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

FORM 10-K

(Mark One)

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

For the Fiscal Year Ended December 31, 2005

or

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

For the transition period from _____ to _____

Commission file number 000-19319

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

Massachusetts (State or other jurisdiction of incorporation or organization)	**04-3039129** (I.R.S. Employer Identification No.)
130 Waverly Street **Cambridge, Massachusetts** (Address of principal executive offices)	**02139-4242** (Zip Code)

Registrant's telephone number, including area code **(617) 444-6100**

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

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

Common Stock, $0.01 Par Value Per Share
Rights to Purchase Series A Junior Participating Preferred Stock
(Title of class)

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

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

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 o

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

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

Large accelerated filer ☒ Accelerated filer o Non-accelerated filer o

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). Yes o 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 The Nasdaq Stock Market on June 30, 2005 was $1,158,946,185.

As of March 14, 2006, the registrant had 109,734,852 shares of common stock outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the definitive Proxy Statement for the 2006 Annual Meeting of Stockholders to be held on May 11, 2006 are incorporated by reference into Part III of this Annual Report on Form 10-K.

FORM 10-K

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The "Company," "Vertex," "we" and "us," 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 a biotechnology company in the business of discovering, developing and commercializing small molecule drugs for the treatment of serious diseases. We continue to make progress toward our goal of becoming a profitable pharmaceutical company with industry-leading capabilities in research, development and commercialization of pharmaceutical products. We intend to continue investing in and building these capabilities as we advance our product candidates to market. Our corporate purpose, which we use to guide our activities and which we believe is an important component of our past and future success, is to innovate to redefine health and transform lives with new medicines.

We have a number of drug candidates in development, including compounds targeting hepatitis C virus ("HCV") infection, rheumatoid arthritis ("RA"), cystic fibrosis, cancer, pain and HIV infection. Our corporate strategy is to retain principal responsibility for the development and commercialization of some of our proprietary drug candidates in certain major markets, concentrating a significant part of our overall development and commercialization resources on those drug candidates once we select them. We intend to rely on collaborators to conduct development and commercialization of certain of our other drug candidates either worldwide or in markets upon which we are not currently focused. We are concentrating most of our drug development resources at the present time on three compounds: VX-950 for the treatment of chronic HCV infection, VX-702 for the treatment of RA and VX-770 for the treatment of cystic fibrosis.

Collaborations will continue to be a key component of our corporate strategy. We currently are collaborating with GlaxoSmithKline plc, Merck & Co., Inc., Cystic Fibrosis Foundation Therapeutics Incorporated, Novartis Pharma AG, Mitsubishi Pharma Corp., Kissei Pharmaceutical Co., Ltd. and other companies. Collaborations provide us with financial support and other valuable resources for our research programs, development resources for our clinical drug candidates and marketing and sales support for our products and product candidates. We have a collaboration agreement with GlaxoSmithKline that has resulted in our two marketed products to date, the HIV protease inhibitor Agenerase and its prodrug Lexiva/Telzir, and the development of a third HIV protease inhibitor, brecanavir (VX-385), which is completing Phase IIb development as an FDA "Fast Track" designee. Through our collaborations with Novartis, Merck and Avalon Pharmaceuticals, Inc., four Vertex-discovered compounds are in development for the treatment of cancer. Our two Far East collaborators, Mitsubishi and Kissei, are committing resources to develop VX-950 and VX-702, respectively, in the Far East, and providing financial support for our efforts in the rest of the world. VX-409, for pain, is being developed by GlaxoSmithKline through our worldwide collaboration relating to certain sub-type selective sodium channel modulators.

We plan to continue adding promising potential products to our development pipeline through our ongoing commitment to discovery research. Our drug design approach integrates biology, chemistry, biophysics, automation and information technologies intended to make the drug discovery process efficient and productive. Our drug discovery expertise is a principal factor in the creation of our pipeline, which includes a number of potentially breakthrough compounds. In addition to our efforts to research and develop kinase inhibitors, we currently are conducting a research program in the area of ion channel modulation. We expect that future development candidates from our programs will be focused on a wide variety of diseases and conditions, including cancer, cystic fibrosis and pain.

We also will seek to opportunistically license and acquire technologies, resources and products that have the potential to strengthen our drug discovery platform, product pipeline and commercial capabilities.

Our internet address is *www.vrtx.com*. Our annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K, and all amendments to those reports, are available to you free of charge through the "Investors" 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.

Vertex was incorporated in Massachusetts in 1989, and our principal executive offices are located at 130 Waverly Street, Cambridge, Massachusetts 02139. We have research sites located in San Diego, California, Iowa City, Iowa and Milton Park, U.K.

COMMERCIAL PRODUCTS AND CLINICAL DEVELOPMENT PROGRAMS

Our product pipeline currently includes the following:

Product Candidate	Clinical Indication(s)	Development Phase	Company with Marketing Rights (Region)
Vertex-Led Programs			
Principal Areas of Focus			
VX-950	Chronic HCV infection	Phase II	Mitsubishi (Far East); Vertex (Rest of World)
VX-702	Rheumatoid arthritis and other inflammatory diseases	Phase II	Kissei (Far East); Vertex (Rest of World; Co-exclusive in certain Far East countries)
VX-770	Cystic fibrosis	Preclinical	Vertex (Worldwide)
Other			
VX-692	Bacterial infection	Preclinical	Vertex (Worldwide)
VX-883	Bacterial infection	Preclinical	Vertex (Worldwide)
VX-271	Oncology	Preclinical	Vertex (Worldwide)
VX-166	Sepsis/Acute liver disease	Preclinical	Vertex (Worldwide)
VX-765	Psoriasis	Phase II	Vertex (Worldwide)
pralnacasan (VX-740)	Rheumatoid arthritis and other inflammatory diseases	Phase II	Vertex (Worldwide)
merimepodib (VX-497)	Chronic HCV infection	Phase II	Vertex (Worldwide)
Collaborator-Led Programs			
Lexiva/Telzir (fosamprenavir calcium)*	HIV infection and AIDS	Marketed	GlaxoSmithKline (Worldwide)
brecanavir (VX-385)	HIV infection and AIDS	Phase II	Vertex (Far East); GlaxoSmithKline (Rest of World)
VX-680	Oncology	Phase I	Merck (Worldwide)
VX-667	Oncology	Preclinical	Merck (Worldwide)
VX-409	Pain	Preclinical	GlaxoSmithKline (Worldwide)
VX-944	Oncology	Phase I	Avalon Pharmaceuticals (Worldwide)
VX-322/VX-398	Oncology	Preclinical	Novartis (Worldwide)

* Fosamprenavir calcium is marketed under the trade names "Lexiva" in North America and "Telzir" in the European Union. Lexiva/Telzir is a prodrug of amprenavir (marketed as Agenerase), our first drug for the treatment of HIV infection and AIDS. Lexiva/Telzir has replaced Agenerase in worldwide markets.

Principal Areas of Focus

VX-950 (oral hepatitis C protease inhibitor for the treatment of chronic hepatitis C viral infection)

VX-950 is Vertex's lead oral hepatitis C protease inhibitor, and one of the most advanced of a new class of antiviral treatments in development targeting HCV infection. VX-950 is designed to inhibit NS3-4A serine protease, an enzyme thought to be necessary for HCV replication. The FDA has granted "Fast-Track" designation to VX-950, because chronic HCV infection is a serious and life-threatening disease and VX-950 has the potential to shorten the duration of therapy compared to the current standard of care. Treatment with VX-950 could result in improved sustained virologic response rates and a more favorable adverse event profile. Vertex currently is conducting a broad Phase II development program to determine the safety and antiviral activity of VX-950.

Background: Treatment of Chronic Hepatitis C Virus Infection

HCV infection causes chronic inflammation in the liver. The World Health Organization estimates that there are as many as 170 million people chronically infected with HCV worldwide and that an additional 3 million to 4 million people are infected each year. Chronic HCV infection results in liver cirrhosis in 10% to 20% of patients, and 1% to 5% of chronic HCV patients worldwide develop liver cancer over a period of 20 to 30 years. Reports published by the American Association for the Study of Liver Disease have estimated that approximately 3.4 million Americans are chronically infected with HCV, and the American Liver Foundation estimates that 10,000 to 12,000 Americans die as a result of HCV infection each year.

Currently, there is no vaccine available to prevent HCV infection. The current standard treatment for HCV infection is a combination of pegylated interferon and ribavirin administered for up to 48 weeks. This treatment regimen is associated with significant side effects, including fatigue, flu-like symptoms, depression and anemia. Among patients who begin treatment, approximately 50% of patients infected with genotype 1 HCV, the most common HCV genotype in the United States, fail to either complete treatment or show a long-term sustained response to therapy. As a result, new safe and effective treatment options for HCV infection are needed. We believe that therapeutics that directly target viral replication, such as VX-950, may significantly increase the number of patients who achieve a sustained viral response to drug therapy.

VX-950 Development Program

In early 2006, we obtained preliminary results from the first Phase II clinical trial of VX-950. This 28-day trial enrolled 12 treatment-naïve patients infected with genotype 1 HCV. The patients' distribution of baseline plasma HCV RNA values upon entering the trial was typical for a treatment-naïve patient population. At the end of treatment, HCV RNA was undetectable in all 12 patients. There were no treatment discontinuations, no serious adverse events reported and no evidence of viral breakthrough during treatment. A detailed safety analysis is ongoing.

Patients in the Phase II trial received VX-950 in a tablet formulation at a dose of 750 mg every eight hours for 28 days in combination with standard doses of Pegasys® (pegylated interferon alfa-2a) ("peg-IFN") and Copegus® (ribavirin) ("RBV"). At the end of 28 days, patients completed dosing with VX-950 and, as required by the trial protocol, continued treatment with peg-IFN and RBV. This 28-day, Phase II trial was not designed to evaluate sustained viral responses in patients receiving VX-950.

Preliminary results from the trial are as follows:

- At the end of week 1 (day 8 of VX-950 dosing), plasma HCV RNA was below the limit of quantitation (< 30 IU/mL, as measured by the Roche TaqMan® assay) in 6 of 12 patients and undetectable (< 10 IU/mL, Roche TaqMan® assay) in 2 of 12 patients.

- At the end of week 2, plasma HCV RNA was below the limit of quantitation in 11 of 12 patients and undetectable in 3 of 12 patients.

- At the end of week 3, plasma HCV RNA was below the limit of quantitation in 12 of the 12 patients and undetectable in 9 of 12 patients.

- At the end of VX-950 dosing (end of week 4; day 28), plasma HCV RNA was undetectable in all 12 patients.

We have completed three-month animal toxicology studies of VX-950 that we believe will support clinical trials of VX-950 of up to three months' duration. We submitted data from these toxicology studies and the 28-day Phase II clinical trial to the FDA in the first quarter of 2006. Subject to FDA agreement, we plan to initiate a three-month Phase II trial of VX-950 in more than 200 HCV patients in the second quarter of 2006. We expect that this trial will include a comparison to the current standard of care in HCV therapy. We also plan to initiate additional trials of VX-950 throughout 2006, including a Phase II trial in patients who have failed prior therapy.

The 28-day Phase II trial was the third in a series of clinical trials of VX-950 in HCV-infected patients designed to evaluate safety, pharmacokinetics and antiviral activity, in order to guide the design of larger, longer-duration Phase II trials. The first two such trials were Phase Ib trials conducted in 2005—a trial of VX-950 as monotherapy completed early in the year (the "Phase Ib monotherapy trial"), and a trial of VX-950 dosed together with peg-IFN completed later in the year (the "Phase Ib combination therapy trial").

The Phase Ib monotherapy trial enrolled 34 patients with chronic genotype 1 HCV infection who were treated for 14 days with placebo or one of three dose regimens of VX-950. In the trial, VX-950 was well tolerated, with no serious adverse events or treatment discontinuations reported, and demonstrated potent antiviral activity. Patients treated with 750 mg of VX-950 every eight hours achieved a median $4.4\log_{10}$ (equivalent to 25,000-fold) reduction in plasma HCV RNA at the end of 14 days of treatment. A median reduction in HCV RNA of greater than $2\log_{10}$ was seen in each of the other two VX-950 dose groups at the end of 14 days of treatment. Every patient receiving VX-950 achieved greater than a $2\log_{10}$ reduction in HCV RNA within the first three days of treatment.

At the end of 14 days of treatment in the Phase Ib monotherapy trial, plasma HCV RNA was below the limit of quantitation in four of eight patients in the 750 mg dose group and was undetectable in two of those four patients. Higher ranges of VX-950 blood concentrations were associated in the Phase Ib monotherapy trial with higher HCV RNA reductions to the responses established at lower blood concentrations of VX-950.

Elevated ALT levels are common in HCV patients and are considered to be a marker of liver injury due to HCV infection. Median serum ALT declines of 25 to 32 U/L were observed in all VX-950 dose groups in the Phase Ib monotherapy trial. In the placebo group, a median 8 U/L increase was observed. Prior to treatment with VX-950, serum ALT levels were elevated in approximately 70% of patients in the trial. In the VX-950 dose groups, 83% (15 of 18) of patients with elevated ALT levels at baseline (prior to treatment) had achieved normalization of ALT levels at day 14, compared to zero in the six patient placebo group. Mean levels of serum neopterin also were observed to decrease with VX-950 treatment in the trial. Decreased neopterin levels may be a further signal of a reduction in liver inflammation associated with HCV infection.

Researchers analyzed the sequences of the HCV NS3-4A protease gene in samples isolated from trial patients prior to and following treatment with VX-950 in the Phase Ib monotherapy trial, in order to characterize HCV protease variants that may emerge during treatment with a direct-acting antiviral compound such as VX-950. In the group of patients that demonstrated continued viral decline during treatment, virus could first be isolated in a sequencing assay within 7 to 10 days after completion of treatment. In this group, wild-type virus predominated during the post-treatment period. Some variants were detected that displayed a minimally-reduced sensitivity to VX-950 *in vitro*. In the other groups of patients who received VX-950, genetic sequence changes associated with reduced sensitivity to VX-950 *in vitro* were detected at the end of dosing, including some variants with moderately to highly reduced sensitivity to VX-950. However, these changes in gene sequences also appeared to result in reduced viral fitness. In particular, the frequency of the variant with the highest level of reduced drug sensitivity, A156V/T, diminished markedly between the end-of-dosing and post-treatment analysis, indicating

significantly reduced *in vivo* fitness relative to wild-type virus. Published *in vitro* data suggest that the A156V/T variant also may retain sensitivity to interferon. We believe that these results provide a strong rationale for study of the combination of VX-950 and interferon to achieve optimal response rates.

Later in 2005, we conducted the Phase Ib combination therapy trial, a 14-day, randomized, blinded, placebo-controlled trial to evaluate the safety, tolerability and pharmacodynamics of VX-950 when combined with peg-IFN. The antiviral activity of the combination through 14 days was significantly greater in this trial than the activity of VX-950 administered as a single agent, and was much greater than peg-IFN alone. In addition, VX-950 appeared to be well-tolerated when dosed alone and in combination with peg-IFN. All patients completed dosing and no serious adverse events were reported.

