenant has elected to exercise an Extension Right by delivering notice to Landlord as required in this Section 40(a) , Tenant and, except as otherwise provided in Section 40(d) and Section 40(f) below, Landlord, shall have no right thereafter to rescind or elect not to extend the term of the Lease for such Extension Term.

(b) **Arbitration** .

(iii) Within 10 days of Tenant's notice to Landlord of its election (or deemed election) to arbitrate Market Rate and escalations, each party shall deliver to the other a proposal containing the Market Rate and escalations that the submitting party believes to be correct (" **Extension Proposal** "). If either party fails to timely submit an Extension Proposal, the other party may send a notice to such party indicating the failure and stating that if an Extension Proposal is not sent within 10 days after such second notice, the party's submitted proposal shall determine the Base Rent and escalations for the Extension Term. If either party fails to timely submit an Extension Proposal following such second notice, the party's submitted proposal shall determine the Base Rent and escalations for the Extension Term. If both parties submit Extension Proposals, then Landlord and Tenant shall meet within 7 days after delivery of the last Extension Proposal and make a good faith attempt to mutually appoint a single Arbitrator (and defined below) to determine the Market Rate and escalations. If Landlord and Tenant are unable to agree upon a single Arbitrator, then each shall, by written notice delivered to the other within 10 days after the meeting, select an Arbitrator. If either party fails to timely give notice of its selection for an Arbitrator, the other party's submitted proposal shall determine the Base Rent for the Extension Term. The 2 Arbitrators so appointed shall, within 5 business days after their appointment, appoint a third Arbitrator. If the 2 Arbitrators so selected cannot agree on the selection of the third Arbitrator within the time above specified, then either party, on behalf of both parties, may request such appointment of such third Arbitrator by application to any state court of general jurisdiction in the jurisdiction in which the Premises are located (or, if the state court does not agree to make such appointment, such appointment of such third Arbitrator shall be made by the President of the Greater San Diego Association of Realtors (or, if such President has previously worked for either party, the most immediate past President of the San Diego Association of Realtors not having such a conflict)), upon 10 days prior written notice to the other party of such intent.

(iv) The decision of the Arbitrator(s) shall be made within 30 days after the appointment of a single Arbitrator or the third Arbitrator, as applicable. The decision of the single Arbitrator shall be final and binding upon the parties. The average of the two closest Arbitrators in a three Arbitrator panel shall be final and binding upon the parties. Each party shall pay the fees and expenses of the Arbitrator appointed by or on behalf of such party and the fees and expenses of the third Arbitrator shall be borne equally by both parties. If the Market Rate and escalations are not determined by the first day of the Extension Term, then Tenant shall pay Landlord Base Rent in an amount equal to the Base Rent in effect immediately prior to the Extension Term and increased by the Rent Adjustment Percentage until such determination is made. After the determination of the Market Rate and escalations, the parties shall make any necessary adjustments to such payments made by Tenant. Landlord and Tenant shall then execute an amendment recognizing the Market Rate and escalations for the Extension Term.

(v) An " **Arbitrator** " shall be any person appointed by or on behalf of either party or appointed pursuant to the provisions hereof and: (i) shall be (A) a member of the American Institute

of Real Estate Appraisers with not less than 10 years of experience in the appraisal of improved office and high tech industrial real estate in the greater San Diego metropolitan area, or (B) a licensed commercial real estate broker with not less than 15 years' experience representing landlords and/or tenants in the leasing of high tech or life sciences space in the greater San Diego metropolitan area, (ii) devoting substantially all of their time to professional appraisal or brokerage work, as applicable, at the time of appointment and (iii) be in all respects impartial and disinterested.

(c) **Rights Personal** . Extension Rights are personal to Vertex Pharmaceuticals Incorporated and are not assignable without Landlord's consent, which may be granted or withheld in Landlord's sole discretion separate and apart from any consent by Landlord to an assignment of Tenant's interest in the Lease, except that they may be assigned in connection with any Permitted Assignment of this Lease.

(d) **Exceptions** . Notwithstanding anything set forth above to the contrary, Extension Rights shall, at Landlord's option, not be in effect and Tenant may not exercise any of the Extension Rights:

(i) during any period of time that Tenant is in Default under any provision of this Lease; or

(ii) if Tenant has been in Default under any provision of this Lease 3 or more times, whether or not the Defaults are cured, during the 12 month period immediately prior to the date that Tenant intends to exercise an Extension Right, whether or not the Defaults are cured.

(e) **No Extensions** . The period of time within which any Extension Rights may be exercised shall not be extended or enlarged by reason of Tenant's inability to exercise the Extension Rights.

(f) **Termination** . The Extension Rights shall, at Landlord's option, terminate and be of no further force or effect even after Tenant's due and timely exercise of an Extension Right, if, after such exercise, but prior to the commencement date of an Extension Term, (i) Tenant fails to timely cure any default by Tenant under this Lease; or (ii) Tenant has Defaulted 3 or more times during the period from the date of the exercise of an Extension Right to the date of the commencement of the Extension Term, whether or not such Defaults are cured.

41. **The Alexandria at Torrey Pines** .

(a) **Generally** . ARE-SD Region No. 17, LLC, a Delaware limited liability company (" **ATP Landlord** ") has constructed certain amenities at the property owned by ATP Landlord located at 10996 Torreyana Road, San Diego, California (" **The Alexandria** "), which include, without limitation, shared conference facilities (" **Shared Conference Facilities** "), a fitness center and restaurant (collectively, the " **Amenities** ") for non-exclusive use by (a) Tenant, (b) other tenants of the Project, (c) Landlord, (d) the tenants of ATP Landlord, (e) ATP Landlord, (e) other affiliates of Landlord, ATP Landlord and Alexandria Real Estate Equities, Inc. (" **ARE** "), (f) the tenants of such other affiliates of Landlord, ATP Landlord and ARE, and (g) any other parties permitted by ATP Landlord (collectively, " **Users** "). Landlord, ATP Landlord, ARE, and all affiliates of Landlord, ATP Landlord and ARE may be referred to collectively herein as the " **ARE Parties** ." Notwithstanding anything to the contrary contained herein, Tenant acknowledges and agrees that ATP Landlord shall have the right, at the sole discretion of ATP Landlord, to discontinue the availability of The Alexandria at any time; provided, however, in no event shall ATP Landlord discontinue Tenant's rights to use the Amenities while continuing the rights of other tenants of the Project or the rights of tenants of affiliates of Landlord, ATP Landlord and ARE (or their respective successors or assigns) to use the Amenities. ATP Landlord shall have the sole right to determine all matters related to the Amenities including, without limitation, relating to the reconfiguration, relocation, modification or removal of any of the Amenities at The Alexandria and/or to revise, expand or discontinue any of the services (if any) provided in connection with the Amenities. Tenant acknowledges and agrees that Landlord has not made any representations or warranties regarding the continued availability of any of the Amenities and that Tenant is not entering into this Lease with an expectation that the Amenities shall continue to be available to Tenant throughout the Term.

(b) **License** . Commencing on the mutual execution and delivery of this Lease by the parties, and so long as (i) The Alexandria and the Project continue to be owned by affiliates of ARE, (ii) The Alexandria continues to be operated as an amenities center, and (iii) ATP Landlord continues to make the Amenities available for use by Tenant, Tenant shall have the non-exclusive right to the use of the available Amenities in common with other Users pursuant to the terms of this Section 41 . A total of 388 passes to the fitness center shall be issued to Tenant for its employees (but, following the Rent Commencement Date, the persons using such passes must be employed at the Premises). Neither Tenant nor its employees shall have any right to access and/or use the Amenities unless Tenant and its employees have entered into license and use agreements (including indemnification and waiver agreements required by ATP Landlord) with respect to such Amenities which are in form and content reasonably acceptable to Landlord and/or ATP Landlord (the " **Standard Use Agreements** "). If, during the Base Term, the Amenities in their entirety become materially unavailable for use by Tenant (for any reason other than a Default by Tenant under this Lease or the default by Tenant of any Standard Use Agreements or other agreement(s) relating to the use of the Amenities by Tenant) for a period in excess of 15 consecutive days, then, commencing on the date that the Amenities in their entirety become materially unavailable for use by Tenant and continuing for the period that the Amenities in their entirety remain materially unavailable for use by Tenant, the Base Rent due under this Lease shall be reduced by an amount equal to $0.18 per rentable square foot of the Premises per month escalated on each date that Base Rent is adjusted pursuant to the schedule set forth on page 1 of this by multiplying the amount payable immediately before such adjustment date by 2.9% (for example, on the first day of the 61 st month of the Base Term, the $0.18 per rentable square foot of the Premises per month would be escalated by 2.9% to $0.18522 per rentable square foot of the Premises per month and on the first day of the 73 rd month of the Base Term, the $0.18522 per rentable square foot of the Premises per month to $0.19 per rentable square foot of the Premises, and so on).

(c) **Shared Conference Facilities** . Use by Tenant of the Shared Conference Facilities and restaurant at The Alexandria shall be in common with other Users with scheduling procedures reasonably determined by ATP Landlord. ATP Landlord reserves the right to exercise its reasonable discretion in the event of conflicting scheduling requests among Users. Tenant hereby acknowledges that (i) Biocom/San Diego, a California non-profit corporation (" **Biocom** ") has the right to reserve the Shared Conference Facilities and any reservable dining area(s) included as part of the Amenities at The Alexandria for up to 50% of the time that such Shared Conference Facilities and reservable dining area(s) are available for use by Users each calendar month, and (ii) Illumina, Inc., a Delaware corporation, has the exclusive use of the main conference room within the Shared Conference Facilities for up to 4 days per calendar month.

Any vendors engaged by Tenant in connection with Tenant's use of the Shared Conference Facilities shall be professional vendors holding any required licenses. ATP Landlord shall have the right to reasonably approve any vendors utilized by Tenant in connection with Tenant's use of the Shared Conference Facilities. Prior to any entry by any such vendor onto The Alexandria, Tenant shall deliver to Landlord a copy of the contract between Tenant and such vendor and certificates of insurance from such vendor evidencing industry standard commercial general liability, automotive liability, and workers' compensation insurance. Tenant shall cause all such vendors utilized by Tenant to provide a certificate of insurance naming Landlord, ARE, and ATP Landlord as additional insureds under the vendor's liability policies. Notwithstanding the foregoing, Tenant shall be required to use the food service operator used by ATP Landlord at The Alexandria for any food service or catered events held by Tenant in the Shared Conference Facilities.

Tenant shall, at Tenant's sole cost and expense, (i) be responsible for the set-up of the Shared Conference Facilities in connection with Tenant's use (including, without limitation ensuring that Tenant has a sufficient number of chairs and tables and the appropriate equipment), and (ii) surrender the Shared Conference Facilities after each time that Tenant uses the Shared Conference Facilities free of Tenant's personal property, in substantially the same set up and same condition as received, subject to casualty, and free of any debris and trash. If Tenant fails to restore and surrender the Shared Conference Facilities as required by sub-section (ii) of the immediately preceding sentence, such failure shall constitute a " **Shared Facilities Failure** ." Each time that Landlord or ATP Landlord reasonably determines that Tenant has committed a Shared Facilities Failure, Tenant shall be required to pay Landlord a penalty within 5 days after

notice from Landlord of such Shared Facilities Failure. The penalty payable by Tenant in connection with the first Shared Facilities Failure shall be $200. The penalty payable shall increase by $50 for each subsequent Shared Facilities Failure (for the avoidance of doubt, the penalty shall be $250 for the second Shared Facilities Failure, shall be $300 for the third Shared Facilities Failure, etc.). In addition to the foregoing, Tenant shall be responsible for reimbursing ATP Landlord or Landlord, as applicable, for all costs expended by ATP Landlord or Landlord, as applicable, in repairing any damage to the Shared Conference Facilities, the Amenities, or The Alexandria caused by Tenant or any Tenant Related Party. The provisions of this Section 41(c) shall survive the expiration or earlier termination of this Lease.