The Phase Ib combination therapy trial enrolled 20 treatment-naïve patients infected with chronic genotype 1 HCV. Patients were randomized to three treatment groups: those who received a tablet formulation of VX-950 at a dose of 750 mg every eight hours in combination with a standard dose of peg-IFN (n=8), those who received the same dose of VX-950 administered alone (n=8) and those who received a standard dose of peg-IFN alone (n=4). The median viral load for all patients at the beginning of the trial was $6.65\log_{10}$ IU/mL HCV RNA (approximately 4,400,000 IU/mL). In this trial, the combination of VX-950 and peg-IFN produced an initial median reduction in plasma HCV RNA of more than $3\log_{10}$ in the first two days of treatment, followed by continued decline to a median $5.5\log_{10}$ reduction in plasma HCV RNA at day 14, which equates to a 300,000-fold reduction in viral levels. Six of eight patients receiving the combination of VX-950 and peg-IFN achieved plasma HCV RNA levels below the limit of quantitation at 14 days, and plasma HCV RNA levels were undetectable in four of those six patients. Adverse events in the patients receiving VX-950 alone were reported as mild, with one incident of skin itching of moderate severity. Typical interferon-related side effects, of mild to moderate severity, were reported in the patients that received peg-IFN along with VX-950 or placebo. The only clinically significant laboratory finding of abnormality was a finding of neutropenia (a blood disorder which can arise as a side effect of certain drug treatments) in one patient who received peg-IFN plus placebo. Neutropenia has previously been reported in patients receiving peg-IFN. Complete data from the trial will be presented at a medical conference later this year.

We have conducted viral kinetic analyses of the results in both the Phase Ib monotherapy trial and the Phase Ib combination therapy trial. In these analyses we have estimated the viral decline that might be expected, with dosing beyond 14 days, in patients who achieved HCV RNA levels below the limit of quantitation at the end of dosing. The results of this simulation suggest that it may be possible to achieve sustained virologic response by including VX-950 in a treatment regimen of approximately 12 weeks' duration. We plan to test this hypothesis in future clinical trials.

In November 2004, we completed a Phase Ia clinical trial of VX-950 in healthy volunteers designed to assess the safety, tolerability and pharmacokinetics in escalating, single doses of VX-950 ranging from 25 mg to 1250 mg. In this trial, no dose-limiting toxicities were identified, and blood serum levels of VX-950 were observed that are associated with potent antiviral activity in laboratory experiments. In preclinical trials VX-950 showed potent and sustained anti-HCV activity in both an *in vitro* replicon system and in infectious viral assays.

We hold worldwide marketing rights to VX-950, except for Japan and certain Far East countries, where we are collaborating with Mitsubishi Pharma Corporation. We may consider entering into a collaborative arrangement for the development and/or commercialization of VX-950 outside North America and the Mitsubishi territory. VX-950 was discovered in our collaboration, now ended, with Eli Lilly and Company. We hold worldwide rights to all other second-generation HCV protease inhibitors discovered by us during our collaboration with Eli Lilly. We will owe Eli Lilly royalties on any future sales of VX-950 and certain other HCV protease inhibitors.

VX-702 (oral p38 MAP kinase inhibitor for the treatment of rheumatoid arthritis)

VX-702 is our lead oral p38 mitogen-activated protein ("MAP") kinase inhibitor, which we are currently developing for the treatment of RA. Based on clinical trials and non-clinical studies, we

believe that VX-702 may be a potent therapy in an inflammatory disorder such as RA. We currently are conducting a broad Phase II development program to assess the safety and efficacy of VX-702. Our collaborator, Kissei Pharmaceuticals, currently is conducting a Phase I clinical trial of VX-702 in Japan. In our recently concluded three-month Phase II trial of VX-702 in RA patients, VX-702 was well-tolerated through 12 weeks of dosing, and demonstrated statistically significant clinical effects on signs and symptoms of RA. The preliminary results from this trial support our plans to advance our clinical program for VX-702 and to initiate by mid-2006 clinical studies of VX-702 on a background of methotrexate, a commonly used therapy for RA. We expect to file an IND application with the FDA in 2006 to support clinical trials of VX-702 in the United States.

Background

Rheumatoid Arthritis

Rheumatoid arthritis, a systemic disease, is the most common form of inflammatory arthritis. RA has a prevalence of about 1% of the worldwide population and an annual incidence of 3 cases per 10,000 adults. RA causes pain, swelling and loss of function in affected joints. The disease is often accompanied by significant morbidity and mortality. Depending on the severity of the disease, the risk of disability can be as high as 33%, and mortality can be raised by as much as 52%. Patients with RA also have a significant impairment in their quality of life.

The current standard treatment for RA is administration of a disease-modifying anti-rheumatic drug ("DMARD"), most commonly methotrexate. Over the last few years, there has been a rapid increase in the use of injectable anti-tumor necrosis factor ("TNF") agents such as Remicade® (infliximab) and Enbrel® (etanercept), generally on a background of methotrexate, when disease activity is not controlled by DMARDs and non-steroidal anti-inflammatory drugs. We believe that an oral agent that successfully targets TNF production may provide an attractive treatment option for patients with this debilitating disease.

p38 MAP Kinase Inhibitors for Inflammatory Diseases

The MAP kinases are a family of structurally-related human enzymes involved in intracellular signaling pathways that enable cells to respond to their environment. The p38 MAP kinase is involved in a variety of cellular processes, including the onset and progression of inflammation. When activated, the p38 MAP kinase triggers production of multiple cytokines, including interleukin-1 ("IL-1"), TNF-alpha and interleukin-6 ("IL-6"). Excess levels of IL-1 and TNF-alpha are associated with a broad range of acute and chronic inflammatory diseases.

We have extensive preclinical and clinical experience with p38 MAP kinase inhibitors, which we believe may be a powerful and broadly useful new class of oral anti-inflammatory drugs.

VX-702 Development Program

In March 2006, we obtained preliminary results from our three-month Phase II 315-patient trial of VX-702 (the "VeRA" trial). A total of 278 patients completed 12 weeks of treatment in this double-blind, randomized and placebo-controlled trial. The trial was conducted at more than 40 centers in Eastern and Central Europe. Patients received either 5 mg or 10 mg of VX-702 once daily, or placebo. In addition to VX-702, patients could receive certain disease-modifying anti-rheumatic drugs (DMARDs), but could not receive methotrexate or anti-TNF therapies. At the end of 12 weeks, patients completed dosing with VX-702 and were evaluated for improvement in clinical signs and symptoms according to American College of Rheumatology ("ACR") criteria ("ACR_{20}"). ACR_{20} is a standardized measure based on a patient's attainment of at least a 20% improvement in ACR-specified indicators of RA activity.

VX-702 met its primary objectives in the VeRA study. Preliminary analyses indicate that treatment with VX-702 in the VeRA trial led to a dose-dependent, statistically significant increase in week 12 ACR_{20} response rates, the primary endpoint of the clinical trial. Thirty percent of patients receiving placebo, 38% of patients receiving 5 mg daily of VX-702 and 40% of patients receiving 10 mg daily of

VX-702 achieved an ACR_{20} response at week 12 (p=0.04; Jonckheere-Terpstra test for increasing dose-response). In addition, 32% of placebo patients, 41% of 5 mg VX-702-treated patients and 44% of 10 mg VX-702-treated patients achieved a EULAR (moderate or good) response (p=0.01). Dose-dependent statistically significant effects also were seen on tender joint counts (p=0.007), swollen joint counts (p=0.003), disease activity score (DAS28; p=0.02) and morning stiffness (p=0.03). We currently are conducting ongoing analyses of additional clinical measures and biomarkers.

Clinical trials of a number of other p38 MAP kinase inhibitors have demonstrated dose-dependent elevations in liver enzymes, which generally are thought to be markers for liver injury. In 2004, we completed a 28-day study of VX-702 in healthy volunteers designed specifically to evaluate the effect of VX-702 on liver enzymes. This trial showed some transient elevations in liver enzymes in a small number of subjects. However, the magnitude of those enzyme elevations did not reach clinical significance and did not require discontinuation of dosing. The enzyme levels returned to normal during continued dosing. In the VeRA trial, no clinically significant adverse effects were seen in liver function tests.

Also in 2004, we completed a Phase IIa double-blind, randomized, placebo-controlled, dose-escalation clinical trial of VX-702 for the treatment of patients with acute coronary syndrome ("ACS") undergoing percutaneous coronary intervention ("PCI"), such as stent placement. p38 MAP kinase regulates the production of key inflammatory cytokines implicated in the pathogenesis of ACS. This Phase IIa trial of VX-702 was designed to evaluate the safety, tolerability and pharmacokinetics of VX-702 in 45 unstable angina patients with elevated c-reactive protein ("CRP") levels, a marker of inflammation measured in the blood, undergoing PCI. In this Phase IIa ACS trial, there were no clinically significant differences between treatment and placebo groups with respect to adverse events, and VX-702 met pre-established safety and pharmacokinetic objectives. During routine (non-continuous) electrocardiogram monitoring in the Phase IIa ACS trial, small (not clinically significant) changes in QT interval (a measure of electrical conduction within the heart) were seen in the patients treated with VX-702. Also in the Phase IIa ACS trial, during Holter (continuous electrocardiogram) monitoring conducted for 72 hours, we observed asymptomatic ventricular ectopy ("VE") (ventricular extra beats), which was present in all treatment groups but at a higher incidence for VX-702 treatment groups. The significance of these events was unclear after the Phase IIa ACS trial. In the VeRA trial, we performed extensive ambulatory and 12-lead electrocardiographic monitoring on patients throughout the trial. No differences in VE activity or cardiac arrythmias were observed between placebo and treated patients. On digital electrocardiograms, from baseline to end of treatment, a minimal (average approximately 1.5% or less for each group) dose-dependent increase in the Fridericia rate-corrected QT interval (QTcF) was seen in the VX-702 treatment groups. No patient experienced a clinically significant (60 msec, or approximately 15%) increase in QTcF at any time in the trial.

A preliminary analysis of VeRA trial data also indicates that VX-702 was well-tolerated. Premature discontinuations for adverse events were low across the trial arms: placebo (2%), 5 mg (3%) and 10 mg (5%). No clinically significant effects were seen on laboratory parameters, including liver function tests. The most common adverse events that led to treatment discontinuation in patients receiving VX-702 were seen in two patients each and were: gastroenteritis, nausea/vomiting, rash, and renal impairment (increased serum creatinine levels to 1.2 to 1.5 times upper limit of normal). Based on preliminary analysis, the most common adverse events were generally mild or moderate and were: infection (5% of placebo patients and 10% of VX-702 patients), gastrointestinal disorders (6% placebo and 8% VX-702), and skin disorders (0% placebo and 9% VX-702).

By mid-2006, we expect to initiate clinical trials of VX-702 on a background of methotrexate, including a three-month dose-ranging Phase II clinical trial in more than 200 patients at centers in Europe. Doses in this planned trial will be determined based on final analysis of the VeRA trial.

We hold worldwide development and commercialization rights to VX-702, except for Japan and certain Far East countries, where we are collaborating with Kissei Pharmaceutical Co., Ltd.

VX-770 (oral CFTR potentiator for the treatment of cystic fibrosis)

VX-770 is a small molecule compound designed to potentiate the gating activity of the cystic fibrosis transmembrane regulator ("CFTR") protein, a chloride ion transporter on the cell surface that is functionally defective in patients with cystic fibrosis. We expect to file an investigational new drug ("IND") application with the FDA and initiate our first clinical trial of VX-770 in the first half of 2006.

Cystic fibrosis is a genetic disease afflicting approximately 30,000 people in the United States. The symptoms of cystic fibrosis, particularly the development of thick mucous that causes lung tissue inflammation and, ultimately, irreversible lung damage, are caused by defects in the CFTR protein. A leading hypothesis is that mucous accumulates in the lung due to improper water and salt (including chloride ion) transport across the cell surface membrane. Using our expertise in ion channels, including high-content cell assays and medicinal chemistry, we have identified selective ion channel modulators for the treatment of cystic fibrosis. CFTR potentiator compounds such as VX-770 may work by increasing the frequency during which the CFTR channel is open, which could result in an increase in chloride transport across the cell membrane. In laboratory studies involving bronchial epithelial cells isolated from cystic fibrosis patients, our researchers have demonstrated that potentiator compounds may improve CFTR function.

VX-770 was discovered in our ongoing research collaboration with Cystic Fibrosis Foundation Therapeutics Incorporated ("CFFT") and with the support and participation of the Cystic Fibrosis Foundation. We hold worldwide development and commercialization rights to VX-770. We will owe CFFT royalties on any future sales of VX-770.

Other Vertex-Led Programs

VX-692 and VX-883 (gyrase inhibition for the treatment of bacterial infection)

VX-692 and VX-883 are novel, Vertex-discovered antibiotics currently in preclinical development that target both DNA gyrase and topoisomerase IV. DNA gyrase and topoisomerase IV are enzymes that are essential to bacteria during the replication process. DNA gyrase and topoisomerase IV inhibitors already on the market have proven to be potent, broad-spectrum antibiotics and are used to treat a variety of common Gram-positive and Gram-negative bacterial infections in various treatment settings. While existing gyrase and topoisomerase IV inhibitors work by interacting with the gyrA and parC subunits of DNA gyrase and topoisomerase IV, VX-692 and VX-883 target the gyrB and parE subunits. Each of VX-692 and VX-883 is active against Gram-positive and Gram-negative bacterial pathogens prevalent in both community and hospital settings, including certain pathogens that are less susceptible to other classes of antibiotics, such as agents targeting the other subunits of gyrase and topoisomerase IV. Accordingly, we believe that VX-692 and VX-883 warrant further investigation to determine if they may be useful in treating infections caused by drug resistant bacteria, a major and growing problem with currently marketed antibiotics.

We hold worldwide development and commercial rights to both VX-692 and VX-883, and we are evaluating the possibility of entering into a collaborative relationship to advance the development of either or both of these compounds.

VX-271 (kinase inhibition for the treatment of oncology indications)

VX-271 is a novel, Vertex-discovered kinase inhibitor currently in preclinical development. Kinases have been implicated in a wide range of oncology indications, and we believe that kinase inhibition may offer a therapeutic opportunity against a broad array of human tumors. We hold worldwide development and commercialization rights to VX-271, and we may consider entering into a collaborative arrangement to advance its development.

VX-166 (caspase inhibition for the treatment of sepsis)

VX-166 is a novel, Vertex-discovered inhibitor of multiple caspases being investigated for the treatment of sepsis and acute liver disease. Inhibition of caspases has been shown to inhibit apoptosis. We have demonstrated in animal models that inhibition of apoptosis may be useful in the treatment of sepsis and acute liver disease. We hold worldwide rights to VX-166, and we may consider entering into a collaborative arrangement to advance its development.

VX-765 and pralnacasan (ICE inhibition for the treatment of inflammatory diseases)

We discovered and have completed certain development activities with respect to two interleukin-1 converting enzyme ("ICE") inhibitors for the treatment of inflammatory diseases, VX-765 and pralnacasan. ICE is an enzyme that controls the release of active IL-1b (one of two forms of IL-1) and IL-18 from white blood cells into the bloodstream and within tissues. IL-1 and IL-18 are cytokines that mediate a wide range of immune and inflammatory responses in many cell types. Elevated IL-1 and IL-18 levels have been correlated with disease states in a number of acute and chronic inflammatory diseases.

During 2005, we completed the clinical portion of our four week, Phase IIa clinical trial of VX-765, for the treatment of psoriasis in 68 patients. We expect that data from this trial will be reported in 2006. Earlier Phase I clinical trials of VX-765 in healthy volunteers demonstrated a dose-dependent decrease in levels of IL-18, the first time this has been demonstrated for any therapeutic agent. Data from preclinical studies show that VX-765 reduces inflammation and cytokine levels in animal dermatitis and arthritis models.

Our first generation ICE inhibitor, pralnacasan, was developed in collaboration with Sanofi-Aventis (then Aventis). In 2005, our collaboration with Sanofi-Aventis terminated, and all rights to pralnacasan reverted to us. Phase II clinical trials of pralnacasan conducted by Aventis suggested that treatment with pralnacasan was well tolerated, produced positive anti-inflammatory effects in patients with RA and led to dose-dependent suppression of the production of IL-1b. Aventis also conducted a Phase II clinical trial of pralnacasan in patients with osteoarthritis. In that trial, there was improvement (29% to 35%) in the primary endpoint in four treatment groups, including the placebo group, during the 12 weeks of the trial, but there were no statistically significant differences in the primary endpoint of the trial between placebo treatment and any of the pralnacasan treatment groups. However, statistically significant changes in some urine and serum markers of bone and cartilage turnover were observed. In 2003, Aventis and Vertex voluntarily suspended the clinical development of pralnacasan pending full analysis of findings that emerged from a nine-month nonclinical toxicology study. In that nonclinical study, high doses of pralnacasan were associated with the development of fibrosis in circumscribed areas of the liver of one species of animal. Nonclinical toxicology studies designed to explore this toxicology issue were completed in 2005, and we expect data from those nonclinical studies to be presented at a medical conference in 2006.

We believe these results warrant further study and we may consider entering into a collaborative arrangement to advance the development of either or both of VX-765 and pralnacasan, to which we hold worldwide development and commercialization rights.

Merimepodib (VX-497) (IMPDH inhibition for the treatment of chronic HCV infection)

We currently are conducting a Phase IIb clinical trial of merimepodib, an oral, small molecule inhibitor of inosine 5-monophosphate dehydrogenase ("IMPDH") for the treatment of chronic HCV infection. This double-blind, placebo-controlled, randomized trial (referred to as the "METRO" trial) is designed to study the administration of merimepodib with peg-IFN and RBV in patients who did not respond to prior treatment with peg-IFN and RBV. The goal of the METRO trial is to evaluate the safety, pharmacokinetics and efficacy of merimepodib in combination with peg-IFN and RBV. The primary endpoint of the trial is to evaluate the antiviral activity of merimepodib in combination with peg-IFN and RBV and perform an assessment of the proportion of merimepodib-treated patients who achieve a sustained virologic response, compared to placebo, at week 72 (end of follow up). We expect to complete the METRO trial in 2006. In the HCV field, we are currently focusing our efforts on the development of direct antivirals such as VX-950. Therefore, we currently do not plan to conduct additional merimepodib clinical trials after the METRO trial is completed.

We hold worldwide development and commercialization rights to merimepodib.

Collaborator-Led Programs

Lexiva/Telzir and brecanavir: HIV protease inhibition for the treatment of HIV/AIDS (GlaxoSmithKline plc)

Infection with HIV can lead to AIDS, a severe, life-threatening impairment of the immune system. The Joint United Nations Programme on HIV/AIDS estimates that approximately 40.3 million individuals worldwide are infected with HIV. The United States National Institutes of Health has estimated that there may be as many as 950,000 individuals in the United States infected with HIV. There are four classes of antiviral drugs approved for the treatment of HIV infection and AIDS: nucleoside reverse transcriptase inhibitors, such as AZT and 3TC; non-nucleoside reverse transcriptase inhibitors, such as efavirenz; the fusion inhibitor enfuvirtide; and HIV protease inhibitors ("HIV PIs"). HIV PIs are used as part of combination regimens for the treatment of HIV. HIV PIs block the cleavage of HIV polyproteins into active proteins, and result in the production of non-infectious viral particles. The HIV PI ritonavir has been shown to significantly boost the levels of certain other PIs in the bloodstream and therefore co-administration of HIV PIs with ritonavir has become progressively more frequent in clinical practice as a strategy for achieving maximum antiviral activity, reducing the likelihood of treatment failure (viral breakthrough), and lowering the overall pill count for patients. Sales of HIV PIs in the United States exceeded $1.2 billion in 2005, an increase of approximately 11% from 2004. The United States market for HIV PIs is highly competitive, with nine different HIV PIs approved by the FDA for sale.

Lexiva/Telzir

Our second generation HIV PI, fosamprenavir calcium, is marketed under the name Lexiva in the United States and under the name Telzir in the European Union. Lexiva/Telzir was co-discovered by us and GlaxoSmithKline and was developed by GlaxoSmithKline pursuant to our collaboration with them. GlaxoSmithKline has worldwide marketing rights for Lexiva/Telzir, and we have the right to conduct certain promotional and educational activities for Lexiva/Telzir in the United States and the European Union. We also have the right, which we have not yet exercised, to supply bulk drug substance to GlaxoSmithKline. We receive royalties on GlaxoSmithKline's sales of Lexiva/Telzir.

Lexiva was launched in the United States in late 2003, and in certain European Union countries in the third quarter of 2004. In 2005, Lexiva was the fourth largest (measured in terms of sales revenue) HIV PI inhibitor in the United States, excluding ritonavir, and it currently holds an approximate 11% share of the United States HIV PI market (also excluding ritonavir). Lexiva/Telzir is currently marketed in over 40 countries worldwide, including the United States, France, Germany, Spain, Italy, the United Kingdom and Canada.

Lexiva/Telzir is a prodrug of amprenavir, our first generation HIV PI, which also was discovered and developed under our collaboration with GlaxoSmithKline and marketed under the name Agenerase. Lexiva/Telzir has replaced Agenerase in worldwide markets. A prodrug is an inactive compound that is metabolized by the body to become the active drug. Due to the physical properties of prodrugs such as Lexiva/Telzir, it is possible to achieve a higher effective dose of the active drug for each prodrug pill administered, resulting in a smaller pill burden for patients.

Brecanavir (VX-385)

Brecanavir (VX-385) is the third novel, orally available HIV PI to enter clinical development from our HIV collaboration with GlaxoSmithKline. Brecanavir is an aspartyl protease inhibitor, and is chemically distinct from Lexiva/Telzir and other currently marketed PIs. Brecanavir is currently in Phase II clinical development and has received "Fast Track" designation from the FDA. GlaxoSmithKline is currently conducting a 105-patient Phase IIb clinical trial of brecanavir in combination with retonavir in North America, Europe and Australia. We expect that the results of this Phase IIb clinical trial will be presented at a medical conference in late 2006. We also expect that GlaxoSmithKline will commence a Phase III clinical trial program for brecanavir in 2006.

In 2005, GlaxoSmithKline reported interim 24-week results from an open label, 48-week Phase IIa study of brecanavir. In this clinical trial, 31 HIV-1 infected adults received 300mg of brecanavir twice-daily, boosted with 100mg of ritonavir, in combination with one of two nucleoside reverse transcriptase inhibitors (based on patient medical history and viral genotype). The interim findings suggested potent antiviral activity for brecanavir in both HIV PI-sensitive and HIV PI-resistant HIV-infected adults participating in the clinical trial. At week 24, 81% of the patients had plasma HIV-1 RNA below the limit of detection in standard assays (< 400 copies/mL of blood) and 77% of the patients had viral load below the limit of detection in ultrasensitive assays (< 50 copies/mL of blood). Patients with HIV PI-sensitive and highly HIV PI-resistant virus had similar response rates. An interim safety assessment suggested that brecanavir was well-tolerated: few Grade 2 to 4 (Common Toxicity Criteria scale) drug-related adverse events and no serious adverse events were observed. Most adverse events were reported as mild and did not require treatment modification or discontinuation. We expect final results of this trial will be announced in 2006.

We hold development and commercialization rights to brecanavir in the Far East, and GlaxoSmithKline holds development and commercialization rights to brecanavir in the rest of the world.

VX-680 and VX-667: Aurora kinase inhibition for the treatment of cancer (Merck & Co., Inc.)

We are collaborating with Merck in the research and development of Aurora kinase inhibitors, including VX-680 and a follow-on compound, which we have designated VX-667. Aurora kinases are enzymes thought to play multiple roles in the development and progression of cancer, acting as regulators of cell proliferation, transforming normal cells into cancer cells and downregulating p53, one of the body's natural tumor suppressors. We believe that inhibitors of Aurora kinases may be useful as highly targeted treatments for a range of oncology indications.

VX-680 is a potent inhibitor of Aurora kinases and of Flt-3 kinase, a receptor tyrosine kinase that is known to be inappropriately activated in several different types of leukemia. Vertex researchers published the three-dimensional atomic structure of Aurora-A kinase in 2002, and published the structure of Flt-3 kinase in January 2004. We also presented preclinical data in a number of research and medical venues in 2003 suggesting that VX-680 should be further investigated to determine its potential to treat several different cancer types for which there are currently few or no available treatments. In a paper published in February 2004, researchers at Vertex reported demonstrating for the first time that a selective small molecule inhibitor of Aurora kinase (VX-680) inhibited tumor growth and induced tumor regression in xenograft models of human pancreatic and colon cancer. In

addition, Vertex researchers have presented data showing that VX-680 prolonged survival and induced sustained remission in an oncogene-driven model of acute myelocytic leukemia.

Merck presently is conducting three Phase I clinical trials of VX-680 in patients with hematologic cancers, with recurrent or non-responsive solid tumors, and with certain cancers for which standard therapy does not currently exist. In late 2005, Merck demonstrated that dosing VX-680 in patients with solid tumor cancers could produce observed changes in the activity of a clinically relevant biomarker. We expect that Merck will report the Phase I clinical data for VX-680 in 2006, and also will initiate Phase II clinical development this year.

In 2005, Merck also selected VX-667, an Aurora kinase inhibitor, for preclinical development. Merck holds worldwide development and commercialization rights to VX-680 and VX-667.

VX-409: Selective sodium channel modulation for the treatment of pain (GlaxoSmithKline plc)

We are collaborating with GlaxoSmithKline in the clinical development of VX-409, an oral, subtype-selective sodium channel modulator, for the treatment of pain. Worldwide prescription drug sales for the treatment and management of pain were more than $20 billion in 2004. VX-409 has been shown to be orally bioavailable and highly active, with a good safety profile, in nonclinical models of both neuropathic and inflammatory pain. VX-409 was discovered through our San Diego-based ion channel research program using the capabilities and proprietary technologies that are unique to that site. We expect that GlaxoSmithKline will initiate Phase I clinical development of VX-409 early in 2007.

GlaxoSmithKline holds worldwide development and commercialization rights to VX-409.

VX-944: IMPDH inhibition for the treatment of cancer (Avalon Pharmaceuticals, Inc.)

We are collaborating with Avalon Pharmaceuticals in the development of VX-944, an IMPDH inhibitor for the treatment of advanced hematological malignancies, such as leukemia, lymphoma or myeloma. Recent reports in medical literature and presentations at scientific conferences provide a clinical rationale for the development of IMPDH inhibitors for the treatment of hematologic malignancies. Results from certain preclinical studies of VX-944 indicated that VX-944 inhibited the *in vitro* proliferation of lymphoid and myeloid cells, the principal cells involved in the most common types of human leukemias. VX-944 also significantly prolonged survival in a model of aggressive mouse leukemia. In a single-dose, dose-escalation Phase I clinical trial of VX-944 in healthy volunteers, data indicated that VX-944 was orally bioavailable and well-tolerated.

Avalon initiated a Phase I clinical trial of VX-944 in January 2006. That clinical trial is designed as an open-label, repeat dose-escalation clinical trial for the evaluation of the safety and tolerability of VX-944 in up to 36 adult patients with advanced hematological cancer.

Avalon Pharmaceuticals holds worldwide development and commercialization rights to VX-944.

VX-322: Flt-3/c-kit inhibitor for the treatment of cancer (Novartis Pharma AG)

We are collaborating with Novartis in the preclinical development of VX-322, a dual inhibitor of the flt-3 and c-kit kinases, for the treatment of certain forms of cancer. Flt-3 kinase and c-kit kinase function as molecular switches that regulate the growth of certain cancers. Flt-3 kinase inhibition has attracted significant attention among cancer researchers due to its highly targeted approach to the treatment of certain leukemias as well other hematological malignancies and solid tumors. Flt-3 kinase is abnormally activated or upregulated in a wide range of leukemias, including in more than 70% of patients with acute myelogenous leukemia ("AML"). Specific mutations of flt-3 kinase that are believed to be drivers of cell proliferation are present in up to 40% of AML patients. In addition, the protein c-kit has been found at high levels in 60% to 80% of AML patients. Preclinical studies conducted at Vertex using cells isolated from AML patients suggested that dual flt-3/c-kit inhibition may provide more potent reduction in cell proliferation than is provided by inhibition of flt-3 kinase or c-kit kinase alone. Current treatment for AML generally involves aggressive chemotherapy with "non-specific"

agents that cannot discriminate between healthy and diseased cells, resulting in significant toxicity and limited efficacy. New targeted approaches hold the potential to transform the treatment of AML, reducing side effects, improving tolerability and increasing the efficacy of chemotherapeutic regimens.

Novartis holds worldwide development and commercialization rights to VX-322, and an option to obtain similar rights to VX-398, a back-up compound to VX-322.

RESEARCH PROGRAMS

Vertex Drug Design Platform and Drug Discovery Strategy

We believe that our integrated drug design approach has significantly enhanced our ability to discover and develop small molecule drug candidates directed at biologically complex targets, including novel targets identified by genomic research. We believe that our approach has been validated through our ability to interest prospective collaborators in our research output and by our success in moving drug candidates into clinical trials.

Integrated Drug Design Approach. Our drug design platform integrates biology, biophysics, chemistry, automation and information technologies in a coordinated and simultaneous fashion throughout the discovery process. The goal of our integrated, interdisciplinary approach is to make the drug discovery and development process more efficient and productive.

Focused Drug Discovery in Target-Rich Gene Families. We have pioneered a novel approach to drug discovery in target-rich gene families, which are groups of genes with similar sequences that code for structurally similar proteins. We organize and cluster targets within a gene family according to how they interact with chemical inhibitors, which allows us to use high-throughput screening technologies, informatics and medicinal chemistry to rapidly identify drug-like classes of compounds in parallel for multiple targets. Along with this approach, we use a variety of biological and chemical methodologies that interrogate the function of newly discovered proteins in order to focus our drug discovery and development efforts on the most promising targets within the most promising gene families. We believe that our systematic application of this drug discovery approach is increasing the speed and efficiency of drug design efforts directed at novel biological targets, and is securing valuable intellectual property for us in gene families of interest.

Technology Platform

We employ a variety of technologies and use information from a number of different scientific disciplines as part of our integrated technology platform. The most significant of them are as follows.

- *Functional Genomics.* We use functional genomics techniques, such as gene knock-out mice, to help guide target selection and test the potential of chemical compounds in disease models. We also use antisense, siRNA, dominant negative cell lines, transcriptional profiling, proteomics and other biological approaches to better characterize the role played by specific targets in cellular processes.

- *Biophysics.* We generate atomic structural information on molecular targets using X-ray crystallography and nuclear magnetic resonance ("NMR") spectroscopy to guide design and optimization of lead classes of drugs.