(d) **Rules and Regulations** . Tenant shall be solely responsible for paying for any and all ancillary services (e.g., audio visual equipment) provided to Tenant, all food services operators and any other third party vendors providing services to Tenant at The Alexandria. Tenant shall use the Amenities (including, without limitation, the Shared Conference Facilities) in compliance with all applicable Legal Requirements and any reasonable rules and regulations imposed by ATP Landlord or Landlord from time to time (which rules shall not be enforced in a discriminatory manner) and in a manner that will not interfere with the rights of other Users. The use of Amenities other than the Shared Conference Facilities by employees of Tenant shall be in accordance with the terms and conditions of the License Agreements. Neither ATP Landlord nor Landlord (nor, if applicable, any other affiliate of Landlord) shall have any liability or obligation for the breach of any rules or regulations by other Users with respect to the Amenities. Tenant shall not make any alterations, additions, or improvements of any kind to the Shared Conference Facilities, the Amenities or The Alexandria.

Tenant acknowledges and agrees that ATP Landlord shall have the right at any time and from time to time to reconfigure, relocate, modify or remove any of the Amenities at The Alexandria and/or to revise, expand or discontinue any of the services (if any) provided in connection with the Amenities.

(e) **Waiver of Liability and Indemnification** . Tenant warrants that it will use reasonable care to prevent damage to property and injury to persons while on The Alexandria. To the extent permitted by applicable law, Tenant waives any claims it or any Tenant Parties may have against any ARE Parties relating to, arising out of or in connection with the Amenities and any entry by Tenant and/or any Tenant Parties onto The Alexandria, except to the extent caused by the willful misconduct or gross negligence of any ARE Party, and Tenant releases and exculpates all ARE Parties from any liability relating to, arising out of or in connection with the Amenities and any entry by Tenant and/or any Tenant Parties onto The Alexandria. Tenant hereby agrees to indemnify, defend, and hold harmless the ARE Parties from any claim of damage to property or injury to person relating to, arising out of or in connection with (i) the use of the Amenities by Tenant or any Tenant Parties, and (ii) any entry by Tenant and/or any Tenant Parties onto The Alexandria, except to the extent caused by the willful misconduct or negligence of any ARE Party. The provisions of this Section 41 shall survive the expiration or earlier termination of this Lease.

(f) **Insurance** . As of the mutual execution and delivery of this Lease by the parties, Tenant shall cause ATP Landlord to be named as an additional insured under the commercial general liability policy of insurance that Tenant is required to maintain pursuant to Section 17 of this Lease.

42. **Roof Equipment** . As long as Tenant is not in Default under this Lease, Tenant shall have the right at its sole cost and expense, subject to compliance with all Legal Requirements (including, without limitation, any height limitations imposed by the City of San Diego with Tenant acknowledging and agreeing that the planned height of the Building may result in Tenant not having any rights under this Section 42), to install, maintain, and remove on the top of the roof of the Building one or more satellite dishes, communication antennae and other equipment for the transmission or reception of communication of signals, mechanical equipment, heat exchangers or other similar equipment (all of which having a diameter and height reasonably acceptable to Landlord) as Tenant may from time to time desire (collectively, " **Roof Equipment** ") on the following terms and conditions:

(a) **Requirements** . Tenant shall submit to Landlord (i) the plans and specifications for the installation of the Roof Equipment, (ii) copies of all required governmental and quasi-governmental permits, licenses, and authorizations that Tenant will and must obtain at its own expense, with the cooperation of Landlord, if necessary for the installation and operation of the Roof Equipment, and (iii) an insurance policy or certificate of insurance evidencing insurance coverage as required by this Lease and any other insurance as reasonably required by Landlord for the installation and operation of the Roof Equipment. Landlord shall not unreasonably withhold or delay its approval for the installation and operation of the Roof Equipment; provided , however , that Landlord may reasonably withhold its approval if the installation or operation of the Roof Equipment (A) may damage the structural integrity of the Building, (B) may void, terminate, or invalidate any applicable roof warranty, (C) may reduce the leasable space in the Building, or (D) is not properly screened from the viewing public to Landlord's reasonable satisfaction.

(b) **No Damage to Roof** . If installation of the Roof Equipment requires Tenant to make any roof cuts or perform any other roofing work, such cuts shall only be made to the roof area of the Building located directly above the Premises and only in the manner designated in writing by Landlord; and any such installation work (including any roof cuts or other roofing work) shall be performed by Tenant, at Tenant's sole cost and expense by a roofing contractor designated by Landlord or otherwise reasonably approved by Landlord. If Tenant or its agents shall otherwise cause any damage to the roof during the installation, operation, and removal of the Roof Equipment such damage shall be repaired promptly at Tenant's expense and the roof shall be restored in the same condition it was in before the damage, ordinary wear and tear excepted. Landlord shall not charge Tenant Additional Rent for the installation and use of the Roof Equipment. If, however, Landlord's insurance premium or Tax assessment increases as a result of the Roof Equipment, Tenant shall pay such increase as Additional Rent within thirty (30) days after receipt of a reasonably detailed invoice from Landlord. Tenant shall not be entitled to any abatement or reduction in the amount of Rent payable under this Lease if for any reason Tenant is unable to use the Roof Equipment. In no event whatsoever shall the installation, operation, maintenance, or removal of the Roof Equipment by Tenant or its agents void, terminate, or invalidate any applicable roof warranty.

(c) **Protection** . The installation, operation, and removal of the Roof Equipment shall be at Tenant's sole risk. Tenant shall indemnify, defend, and hold Landlord harmless from and against any and all claims, costs, damages, liabilities and expenses (including, but not limited to, attorneys' fees) of every kind and description that may arise out of or be connected in any way with Tenant's installation, operation, or removal of the Roof Equipment.

(d) **Removal** . At the expiration or earlier termination of this Lease or the discontinuance of the use of the Roof Equipment by Tenant, Tenant shall, at its sole cost and expense, remove the Roof Equipment from the Building. Tenant shall leave the portion of the roof where the Roof Equipment was located in good order and repair, reasonable wear and tear excepted. If Tenant does not so remove the Roof Equipment, Tenant hereby authorizes Landlord to remove and dispose of the Roof Equipment and charge Tenant as Additional Rent for all costs and expenses incurred by Landlord in such removal and disposal. Tenant agrees that Landlord shall not be liable for any Roof Equipment or related property disposed of or removed by Landlord.

(e) **No Interference** . The Roof Equipment shall not interfere with the proper functioning of any telecommunications equipment or devices that have been installed prior to the installation of the Roof Equipment.

(f) **Relocation** . Landlord shall have the right, at its expense (but not as an Operating Expense) and after 60 days prior notice to Tenant, to relocate the Roof Equipment to another site on the roof of the Building as long as such site reasonably meets Tenant's sight line and interference requirements and does not unreasonably interfere with Tenant's use and operation of the Roof Equipment.

(g) **Access** . Landlord grants to Tenant the right of ingress and egress on a 24 hour 7 day per week basis to install, operate, and maintain the Roof Equipment. Before receiving access to the roof of the

Building, Tenant shall give Landlord at least 24 hours' advance written or oral notice, except (i) in emergency situations, in which case reasonable advance oral notice shall be given by Tenant and (ii) access for standard, periodic maintenance, in which case a one-time notice to Landlord of the nature of the maintenance and the general frequency of the access shall be adequate. Landlord shall supply Tenant with the name, telephone, and pager numbers of the contact individual(s) responsible for providing access during emergencies.

(h) **Appearance** . If permissible by Legal Requirements and reasonably practicable, the Roof Equipment shall be painted the same color as the exterior structural painted elements of the Building.

(i) **Intentionally Omitted** .

(j) **No Assurance of Roof Equipment** . Notwithstanding anything to the contrary contained herein, Tenant acknowledges and agrees that (i) Landlord shall have no obligation to alter any plans Landlord may have, now or in the future, for the height of the Building so that Tenant may exercise or use any of its rights under this Section 42 and (ii) Landlord may use the full height allocated to the Project so that Tenant will not have the right to exercise or use any of its rights under this Section 42 in which case Tenant shall have no further rights under this Section 42 . Notwithstanding the foregoing, Tenant shall have the right to pursue, so long as Landlord's development, use or operation of the Building is not materially adversely affected and the Building structure and Building Systems are not materially adversely affected, at Tenant's sole cost and expense, approvals and/or permits required from the applicable Governmental Entities for the installation and maintenance by Tenant of Roof Equipment which would exceed any height requirements imposed by applicable Governmental Entities, and if Tenant obtains such approvals and/or permits, Tenant shall have the right to install and maintain such Roof Equipment which would exceed such height requirements subject to the terms of this Section 42 . Landlord shall reasonably cooperate, at no cost to Landlord, in Tenant's efforts to obtain approvals and/or permits

43. **Emergency Generator** . Subject to Tenant complying with all of the provisions of this Lease including, without limitation, Section 12 hereof, and all applicable Legal Requirements and Landlord's rules and regulations, Tenant shall have the right, at Tenant's sole cost and expense, to install an emergency generator and related tanks and equipment (collectively, " **Emergency Generator** ") in a location at the Project reasonably acceptable to both Landlord and Tenant (" **Generator Area** "). All such improvements to the Generator Area shall be of a design and type and with screening acceptable to Landlord, in Landlord's reasonable discretion. Landlord shall have the right, in its sole and absolute discretion, to require Tenant to remove any such Emergency Generator installed by Tenant and restore the Generator Area to its original use and condition, free of any debris and trash and free of any Hazardous Materials, upon the expiration or earlier termination of the Term. Landlord shall have no obligation to make any repairs or improvements to the Emergency Generator or the Generator Area and Tenant shall maintain the same, at Tenant's sole cost and expense, in good repair and condition during the Term as though the same were part of the Premises.

44. **LEED Certification** . Tenant agrees to reasonably cooperate with Landlord and to use commercially reasonable efforts to comply with measures reasonably implemented by Landlord with respect to the Building and/or the Project in connection with Landlord's efforts, if any, to obtain a Leadership in Energy and Environmental Design (LEED) certificate for Landlord's Work. Tenant shall have the right, at its sole discretion and at Tenant's sole cost and expense, to pursue LEED certification for the Tenant's Work.

45. **Learning Lab** .