- *Computer-based Modeling.* We apply advanced proprietary computational modeling tools to guide the evaluation and selection of compounds for synthesis. During our virtual ("*in silico*") screening process, candidate compounds are selected for synthesis and screening. We use proprietary algorithms to sort and filter compounds for specific properties in order to seek compounds that are more likely to become development candidates.

- *Pharmacokinetics and Pharmacology.* We employ a number of approaches to obtain predictive information on the bioavailability, pharmacokinetic profile and efficacy of potential drug

candidates. These approaches include *in vitro* metabolism and toxicological studies and *in vivo* assessment of leads in predictive animal models.

- *Assay Development.* We use modern cell biology, enzymology, and screening techniques to develop high-throughput assays which provide high-quality information to support drug discovery. Many of these assays are built upon a number of gene reporter technologies such as green fluorescent protein and beta lactamase. We also are utilizing our assay capabilities to develop novel proprietary *in vitro* assays to rapidly establish ADME/toxicology profiles for compounds in our screening library.

- *High-Throughput Screening.* We conduct assays for most enzyme and receptor targets using very high-throughput screening approaches, many of which are proprietary. These assays enable us to rapidly generate large numbers of lead compounds and drug candidates across targets from many different gene families. These approaches integrate compound management, plate replication with miniaturized screening, hit (potential lead) identification and follow-up.

- *Instrumentation.* We have a dedicated research and application development group, which is responsible for designing and building automated solutions to address many of the more repetitive and labor-intensive aspects and processes of drug discovery. For example, most of our ion channel research is conducted using E-VIPR, our proprietary screening technology that uses fluorescent probes and waves of electrical stimulation to study ion channels. E-VIPR provides an automated, high-throughput platform that enables us to collect high quality data at speeds up to a thousand times faster than patch clamping.

Current Research Programs

Our past drug discovery efforts have produced a variety of drug candidates that are currently in preclinical or clinical development. We believe our ongoing research programs, particularly those directed at the kinase and ion channel gene families, continue to create potential value for Vertex by generating new product candidates in areas of significant unmet medical need. These programs include research targeting certain kinases, ion channels, g-protein coupled receptors and HCV protease inhibitors.

Kinase Program

We have a broad-based drug discovery effort targeting the human protein kinase family, of which there are more than 500 members. Protein kinases are enzymes that play a key role in transmitting signals between and within cells. Kinases exert their effect by phosphorylating other proteins, which then become activated and perform a specific function. Kinase activity has been implicated in many major diseases, including cancer and autoimmune, inflammatory, cardiovascular, metabolic, and neurological diseases. As a result, we believe that kinases are ideal targets for therapeutic intervention. The clinical success of the oncology drugs Gleevec® (imatinib mesylate) and Tarceva® (erlotinib) offer examples of how small molecule kinase inhibitors can be tailored to address specific diseases.

Under our collaboration with Novartis, we have conducted extensive parallel drug design efforts within the kinase target family. To date, three development stage kinase inhibitors, VX-680, VX-322 and VX-271, have emerged from that collaboration, the research portion of which ends in April 2006. In 2004, we entered into a collaboration with Merck for the development of VX-680, an Aurora kinase inhibitor, in cancer, and for continuing collaborative research in the area of Aurora kinase inhibition. We expect the joint research effort with Merck to continue until June 2006.

We have drug discovery efforts underway targeting kinases that play a role in the development and progression of cancer, inflammation and autoimmune disease.

Our extensive drug discovery efforts involving numerous targets in the kinase gene family continue to refine our understanding of kinase biology and the design of kinase inhibitors. Our researchers have determined the atomic structure of more than 25 kinase drug targets and hundreds of kinase/inhibitor co-complexes. This information is of critical importance in the design of selective inhibitors for ongoing research projects. We also have designed a diverse library of proprietary kinase inhibitors and we continue to expand that library. We apply all of these tools with the objective of determining and optimizing new chemical scaffolds against targets of interest in the area of kinase inhibition.

Ion Channel Program

We are conducting a broad-based drug discovery program targeting the ion channel family. Ion channels are a gene family of more than 650 proteins that act as cellular gatekeepers, controlling the flow of ions across cell membranes. The ion channel family contains numerous drugable targets representing potential therapeutic intervention points for a variety of indications, including cystic fibrosis, pain and inflammatory, cardiovascular and metabolic diseases. Existing therapies such as amlodipine and nifedipine, which are calcium channel blockers for the treatment of hypertension, and lamotrigine and carbamazepine, which are sodium channel inhibitors for the treatment of epilepsy, provide a strong rationale for developing drugs targeting ion channels.

Our ion channel research extends across several ion channel subfamilies, including sodium channels and calcium channels, and is principally focused at present on the design and development of small-molecule drugs for the treatment of pain and cystic fibrosis. For example, specific sodium channels have been shown to increase in expression and function in peripheral nerve cells at the site of injury, making them novel and attractive targets for the treatment of neuropathic pain.

We have an ongoing research collaboration with CFFT targeting the CFTR protein. Our research efforts in this collaboration currently are focused on the identification of possible CFTR protein corrector compounds that may work to increase the number of ion channels in certain lung cell membranes of patients with cystic fibrosis. These ion channels may prevent the improper accumulation of water and salt (including chloride ions) that is believed to be the cause of mucous accumulation in the lungs of cystic fibrosis patients.

We are utilizing our expertise in assay development and screening to advance discovery efforts within the ion channel family.

Additional Discovery Efforts

We plan to utilize our proprietary gene family-based platform and experience in structure-based drug design to pursue targets in other medically important gene families. We have significant efforts underway targeting g-protein coupled receptors and back-up HCV protease inhibitors, among other things.

CORPORATE COLLABORATIONS

We have entered into corporate collaborations with pharmaceutical and other companies and organizations that provide financial and other resources, including capabilities in research, development, manufacturing, and sales and marketing, to support our research and development programs. At present, we have the following major corporate collaborations.

GlaxoSmithKline plc

In December 1993, we entered into a collaboration with GlaxoSmithKline covering the research, development and commercialization of HIV protease inhibitors, including Agenerase (amprenavir), Lexiva/Telzir (fosamprenavir calcium) and brecanavir (VX-385). Under the original agreement,

GlaxoSmithKline had exclusive rights to develop and commercialize our HIV PIs in all parts of the world except the Far East. In 2003, we amended the agreement to add the Far East to GlaxoSmithKline's territory for development and commercialization of Lexiva/Telzir. GlaxoSmithKline pays us a royalty on all sales of the HIV PIs covered by the agreement. We have retained certain bulk drug manufacturing rights and certain co-promotion rights in the territories licensed to GlaxoSmithKline. Under the collaborative agreement, GlaxoSmithKline agreed to pay the Company up to $42 million, comprised of an up-front $15 million license payment made in 1993, $14 million of product research funding over five years and $13 million of development and commercialization milestone payments for an initial drug candidate. Research funding under this agreement ended on December 31, 1998 and Vertex has received the entire $42 million referenced above. We began earning a royalty from GlaxoSmithKline in 1999 on sales of Agenerase, in the fourth quarter of 2003 on sales of Lexiva, and in the third quarter of 2004 on sales of Telzir. GlaxoSmithKline is also obligated to pay additional development and commercialization milestone payments for subsequent drug candidates, including brecanavir. If brecanavir is successfully commercialized, GlaxoSmithKline must pay us royalties on any future sales of brecanavir. GlaxoSmithKline bears the costs of development in its territory under the collaboration. GlaxoSmithKline has the right to terminate its agreement with us without cause upon 12 months' notice. Termination of the agreement by GlaxoSmithKline will relieve it of its obligation to make further commercialization and development milestone and royalty payments, and will end any license granted by us to GlaxoSmithKline under the agreement. In June 1996, we and GlaxoSmithKline obtained a worldwide, non-exclusive license under certain G.D. Searle & Co. (now owned by Pharmacia/Pfizer) patents in the area of HIV protease inhibition. We pay Searle a royalty based on sales of Lexiva/Telzir.

In December 2005, we entered into a separate collaboration agreement with GlaxoSmithKline for the development and commercialization of VX-409. Under the terms of the agreement, GlaxoSmithKline has the exclusive right and license to develop and commercialize VX-409 and certain specified back-up compounds worldwide. The agreement provides for a $20 million up-front license payment, which was paid in December 2005, and potentially additional development and commercial milestone payments based on the development of VX-409 and back-up compounds in major pharmaceutical markets across a range of indications. GlaxoSmithKline will also pay us royalties on annual net sales of any pharmaceutical products commercialized under the agreement. Prior to commercial launch of any drug that is covered by the agreement, GlaxoSmithKline can terminate the agreement without cause upon six months' notice to us. Following commercial launch, GlaxoSmithKline can terminate the agreement on one year's notice, unless the termination is the result of a safety issue associated with a drug arising from the collaboration, in which case GlaxoSmithKline may terminate immediately upon notice.

Merck & Co., Inc.

In June 2004, we entered into a global collaboration with Merck to develop and commercialize VX-680, our lead Aurora kinase inhibitor, for the treatment of cancer, and to conduct research targeting the discovery of an additional Aurora kinase inhibitory compound or compounds to follow VX-680. Merck made an up-front license payment of $20 million in June 2004, and the collaboration agreement also provides for research funding of $14 million over the first two years of the collaboration (from June 2004 to June 2006). In addition, the agreement provides for as much as $350 million in milestone payments, including up to $130 million for the successful development of VX-680 in the first oncology indication and additional milestone payments for development of VX-680 and follow-on compounds in subsequent major oncology indications. Two milestone payments under the agreement, totaling $19.5 million, were made in December 2005. Under the agreement, Merck is responsible for worldwide clinical development and commercialization of VX-680 and follow-on candidates (including VX-667, which Merck selected for preclinical development in 2005) and will pay us royalties on product sales. Merck may terminate the agreement at any time without cause upon 90 days' advance written notice, except that six months' advance written notice is required for termination during the second

year of the research term (ending June 2006), or at any time when a product has marketing approval in a major market and the termination is not the result of a safety issue.

Cystic Fibrosis Foundation Therapeutics Incorporated

In May 2004, we entered into a collaboration agreement with Cystic Fibrosis Foundation Therapeutics Incorporated ("CFFT") providing funding for our late-stage cystic fibrosis drug discovery effort. The agreement subsequently was amended to extend the term of the drug discovery effort to March 31, 2008. Under the amended agreement, we retain the right to develop and commercialize any compounds discovered in the course of the research collaboration, and we will pay a royalty to CFFT on the net sales of any drugs discovered in the collaboration. The agreement, as amended, provides for CFFT to make up to $21 million of research payments through December 31, 2005, and for it to fund up to an additional $22 million for further research from January 1, 2006 through March 31, 2008 directed toward CFTR corrector compounds. The agreement also provides that CFFT will make a $1.5 million milestone payment to us upon advancement of the first compound from the research program into clinical development. CFFT has the right to terminate the agreement without cause, effective on June 30, 2006 and June 30, 2007, upon 60 days' prior written notice.

Novartis Pharma AG

In May 2000, we entered into an agreement with Novartis to collaborate on the discovery, development and commercialization of small molecule drugs directed at protein kinases. We amended this collaboration agreement in February 2004. Under the original agreement, we were responsible for drug discovery and clinical proof-of-concept testing of all drug candidates. Novartis agreed to pay us up to $200 million in research funding through April 2006, and to loan us up to $200 million on a non-interest-bearing basis to support our clinical proof-of-concept studies. Under the amended agreement, we will continue to receive research funding through April 2006. Novartis holds an option to develop drug candidates meeting certain pre-agreed criteria. The option is exercisable with respect to each development candidate at the pre-development stage, at which point a $10 million milestone payment will be due from Novartis with up to $25 million in additional pre-commercial milestone payments. Following completion of the six-year research term in April 2006, Novartis' development option with respect to all compounds discovered in the research program will terminate no later than the end of a specified period following delivery by us to Novartis of a final research report. We retain all rights to any candidate not selected by Novartis, as well as to all of our intellectual property generated under the collaboration that is not specific to candidates selected by Novartis for development. As part of the amended agreement, restrictions under the original agreement that limited Novartis' right to pursue kinase research and development outside our collaboration were removed, and the development loan facility was terminated. In November 2004, Novartis accepted VX-322 for preclinical development under the amended terms of our collaboration agreement, and made a $10 million milestone payment. Novartis will have exclusive worldwide development, manufacturing and commercialization rights to VX-322 and any other drug candidates that it accepts from us for development. We will receive royalties on any products that are marketed as part of the collaboration.

Also under the amended agreement, we retained the right either to develop VX-680 to proof-of-concept under the terms of the original agreement, or to elect to remove VX-680, and the Aurora kinases that it targets, from the Novartis collaboration. We exercised this election in June 2004, as part of our collaboration with Merck, described above, and repaid to Novartis approximately $12.5 million in unspent and uncommitted development loans previously advanced on account of VX-680. Outstanding loans relating to collaboration compounds other than VX-680 will be forgiven on a compound-by-compound basis if any such compounds are selected by Novartis for development. All loans not forgiven under the facility will be repayable, without interest, in May 2008. At December 31, 2005, we had approximately $20 million in remaining loans outstanding under the loan facility.

Mitsubishi Pharma Corporation

In June 2004, we entered into a license, development and commercialization agreement with Mitsubishi for the development and commercialization of VX-950, our lead oral HCV protease inhibitor, in Japan and certain other Far East countries. Under the terms of the agreement, Mitsubishi has the right to develop and commercialize VX-950 in its territory, and we have exclusive development and marketing rights to VX-950 in the rest of the world. Under the agreement, we are entitled to receive up to $33 million in payments from Mitsubishi through Phase II clinical development, including a license fee, development milestone payments and contributions to certain drug development costs incurred by us for VX-950. Further cost sharing beyond Phase II clinical development will be determined by Mitsubishi and us based on the design of registration trials for VX-950. We will also be entitled to royalties on sales of VX-950, if approved, in Mitsubishi's territory. Mitsubishi may terminate the agreement at any time without cause upon 60 days' prior written notice.

Kissei Pharmaceutical Co., Ltd.

In September 1997, we entered into a collaboration agreement with Kissei to identify and develop compounds that target p38 MAP kinase. The research phase of the collaboration ended on June 30, 2000, and we have received the full amount of research funding specified under the agreement. We are working with Kissei to develop and commercialize VX-702, which was discovered during our p38 MAP kinase research collaboration. Kissei has exclusive rights to develop and commercialize VX-702 in Japan and certain Far East countries, and co-exclusive rights (with us) in China, Taiwan and South Korea. We retain exclusive marketing rights outside the Far East. Under our agreement, Kissei will pay us development and commercialization milestone payments for the successful development and commercialization of VX-702 in the Far East, including $2.5 million paid in 2005 upon Kissei's submission of regulatory filings in preparation for Phase I clinical trials of VX-702 in Japan. Kissei is providing a portion of the funding for our clinical trials of VX-702 in RA. If VX-702 is approved for sale in Kissei's territory, we will have the right to supply Kissei with bulk drug substance for manufacture by Kissei into drug product. We will receive drug supply payments or royalties on any product sales.

Avalon Pharmaceuticals, Inc.

In February 2005, we entered into a license agreement with Avalon Pharmaceuticals, Inc. for the development and commercialization of the IMPDH inhibitor VX-944 for the treatment of cancer. Under the agreement, Avalon has the exclusive worldwide right and responsibility to develop and commercialize VX-944 for the treatment of cancer. Avalon has made a $5.0 million up-front license payment to us, and has agreed to make additional milestone payments to us for the successful development of VX-944 in multiple oncology indications. Avalon will pay us royalties on any product sales. The agreement provides us with certain rights to co-promote VX-944. Neither Avalon nor Vertex has the right to terminate the agreement other than for cause.

OTHER MATTERS

Intellectual Property

We actively seek protection for our products and proprietary information by means of United States 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. In addition to patents and pending patent applications that relate to potential drug targets, compounds we are developing to modulate those targets, and methods of making or using those compounds, we have several patents and pending patent applications directed to proprietary elements of our drug discovery platform. For example, some of these "platform" patents and applications claim our proprietary E-VIPR ion channel screening technology.

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 Vertex of ideas, developments, discoveries and inventions made by these employees, consultants and advisors in the course of their service to Vertex.

Patents and Pending Patent Applications

We hold issued patents and pending patent applications in the United States, and in foreign countries we deem appropriate, covering intellectual property developed as part of each of our advanced research, development and commercial programs. Our intellectual property holdings include:

- United States and worldwide pending applications covering VX-950, and many other hepatitis C protease inhibitors.
- issued United States patents and pending applications covering assays useful to evaluate potential inhibitors of hepatitis C protease, including patents and applications covering the X-ray crystal structures of hepatitis C protease and the use of those structures to develop hepatitis C protease inhibitors.
- an issued United States patent that covers a class of chemical compounds that includes VX-702 as well as compositions including VX-702 and similar compounds and the use of those compounds to treat p38 MAP kinase related disorders.
- pending United States and foreign patent applications covering potentiators of the CFTR protein and the uses of those potentiators, including VX-770 and many other related compounds.
- issued United States patents that cover classes of chemical compounds, pharmaceutical formulations and uses of the same for treating HIV infection and AIDS. These patents include specific coverage for fosamprenavir and its pharmaceutical formulations, methods of manufacture and methods to treat HIV infection or AIDS-related central nervous system disorders. In addition we have a non-exclusive, worldwide license under certain patent applications claiming HIV PIs. We have an issued patent in the United States and patents and pending applications in other countries claiming amprenavir and related compounds, as well as brecanavir (VX-385).
- issued United States patents and pending patent applications worldwide claiming inhibitors of multiple kinase proteins, including the Aurora kinase/Flt-3 kinase inhibitor VX-680, the Flt-3/c-kit kinase inhibitor VX-322 and the kinase inhibitor VX-271.
- pending United States and foreign patent applications covering modulators of sodium ion channels and uses thereof, including VX-409 and many other related compounds.

- pending United States and foreign patent applications covering bacterial gyrase inhibitors including VX-692 and VX-883 and the use of these compounds for the treatment of bacterial infections.

- issued United States patents that cover classes of chemical compounds, pharmaceutical compositions containing such compounds, and methods of using those compounds to treat or prevent IMPDH-mediated diseases, including HCV infection. These patents claim merimepodib (VX-497) and VX-944, their combination with certain other therapeutic agents and their use for treating HCV infection and other IMPDH-mediated diseases.

- issued United States patents covering several different classes of compounds useful as inhibitors of ICE, as well as pharmaceutical compositions containing those compounds and methods of using those compounds to treat ICE-related diseases. These patents and applications include a series of patents and applications purchased from Sanofi S.A. in July 1997, including a United States patent that covers DNA sequences encoding ICE. We also have applications pending in the United States and other countries claiming VX-765, pralnacasan (VX-740) and related compounds.

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. For example, we have entered into a non-exclusive license arrangement with Chiron Corporation for rights to technology in the HCV area that provides Chiron with certain milestone and royalty payment rights.

Manufacturing

As we advance our proprietary drug candidates through clinical development toward commercialization, we will be required to significantly augment our manufacturing, logistics, supply chain and quality assurance resources. We currently rely on networks of third party manufacturers and suppliers worldwide to synthesize, tablet, and package our drug candidates for clinical trials, and we expect that we will continue to do so to meet our commercial supply needs for those products, if they are approved for sale. We plan to identify and enter into commercial relationships with multiple suppliers of the materials and manufacturing services necessary for the synthesis, tableting and packaging of our drug candidates and, if approved for sale, our drugs. We believe that this approach will reduce our risk of supply chain disruption by limiting our reliance on any one supplier or manufacturer. There is no assurance, however, that we will be able to establish a second source for each stage of manufacturing and supplying our drug candidates and/or commercial products. We currently are seeking to reduce our VX-950 supply chain risk by identifying and engaging additional vendors for various processes in the manufacture and supply of VX-950 tablets.

We are focusing resources on the development of systems and processes to track, monitor and oversee our manufacturers' and suppliers' activities. We evaluate the performance of our third party manufacturers and suppliers and confirm their continuing capabilities to meet our needs efficiently and economically.

We have established a quality assurance program intended to ensure that our third-party manufacturers and suppliers produce our compounds in accordance with the FDA's current Good Manufacturing Practices, or cGMP, and other applicable regulations. We expect that we may need to increase our quality assurance resources in connection with the commercial launch of any drug product.

The production of our drug candidates is based in part on technology that we believe to be proprietary. We license this technology to our suppliers and manufacturers to enable them to manufacture drug candidates for us. However, in the course of their services, a contract manufacturer may develop process technology related to the manufacture of our drug candidates that the

manufacturer owns, either independently or jointly with us. This might increase our reliance on that manufacturer or require us to obtain a license from that manufacturer if we wished to have our products manufactured by other suppliers utilizing the same process.

Commercial manufacturing of Lexiva/Telzir is being done by GlaxoSmithKline. We retain the option to manufacture a portion of GlaxoSmithKline's requirements for bulk drug substance for Lexiva/Telzir. If we were to exercise that option, we believe we would need to rely upon one or more contract manufacturers to manufacture the bulk drug substance on our behalf.

Competition

We are engaged in biopharmaceutical fields characterized by extensive research efforts, rapid technological progress and intense competition. There are many public and private companies, including pharmaceutical companies, chemical companies and biotechnology companies, engaged in developing products for the same human therapeutic applications as those we are targeting. Many of our competitors have substantially greater financial, technical and human resources than we do and are more experienced in the development of new drugs than we are. In order for us to compete successfully, we may need to demonstrate improved safety, efficacy, ease of manufacturing and market acceptance of our products over the products of our competitors that have or will receive regulatory approval for marketing.

A variety of companies are attempting to develop new treatments for HCV infection. Schering-Plough Corporation is developing SCH503034, an orally available HCV protease inhibitor, for which it is currently conducting a Phase II clinical trial. SCH503034 received "Fast Track" designation from the FDA in early 2006. Idenix Pharmaceuticals, Inc. is developing valopicitabine, an orally available inhibitor of HCV RNA polymerase, which is responsible for synthesizing viral RNA during HCV replication. Valopicitabine is currently in Phase II trials, and Idenix has announced plans to commence Phase III clinical trials of this compound in the first half of 2006. There may be other potential HCV treatments in research or early development.

A wide range of drugs are being investigated for the treatment of RA, including several drugs that are currently being marketed for other indications, such as Prograf® (tacrolimus), an immunosuppressant. Bristol-Myers Squibb recently received marketing approval from the FDA for Orencia® (abatacept), an intravenous T-cell co-stimulator for the treatment of RA. Roche is in Phase III development of Actemra® (tocilizumab), an IL-6 monoclonal antibody. In February 2006, Genentech and Biogen Inc. received approval from the FDA to market Rituxan (rituximab), Genentech Inc.'s drug product currently sold as a lymphoma treatment, in combination with methotrexate for the treatment of RA. In the field of p38 MAP kinase inhibitors for the treatment of RA, over the last three years a number of companies, including Vertex, Amgen Inc., GlaxoSmithKline, Bristol-Myers Squibb Company, Boerhinger Ingelheim GmbH, Takeda Pharmaceuticals, Co., Ltd. and Scios, Inc. have initiated Phase I clinical trials. Of these, to date, Vertex, Boerhinger Ingelheim, Scios and Takeda have announced advancement of drug candidates to Phase II clinical trials. The commercialization of any of the therapies or other novel treatments for RA by Vertex competitors may adversely alter the competitive landscape for VX-702.

Several companies are engaged in the process of developing treatments for cystic fibrosis. For example, PTC Therapeutics, Inc. has recently announced the commencement of several Phase II clinical trials for PTC124, a drug candidate that targets nonsense genetic mutations which can cause cystic fibrosis in some populations. Altus Pharmaceuticals, Inc. is developing TheraCLEC, an orally delivered enzyme replacement therapy for the treatment of pancreatic insufficiency, a condition that affects many cystic fibrosis patients. Inspire Pharmaceuticals Inc. currently is conducting Phase III clinical trials of denufosol tetrasodium, an inhaled molecule that activates an alternate chloride channel in the airway of cystic fibrosis patients.

In the field of HIV protease inhibition, Abbott Laboratories, Bristol-Myers Squibb, Gilead Sciences, Inc., Johnson & Johnson and Pfizer Inc., among others, have other HIV PIs in various stages

of development. In addition to the nine currently marketed protease inhibitors, each of these compounds and others that may be in research or development may eventually compete with Lexiva/Telzir and, if it is successfully developed, brecanavir.

Government Regulation

Our development, manufacture and potential sale of therapeutics are subject to extensive regulation by United States and foreign governmental authorities. In particular, pharmaceutical products are subject to rigorous preclinical, nonclinical and clinical testing and to other approval requirements by the FDA in the United States under the Food, Drug and Cosmetic Act, and by comparable agencies in most foreign countries. Although we have summarized the FDA process below, other countries may have different approval processes with which we will need to comply if we seek to conduct clinical trials or obtain marketing approval in those countries. In addition, even if we ultimately intend to seek initial marketing approval in the United States, we may conduct early clinical trials in other countries, for a variety of reasons, and therefore our initial Investigational New Drug ("IND") filing in the United States may not occur until after one or more foreign-sited clinical trials.

Approval Process

As an initial step in the FDA regulatory approval process, short term preclinical studies typically are conducted in animals to help identify potential safety problems which might be associated with administration of the drug candidate being tested over the period of time planned for the initial human trials. For certain diseases, animal models exist that are believed to be predictive of efficacy in humans. For such diseases, a drug candidate is typically tested for efficacy in that animal model. The results of these preclinical safety and disease model studies are submitted to the FDA as a part of the IND which is filed to comply with FDA regulations prior to commencement of human clinical testing in the United States. For several of our drug candidates, no appropriately predictive animal model exists. As a result, no *in vivo* evidence of efficacy will be available until those compounds progress to human clinical trials. A variety of nonclinical studies in a number of animal species, and other nonclinical studies, ordinarily are conducted while human clinical trials are underway, to provide supplemental toxicology and other information and to help provide a foundation for the design of broader and more lengthy human clinical trials as a drug candidate progresses through the review and approval process.

Clinical trials typically are conducted in three sequential phases, although the phases may overlap. Phase I frequently begins with the initial introduction of the drug candidate into healthy human subjects prior to introduction into patients. The drug candidate is then tested in a relatively small number of patients for safety on a preliminary basis, dosage tolerance, absorption, bioavailability, biodistribution, metabolism, excretion, clinical pharmacology and, if possible, for early information on effectiveness. Phase II typically involves studies in a small sample of the intended patient population to assess the efficacy of the drug for a specific indication, to determine dose tolerance and the optimal dose range and to gather additional information relating to safety and potential adverse effects. Phase III trials are undertaken to further evaluate clinical safety and efficacy in an expanded patient population at geographically dispersed study sites, to determine the overall risk-benefit ratio of the drug candidate and to provide an adequate basis for physician labeling. Each trial is conducted in accordance with standards set forth in protocols that detail the objectives of the trial, the parameters to be used to monitor safety and the efficacy criteria to be evaluated. For clinical trials in the United States, each protocol must be submitted to the FDA as part of the IND. Further, each clinical trial must be evaluated by an independent Institutional Review Board ("IRB") at the institution at which the trial will be conducted. The IRB will consider, among other things, ethical factors, the safety of human subjects and the possible liability of the institution.

Data from nonclinical testing and clinical trials are submitted to the FDA in a New Drug Application ("NDA") for United States marketing approval. The process of completing nonclinical and clinical testing and obtaining FDA approval for a new drug is likely to take a number of years and require the expenditure of substantial resources. Preparing an NDA involves considerable data

collection, verification, analysis and expense, and there can be no assurance that approval will be granted on a timely basis, if at all. The approval process is affected by a number of factors, including the severity of the targeted disease, the availability of alternative treatments and the risks and benefits demonstrated in clinical trials. The FDA may deny an NDA if applicable regulatory criteria are not satisfied or may require additional testing or information. Among the conditions for marketing approval is the requirement that the prospective manufacturer's quality control and manufacturing procedures conform to the FDA's cGMP regulations, which must be followed at all times. In complying with standards set forth in these regulations, manufacturers must continue to expend time, money and effort in the area of production and quality control to ensure full technical compliance. Manufacturing establishments, both foreign and domestic, also are subject to inspections by or under the authority of the FDA and by or under the authority of other federal, state or local agencies.

Under the FDA Modernization Act of 1997, the United States FDA may grant "Fast Track designation" to facilitate the development of a drug intended for the treatment of a serious or life-threatening condition if the drug demonstrates the potential to address an unmet medical need. The benefits of Fast Track designation include scheduled meetings with the FDA to receive input on development plans, the option of submitting an NDA in sections (rather than submitting all components simultaneously), and the option of requesting evaluation of studies using surrogate endpoints. Fast Track designation does not necessarily lead to a priority review or accelerated approval of a drug candidate by the FDA. VX-950 and brecanavir have received Fast Track designation by the FDA.

Timing to Approval

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:	Objective:	Estimated Duration:
Discovery	Lead identification and target validation	2 to 4 years
Preclinical	Initial toxicology for preliminary identification of risks for humans; gather early pharmacokinetic data	1 to 2 years
Phase I	Evaluate safety in humans; study how the drug works, metabolizes and interacts with other drugs	1 to 2 years
Phase II	Establish effectiveness of the drug and its optimal dosage; continue safety evaluation	2 to 4 years
Phase III	Confirm efficacy, dosage regime and safety profile of the drug; submit New Drug Application	2 to 4 years
FDA approval	Approval by the FDA to sell and market the drug for the approved indication	6 months to 2 years

A proposed drug candidate may fail at any point during this process. Animal and other nonclinical studies typically are conducted during each phase of human clinical trials.

Post-approval Studies

Even after initial FDA approval has been obtained, further studies, including post-approval trials, may be required to provide additional data on safety and will be required to gain approval for the sale of a product as a treatment for clinical indications other than those for which the product was initially tested and approved. Also, the FDA will require post-approval reporting to monitor the side effects of the drug. Results of post-approval programs may limit or expand the indications for which the drug product may be marketed. Further, if there are any requests for modifications to the initial FDA approval for the drug, including changes in indication, manufacturing process, labeling or manufacturing facilities, a supplemental NDA may be required to be submitted to the FDA.