(a) **General** . Tenant may operate a portion of the Premises in a location selected by Tenant and reasonably acceptable to Landlord but not to exceed 1,500 rentable square feet (the " **Learning Lab** "), as a center for science education providing programs and services for children from and around the San Diego area. Tenant shall be responsible, at Tenant's sole cost and expense for any and all furniture, fixtures and equipment desired by Tenant with respect to the Learning Lab. Tenant shall also be responsible during the Term, at Tenant's sole cost and expense, for all aspects of the staffing and operation of the Learning Lab in compliance with all applicable Legal Requirements and in a Class A manner and for providing all materials

required in connection with such operation of the Learning Lab. The Rentable Area of Premises set forth on page 1 of this Lease includes all of the rentable area of the Premises, including any space that may be included in the Learning Lab. Tenant shall not be required to pay Base Rent with respect to the Learning Lab but shall, commencing on the Rent Commencement Date, pay Operating Expenses with respect to the Learning Lab throughout the Term subject to and in accordance with the terms of Section 5 of this Lease (meaning that the rentable square footage of the Learning Lab (not to exceed 1,500 rsf) shall be deducted from the Rentable Area of Premises as defined on page 1 of this Lease for the purpose of determining Base Rent, but Tenant's Share of Operating Expenses of Building shall not be reduced); provided, however, that if at any time during the Term Tenant ceases operating the Learning Lab as a center for science education as provided in this paragraph or otherwise commences using the Learning Lab in connection with its business operations, Tenant shall be required to pay Base Rent with respect to the Learning Lab at the same rate per rentable square foot as Tenant is then paying with respect to the balance of the Premises. At any time during the Term, Tenant shall have the right to elect by written notice to Landlord to terminate the agreement with Landlord regarding the Learning Lab set forth in this Section 45 , in which event (i) Tenant shall immediately commence paying Base Rent with respect to the Learning Lab at the same rate per rentable square foot as Tenant is then paying with respect to the balance of the Premises, (ii) this Section 45 shall terminate and have no further force or effect, and (iii) Tenant shall continue to have the right as a Permitted Use hereunder, in Tenant's sole discretion, to use all or any portion of the Premises as a center for science education providing programs and services for children from and around the San Diego area, but without the obligations of Sections 45(b) and (c).

(b) **Signage** . Landlord and Tenant shall develop a mutually acceptable logo that represents the involvement of both Landlord (or, if designated by Landlord, an affiliate of Landlord) and Tenant with the Learning Lab, which logo shall, during any period that Tenant operates the Learning Lab as an educational facility pursuant to Section 45(a) above, be included on signage at the entry of the Learning Lab and at other locations within the Learning Lab reasonably acceptable to Landlord and Tenant. Tenant shall not use the logo other than as expressly provided in this Section 45(b) and, if requested to do so by Landlord, Tenant shall promptly remove any reference to Landlord (or Landlord's affiliate, if applicable) from the logo.

(c) **Calendar of Events** . Tenant shall provide Landlord with reasonable advance notice of all events being held at the Learning Lab while the Learning Lab operates as an educational facility pursuant to Section 45(a) above so that Landlord may, if it so elects and without any obligation to do so, attend any such events.

46. **Miscellaneous** .

(a) **Notices** . All notices or other communications between the parties shall be in writing and shall be deemed duly given upon delivery or refusal to accept delivery by the addressee thereof if delivered in person, or upon actual receipt if delivered by reputable overnight guaranty courier, addressed and sent to the parties at their addresses set forth above. Landlord and Tenant may from time to time by written notice to the other designate another address for receipt of future notices.

(b) **Joint and Several Liability** . If and when included within the term " **Tenant** ," as used in this instrument, there is more than one person or entity, each shall be jointly and severally liable for the obligations of Tenant.

(c) **Financial Information** . Tenant shall furnish Landlord with true and complete copies of (i) Tenant's most recent audited annual financial statements within 180 days of the end of each of Tenant's fiscal years during the Term, and (ii) Tenant's most recent unaudited quarterly financial statements within 90 days of the end of each of Tenant's first three fiscal quarters of each of Tenant's fiscal years during the Term. So long as Tenant or Tenant's parent entity (to the extent that the Tenant's financial statements are consolidated with those of its parent entity and separate financial statements are not maintained with respect to Tenant) is a "public company" and its financial information is publicly available, then the foregoing delivery requirements of this Section 44(c) shall not apply.

(d) **Recordation** . Neither this Lease nor a memorandum of lease shall be filed by or on behalf of Tenant in any public record. Notwithstanding the foregoing, upon Tenant's request and at Tenant's sole cost and expense, Landlord shall execute and properly notarize a memorandum of lease prepared by Tenant which memorandum shall contain only the following information and any other additional information that may be required by applicable law: (i) the names of the parties to this Lease, (ii) description of the Premises and the Project, and (iii) the Term. Tenant shall file such memorandum of lease, at Tenant's sole cost. If Tenant fails, after written request from Landlord, to record a termination of the memorandum on the expiration or earlier termination of this Lease, Tenant shall be responsible for any damages suffered by Landlord (from any cause including, without limitation, resulting from any indemnities or certifications which may be made by Landlord in favor of third parties). The provisions of this Section 46(d) shall survive the expiration or earlier termination of this Lease.

(e) **Interpretation** . The normal rule of construction to the effect that any ambiguities are to be resolved against the drafting party shall not be employed in the interpretation of this Lease or any exhibits or amendments hereto. Words of any gender used in this Lease shall be held and construed to include any other gender, and words in the singular number shall be held to include the plural, unless the context otherwise requires. The captions inserted in this Lease are for convenience only and in no way define, limit or otherwise describe the scope or intent of this Lease, or any provision hereof, or in any way affect the interpretation of this Lease.

(f) **Not Binding Until Executed** . The submission by Landlord to Tenant of this Lease shall have no binding force or effect, shall not constitute an option for the leasing of the Premises, nor confer any right or impose any obligations upon either party until execution of this Lease by both parties.

(g) **Limitations on Interest** . It is expressly the intent of Landlord and Tenant at all times to comply with applicable law governing the maximum rate or amount of any interest payable on or in connection with this Lease. If applicable law is ever judicially interpreted so as to render usurious any interest called for under this Lease, or contracted for, charged, taken, reserved, or received with respect to this Lease, then it is Landlord's and Tenant's express intent that all excess amounts theretofore collected by Landlord be credited on the applicable obligation (or, if the obligation has been or would thereby be paid in full, refunded to Tenant), and the provisions of this Lease immediately shall be deemed reformed and the amounts thereafter collectible hereunder reduced, without the necessity of the execution of any new document, so as to comply with the applicable law, but so as to permit the recovery of the fullest amount otherwise called for hereunder.

(h) **Choice of Law** . Construction and interpretation of this Lease shall be governed by the internal laws of the state in which the Premises are located, excluding any principles of conflicts of laws.

(i) **Time** . Time is of the essence as to the performance of Tenant's obligations under this Lease.

(j) **OFAC** . Tenant and Landlord are currently (a) in compliance with and shall at all times during the Term of this Lease remain in compliance with the regulations of the Office of Foreign Assets Control (" **OFAC** ") of the U.S. Department of Treasury and any statute, executive order, or regulation relating thereto (collectively, the " **OFAC Rules** "), (b) not listed on, and shall not during the term of this Lease be listed on, the Specially Designated Nationals and Blocked Persons List, Foreign Sanctions Evaders List, or the Sectoral Sanctions Identification List, which are all maintained by OFAC and/or on any other similar list maintained by OFAC or other governmental authority pursuant to any authorizing statute, executive order, or regulation, and (c) not a person or entity with whom a U.S. person is prohibited from conducting business under the OFAC Rules.

(k) **Incorporation by Reference** . All exhibits and addenda attached hereto are hereby incorporated into this Lease and made a part hereof. If there is any conflict between such exhibits or addenda and the terms of this Lease, such exhibits or addenda shall control.

(l) **Entire Agreement** . This Lease, including the exhibits attached hereto, constitutes the entire agreement between Landlord and Tenant pertaining to the subject matter hereof and supersedes all prior and contemporaneous agreements, understandings, letters of intent, negotiations and discussions, whether oral or written, of the parties, and there are no warranties, representations or other agreements, express or implied, made to either party by the other party in connection with the subject matter hereof except as specifically set forth herein.

(m) **No Accord and Satisfaction** . No payment by Tenant or receipt by Landlord of a lesser amount than the monthly installment of Base Rent or any Additional Rent will be other than on account of the earliest stipulated Base Rent and Additional Rent, nor will any endorsement or statement on any check or letter accompanying a check for payment of any Base Rent or Additional Rent be an accord and satisfaction. Landlord may accept such check or payment without prejudice to Landlord's right to recover the balance of such Rent or to pursue any other remedy provided in this Lease.

(n) **Hazardous Activities** . Notwithstanding any other provision of this Lease, Landlord, for itself and its employees, agents and contractors, reserves the right to refuse to perform any repairs or services in any portion of the Premises which, pursuant to Tenant's routine safety guidelines, practices or custom or prudent industry practices, require any form of protective clothing or equipment other than safety glasses. In any such case, Tenant shall contract with parties who are acceptable to Landlord, in Landlord's reasonable discretion, for all such repairs and services, and Landlord shall, to the extent required, equitably adjust Tenant's Share of Operating Expenses in respect of such repairs or services to reflect that Landlord is not providing such repairs or services to Tenant.

(o) **Redevelopment of Project** . Tenant acknowledges that Landlord, in its sole discretion, may, subject to the terms of the fourth sentence of Section 1 and the limitations set forth in this Section 46(o) , from time to time expand, renovate and/or reconfigure the Project as the same may exist from time to time and, in connection therewith or in addition thereto, as the case may be, from time to time without limitation: (a) change the shape, size, location, number and/or extent of any improvements, buildings, structures, lobbies, hallways, entrances, exits, parking and/or parking areas relative to any portion of the Project; (b) modify, eliminate and/or add any buildings, improvements, and parking structure(s) either above or below grade, to the Project, the Common Areas and/or any other portion of the Project and/or make any other changes thereto affecting the same; and (c) make any other changes, additions and/or deletions in any way affecting the Project and/or any portion thereof as Landlord may elect from time to time, including without limitation, additions to and/or deletions from the land comprising the Project, the Common Areas and/or any other portion of the Project; provided, however, in no event may Landlord make any changes to the Building (including the subterranean parking garage) or, subject to the terms of the immediately following paragraph, reduce the parking spaces available to Tenant and in no event shall Tenant's use of the Exclusive Use Areas including, but not limited to, the courtyard/meadow area located on the east side of the Building facing the canyons be materially or adversely affected. Landlord shall consult with Tenant if Landlord plans to make any changes to the Project pursuant to this Section 46(o) that would materially adversely affect the entrance to the Building. Notwithstanding anything to the contrary contained in this Lease, Tenant shall have no right to seek damages (including abatement of Rent) or to cancel or terminate this Lease because of any proposed changes, expansion, renovation or reconfiguration of the Project nor shall Tenant have the right to restrict, inhibit or prohibit any such changes, expansion, renovation or reconfiguration; provided, however, Landlord shall not change the size, dimensions, location or Tenant's Permitted Use of the Premises (including the subterranean parking garage).

If, at any time during the Term, Landlord elects to expand, renovate and/or reconfigure the Project pursuant to the immediately preceding paragraph, Landlord shall have the right, exercisable upon 30 days prior written notice to Tenant to relocate all or any portion of Tenant's parking spaces hereunder on a temporary basis during such expansion, renovation and/or reconfiguration to one or more locations designated by Landlord in the Torrey Pines area of San Diego within a one-mile radius of the Premises. Landlord shall, at Landlord's sole cost and expense (and not as an Operating Expense), provide a shuttle service between such locations and the Project.

[Signatures on next page]

IN WITNESS WHEREOF, Landlord and Tenant have executed this Lease as of the day and year first above written.