Other Regulations

Pursuant to the Drug Price Competition and Patent Term Restoration Act of 1984, under certain conditions a sponsor may be granted marketing exclusivity for a period of five years following FDA approval of certain drug applications. During this period, third parties would not be permitted to obtain FDA approval for a similar or identical drug through an Abbreviated NDA, which is the application form typically used by manufacturers seeking approval of a generic drug. The statute also allows a patent owner to extend the term of the patent for a period equal to one-half the period of time elapsed between the filing of an IND and the filing of the corresponding NDA plus the period of time between the filing of the NDA and FDA approval. We intend to seek the benefits of this statute, but there can be no assurance that we will be able to obtain any such benefits.

Whether or not FDA approval has been obtained, approval of a drug product by regulatory authorities in foreign countries must be obtained prior to the commencement of commercial sales of the product in such countries. Historically, the requirements governing the conduct of clinical trials and product approvals, and the time required for approval, have varied widely from country to country.

In addition to the statutes and regulations described above, we are also subject to regulation under the Occupational Safety and Health Act, the Environmental Protection Act, the Toxic Substances Control Act, the Resource Conservation and Recovery Act and other present and potential future federal, state and local regulations.

Employees

As of December 31, 2005, we had 813 employees (806 full time, 7 part time), including 565 in research and development and 248 in general and administrative functions. Of these employees, 80 were located at our U.K. research and development facility, 158 were located at our facility in San Diego, California and 576 were based at our Cambridge, Massachusetts headquarters. Our scientific staff members (approximately 375 of whom hold Ph.D. and/or M.D. degrees) have diversified experience and expertise in molecular and cell biology, biochemistry, animal pharmacology, 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 employees are not covered by a collective bargaining agreement, and we consider our relations with our employees to be good.

EXECUTIVE OFFICERS AND DIRECTORS

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

Name	Age	Position
Joshua S. Boger, Ph.D.	54	Chairman, President and Chief Executive Officer
John J. Alam, M.D.	44	Executive Vice President, Medicines Development, and Chief Medical Officer
Victor A. Hartmann, M.D.	56	Executive Vice President, Strategic and Corporate Development
Peter Mueller, Ph.D.	49	Executive Vice President, Drug Innovation and Realization, and Chief Scientific Officer
Ian F. Smith, C.P.A., A.C.A.	40	Executive Vice President and Chief Financial Officer
Kenneth S. Boger	59	Senior Vice President and General Counsel
Richard C. Garrison	57	Senior Vice President, Organizational Development
Lynne H. Brum	42	Vice President, Strategic Communications
Johanna Messina Power, C.P.A	33	Vice President and Corporate Controller
Eric K. Brandt	43	Director
Roger W. Brimblecombe, Ph.D., D.Sc.	76	Director
Stuart J.M. Collinson, Ph.D.	46	Director
Eugene H. Cordes, Ph.D	69	Director
Matthew W. Emmens	54	Director
Bruce I. Sachs	46	Director
Charles A. Sanders, M.D.	74	Director
Eve E. Slater, M.D., F.A.C.C.	60	Director
Elaine S. Ullian	58	Director

Dr. Joshua Boger is a founder of Vertex. He has been Chief Executive Officer since 1992 and Chairman of the Board since 1997. He was our President from our inception in 1989 until December 2000, and was again appointed our President in 2005. He was our Chief Scientific Officer from 1989 until May 1992. Dr. Boger has been a director since Vertex's inception. 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. Dr. Boger is the brother of Mr. Kenneth Boger, the Company's Senior Vice President and General Counsel.

Dr. Alam currently serves as our Executive Vice President, Medicines Development, and Chief Medical Officer, a position he has held since February 2006. From January 2001 to February 2006, he served as our Senior Vice President of Drug Evaluation and Approval. From October 1997 to January 2001, he was our Vice President of Clinical Development. From 1991 to 1997, Dr. Alam held a variety of positions with Biogen, Inc., including Director of Medical Research and Program Executive (beta interferon) for Avonex. Prior to joining Biogen, Dr. Alam was a Research Fellow at the Dana Farber Cancer Institute and completed an internal medicine residency at The Brigham and Women's

Hospital in Boston. Dr. Alam holds an M.D. from Northwestern University Medical School and an S.B. in chemical engineering from the Massachusetts Institute of Technology.

Dr. Hartmann, our Executive Vice President, Strategic and Corporate Development, joined Vertex in February 2005. From 2000 to 2005, Dr. Hartmann served as the Senior Vice President, Global Business Development and Licensing, for Novartis Pharma AG. He served as Vice President, Head of Scientific and Business Evaluation at Novartis from 1999 to 2000. Dr. Hartmann served as Vice President and Head of Global Portfolio Management of Sandoz Pharma Ltd. (later Novartis AG) from 1995 to 1999. Dr. Hartmann joined Sandoz as Vice President and Head of Clinical Research and Development in 1994. Dr. Hartmann received his medical degree from the University of Bonn, Germany, and a bachelor's degree from Macalester College.

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

Mr. Smith currently serves as 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 Vertex, 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 Board of Directors of Predix Pharmaceuticals, Inc. and TolerRx Inc. 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. Kenneth Boger currently serves as our Senior Vice President and General Counsel, a position he has held since 2001. He came to Vertex from the law firm of Kirkpatrick & Lockhart LLP, now known as Kirkpatrick & Lockhart Nicholson Graham LLP, where he was a partner specializing in business and corporate law and was a member of the firm's Management Committee. Prior to the merger of Kirkpatrick & Lockhart with the Boston law firm of Warner & Stackpole LLP in 1999, Mr. Boger was a partner at Warner & Stackpole, where he served on its Executive Committee from 1988 to 1997. Mr. Boger holds an A.B. in history from Duke University, an M.B.A. from the Graduate School of Business at the University of Chicago, and a J.D. from Boston College Law School. Mr. Boger is the brother of Dr. Joshua Boger, the Company's Chairman, President and Chief Executive Officer.

Mr. Garrison, our Senior Vice President, Organizational Development, joined Vertex in that role in December 2005. From June 2001 to December 2005, Mr. Garrison was the founder and President of Bink Inc., a strategic consulting firm. From September 1999 to May 2001, he served as the Chairman of Holland Mark Edmund Ingalls, an advertising firm. For the 18 years ending in 1999, Mr. Garrison was the Chairman and CEO of Ingalls, Quinn & Johnson, one of New England's largest advertising agencies. Mr. Garrison holds a B.A. in English from Princeton University.

Ms. Brum is currently our Vice President, Strategic Communications, a position she has held since January 2006. Since joining Vertex in 1994, Ms. Brum has served in various capacities, including Director, Corporate Communications (from 1994 to 1998), Vice President of Corporate Communications and Market Development (from 1998 to 2001), Vice President, Corporate Development and Communications (2001 to 2003), and Vice President, Corporate Communications and Financial Planning (from 2003 to 2006). Ms. Brum came to Vertex from Feinstein Kean Healthcare, a communications and business consulting practice, where she was a Vice President. Previously, she held corporate communications and research positions at Biogen, Inc. Ms. Brum holds an M.B.A. from the Simmons Graduate School of Management, and a B.A. in biological sciences from Wellesley College.

Ms. Messina Power currently serves as our Vice President and Corporate Controller. Since joining the Company in 1999, Ms. Messina Power also has served us as Assistant Corporate Controller (from 1999 to 2000) and Corporate Controller (from 2000 to 2006). Prior to joining us, Ms. Messina Power was employed as an accountant by PricewaterhouseCoopers LLP, an accounting firm, from 1995 to 1999. She holds a B.S. in accounting from Boston College, and is a Certified Public Accountant.

Mr. Brandt has been a member of our Board of Directors since 2003. He is the President, Chief Executive Officer and a member of the Board of Directors of Avanir Pharmaceuticals, which he joined in 2005. Prior to joining Avanir, Mr. Brandt held various positions at Allergan Inc. from 1999 to 2005, including Executive Vice President, Finance and Technical Operations and Chief Financial Officer from February 2005 to September 2005, Executive Vice President, Finance, Strategy and Business Development, and Chief Financial Officer from 2003 until February 2005, and Corporate Vice President and Chief Financial Officer from May 1999 to 2003. From January 2001 to January 2002, he also assumed the duties of President, Global Consumer Eye Care Business, at Allergan. Prior to that, he held various positions with the Boston Consulting Group, most recently serving as Vice President and Partner, and a senior member of the BCG Health Care practice. Mr. Brandt also currently serves as a director of Dentsply International Inc. Mr. Brandt holds a B.S. in chemical engineering from the Massachusetts Institute of Technology and an M.B.A. from Harvard University.

Dr. Brimblecombe has been a member of our Board of Directors since 1993. He served as Chairman of Vanguard Medica Ltd. from 1991 to 2000, as Chairman of Core Group plc from 1997 to 1999, and as Chairman of Oxford Asymmetry International plc from 1997 to 2000. From 1979 to 1990, he held various Vice Presidential posts in SmithKline & French Laboratories' research and development organization. He is currently Chairman of pSivida Ltd. (listed on the Australian Stock Exchange) and a director of Tissue Science Laboratories plc (listed on the AIM market in the United Kingdom). Dr. Brimblecombe also serves as a director of several private companies located in Europe and Singapore. He holds Ph.D. and D.Sc. degrees in pharmacology from the University of Bristol, England.

Dr. Collinson has been a member of our Board of Directors since July 2001. He currently serves as a Partner at Forward Ventures. Prior to our merger with Aurora Biosciences Corporation in 2001, Dr. Collinson served as the President, Chief Executive Officer and Chairman of the Board of Aurora. Dr. Collinson held senior management positions with Glaxo Wellcome from December 1994 to June 1998, most recently serving as Co-Chairman, Hospital and Critical Care Therapy Management Team and Director of Hospital and Critical Care. Dr. Collinson received his Ph.D. in physical chemistry from the University of Oxford, England and his M.B.A. from Harvard University.

Dr. Cordes has been a member of our Board of Directors since 2005, and a member of the Company's Scientific Advisory Board since 1996. Dr. Cordes is the Chairman of Vitae Pharmaceuticals, Inc., a position he has held since January 2002. Prior to joining Vitae Pharmaceuticals, Dr. Cordes was a professor of pharmacy at the University of Michigan. Dr. Cordes received a B.S. degree in chemistry from the California Institute of Technology and a Ph.D. in biochemistry from Brandeis University.

Mr. Emmens has been a member of our Board of Directors since 2004. Mr. Emmens is the Chief Executive Officer, Chairman of the Executive Committee and a member of the Board of Directors of

Shire Pharmaceuticals Group plc. Before joining Shire in 2003, Mr. Emmens served as president of Merck KGaA's global prescription pharmaceuticals business in Darmstadt, Germany. In 1999, he joined Merck KGaA and established EMD Pharmaceuticals, its United States prescription pharmaceutical business. Mr. Emmens held the position of President and Chief Executive Officer at EMD Pharmaceuticals from 1999 to 2001. Prior to this, Mr. Emmens held various positions, including Chief Executive Officer, at Astra Merck, Inc. as well as several positions at Merck & Co., Inc.

Mr. Sachs has been a member of our Board of Directors since 1998. He is a General Partner at Charles River Ventures. 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 CEO of Stratus Computer, Inc. From 1995 to 1997, he served as Executive Vice President and General Manager of the Internet Telecom Business Group at Bay Networks, Inc. From 1993 to 1995, he served as President and Chief Executive Officer at Xylogics, Inc. Mr. Sachs 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.

Dr. Sanders has been a member of our Board of Directors director since 1996 and has served as our lead outside director since 2003. He retired in 1994 as Chief Executive Officer and in 1995 as Chairman of Glaxo Inc. From 1990 to 1995, he served as a member of the board of Glaxo plc. From 1981 to 1989, Dr. Sanders held a number of positions at Squibb Corporation, including that of Vice Chairman. Dr. Sanders has previously served on the boards of Merrill Lynch, Reynolds Metals Co. and Morton International Inc. He is also a director of Biopure Corporation, Cephalon Corporation, Genentech, Inc., Icagen, Inc. and Fisher Scientific International. Dr. Sanders holds an undergraduate degree from the University of Texas, and an M.D. from the University of Texas Southwestern Medical School.

Dr. Slater has been a member of our Board of Directors since 2004. Dr. Slater is board-certified in internal medicine and cardiology and has extensive experience in the pharmaceutical industry, including 19 years in senior management positions at Merck Research Laboratories. Most recently, she was Assistant Secretary for Health at the United States Department of Health and Human Services ("HHS") where she served as Health and Human Services Secretary Tommy Thompson's chief health policy advisor. Prior to joining HHS, Dr. Slater held senior management positions at Merck Research Laboratories from 1983 to 2001, including Senior Vice President of External Policy, Vice President of Corporate Public Affairs, Senior Vice President of Clinical and Regulatory Development, Executive Director of Biochemistry and Molecular Biology and Senior Director of Biochemical Endocrinology. Dr. Slater also serves as a director of AnorMed Inc., VaxGen, Inc., Phase Forward Incorporated and Theravance, Inc. Dr. Slater is a graduate of Vassar College and received her M.D. from Columbia University's College of Physicians and Surgeons.

Ms. Ullian has been a member of our Board of Directors since 1997. Since 1996, she has served as President and Chief Executive Officer of Boston Medical Center. 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 Electron Corporation and Valeant Pharmaceuticals, Inc. Ms. Ullian holds a B.A. in political science from Tufts University and a M.P.H. from the University of Michigan.

SCIENTIFIC ADVISORY BOARD

Our Scientific Advisory Board consists of individuals with demonstrated expertise in various fields who advise us concerning long-term scientific planning, research and development. The Scientific Advisory Board also evaluates our research programs, recommends personnel to us and advises us on

technological matters. The members of the Scientific Advisory Board, which is chaired by Dr. Mark Murcko, our Chief Technology Officer, are:

Mark Murcko, Ph.D.	Vice President and Chief Technology Officer, Vertex Pharmaceuticals Incorporated
Peter Mueller, Ph.D.	Chief Scientific Officer and Executive Vice President, Drug Innovation and Realization, Vertex Pharmaceuticals Incorporated
Paul S. Anderson, Ph.D.	Retired Vice President, Drug Discovery, Bristol-Myers Squibb Company
Steven J. Burakoff, M.D.	Laura and Isaac Perlmutter Professor, New York University School of Medicine; Director, New York University Cancer Institute; Director, Skirball Institute of Biomolecular Medicine, New York University School of Medicine
Lewis C. Cantley, Ph.D.	Chief, Division of Signal Transduction at Beth Israel Deaconess Medical Center and the Harvard Institutes of Medicine
Eugene H. Cordes, Ph.D.	Chairman, Vitae Pharmaceuticals, Inc.; former Professor of Pharmacy, College of Pharmacy and Adjunct Professor of Chemistry, College of Literature, Science and the Arts, University of Michigan, Ann Arbor
Stephen C. Harrison, Ph.D.	Higgins Professor of Biochemistry, Harvard University; Investigator, Howard Hughes Medical Institute; Professor of Biological Chemistry and Molecular Pharmacology and Professor of Pediatrics, Harvard Medical School
Jeremy R. Knowles, D. Phil.	Amory Houghton Professor of Chemistry and Biochemistry, Harvard University
Robert T. Schooley, M.D.	Professor and Head of the Division of Infectious Diseases, University of California, San Diego
Roger Tsien, Ph.D.	Investigator, Howard Hughes Medical Institute; Professor of Pharmacology and Professor of Chemistry and Biochemistry, University of California, San Diego

Other than Dr. Murcko and Dr. Mueller, who are employed by Vertex, and Dr. Cordes, who is a member of our Board of Directors, none of the members of the Scientific Advisory Board is employed by Vertex, and members may have other commitments to or consulting or advisory contracts with their employers or other entities that may restrict their availability. Accordingly, such persons are expected to devote only a small portion of their time to us. In addition to our Scientific Advisory Board, we have established consulting relationships with a number of scientific and medical experts who advise us on a project-specific basis.