TENANT:

VERTEX PHARMACEUTICALS INCORPORATED ,
a Massachusetts corporation

/s/ Ian Smith

By: Ian Smith
Its: Chief Financial Officer

LANDLORD:

ARE-SD REGION NO. 23, LLC ,
a Delaware limited liability company

By: ALEXANDRIA REAL ESTATE EQUITIES, L.P.,
a Delaware limited partnership,
managing member

By: ARE-QRS CORP.,
a Maryland corporation,
general partner

/s/ Gary Dean

By: Gary Dean
Its: SVP RE Legal Affairs

Acknowledging and agreeing to be bound with respect to the applicable obligations set forth in Section 41 of this Lease with respect to the Amenities only:

ARE-SD REGION NO. 17, LLC ,
a Delaware limited liability company

By: ALEXANDRIA REAL ESTATE EQUITIES, L.P.,
a Delaware limited partnership,
managing member

By: ARE-QRS CORP.,
a Maryland corporation,
general partner

/s/ Gary Dean

By: Bary Dean
Its: SVP RE Legal Affairs

Exhibit 10.25

VERTEX PHARMACEUTICALS INCORPORATED
2013 STOCK AND OPTION PLAN

Restricted Stock Unit Award

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

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

[INSERT NAME/ADDRESS]

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

[_____]

3. Purchase price of Shares upon Vesting:

[_____]

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

[_____]

5. Vesting. [INSERT PERFORMANCE BASED OR TIME BASED VESTING CONDITIONS AND SCHEDULE, AS APPLICABLE].

On each vesting date described in the preceding sentence, the Participant shall be entitled to receive the number of shares of Common Stock equal to the number of Shares becoming vested that shall thereafter be delivered by the Company to the Participant in accordance with this Agreement and the Plan within two business days following the applicable vesting date. Except as otherwise provided in Exhibit A of this Agreement, upon any Termination of Service of the Participant for any reason, vesting of the Shares shall immediately cease, and the unvested portion of the Restricted Stock Unit Award shall immediately be forfeited.

6. Agreement with respect to Tax Payments. The Participant acknowledges and agrees that any income or other taxes due from the Participant with respect to the Shares issued pursuant to this Agreement, including on account of the vesting of the Shares, shall be the Participant's responsibility. By accepting this Agreement, the Participant agrees and acknowledges that (i) the Company promptly will withhold from the Participant's pay the amount of taxes the Company is required to withhold upon any vesting of Shares pursuant to this Agreement, and (ii) the Participant shall make immediate payment to the Company in the amount of any tax required to be withheld by the Company in excess of the Participant's pay available for such withholding.

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

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

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

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

11. Plan. The Participant hereby acknowledges receipt of a copy of the Plan as presently in effect and the Prospectus with respect thereto. All of the terms and provisions of the Plan are incorporated herein by reference, and this Restricted Stock Unit Award is subject to those terms and provisions in all respects.

VERTEX PHARMACEUTICALS INCORPORATED

By: _____

EXHIBIT A

Adjustments to Vesting Schedule

A) **Death of the Participant** . If the Participant dies while an Employee, Non-Employee Director, consultant or advisor of the Company or an Affiliate, 100% of the remaining Shares subject to this Restricted Stock Unit Award shall be accelerated and shall be delivered to the Participant's Survivors as soon as practicable, but no more than 90 days, after the Participant's date of death.

B) **Termination for Cause.** If the Participant's employment with the Company is terminated due to Cause, any portion of the Restricted Stock Unit Award that has not vested prior to the date written notice of such termination is provided to the Participant shall be immediately forfeited. If the Company is investigating or evaluating whether the Company will terminate Participant's employment or other service to the Company for Cause, the Company may, at its election, suspend the vesting of this Restricted Stock Unit Award by written notice to the Participant. If after such notification it is determined or otherwise agreed that Participant's service to the Company will not be terminated for Cause, vesting of the Shares shall resume pursuant to the original schedule and any Shares that would have vested during such suspension immediately shall vest. However, if the period of the investigation extends beyond 90 days after the Restricted Stock Unit Award otherwise vests, any Shares that would have otherwise become vested during the period of suspension shall become vested on such 90th day. In such event, any Shares of Common Stock delivered while the Company's investigation is pending shall be non-transferable until the conclusion of the investigation without a determination that Cause for termination exists, and such Common Stock shall be immediately forfeited by the Participant and returned to the Company if the Company determines that Cause for the Participant's termination exists.

C) **Retirement Provision.** If a Participant experiences a Termination of Service other than for Cause, and the Participant is a Qualified Participant (as defined below), then the FCP % of the remaining Shares subject to this Restricted Stock Unit Award that have not previously vested shall vest as of the date of the Termination of Service.

A " Qualified Participant " shall mean a Participant who meets all of the following conditions: (i) he or she is at least fifty-five (55) years old, (ii) he or she has completed at least five (5) full years of service as an Employee and/or a Non-Employee Director to the Company or an Affiliate, (iii) his or her age plus full years of service as an Employee and/or a Non-Employee Director to the Company or an Affiliate is 65 or greater and (iv) he or she has completed a mandatory transitional period of employment with the Company following written notice of the Termination of Service by the Participant, the duration of which will be no fewer than twelve (12) months, except as may be determined by the Company in its sole discretion or as may be required by applicable law.

The " FCP %" shall be equal to (a) the sum of 50% plus 10% for each full year of service as an Employee and/or a Non-Employee Director to the Company or an Affiliate in excess of five (5) full years of service.

[INSERT ADDITIONAL ACCELERATION PROVISIONS, AS APPPLICABLE]

Exhibit 10.27

VERTEX PHARMACEUTICALS
NON-EMPLOYEE DIRECTOR DEFERRED COMPENSATION PLAN
Effective January 1, 2016

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Exhibit 10.27

VERTEX PHARMACEUTICALS NON-EMPLOYEE DIRECTOR DEFERRED COMPENSATION PLAN

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Exhibit 10.27

Vertex Pharmaceuticals
Non-Employee Director Deferred Compensation Plan
Effective January 1, 2016

PURPOSE

The purpose of this Plan is to provide deferred compensation to non-employee directors of Vertex Pharmaceuticals Incorporated. The Plan is not subject to the Employee Retirement Income Security Act of 1974. This Plan is intended to comply with Code Section 409A and the regulations and guidance thereunder. This Plan is a sub-plan of the Vertex Pharmaceuticals Incorporated 2013 Stock and Option Plan, as permitted by section 26 of such plan, and is subject to the terms and conditions of the Stock and Option Plan. This Plan is adopted effective as of January 1, 2016.

ARTICLE 1
Definitions

For purposes of this Plan, unless otherwise clearly apparent from the context, the following phrases or terms shall have the following meanings:

1.1 "Account Balance" means the aggregate number of Deferred Stock Units or cash allocated on account of a Participant's deferrals to the Plan, as adjusted in accordance with Article 3 of the Plan. This account shall be a bookkeeping entry only and shall be utilized solely as a device for the measurement and determination of the number of shares of Common Stock to be paid to or in respect of a Participant pursuant to the Plan.

1.2 "Administrator" means the Committee or such person or persons as may be appointed by the Committee to be responsible for those functions assigned to the Administrator under the Plan.

1.3 "Beneficiary" means one or more persons, trusts, estates or other entities, designated in accordance with Section 4.3, that are entitled to receive benefits under the Plan upon the death of a Participant.

1.4 "Board" means the Board of Directors of Vertex.

1.5 "Change in Control" means an "Acquisition" under the Stock and Option Plan that also constitutes a change in ownership or control event as defined in Treasury Regulation § 1.409A-3(i)(5).

1.6 "Code" means the Internal Revenue Code of 1986, as amended from time to time, and the regulations promulgated thereunder.

1.7 "Committee" means the Management Development & Compensation Committee of the Board, or such other committee as the Board shall appoint from time to time to administer the Plan.

1.8 "Common Stock" means the common stock of Vertex, par value $0.01 per share.

1.9 "Compensation" means (a) all cash compensation, including fees and retainers (but not reimbursement of expenses) paid to a Director for service on the Board or a committee of the Board and (b) Restricted Stock Units that become vested.

1.10 "Deferred Stock Units" means the phantom stock units comprising all or a portion of the Participant's Account Balance, each of which represents one share of Common Stock.

1.11 "Director" means a member of the Board who is not an employee of Vertex.

1.12 "Disability" means that the Participant (a) is unable to engage in any substantial gainful activity by reason of any medically determinable physical or mental impairment that can be expected to result in death or can be expected to last for a continuous period of not less than 12 months; or (b) has been determined to be totally disabled by the Social Security Administration.

1.13 "Effective Date" means the Effective Date of the Plan, which is January 1, 2016.

1.14 "Fair Market Value" of a share of Common Stock on a particular date shall be the mean between the highest and lowest quoted sales prices on such date (the "valuation date") on the securities market where the Common Stock is traded, or if there were no sales on the valuation date, on the next preceding date within a reasonable period (as determined in the sole discretion of the Committee) on which there were sales. If there were no sales on such a market within a reasonable period, the Fair Market Value shall be determined in good faith by the Committee in its sole discretion. The Fair Market Value as determined in this Section 1.14 shall be rounded down to the nearest whole cent if the foregoing calculation results in fractional cents.

1.15 "Participant" means a Director who elects to participate in the Plan in accordance with the terms and conditions of the Plan or a former Director who has an Account Balance in the Plan that has not been fully distributed.

1.16 "Plan" means the Vertex Pharmaceuticals Non-Employee Director Deferred Compensation Plan, which shall be evidenced by this plan document.

1.17 "Plan Year" means the calendar year.

1.18 "Restricted Stock Units" means an award of restricted stock units made to a Director under the Stock and Option Plan for his or her service as a Director, including both annual awards and awards made upon appointment to the Board.

1.19 "Stock and Option Plan" means the Vertex Pharmaceuticals Incorporated 2013 Stock and Option Plan, as amended from time to time, and any successor thereto under which this Plan is an authorized sub-plan.

1.20 "Termination" means the termination of service as a Director for any reason. Whether a Termination has occurred shall be determined in accordance with Treasury Regulation § 1.409A-1(h). Therefore, a Termination shall not occur if the Director becomes an Employee of Vertex even if he or she terminates service as a Director.

1.21 "Vertex" means Vertex Pharmaceuticals Incorporated, a Massachusetts corporation, and its successors.

ARTICLE 2
Eligibility and Enrollment

2.1 Eligibility . All non-employee Directors of Vertex shall be eligible to participate in the Plan.

2.2 Commencement of Participation . As a condition to enrolling in the Plan, each Director shall execute and return to the Administrator any such forms required by the Administrator to elect his or her deferral amounts and designate a Beneficiary.

2.3 Election to Defer . A Participant may make separate periodic elections to defer (a) either 0%, 50%, or 100% of the Participant's cash Compensation to be earned during an applicable Plan Year (or, if applicable, the portion of the Plan Year) and (b) either 0% or 100% of the Restricted Stock Units granted to a Participant that vest not less than 12 months from the date of the election. A deferral election shall be irrevocable once made. The Administrator may limit or decline to accept a deferral election to the extent that it determines that Deferred Stock Units are not available for issuance under the Stock and Option Plan.