ITEM 1A. RISK FACTORS

WE EXPECT TO INCUR FUTURE LOSSES AND WE MAY NEVER BECOME PROFITABLE.

We have incurred significant operating losses each year since our inception and expect to incur a significant operating loss in 2006. We believe that operating losses will continue beyond 2006, even if we receive significant future payments under our existing and future collaborative agreements, because we are planning to make significant investments in research and development, and because we will incur significant selling, general and administrative expenses in the course of researching, developing and commercializing our product candidates. We expect that losses will fluctuate from quarter to quarter and year to year, and that such fluctuations may be substantial. We cannot predict when we will become profitable, if at all.

MANY OF OUR DRUG CANDIDATES ARE STILL IN THE EARLY STAGES OF DEVELOPMENT AND ALL OF OUR DRUG CANDIDATES REMAIN SUBJECT TO CLINICAL TESTING AND REGULATORY APPROVAL. IF WE ARE UNABLE TO SUCCESSFULLY DEVELOP AND TEST OUR DRUG CANDIDATES, WE WILL NOT BE SUCCESSFUL.

The success of our business depends primarily upon our ability to develop and commercialize our drug candidates successfully. Our drug candidates are in various stages of development. Our drug candidates must satisfy rigorous standards of safety and efficacy before they can be approved by the FDA or other regulatory authorities for sale. To satisfy these standards, we must engage in expensive and lengthy testing of our drug candidates. Despite our efforts, our drug candidates may not:

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

Positive results in preclinical studies of a drug candidate may not be predictive of similar results in humans during clinical trials, and promising results from early clinical trials of a drug candidate may not be replicated in later clinical trials. Findings in nonclinical studies conducted concurrently with clinical trials could result in abrupt changes in our development activities, including the possible cessation of development activities associated with a 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.

A number of companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late stage clinical trials even after achieving promising results in early stage development. Accordingly, the results from the completed preclinical studies and clinical trials and ongoing clinical trials for our drug candidates may not be predictive of the results we may obtain in later stage trials, and are not predictive of the likelihood of approval of a drug candidate for commercial sale.

IF WE ARE UNABLE TO OBTAIN U.S. AND/OR FOREIGN REGULATORY APPROVAL, WE WILL BE UNABLE TO COMMERCIALIZE OUR DRUG CANDIDATES.

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

We have limited experience in conducting and managing the clinical trials necessary to obtain regulatory approvals, including approval by the FDA. The time required to complete clinical trials and for the FDA and other countries' regulatory review processes is uncertain and typically takes many

years. Our analysis of data obtained from preclinical and clinical activities is subject to confirmation and interpretation by regulatory authorities, which could delay, limit or prevent regulatory approval. We may also encounter unanticipated delays or increased costs due to government regulation from future legislation or administrative action or changes in FDA policy during the period of product development, clinical trials and FDA regulatory review.

Any delay in obtaining or failure to obtain required approvals could materially adversely affect our ability to successfully commercialize any drug candidate. Furthermore, any regulatory approval to market a drug product may be subject to unexpected limitations on the indicated uses for which we may market the drug product. These limitations may limit the size of the market for the drug product.

We are also subject to numerous foreign regulatory requirements governing the conduct of clinical trials, manufacturing and marketing authorization, pricing and third-party reimbursement. 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. Foreign jurisdictions may have different approval procedures than those required by the FDA and may impose additional testing requirements for our drug candidates.

IF CLINICAL TRIALS FOR OUR DRUG CANDIDATES ARE PROLONGED OR DELAYED, WE MAY BE UNABLE TO COMMERCIALIZE OUR DRUG CANDIDATES ON A TIMELY BASIS, WHICH WOULD REQUIRE US TO INCUR ADDITIONAL COSTS AND WOULD DELAY OUR RECEIPT OF ANY PRODUCT REVENUE.

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

- ongoing discussions with the FDA or comparable foreign authorities regarding the scope or design of our clinical trials;
- delays in receiving or the inability to obtain required approvals from IRBs or other reviewing entities at clinical sites selected for participation in our clinical trials;
- delays in enrolling volunteers and patients into clinical trials;
- a lower than anticipated retention rate of volunteers and patients in clinical trials;
- the need to repeat clinical trials as a result of inconclusive results or unforeseen complications in testing;
- inadequate supply or deficient quality of drug candidate materials or other materials necessary for the conduct of our clinical trials;
- unfavorable FDA inspection and review of a clinical trial site or records of any clinical or preclinical investigation;
- serious and unexpected drug-related side effects experienced by participants in our clinical trials; or
- the placement by the FDA of a clinical hold on a trial.

Our ability to enroll patients in our clinical trials in sufficient numbers and on a timely basis will be 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 and the eligibility criteria for the clinical trial. In addition, subjects may drop out of our clinical trials, and thereby possibly 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. While all or a portion of these additional costs may be covered by payments under our collaborative agreements, we bear all of the costs for our development candidates for which we have no financial support from a collaborator.

We, the FDA or other applicable regulatory authorities may suspend clinical trials of a drug candidate at any time if we or they believe the subjects or patients participating in such clinical trials are being exposed to unacceptable health risks or for other reasons.

We cannot predict whether any of our drug candidates will encounter problems during clinical trials which will cause us or regulatory authorities to delay or suspend these trials, or which will delay the analysis of data from these trials. In addition, it is impossible to predict whether legislative changes will be enacted, or whether FDA regulations, guidance or interpretations will be changed, or what the impact of such changes, if any, may be. If we experience any such problems, we may not have the financial resources to continue development of the drug candidate that is affected or the development of any of our other drug candidates.

IF OUR PROCESSES AND SYSTEMS ARE NOT COMPLIANT WITH REGULATORY REQUIREMENTS, WE COULD BE SUBJECT TO DELAYS IN FILING NEW DRUG APPLICATIONS OR RESTRICTIONS ON MARKETING OF PRODUCTS AFTER THEY HAVE BEEN APPROVED.

We currently are developing drug product candidates for regulatory approval for the first time since the Company's inception, and are in the process of implementing regulated processes and systems required to obtain and maintain regulatory approval for our product candidates. Certain of these processes and systems for conducting clinical trials and manufacturing material must be compliant with regulatory requirements before we can apply for regulatory approval for our drug product candidates. These processes and systems will be subject to continual review and periodic inspection by the FDA and other regulatory bodies. If we are unable to achieve compliance in a timely fashion, we may experience delays in filing for regulatory approval for our drug product candidates. In addition, any later discovery of previously unknown problems or safety issues with approved products or manufacturing processes, or failure to comply with regulatory requirements, may result in restrictions on such products or manufacturing processes, withdrawal of products from the market, the imposition of civil or criminal penalties or a refusal by the FDA and/or other regulatory bodies to approve pending applications for marketing approval of new 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 collaboration agreements that transfer responsibility for complying with specified regulatory requirements, such as filing and maintenance of marketing authorizations and safety reporting, to our collaborator. If our collaborators do not fulfill these regulatory obligations, any products for which we or they obtain approval may be withdrawn from the market, which would have a material adverse effect on our business.

EVEN IF WE OBTAIN REGULATORY APPROVALS, OUR DRUG CANDIDATES WILL BE SUBJECT TO ONGOING REGULATORY REVIEW. IF WE FAIL TO COMPLY WITH CONTINUING U.S. AND APPLICABLE FOREIGN REGULATIONS, WE COULD LOSE THOSE APPROVALS, AND OUR BUSINESS WOULD BE SERIOUSLY HARMED.

Even if we receive regulatory approval of any drug candidates that we are developing, we will be subject to continuing regulatory review, including the review of clinical results that are reported after our drug candidates become commercially available, approved drugs. Since drugs are more widely used by patients once approval has been obtained, side effects and other problems may be observed after approval that were not seen or anticipated during pre-approval clinical trials. In addition, the manufacturers and the manufacturing facilities we engage to make any of our drug candidates will also be subject to periodic review and inspection by the FDA. The subsequent discovery of previously unknown problems with the drug, manufacturers or manufacturing facilities may result in restrictions on the drug, manufacturers or facilities, including withdrawal of the drug from the market or our inability to use the facilities to make our drug. If we fail to comply with applicable continuing regulatory requirements, we may be subject to fines, suspension or withdrawal of regulatory approval, product recalls and seizures, operating restrictions and criminal prosecutions.

OUR DRUG DEVELOPMENT EFFORTS ARE DATA-DRIVEN AND THEREFORE POTENTIALLY SUBJECT TO ABRUPT CHANGES IN EXPECTED OUTCOMES.

Small molecule drug discovery and development involve, initially, the identification of chemical compounds which may have promise as treatments for specific diseases. Once identified as drug candidates, compounds are subjected to years of testing in a laboratory setting, in animals and in people. Our ultimate objective is to determine whether the compounds have physical characteristics, both intrinsically and in animal and human systems and including a toxicological profile, that are compatible with clinical and commercial success in treatment of the disease being targeted. Throughout this process, experiments are conducted and data are gathered that could reinforce a decision to move to the next step in the evaluation process for a particular drug candidate, could result in uncertainty over the proper course to pursue, or could result in the termination of further drug development efforts with respect to the compound being evaluated. We monitor the results of our discovery research and our nonclinical studies and clinical trials and regularly evaluate and re-evaluate our portfolio investments with the objective of balancing risk and potential return in view of new data and scientific, business and commercial insights. This process can result in relatively abrupt changes in focus and priority as new information comes to light and we gain additional insights into ongoing programs and potential new programs.

WE DEPEND ON THIRD PARTY MANUFACTURERS AND SUPPLIERS, AND AS A RESULT WE MAY BE SUBJECT TO MANUFACTURING AND SUPPLY DISRUPTIONS OUTSIDE OF OUR CONTROL.

We expect that we will need to significantly augment our manufacturing, supply chain and quality assurance resources for our later-stage drug product candidates. We have no experience in manufacturing pharmaceutical products and in conducting manufacturing testing programs required to obtain FDA and other regulatory approvals, and there can be no assurance that we will develop those capabilities successfully. If we are unable to establish these capabilities, we may be unable to achieve our development and commercialization goals. We are currently relying on networks of third party manufacturers and suppliers worldwide to synthesize, tablet, and package our drug candidates for clinical trials and we expect that we will continue to do so to meet our commercial supply needs for these products, if they are approved for sale. As a result of our reliance on these third party manufacturers and suppliers, some of whom currently are our sole source for clinical trial material, we may be subject to significant supply disruptions outside of our control. These supply disruptions may result from a number of factors including shortages in product raw materials, labor or technical difficulties, regulatory inspections or restrictions, and shipping and customs delays. We plan to identify and enter into commercial relationships with multiple suppliers of the materials and manufacturing services necessary for the synthesis, tableting and packaging of our drug candidates and, if approved for sale, our drugs. We expect that this approach will reduce our risk of supply chain disruptions by reducing our reliance on any one manufacturer or supplier, but we will remain vulnerable to disruptions arising from performance failure by a vendor in our manufacturing supply chain, particularly if we are unable to secure second sources for necessary products and services. Any supply disruptions could impact the timing of our clinical trials and the commercial launch of any approved pharmaceutical products. Furthermore, we may be required to modify our production methods to permit us to economically manufacture our products for commercial launch and sale. Upon approval of a pharmaceutical product for sale, if any, we similarly may be at risk of supply chain disruption for our commercial drug supply. These modifications may require us to reevaluate our resources and the resources of our third party manufacturers and suppliers, which could result in abrupt changes in our production methods and supplies. The production of our drug candidates is based in part on technology that we believe to be proprietary. We have licensed this technology to enable our third party manufacturers and suppliers to manufacture drug candidates for us. However, in the course of their services, a contract manufacturer may develop process technology related to the manufacture of our 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 manufactured by other suppliers utilizing the same process.

WE RELY ON THIRD PARTIES TO CONDUCT OUR CLINICAL TRIALS, AND THOSE THIRD PARTIES MAY NOT PERFORM SATISFACTORILY, INCLUDING FAILING TO MEET ESTABLISHED DEADLINES FOR THE COMPLETION OF SUCH TRIALS.

We do not have the ability to independently conduct clinical trials for our drug candidates, and we rely on third parties such as contract research organizations, medical institutions and clinical investigators to enroll qualified patients and conduct our clinical trials. Our reliance on these third parties for clinical development activities reduces our control over these activities. Accordingly, these third-party contractors may not complete activities on schedule, or may not conduct our clinical trials in accordance with regulatory requirements or our trial design. To date, we believe our contract research organizations and other similar entities with which we are working generally have performed well. However, if these third parties do not successfully carry out their contractual duties or meet expected deadlines, we may be required to replace them. Although we believe that there are a number of other third-party contractors we could engage to continue these activities, it may result in a delay of the affected trial. Accordingly, our efforts to obtain regulatory approvals for and commercialize our drug candidates may be delayed.

OUR SALES AND MARKETING EXPERIENCE IS LIMITED.

We have limited experience in marketing and selling pharmaceutical products. We must either develop a marketing and sales force or enter into arrangements with third parties to market and sell any of our product candidates that are approved by regulatory authorities. We do not know whether we will be able to enter into marketing and sales agreements with others on acceptable terms, if at all. We may not be able to successfully develop our own sales and marketing force for drug candidates for which we have retained marketing or co-promotion rights. As we develop our own marketing and sales capability, we may be competing with other companies that currently have experienced and well-funded marketing and sales operations. We have granted exclusive marketing rights for Lexiva/Telzir, brecanavir (VX-385) and VX-409 to GlaxoSmithKline worldwide (except for brecanavir in the Far East where we have retained rights), and for VX-680 and VX-667 to Merck. Avalon Pharmaceuticals has exclusive, worldwide marketing rights to VX-944. Mitsubishi has exclusive marketing rights to VX-950 in Japan and certain Far East countries. In addition, we have granted marketing rights to VX-702 to Kissei in the Far East and to VX-322 to Novartis worldwide. Even though we retain some co-promotion rights in some collaborations, to the extent that our collaborators have commercial rights to our products, any revenues we receive from those products will depend primarily on the sales and marketing efforts of others.

WE MAY NEED TO RAISE ADDITIONAL CAPITAL THAT MAY NOT BE AVAILABLE.

We expect to incur substantial research and development and related supporting expenses as we design and develop existing and future compounds, undertake clinical trials of drug candidates resulting from such compounds, and build our manufacturing, regulatory, development and commercial capabilities. We also expect to incur substantial administrative and commercialization expenditures in the future and substantial expenses related to the filing, prosecution, defense and enforcement of patent and other intellectual property claims. We may need to make significant capital investment in building our manufacturing capacity and creating pre-launch inventory for one or more of our potential products. We anticipate that we will finance these substantial cash needs with:

- cash received from our existing collaborative agreements;
- cash received from new collaborative agreements;
- Lexiva/Telzir royalty revenue;
- existing cash reserves, together with interest earned on those reserves; and
- future product sales to the extent that we market products directly.