2.4 Date for Filing Elections . Each Director may elect to defer Compensation by executing and returning to the Administrator the required forms. The elections must be made by the following deadlines:

2.4.1 For deferrals of cash Compensation, the election must be made no later than the end of the Plan Year preceding the Plan Year in which the cash Compensation is to be earned. If a Director first becomes eligible for this Plan during a Plan Year, an election to defer cash Compensation to be earned for the remainder of that Plan Year shall be made within 30 days of the initial date of eligibility for this Plan.

2.4.2 For deferrals of Restricted Stock Units, the election must be made on or before the earliest to occur of (i) the 30th day after the Director obtains the legally binding right to the grant of Restricted Stock Units and (ii) 12 months prior to the date that the substantial risk of forfeiture with respect to such Restricted Stock Units lapses (other than due to death, Disability or a Change in Control). Such election shall comply with Treasury Regulation Section 1.409A-2(a)(5).

The Administrator shall establish from time to time such other enrollment requirements as it determines in its sole and absolute discretion are necessary.

ARTICLE 3
Vesting and Earnings Crediting

3.1 Withholding of Compensation; Conversion into Deferred Stock Units . Compensation shall be withheld as elected by the Participant at the time the Compensation otherwise would have been paid to the Participant. The dollar value of the amount withheld will be converted into Deferred Stock Units (including fractions thereof) by dividing the amount withheld by the Fair Market Value of a share of Common Stock as of the date such Compensation would otherwise have been paid to the Director; and such Deferred Stock Units will be credited to the Participant's Account Balance at such time.

3.2 Crediting of Dividends and Distributions . Dividend equivalents shall be credited to each Deferred Stock Unit on each dividend payment date (based on Deferred Stock Units held as of the dividend record date) to the extent of any dividends issued on Common Stock. Such dividend equivalents shall themselves be converted into Deferred Stock Units as of the dividend payment date by dividing the amount of the dividend equivalents by the Fair Market Value of the Common Stock as of the applicable dividend payment date. Any such additional Deferred Stock Units (or fraction thereof) resulting from dividend equivalent credits shall be treated as Deferred Stock Units and credited to the Participant's Account Balance. The right to credits for dividend equivalents shall survive the termination of this Plan and the termination of the Stock and Option Plan until the Deferred Stock Units have been distributed pursuant to Section 4.1.

3.3 Substitution of Cash . If the Administrator determines that Deferred Stock Units are not available for issuance under the Stock and Option Plan for any reason, the Administrator shall credit the Participant's Account Balance with cash in lieu of the Deferred Stock Units that the Participant would otherwise be entitled to. Cash credited to a Participant's Account Balance shall be credited with interest on a monthly basis at the prime rate plus one percent (1%) per annum. Such credits shall continue until the Account Balance has been distributed pursuant to Section 4.1 or until such cash is converted to Deferred Stock Units in accordance with the last sentence of this Section 3.3. If additional Deferred Stock Units subsequently become available for issuance under the Stock and Option Plan, the Administrator shall, as of the date the additional Deferred Stock Units become available for issuance, automatically convert any cash in the Participant's Account Balance into Deferred Stock Units by dividing the amount of cash in the Participant's Account Balance by the Fair Market Value of a

share of Common Stock as of the date the additional Deferred Stock Units become available for issuance; and such Deferred Stock Units will be credited to the Participant's Account Balance at such time.

3.4 Vesting. A Participant shall at all times be one hundred percent (100%) vested in his or her Account Balance.

ARTICLE 4
Distribution of Benefits

4.1 Distribution Events. Upon the earliest to occur of (a) the Termination of the Director's service on the Board, (b) a Change in Control, (c) the Director's Disability or (d) the Director's death, the Participant (or his or her Beneficiary in the event of the Participant's death) shall receive a lump sum distribution of whole shares of Common Stock equal to the sum of (i) the number of Deferred Stock Units in his or her Account Balance plus (ii) such number of shares of Common Stock as is equal to the amount of cash in the Account Balance on the date of distribution divided by the Fair Market Value of a share of Common Stock as of such date. The distribution shall be made no later than the 15th day of the third month after the event described above that results in the distribution.

4.2 Form of Benefit. A Participant or his or her Beneficiary entitled to a distribution under Section 4.1 shall receive his or her Account Balance as a lump sum payable in whole shares of Common Stock. No fractional shares of Common Stock will be issued under the Plan. If the calculation of the total number of shares of Common Stock to be issued under this Plan results in fractional shares, then the number of shares of Common Stock will be rounded up to the nearest whole share of Common Stock. Notwithstanding the foregoing, if the Administrator determines that Common Stock may not be distributed to a Participant for any reason under the Stock and Option Plan, the Administrator shall, in lieu of Common Stock, make a cash payment to the Participant in an amount equal to the aggregate Fair Market Value of the Common Stock the Participant otherwise would have received.

4.3 Designation of Beneficiary. A Participant may designate a Beneficiary by so notifying the Administrator in writing, in a form acceptable to the Administrator, at any time before the Participant's death. A Participant may revoke any Beneficiary designation or designate a new Beneficiary at any time without the consent of a Beneficiary or any other person. If no Beneficiary is designated or no designated Beneficiary survives the Participant, distribution or payment shall be made to the Participant's spouse or, if the Participant does not have a surviving spouse, to his or her estate. If the Administrator has any doubt as to the proper Beneficiary to receive distribution or payments pursuant to this Plan, the Administrator shall have the right, exercisable in its sole discretion, to withhold such payments until this matter is resolved to the Administrator's satisfaction.

4.4 Delay of Distribution or Payment. A distribution or payment otherwise required to be made under the terms of the Plan may be delayed solely to the extent necessary under the following circumstances, provided that the distribution or payment is made as soon as possible within the first taxable year of the Participant after the reason for delay no longer applies:

4.4.1 Violation of Law. The Administrator reasonably determines that making the distribution or payment will violate Federal securities or other applicable laws; or

4.4.2 Other Permitted Event. Upon such other events and conditions as the Commissioner of Internal Revenue shall prescribe in generally applicable guidance.

This Section 4.4 shall be applied to similarly-situated Participants in a reasonably consistent basis.

4.5 Acceleration of Distribution or Payment. Notwithstanding the foregoing, a distribution or payment hereunder may be accelerated, with the consent of the Administrator, under the following circumstances:

4.5.1 Compliance with Domestic Relations Order. To permit distribution or payment to an individual other than the Participant as necessary to comply with the provisions of a domestic relations order (as defined in Code Section 414(p)(1)(B));

4.5.2 Conflicts of Interest. To permit distribution or payment as necessary to comply with the provisions of a Federal government ethics agreement or to avoid violation of an applicable Federal, state, local or foreign ethics law or conflicts of interest law; or

4.5.3 Tax Event. Upon a good faith, reasonable determination by the Administrator, and upon advice of counsel, that the

Plan fails to meet the requirements of Code Section 409A and regulations thereunder. Such distribution or payment may not exceed the amount required to be included in income as a result of the failure to comply with the requirements of Code Section 409A.

ARTICLE 5
Administration

5.1 Committee Duties. This Plan shall be administered by the Administrator. The Administrator also shall have the discretion and authority to make, amend, interpret, and enforce all appropriate rules and regulations for the administration of this Plan and decide or resolve any and all questions including interpretations of this Plan, as may arise in connection with the Plan. All such interpretations or decisions by the Administrator shall be final, conclusive and binding on all Participants and any Beneficiary or other person claiming under or through any Participant, in the absence of clear and convincing evidence that the Administrator acted arbitrarily and capriciously. The Administrator shall have the authority to deviate from the literal terms of the Plan to the extent it shall determine to be necessary or appropriate to operate the Plan in compliance with the provisions of applicable law. Any individual serving on the Committee, or as the Administrator, who is a Participant will not vote or act on any matter relating solely to himself or herself.

5.2 Agents. In the administration of this Plan, the Administrator may, from time to time, employ agents and delegate to them such administrative duties as it sees fit and may from time to time consult with counsel, including counsel to Vertex.

5.3 Indemnity of Committee and Administrator. Vertex shall indemnify and hold harmless the members of the Committee and the Administrator against any and all claims, losses, damages, expenses or liabilities arising from any action or failure to act with respect to this Plan, except in the case of willful misconduct by the Committee or any of its members, or the Administrator.

ARTICLE 6
Miscellaneous

6.1 Unsecured General Creditor. Participants and their Beneficiaries, heirs, successors and assigns shall have no legal or equitable right, interest or claim in any property or assets of Vertex. Vertex's obligation under the Plan shall be merely that of an unfunded and unsecured promise to pay money or issue Common Stock in the future with respect to its Participants.

6.2 Vertex's Liability. Vertex's liability for the distribution or payment of benefits shall be defined only by the Plan. Vertex shall have no obligation to a Participant or Beneficiary under the Plan except as expressly provided in the Plan.

6.3 Taxes. It shall be the sole responsibility of the Participant to properly account for and to pay any income and self-employment tax payable on amounts deferred or benefits paid under this Plan.

6.4 No Rights as a Shareholder. No Participant shall have rights as a shareholder, including voting rights, with respect to any Deferred Stock Units that are held for his or her benefit under the Plan.

6.5 Nonassignability. Neither a Participant nor any other person shall have any right to commute, sell, assign, transfer, pledge, anticipate, mortgage, or otherwise encumber, transfer, hypothecate or convey in advance of actual receipt, the amounts, if any, payable hereunder, or any part thereof, which amounts are, and all rights to which are, expressly declared to be unassignable and non-transferable. No part of the amounts payable shall, prior to distribution or payment, be subject to seizure or sequestration for the payment of any debts, judgments, alimony or separate maintenance owed by a Participant or any other person, nor be transferable by operation of law in the event of a Participant's or any other person's bankruptcy or insolvency. Notwithstanding the foregoing, Vertex shall comply with the terms of a domestic relations order applicable to a Participant's interest in the Plan, provided that such order does not require the distribution or payment of benefits in a manner or amount, or at a time, inconsistent with the terms of the Plan. Vertex shall have no liability to any Participant or Beneficiary to the extent that his or her benefit is reduced in accordance with the terms of a domestic relations order that Vertex applies in good faith.

6.6 Adjustments. Upon the occurrence of any of the following events, a Participant's rights with respect to any Deferred Stock Units shall be adjusted as hereinafter provided:

6.6.1 Stock Splits. If the shares of Common Stock shall be subdivided or combined into a greater or smaller number of shares, the number of Deferred Stock Units shall be appropriately increased or decreased.

6.6.2 Consolidations or Mergers. In the event of a consolidation or merger in which Vertex is not the surviving corporation or which results in the acquisition of substantially all Vertex's outstanding stock by a single person or entity or by a group of persons and/or entities acting in concert, or in the event of the sale or transfer of substantially all Vertex's assets (any of the foregoing, an "Acquisition"), if such Acquisition does not result in a Change in Control, all outstanding Deferred Stock Units at the time of the Acquisition shall be assumed by the surviving or acquiring entity or an affiliate thereof or replaced with rights with a value immediately after the Acquisition equivalent to the aggregate value of the Deferred Stock Units immediately before such Acquisition. If the Acquisition results in a Change in Control, Deferred Stock Units shall be payable pursuant to Section 4.1.

6.6.3 Recapitalization or Reorganization. In the event of a recapitalization or reorganization of Vertex that does not result in a Change in Control, pursuant to which securities of Vertex or of another corporation are issued with respect to the outstanding shares of Common Stock, a Participant shall be entitled to replacement rights with an aggregate value equivalent to that of the Deferred Stock Units that constituted the Participant's Account Balance immediately prior to such recapitalization or reorganization. If the recapitalization or reorganization results in a Change in Control, Deferred Stock Units shall be payable pursuant to Section 4.1.

6.6.4 Adjustments to Deferred Stock Units. Upon the happening of any of the events described in Sections 6.6.1, 6.6.2 or 6.6.3, any outstanding Deferred Stock Units shall be appropriately adjusted to reflect the events described in such Sections. The Administrator shall determine the specific adjustments to be made under this Section 6.6.4.

6.7 Issuances of Securities. Except as expressly provided herein, no issuance by Vertex of shares of stock of any class, or securities convertible into shares of stock of any class, shall affect, and no adjustment by reason thereof shall be made with respect to, the number of Deferred Stock Units to which a Participant or Beneficiary is entitled. Except as expressly provided herein, no adjustments shall be made for dividends paid in cash or in property (including without limitation, securities) of Vertex.

6.8 Dissolution or Liquidation of Vertex. Upon the dissolution or liquidation of Vertex (other than in connection with a transaction subject to the provisions of Section 6.6.2), all Deferred Stock Units under this Plan shall be liquidated and paid in cash to Participants based upon the Fair Market Value of the Common Stock as of the date of such liquidation or dissolution to the extent permitted under Code Section 409A and the regulations thereunder.

6.9 Coordination with Other Benefits. The benefits provided for a Participant or Beneficiary under the Plan are in addition to any other benefits available to such Participant under any other plan or program of Vertex. The Plan shall

supplement and shall not supersede, modify or amend any other such plan or program except as expressly may be provided otherwise.

6.10 Amendment and Termination . The Plan may at any time or from time to time be amended, modified, or terminated by the Board. No amendment, modification, or termination shall, without the consent of a Participant, adversely affect the amount of the Participant's (or Beneficiary's) benefit. Upon termination of the Plan, the Committee may elect to (a) treat each Participant's Account Balance, and make payments or distribution thereon, as if the Plan had not terminated; or (b) to the extent permitted by Code Section 409A and regulations thereunder, make a lump sum distribution or payment on each Participant's Account Balance in accordance with Article 4 of this Plan.

6.11 Distributions or Payments to Minors or Persons Under Legal Disability . If any Participant or Beneficiary is determined by the Administrator to be incompetent by reason of physical or mental disability (including minority), the Administrator may cause a distribution or payment due to such person to be made to another person for his or her benefit without responsibility on the part of the Administrator or Vertex to follow the application of such funds.

6.12 No Special Rights . Nothing contained in this Plan shall confer upon any Participant any right with respect to the continuation of his or her service with on the Board.

6.13 Claims Procedure . Any Participant, contingent annuitant or beneficiary under the Plan (a "Claimant") who believes that he or she is entitled to receive a benefit under the Plan, including one greater than that initially determined by the Administrator or its delegate, may file a claim in writing with the Administrator. The Administrator shall, within 90 days of the receipt of a claim, either allow or deny the claim in writing, subject to extension as described below. A denial of a claim shall be written in a manner calculated to be understood by the Claimant and shall include: (a) the specific reason or reasons for the denial; (b) specific references to pertinent Plan provisions on which the denial is based; (c) a description of any additional material or information necessary for the Claimant to perfect the claim and an explanation of why such material or information is necessary; and (d) an explanation of the Plan's claims review procedures. After denial of a claim, a Claimant may request and receive reasonable access to and copies of relevant documents, records and other information in Vertex's possession free of charge. Relevant documents, records and other information are those that: (1) were relied on in making the determination; (2) were submitted, considered or generated in the course of making the determination; or (3) demonstrate compliance with the Plan's administrative processes or safeguards.

A Claimant (or his or her duly authorized representative) whose claim is denied may, within 60 days after receipt of denial of the claim: (i) submit a written request to the Administrator for review of the decision by the Committee; (ii) review pertinent documents; and (iii) submit issues and comments in writing. The Committee or its delegate shall notify the Claimant of its decision on review within 60 days of receipt of a request for review. The decision on review shall be written in a manner calculated to be understood by the Claimant and shall include specific reasons for the decision and specific references to the pertinent Plan provisions on which the decision is based.

The 90-day and 60-day periods described above may be extended at the discretion of the Administrator or Committee, as the case may be, for a second 90- or 60-day period, as the case may be, provided that written notice of the extension is furnished to the Claimant prior to the termination of the initial period, indicating the special circumstances requiring such extension of time and the date by which a final decision is expected.

Claimants shall not be entitled to challenge the Administrator's or Committee's determinations in judicial or administrative proceedings without first complying with the procedures in the Plan. The decisions made pursuant to this Section 6.13 are final and binding on Claimants and any other party; provided, however, that a Claimant who has exhausted the administrative claims procedure set forth in the Plan may seek review of his or her claim before a court of competent jurisdiction within 12 months of the date such claim is finally denied.

6.14 Furnishing Information . A Participant or his or her Beneficiary will cooperate with the Committee by furnishing any and all information requested by the Committee and take such other actions as may be requested in order to facilitate the administration of the Plan and the distribution or payment of benefits hereunder, including but not limited to taking such physical examinations as the Committee may deem necessary.

6.15 Captions . The captions of the articles, sections and paragraphs of this Plan are for convenience only and shall not control or affect the meaning or construction of any of its provisions.

6.16 Governing Law . The Plan will be administered in accordance with the laws of The Commonwealth of Massachusetts, without reference to its principles of conflicts of laws.

6.17 **Notice.** Any notice or filing required or permitted to be given to the Committee under this Plan shall be sufficient if in writing and hand-delivered, or sent by registered or certified mail, to:

Vertex Pharmaceuticals Incorporated
Attn: Employee Benefits
50 Northern Ave.
Boston, MA 02210

Such notice shall be deemed given as of the date of delivery or, if delivery is made by mail, as of the date shown on the postmark on the receipt for registration or certification.

Any notice or filing required or permitted to be given to a Participant under this Plan shall be sufficient if in writing and hand-delivered, or sent by mail, to the last known address of the Participant.

6.18 **Successors.** The provisions of this Plan shall bind and inure to the benefit of Vertex and its successors and assigns, and the Participant, the Participant's Beneficiaries, and their permitted successors and assigns.

6.19 **Validity.** In case any provision of this Plan shall be illegal or invalid for any reason, said illegality or invalidity shall not affect the remaining parts hereof, but this Plan shall be construed and enforced as if such illegal or invalid provision never had been inserted herein.

6.20 **Sub-Plan.** This Plan is a sub-plan of the Stock and Option Plan, and the Deferred Stock Units provided in this Plan shall be Stock Rights that are subject to the Stock and Option Plan.

Exhibit 10.34

EMPLOYMENT AGREEMENT

This Employment Agreement (this " Agreement ") is made and entered into as of this 12th day of December, 2014, by and between Vertex Pharmaceuticals Incorporated, a Massachusetts corporation (together with its successors and assigns, the " Company "), and David Altshuler, M.D., Ph.D. (the " Executive ").

W I T N E S S E T H

WHEREAS, the Company is employing the Executive as the Company's Executive Vice President, Global Research, & Chief Scientific Officer;

WHEREAS, the Executive has been designated as a member of the Executive and Management Committees of the Company; and

WHEREAS, the Executive has agreed as a condition precedent to the foregoing to resign from the Board of Directors, and the Company has accepted said resignation;

NOW, THEREFORE, in consideration of the premises and mutual covenants contained herein and for other good and valuable consideration, the receipt of which mutually is acknowledged, the Company and the Executive (each individually a " Party ", and together the " Parties ") agree as follows:

1. DEFINITIONS.

" Base Salary " shall mean the Executive's base salary in accordance with Section 4 below.

" Board " shall mean the Board of Directors of the Company.

" Cause " shall mean (i) the Executive is convicted of a crime involving moral turpitude, (ii) the Executive commits a material breach of any provision of this Agreement not involving the performance or nonperformance of duties, or (iii) the Executive, in carrying out the Executive's duties, acts or fails to act in a manner that is determined, in the sole discretion of the Board, after written notice of any such act or failure to act and a reasonable opportunity to cure the deficiency has been provided to the Executive, to be (A) willful gross neglect or (B) willful gross misconduct resulting, in either case, in material harm to the Company unless such act, or failure to act, was believed by the Executive, in good faith, to be in the best interests of the Company.

" Change of Control " shall have the meaning set forth in the Change of Control Agreement.

" Change of Control Agreement " shall mean the Change of Control letter agreement between the Company and the Executive of even date herewith.

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

" Common Stock " shall mean the common stock of the Company.

" Disability " or " Disabled " shall mean a disability as determined under the Company's long-term disability plan or program in effect at the time the disability first occurs, or if no such

plan or program exists at the time of disability, then a "disability" as defined under Section 22(e)(3) of the Code.

" Effective Date " shall mean January 12, 2015.

" Good Reason " shall mean that, without the Executive's consent, one or more of the following events occurs:

(i) the Executive's duties are materially diminished to an extent that results in either (A) the Executive no longer being an "officer," as such term is defined in Rule 16a-1(f) promulgated under the Securities Exchange Act of 1934; or (B) the Executive ceases to be a member of the executive management team of the Company; or

(ii) the Executive's Base Salary is decreased unless such reduction is part of an across-the-board proportionate reduction in the salaries of the Company's senior management team; or

(iii) the office to which the Executive is assigned is relocated to a place 35 or more miles away and such relocation is not at the Executive's request or with the Executive's prior agreement (and other than, for Executives assigned to the Company's principal executive offices, in connection with a change in location of the Company's principal executive offices);

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

" Severance Payment " shall mean an amount equal to the sum of the Base Salary in effect on the date of termination of Executive's employment, plus the amount of the Target Bonus for the Executive for the year in which the Executive's employment is terminated; provided, however, that if the Executive terminates the Executive's employment for Good Reason based on a reduction in Base Salary, then the Base Salary to be used in calculating the Severance Payment shall be the Base Salary in effect immediately prior to such reduction in Base Salary.

" Target Bonus " shall mean the target cash bonus for which the Executive is eligible on an annual basis, at a level consistent with the Executive's title and responsibilities, under the Company's bonus program then in effect and applicable to the Company's senior executives generally.

2. TERM OF EMPLOYMENT.

The Company hereby employs the Executive, and the Executive hereby accepts such employment, continuing until termination in accordance with the terms of this Agreement. The

period during which the Executive is employed hereunder is referred to in this Agreement as the " term of employment. "

3. POSITION.

On the Effective Date, the Executive is employed as the Company's Executive Vice President, Global Research, & Chief Scientific Officer, reporting to the Company's President & Chief Executive Officer.

4. BASE SALARY.

The Executive's annualized Base Salary as of the date of this Agreement is $550,000, payable in accordance with the regular payroll practices of the Company. The Base Salary shall be reviewed no less frequently than annually, and any changes thereto (which shall thereafter be deemed the Executive's Base Salary) shall be solely within the discretion of the Board.

5. TARGET BONUS PROGRAM.

During the term of employment, the Executive shall be eligible to participate in the Company's Target Bonus program (and other cash incentive compensation programs) applicable to the Company's senior executives, as any such programs are established and modified from time to time by the Board in its sole discretion, and in accordance with the terms of such program.

6. INCENTIVE COMPENSATION PROGRAMS/SIGN-ON AWARDS.

(a) During the term of employment, the Executive shall be eligible to participate in the Company's incentive compensation programs applicable to the Company's senior executives, as such programs may be established and modified from time to time by the Board in its sole discretion.

(b) **Sign-On Cash Bonus** : The Executive shall receive a sign-on cash bonus in the amount of $250,000 payable (with appropriate deductions as required by law) to the Executive at the first regular pay date applicable to the Executive after the Effective Date. If the Executive terminates this Agreement without Good Reason, and other than as a result of death or Disability, during the period commencing on the Effective Date and ending on the first anniversary of the Effective Date, the Executive shall repay the sign-on cash bonus to the Company within 30 days of such termination.

(c) **Sign-On Restricted Stock Grant** : The Executive will purchase, in accordance with the terms of a Restricted Stock Award agreement executed and delivered to the Company by the Executive on the Effective Date (the " Grant Date "), 75,000 shares of the Company's Common Stock, at a purchase price per share of $0.01. This grant, including but not limited to the vesting schedule and the Company's right to repurchase these shares, shall be subject to the other terms and conditions specified in a separate Restricted Stock Award agreement attached hereto as Exhibit A .

(d) **Continued Vesting of Option Grant During Board Service:** The Company hereby amends the Executive's May 24, 2012 Stock Option Grant consistent with this Employment Agreement, such that the Executive will continue to vest the options subject to such

grant on a quarterly basis following his resignation of Board service, during the interim period prior to his commencing employment with the Company and thereafter for so long as he continues as an employee or director of the Company; provided that such grant will terminate with respect to any unvested portion if Executive does not commence employment with the Company as set forth herein by January 12, 2015.

7. EMPLOYEE BENEFIT PROGRAMS.

During the term of employment, the Executive shall be entitled to participate in all employee welfare and pension benefit plans, programs and/or arrangements offered by the Company to its senior executives, as such plans, programs and arrangements may be amended from time to time, to the same extent and on the same terms applicable to other senior executives. Nothing in this section shall preclude the Company from amending or terminating any of its employee benefit plans, programs or arrangements.

8. VACATION.

During the term of employment, the Executive shall be entitled to paid vacation days each calendar year in accordance with the Company's vacation policy then in effect.

9. TERMINATION OF EMPLOYMENT.

(a) **Termination in Connection with a Change of Control** . To the extent the Executive is entitled, in connection with the Executive's termination of employment, to severance or other benefits under the Change of Control Agreement, the Executive shall not be entitled to corresponding benefits under this Section 9.

(b) **Termination by the Company for Cause; or Termination by the Executive without Good Reason.** If the Company terminates the Executive's employment for Cause, or if the Executive voluntarily terminates the Executive's employment, other than for Good Reason, death or Disability, the term of employment shall end as of the date specified below, and the Executive shall be entitled to the following:

(i) Base Salary earned by Executive but not paid through the date of termination of Executive's employment under this Section 9(b); and

(ii) any amounts earned, accrued or owing to the Executive but not yet paid under Sections 5, 6, or 7 above.

Termination by Company for Cause shall be effective as of the date noticed by the Company. Voluntary termination by Executive other than for Good Reason, death or Disability shall be effective upon 90 days' prior written notice to the Company and shall not be deemed a breach of this Agreement.

(c) **Termination by the Company Without Cause; or Termination by the Executive for Good Reason.** If the Executive's employment is terminated by the Company without Cause (other than due to death or Disability), or is terminated by the Executive for Good Reason (in accordance with the notice and cure provisions set forth in the definition of "Good Reason" above), the Executive shall be entitled to the following (provided that, with respect to (iii) and (v) such amounts shall be subject to and in exchange for a general release of all claims against

the Company, its subsidiaries, and their officers, directors, agents and representatives, which is executed by Executive and becomes enforceable and non-revocable within 60 days of the date of termination):

(i) Base Salary earned by Executive but not paid through the date of termination of Executive's employment under this Section 9(c);

(ii) all incentive compensation awards earned by Executive but not paid prior to the date of termination of Executive's employment under this Section 9(c);

(iii) a cash payment to the Executive in an amount equal to the Severance Payment, payable within ten days after the execution of a general release and expiration, without revocation, of any applicable revocation periods under the general release provided that if the 60-day period during which the release is required to become effective and irrevocable begins in one calendar year and ends in another calendar year, the Severance Payment shall not be made before the first day of the second calendar year;

(iv) any amounts earned, accrued or owing to the Executive but not yet paid under Sections 5, 6 or 7 above;

(v) if COBRA coverage is elected by the Executive, the Company shall pay the cost of insurance continuation premiums on the Executive's behalf (whether or not covered by COBRA) to continue standard medical, dental and life insurance coverage for the Executive (or the cash equivalent of same in the event the Executive is ineligible for continued coverage) until the earlier of:

(A) the date 12 months after the date the Executive's employment is terminated; or

(B) the date, or dates, on which the Executive receives equivalent coverage and benefits under the plans, programs and/or arrangements of a subsequent employer (such coverage and benefits to be determined on a coverage-by-coverage or benefit-by-benefit basis).

If Executive is a "specified employee" under Section 409A(a)(2)(B)(i) of the Code, any payment of "nonqualified deferred compensation" (as defined under Section 409A of the Code and related guidance) attributable to a "separation from service" (as defined under Section 409A of the Code and related guidance) shall not commence until the first full business day that is more than six months after the applicable separation from service (" Deferred Payment Date "). Any payments that would otherwise have been made between the separation from service and the Deferred Payment Date, but for this paragraph, shall be made in a lump sum on the Deferred Payment Date. Payments that, in any case, are scheduled to be made after the Deferred Payment Date shall continue according to the applicable payment schedule. To the extent that the termination of the Executive's employment does not constitute a separation of service under Section 409A(a)(2)(A)(i) of the Code (as the result of further services that reasonably are anticipated to be provided by the Executive to the Company at the time the Executive's employment is terminated), the payment of any nonqualified deferred compensation will be further delayed until the date that is the first full business day that is more than six months after

the date of a subsequent event constituting a separation of service under Section 409A(a)(2)(A)(i) of the Code.

10. ASSIGNABILITY; BINDING NATURE.

This Agreement shall be binding upon and inure to the benefit of the Parties and their respective successors, heirs (in the case of the Executive) and assigns. No rights or obligations of the Company under this Agreement may be assigned or transferred by the Company except that such rights or obligations may be assigned or transferred pursuant to a merger or consolidation in which the Company is not the continuing entity, or the sale or liquidation of all or substantially all of the assets of the Company; provided , however , that the assignee or transferee is the successor to all or substantially all of the assets of the Company and such assignee or transferee assumes the liabilities, obligations and duties of the Company, as contained in this Agreement, either contractually or as a matter of law.

11. REPRESENTATIONS.

The Company represents and warrants that it is fully authorized and empowered to enter into this Agreement, and that the performance of its obligations under this Agreement will not violate any agreement between it and any other person, firm or organization. The Executive represents and warrants that no agreement exists between her and any other person, firm or organization that would be violated by the performance of the Executive's obligations under this Agreement.

12. INDEMNIFICATION; INSURANCE.

The Executive shall at all times be indemnified and eligible for advancement of expenses on the same basis as is provided for the Company's other executive officers and in accordance with the provisions of the Company's charter and by-laws then in effect. The Executive shall also be covered under all of the Company's policies of liability insurance maintained for the benefit of its directors and officers on the same basis as is provided for its other executive officers.

13. ENTIRE AGREEMENT; TERMINATION.

This Agreement, the agreements referenced herein and the Employee Non-Disclosure, Non-Competition & Inventions Agreement between the Executive and the Company contain the entire understanding and agreement between the Parties concerning the subject matter hereof and supersedes all prior agreements, understandings, discussions, negotiations and undertakings, whether written or oral, between the Parties with respect thereto. Subject to the terms of this Agreement, the Company shall be entitled to terminate the Executive's employment at any time, and the Executive may terminate the Executive's employment by the Company, at any time subject to the provisions of Section 9(b) of this Agreement, in each case by written notice provided in accordance with Section 20 of this Agreement.

14. AMENDMENT OR WAIVER.

No provision in this Agreement may be amended unless such amendment is agreed to in writing and signed by the Executive and an authorized officer of the Company provided that the Company may, without the Executive's consent, unilaterally adopt amendments that may be

required so that this Agreement continues to comply with applicable law or regulations, including without limitation Section 409A of the Code, provided such amendments do not adversely affect the benefits to the Executive under this Agreement. No waiver by either Party of any breach by the other Party of any condition or provision contained in this Agreement to be performed by such other Party shall be deemed a waiver of a similar or dissimilar condition or provision at the same or any prior or subsequent time. Any waiver must be in writing and signed by the Executive or an authorized officer of the Company, as the case may be.

15. SEVERABILITY.

If any provision or portion of this Agreement shall be determined to be invalid or unenforceable for any reason, in whole or in part, the remaining provisions of this Agreement shall be unaffected thereby and shall remain in full force and effect to the fullest extent permitted by law.

16. SURVIVORSHIP.

The respective rights and obligations of the Parties hereunder shall survive any termination of the Executive's employment to the extent necessary to the intended preservation of such rights and obligations.

17. BENEFICIARIES/REFERENCES.

The Executive shall be entitled, to the extent permitted under any applicable law, to select and change a beneficiary or beneficiaries to receive any compensation or benefit payable hereunder following the Executive's death by giving the Company written notice thereof. In the event of the Executive's death or a judicial determination of the Executive's incompetence, reference in this Agreement to the Executive shall be deemed, where appropriate, to refer to the Executive's beneficiary, estate or other legal representative.

18. GOVERNING LAW/JURISDICTION.

This Agreement shall be governed by and construed and interpreted in accordance with the laws of The Commonwealth of Massachusetts without reference to principles of conflict of laws.

19. RESOLUTION OF DISPUTES.

Any disputes arising under or in connection with this Agreement may, at the election of the Executive or the Company, be resolved by binding arbitration, to be held in Massachusetts in accordance with the Rules and Procedures of the American Arbitration Association. If arbitration is elected, the Executive and the Company shall mutually select the arbitrator. If the Executive and the Company cannot agree on the selection of an arbitrator, each Party shall select an arbitrator and the two arbitrators shall select a third arbitrator, and the three arbitrators shall form an arbitration panel that shall resolve the dispute by majority vote. Judgment upon the award rendered by the arbitrator or arbitrators may be entered in any court having jurisdiction thereof. Costs of the arbitrator or arbitrators and other similar costs in connection with an arbitration shall be shared equally by the Parties; all other costs, such as attorneys' fees incurred by each Party, shall be borne by the Party incurring such costs.

20. NOTICES.

All notices that are required or permitted hereunder shall be in writing and sufficient if delivered personally, sent by facsimile (and promptly confirmed by personal delivery, registered or certified mail or overnight courier), sent by nationally-recognized overnight courier or sent by registered or certified mail, postage prepaid, addressed as follows:

If to the Company: Vertex Pharmaceuticals Incorporated
50 Northern Avenue
Boston, MA 02210
Attn: Chief Executive Officer
with copies to:
the Chief Legal Officer

If to the Executive: at the Executive's home address listed in the Company records.

Any such notice shall be deemed to have been given: (a) when delivered if personally delivered or sent by facsimile on a business day; (b) on the business day after dispatch if sent by nationally-recognized overnight courier; and/or (c) on the fifth business day following the date of mailing if sent by mail.

21. HEADINGS.

The headings of the sections contained in this Agreement are for convenience only and shall not be deemed to control or affect the meaning or construction of any provision of this Agreement.

22. COUNTERPARTS.

This Agreement may be executed in two or more counterparts.

23. SECTION 409A COMPLIANCE.

It is the intention of the Company and the Executive that this Agreement and the payments provided for herein meet the requirements of Section 409A of the Code, to the extent applicable to this Agreement and such payments. The Company and the Executive agree to cooperate in good faith in preparing and executing, at such time as sufficient guidance is available under Section 409A and from time to time thereafter, such amendments to this Agreement, if any, as the Executive may reasonably request solely for the purpose of assuring that this Agreement and the payments provided hereunder meet the requirements of Section 409A. Nothing in this Section 23 shall require the Company to increase the Executive's compensation or make the Executive whole for any requested changes.

24. TAX WITHHOLDING; NO GUARANTEE OF ANY TAX CONSEQUENCES.

All payments hereunder shall be subject to all applicable withholding for any federal, state or local income taxes including any excise taxes under the Code. Notwithstanding any other provision of this Agreement to the contrary or other representation, the Company does not

in any way guarantee the tax consequences of any payment or compensation under this Agreement including, without limitation, under Section 409A of the Code.

IN WITNESS WHEREOF, the undersigned have executed this Agreement as of the date first written above.

Vertex Pharmaceuticals Incorporated

/s/ Jeffrey M. Leiden
Jeffrey M. Leiden, M.D., Ph.D.
Chairman, President & Chief Executive Officer

Executive

/s/ David Altshuler
David Altshuler, M.D., Ph.D.

Exhibit 10.35

December 10, 2014

David Altshuler, M.D., Ph.D.
61 Dean Road
Brookline, MA 02445

RE: Change of Control Agreement

Dear David:

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

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

1. " Cause " shall mean:

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

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

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

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

2. " Change of Control " shall mean that:

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

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

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

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

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

(a) You suffer a material reduction in the authorities, duties or job title and responsibilities associated with your position as Executive Vice President, Global Research, & Chief Scientific Officer for the Company as of the date hereof;

(b) your annual base salary is decreased;

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

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

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

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

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

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

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

then, you shall receive the following benefits:

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

(a) (i) your annual base salary (provided, however, that if you terminate your employment for Good Reason based on a reduction in your annual base salary, then the annual base salary to be used in calculating the Severance Payment shall be your annual base salary in effect immediately prior to such reduction in annual base salary) plus your target bonus under any bonus program applicable to you for the year in which the Termination Date occurs; plus

(b) a prorata portion of your target bonus for the portion of the year in which the Termination Date occurs under any bonus program applicable to you; plus

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

Except with respect to any portion of the Severance Payment that is delayed as set forth in this paragraph, the Severance Payment shall be made in cash within ten days after the execution by you of the general release referred to above and expiration without revocation of any applicable revocation periods under such general release (or, if the Change of Control resulting in your becoming entitled to such benefits occurs after such execution and expiration, within ten days after the Change of Control), provided that, if the 60-day period during which the general release is required to become effective and irrevocable begins in one calendar year and ends in another calendar year, the Severance Payment shall not be made before the first day of the second calendar year. The Severance Payment shall be divided into two portions, consisting of a portion that does not constitute "nonqualified deferred compensation" within the meaning of Section 409A of the Code and a portion, if

any, that does constitute nonqualified deferred compensation. If you are a "specified employee" as defined in Section 409A(a)(2)(B)(i) of the Code, the commencement of the delivery of any such payments that constitute nonqualified deferred compensation payable upon a "separation from service" under Section 409A(a)(2)(A)(i) of the Code will be delayed until the first business day that is more than six months after your Termination Date. The determination of whether, and the extent to which, any of the payments to be made to you hereunder are nonqualified deferred compensation shall be made after the application of all applicable exclusions, including those set forth under Treasury Reg. § 1.409A-1(b)(9). Any payments that are intended to qualify for the exclusion for separation pay due to involuntary separation from service set forth in Reg. §1.409A-1(b)(9)(iii) must be paid no later than the last day of the second taxable year following the taxable year in which the Termination Date occurs. To the extent that the termination of your employment does not constitute a separation of service under Section 409A(a)(2)(A)(i) of the Code (as the result of further services that are reasonably anticipated to be provided by you to the Company at the time your employment is terminated), the payment of any non-qualified deferred compensation will be further delayed until the first business day that is more than six months after the date of a subsequent event constituting a separation of service under Section 409A(a)(2)(A)(i) of the Code.

2. *Accelerated Vesting.*

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

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

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

3. *Continued Insurance Coverage* . If COBRA coverage is elected by you, the Company shall pay the cost of insurance continuation premiums on your behalf (whether or not covered by COBRA) to continue standard medical, dental and life insurance coverage for you (or the cash equivalent of same if you are ineligible for continued coverage) until the earlier of (i) the date 12 months after the Termination Date or (ii) the date you begin receiving substantially equivalent coverage and benefits through a subsequent employer.

4. *No Mitigation.* You shall not be required to mitigate the amount of the Severance Payment or any other benefit provided under this Agreement by seeking other employment or

otherwise, nor shall the amount of any payment or benefit provided for in this Agreement be reduced (except as provided in Article II Section 3(ii)) by any compensation earned by you as the result of other employment, by retirement benefits, or be offset against any amount claimed to be owed by you to the Company or otherwise (except for any required withholding taxes); provided, that if the Company makes any other severance payments to you under any other program or agreement, such amounts shall be offset against the payments the Company is obligated to make pursuant to this Agreement.

III. *Miscellaneous* .

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

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

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

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

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

Very truly yours,

Vertex Pharmaceuticals Incorporated

By: /s/ Jeffrey Leiden

Jeffrey M. Leiden, M.D., Ph.D.

Chairman, President & Chief Executive Officer

ACCEPTED AND AGREED:

/s/ David Altshuler
David Altshuler, M.D., Ph.D.

Exhibit 10.41

Vertex Employee Compensation Plan

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

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

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

On February 2, 2016, the Board of Directors determined the cash bonus awards related to the fiscal year ended December 31, 2015 and annual salaries effective February 2016. In addition, the Board of Directors granted our named executive officers equity grants under the 2013 Stock and Option Plan which will be described in detail in our 2016 proxy statement. These grants reflect a transition from a share-based approach to a value-based approach. The grants included performance share units that will only vest based on achievement of financial or business goals.

Exhibit 10.42

Vertex Pharmaceuticals Non-Employee Board Compensation

Annual Retainer	$85,000
Committee Chair Compensation	
Audit & Finance Committee Chair	$30,000 annual retainer
Management Development & Compensation Committee Chair	$25,000 annual retainer
Corporate Governance & Nominating Committee Chair	$20,000 annual retainer
Science & Technology Committee Chair	$20,000 annual retainer
Committee Membership Fee (Non Chairs)	
Audit & Finance Committee Member	$15,000 annual retainer
Management Development & Compensation Committee Member	$10,000 annual retainer
Corporate Governance & Nominating Committee Member	$10,000 annual retainer
Science & Technology Committee Member	$10,000 annual retainer
Lead Independent Director Compensation	$40,000 annual retainer

Equity Grants

Upon first election to the Board, a $550,000 value-based award, based on a 50/50 mix of restricted stock and options

- Options vesting quarterly over four years
- Restricted stock vesting annually over four years

On June 1 on each year of service, a $550,000 value-based award, based on a 50/50 mix of restricted stock and options

- Options are fully vested upon grant
- Restricted shares cliff vest on the 1 year anniversary of the grant date

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

Exhibit 21.1

Subsidiaries of Vertex Pharmaceuticals Incorporated

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

Vertex Securities Corporation, a Massachusetts corporation

Vertex Pharmaceuticals (Distribution) Incorporated, a Delaware corporation

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

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

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

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

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

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

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

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

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

Vertex Holdings, Inc., a Delaware corporation

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

Vertex Pharmaceuticals (Switzerland) Sàrl, a Swiss company

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

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

Vertex Pharmaceuticals (France) SAS, a French company

Vertex Pharmaceuticals (Germany) GmbH, a German company

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

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

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

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

Vertex (Brazil) Participações LTDA, a Brazilian company (4)

Vertex Pharmaceuticals GmbH, an Austrian company (6)

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

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

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

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

Exhibit 23.1

Consent of Independent Registered Public Accounting Firm

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

(1) Registration Statement (Form S-3 No. 333-186993) of Vertex Pharmaceuticals Incorporated,
(2) Registration Statement (Form S-8 No. 333-104362) pertaining to the Vertex Pharmaceuticals Incorporated 1996 Stock and Option Plan, as amended,
(3) Registration Statement (Form S-8 Nos. 333-134482, 333-150946, 333-160442, 333-166803 and 333-184787) pertaining to the Vertex Pharmaceuticals Incorporated Amended and Restated 2006 Stock and Option Plan (formerly known as the Vertex Pharmaceuticals Incorporated 2006 Stock and Option Plan),
(4) Registration Statement (Form S-8 No. 333-184784) pertaining to the Vertex Pharmaceuticals Incorporated Employee Stock Purchase Plan, and
(5) Registration Statement (Form S-8 Nos. 333-188737, 333-197466 and 333-206075) pertaining to the Amended and Restated Vertex Pharmaceuticals Incorporated 2013 Stock and Option Plan (formerly known as the Vertex Pharmaceuticals Incorporated 2013 Stock and Option Plan);

of our reports dated February 16, 2016 , with respect to the consolidated financial statements of Vertex Pharmaceuticals Incorporated and the effectiveness of internal control over financial reporting of Vertex Pharmaceuticals Incorporated, included in this Annual Report (Form 10-K) of Vertex Pharmaceuticals Incorporated for the year ended December 31, 2015.

/s/ Ernst & Young LLP

Boston, Massachusetts
February 16, 2016

Exhibit 31.1

CERTIFICATION

I, Jeffrey M. Leiden, certify that:

1. I have reviewed this Annual Report on Form 10-K of Vertex Pharmaceuticals Incorporated;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   a) designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   b) designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   c) evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   d) disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: February 16, 2016

/s/ Jeffrey M. Leiden

Jeffrey M. Leiden

Chief Executive Officer and President

Exhibit 31.2

CERTIFICATION

I, Ian F. Smith, certify that:

1. I have reviewed this Annual Report on Form 10-K of Vertex Pharmaceuticals Incorporated;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   a) designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   b) designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   c) evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   d) disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: February 16, 2016

/s/ Ian F. Smith

Ian F. Smith

Executive Vice President and Chief Financial Officer

Exhibit 32.1

SECTION 906 CEO/CFO CERTIFICATION

Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002 (Subsections (a) and (b) of Section 1350, Chapter 63 of Title 18, United States Code) each of the undersigned officers of Vertex Pharmaceuticals Incorporated, a Massachusetts corporation (the "Company"), does hereby certify, to such officer's knowledge, that:

The Annual Report on Form 10-K for the year ended December 31, 2015 (the "Form 10-K") of the Company fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934, and the information contained in the Form 10-K fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: February 16, 2016

/s/ Jeffrey M. Leiden

Jeffrey M. Leiden
Chief Executive Officer and President

Date: February 16, 2016

/s/ Ian F. Smith

Ian F. Smith
Executive Vice President and Chief Financial Officer

A signed original of this written statement required by Section 906 has been provided to the Company and will be retained by the Company and furnished to the Securities and Exchange Commission or its staff upon request.