We expect that funds from these sources will be sufficient to fund our planned activities for at least the next eighteen months from the date of this filing. If not, it will be necessary to raise additional funds through public offerings or private placements of equity or debt securities or other methods of financing. Even if our financial resources are sufficient to meet our short or intermediate term needs, we may still decide, as we have in the past, to raise additional funds when we believe financial market conditions are favorable. Any equity financings could result in dilution to our then-existing security holders. Any debt financing, if available at all, may be on terms that, among other things, restrict our ability to pay dividends and interest (although we do not intend to pay dividends for the foreseeable future). The required interest payments associated with any significant additional debt financing could materially adversely affect our ability to service our convertible subordinated notes and convertible senior subordinated notes. The terms of any additional debt financing may also, under certain circumstances, restrict or prohibit us from making interest payments on our convertible subordinated notes and convertible senior subordinated notes. If adequate funds are not available, we may be required to curtail significantly or discontinue one or more of our research, drug discovery or development programs (including clinical trials), or attempt to obtain funds through arrangements with collaborators or others that may require us to relinquish rights to certain of our technologies or products in research or development. Additional financing may not be available on acceptable terms, if at all.

IF WE ARE UNABLE TO ATTRACT AND RETAIN COLLABORATORS FOR RESEARCH SUPPORT AND THE DEVELOPMENT AND COMMERCIALIZATION OF OUR PRODUCTS, WE MAY NOT BE ABLE TO FUND OUR RESEARCH, DEVELOPMENT AND COMMERCIALIZATION ACTIVITIES.

Our research, development and commercialization collaborators have agreed to fund portions of our research and development programs and/or to conduct the development and commercialization of specified product candidates and, if they are approved, products. In exchange, we have given them technology, product and marketing rights relating to those products. Some of our corporate collaborators have rights to control the planning and execution of product development and clinical programs. Our collaborators may exercise their control rights in ways that may negatively affect the timing and success of those programs. Our collaborations are subject to termination rights by the collaborators. If any of our collaborators were to terminate its relationship with us, or fail to meet its contractual obligations, that action could have a material adverse effect on our ability to undertake research, to fund related and other programs and to develop, manufacture and market any products that may have resulted from the collaboration. We expect to seek additional collaborative arrangements, which may not be available to us, to provide research support and to develop and commercialize our products in the future. For example, a significant portion of our overall research effort is conducted under our research collaborations with Novartis and Merck, both of which are scheduled to conclude in the first half of 2006. If we are unable to enter into collaborative arrangements that would extend or replace these research collaborations, or to find other means of financing the effort currently devoted to these research programs, our ability to conduct our research, development and commercial activities could be adversely affected to a material degree. Similarly we may choose to enter into collaborative arrangements to advance the development of some of our preclinical and clinical development stage compounds. Even if we are able to establish acceptable collaborative arrangements in the future, they may not be successful.

IF OUR COMPETITORS BRING SUPERIOR PRODUCTS TO MARKET OR BRING THEIR PRODUCTS TO MARKET BEFORE WE DO, WE MAY BE UNABLE TO FIND A MARKET FOR OUR PRODUCTS.

Our products in development may not be able to compete effectively with products that are currently on the market or new products that may be developed by others. There are many other companies developing products for the same indications that we are pursuing in development. In order to compete successfully in these areas, we must demonstrate improved safety, efficacy and ease of

manufacturing and gain market acceptance over competing products that may receive regulatory approval before or after our products, and over those that currently are marketed. Many of our competitors, including major pharmaceutical companies such as GlaxoSmithKline, Merck, Roche, Amgen, Boerhinger Ingelheim, Novartis, Johnson & Johnson and Schering-Plough possess substantially greater financial, technical and human resources than we possess. In addition, many of our competitors have significantly greater experience than we have in conducting preclinical and nonclinical testing and human clinical trials of new pharmaceutical products, scaling up manufacturing operations and obtaining regulatory approvals of products and manufacturing facilities. Accordingly, our competitors may succeed in obtaining regulatory approval for products more rapidly than we do. If we obtain regulatory approval and launch commercial sales of our products, we also will compete with respect to manufacturing efficiency and sales and marketing capabilities, areas in which we currently have limited experience.

IF WE FAIL TO EXPAND OUR HUMAN RESOURCES AND MANAGE OUR GROWTH EFFECTIVELY, OUR BUSINESS MAY SUFFER.

We expect that if our clinical candidates continue to progress in development, we continue to build our commercial organization and our drug discovery efforts continue to generate drug candidates, we will require significant additional investment in personnel, management systems and resources. Our ability to commercialize our products, achieve our research and development objectives, and satisfy our commitments under our collaboration agreements depends on our ability to respond effectively to these demands and expand our internal organization to accommodate additional anticipated growth. If we are unable to manage our growth effectively, there could be a material adverse effect on our business.

IF WE LOSE OUR TECHNOLOGICAL ADVANTAGES, WE MAY NOT BE ABLE TO COMPETE IN THE MARKETPLACE.

We believe that our integrated drug discovery capability gives us a technological advantage over our competitors. However, the pharmaceutical research field is characterized by rapid technological progress and intense competition. As a result, we may not realize the expected benefits from these technologies. For example, a large pharmaceutical company, with significantly more resources than we have, could pursue a systematic approach to the discovery of drugs based on gene families, using proprietary drug targets, compound libraries, novel chemical approaches, structural protein analysis and information technologies. Such a company might identify broadly applicable compound classes faster and more effectively than we do. Further, we believe that interest in the application of structure-based drug design, parallel drug design and related approaches has accelerated as the strategies have become more widely understood. Businesses, academic institutions, governmental agencies and other public and private research organizations are conducting research to develop technologies that may compete with those we use. It is possible that our competitors could acquire or develop technologies that would render our technology obsolete or noncompetitive. For example, a competitor could develop information technologies that accelerate the atomic-level analysis of potential compounds that bind to the active site of a drug target, and predict the absorption, toxicity, and relative ease-of-synthesis of candidate compounds. If we were unable to access the same technologies at an acceptable price, our business could be adversely affected.

THE LOSS OF THE SERVICES OF KEY EMPLOYEES OR THE FAILURE TO HIRE QUALIFIED EMPLOYEES WOULD NEGATIVELY IMPACT OUR BUSINESS AND FUTURE GROWTH.

Because our product 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. Our future success will depend in large part on the continued services of our key scientific and management personnel. We have entered into employment agreements with some individuals 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 employee on relatively short notice. The value to employees of stock-related benefits that vest

over time—such as options and restricted stock—will be significantly affected by movements in our stock price that we cannot control, and may at any point in time be insufficient to counteract more lucrative offers from other companies.

We face intense competition for our scientific personnel from our competitors, our collaborators and other companies throughout our industry. Moreover, the growth of local biotechnology companies and the expansion of major pharmaceutical companies into the Boston area has increased competition for the available pool of skilled employees, especially in technical fields, and the high cost of living in the Boston and San Diego areas makes it difficult to attract employees from other parts of the country. A failure to retain, as well as hire, train and effectively integrate into our organization a sufficient number of qualified scientists and professionals would negatively impact our business and our ability to grow our business. In addition, the level of funding under certain of our collaborative agreements depends on the number of our scientists performing research under those agreements. If we cannot hire and retain the required personnel, funding received under the agreements may be reduced.

IF OUR PATENTS DO NOT PROTECT OUR PRODUCTS, OR OUR PRODUCTS INFRINGE THIRD-PARTY PATENTS, WE COULD BE SUBJECT TO LITIGATION AND SUBSTANTIAL LIABILITIES.

We have numerous patent applications pending in the United States, as well as foreign counterparts in other countries. Our success will depend, in significant part, on our ability to obtain and maintain United States and foreign patent protection for our products, their uses and our processes, to preserve our trade secrets and to operate without infringing the proprietary rights of third parties. We do not know whether any patents will issue from any of our patent applications or, even if patents issue or have issued, that the issued claims will provide us with any significant protection against competitive products or otherwise be valuable commercially. Legal standards relating to the validity of patents and the proper scope of their claims in the pharmaceutical field are still evolving, and there is no consistent law or policy regarding the valid breadth of claims in biopharmaceutical patents or the effect of prior art on them. If we are not able to obtain adequate patent protection, our ability to prevent competitors from making, using and selling similar products will be limited. Furthermore, our activities may infringe the claims of patents held by third parties. Defense and prosecution of infringement or other intellectual property claims, as well as participation in other inter-party proceedings, can be expensive and time-consuming, regardless of whether or not the outcome is favorable to us. If the outcome of any such litigation or proceeding were adverse, we could be subject to significant liabilities to third parties, could be required to obtain licenses from third parties or could be required to cease sales of affected products, any of which outcomes could have a material adverse effect on our business.

WE DO NOT KNOW WHETHER LEXIVA/TELZIR WILL CONTINUE TO BE COMPETITIVE IN THE MARKET FOR HIV PIs OR IF BRECANAVIR, IF APPROVED, WILL BE SUCCESSFUL IN THE MARKET.

We currently receive royalties from sales of Lexiva/Telzir under our collaboration with GlaxoSmithKline and will receive product royalty payments on sales of brecanavir, if any, if brecanavir is approved for sale. Lexiva/Telzir's share of the worldwide protease inhibitor market may decrease due to competitive forces and market dynamics. Other HIV PIs and a number of other products, including Viread® (tenofovir dispoproxil fumerate), Sustiva® (efavirenz) and Ziagen® (abacavir) are on the market for the treatment of HIV infection and AIDS. Other drugs are still in development by our competitors, including Bristol-Myers Squibb, Boehringer Ingelheim and Johnson & Johnson, which may have better efficacy, fewer side effects, easier administration and/or lower costs than Lexiva/Telzir or brecanavir. Moreover, the growth in the worldwide market for HIV PIs has, to a certain extent, occurred as a result of early and aggressive treatment of HIV infection with a protease inhibitor-based regimen. Changes in treatment strategy, in which treatment is initiated later in the course of infection, or in which treatment is more often initiated with a regimen that does not include a protease inhibitor, may result in reduced use of HIV PIs. As a result, the total market for HIV PIs may decline,

decreasing the sales potential of Lexiva/Telzir and/or brecanavir. Further, although we provide education efforts related to the promotion of Lexiva/Telzir in the United States and key markets in Europe, GlaxoSmithKline directs the majority of the marketing and sales efforts and the positioning of Lexiva/Telzir in the overall market, and we have little control over the direction or success of those efforts. GlaxoSmithKline has the right to terminate its agreement with us without cause upon twelve months' notice, and would have no obligation to pay further royalties to us upon any such termination.

IF PHYSICIANS, PATIENTS AND THIRD-PARTY PAYORS DO NOT ACCEPT OUR FUTURE DRUGS, WE MAY BE UNABLE TO GENERATE SIGNIFICANT REVENUE, IF ANY.

Even if our drug candidates obtain regulatory approval, they may not gain market acceptance among physicians, patients and health care payors. Physicians may elect not to recommend our drugs for a variety of reasons including:

- the timing of the market introduction of competitive drugs;
- lower demonstrated clinical safety and efficacy compared to other drugs;
- lack of cost-effectiveness;
- lack of availability of reimbursement from third-party payors;
- convenience and ease of administration;
- prevalence and severity of adverse side effects;
- other potential advantages of alternative treatment methods; and
- ineffective marketing and distribution support.

If our approved drugs fail to achieve market acceptance, we would not be able to generate significant revenue.

IF THE GOVERNMENT AND OTHER THIRD-PARTY PAYORS FAIL TO PROVIDE COVERAGE AND ADEQUATE PAYMENT RATES FOR OUR FUTURE DRUGS, OUR REVENUE AND PROSPECTS FOR PROFITABILITY WILL BE HARMED.

In both domestic and foreign markets, our sales of any future drugs will depend in part upon the availability of reimbursement from third-party payors. Such third-party payors include government health programs such as Medicare, managed care providers, private health insurers and other organizations. These third-party payors are increasingly attempting to contain healthcare 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 these drugs. As a result, they may not cover or provide adequate payment for our future drugs. We might need to conduct post-marketing studies in order to demonstrate the cost-effectiveness of any future drugs to such payors' satisfaction. Such studies might require us to commit a significant amount of management time and financial and other resources. Our future drugs 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 investment in product development.

Reimbursement rates may 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 are already reimbursed, may be incorporated into existing payments for other products or services, and may reflect budgetary constraints and/or imperfections in Medicare or Medicaid data used to calculate these rates. Net prices for drugs may be reduced by mandatory discounts or rebates required by government health care programs. In addition, legislation has been introduced in Congress that, if enacted, would permit more widespread importation of drugs from foreign countries into the United States, which may include importation from countries where the drugs are sold at lower prices than in the United States. Such legislation, or similar regulatory changes or relaxation of laws that restrict imports of drugs from other countries, could reduce the net price we receive for our marketed drugs.

RECENT FEDERAL LEGISLATION WILL INCREASE THE PRESSURE TO REDUCE PRICES OF PHARMACEUTICAL PRODUCTS PAID FOR BY MEDICARE, WHICH COULD ADVERSELY AFFECT OUR REVENUES, IF ANY.

The Medicare Prescription Drug Improvement and Modernization Act of 2003, or MMA, changed the way Medicare will cover and pay for pharmaceutical products. The legislation expanded Medicare coverage for drug purchases by the elderly and eventually will introduce a new reimbursement methodology based on average sales prices for drugs. In addition, this legislation provides authority for limiting the number of drugs that will be covered in any therapeutic class. As a result of this legislation and the expansion of federal coverage of drug products, we expect that there will be additional pressure to contain and reduce costs. These cost reduction initiatives and other provisions of this legislation could decrease the coverage and price that we receive for any approved products and could seriously harm our business. 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 reimbursement rates, and any reduction in reimbursement that results from the MMA may result in a similar reduction in payments from private payors.

OUR BUSINESS HAS A SUBSTANTIAL RISK OF PRODUCT LIABILITY CLAIMS. IF WE ARE UNABLE TO OBTAIN APPROPRIATE LEVELS OF INSURANCE, A PRODUCT LIABILITY CLAIM COULD ADVERSELY AFFECT OUR BUSINESS.

Our business exposes us to significant potential product liability risks that are inherent in the development, manufacturing and sales and marketing of human therapeutic products. We currently have clinical trial insurance and will seek to obtain product liability insurance prior to the sales and marketing of any of our drug candidates. However, our insurance may not provide adequate coverage against potential liabilities. Furthermore, clinical trial and product liability insurance is becoming increasingly expensive. As a result, we may be unable to maintain current amounts of insurance coverage or obtain additional or sufficient insurance at a reasonable cost to protect against losses that could have a material adverse effect on us. If a claim is brought against us, we might be required to pay legal and other expenses to defend the claim, as well as uncovered damages awards resulting from a claim brought successfully against us. 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.

IF WE DO NOT COMPLY WITH LAWS REGULATING THE PROTECTION OF THE ENVIRONMENT AND HEALTH AND HUMAN SAFETY, OUR BUSINESS COULD BE ADVERSELY AFFECTED.

Our research and development efforts involve the controlled use of hazardous materials, chemicals and various radioactive compounds. Although we believe that our safety procedures for handling and disposing of these materials comply with the standards prescribed by state and federal regulations, the risk of 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 are also 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. Due to the small amount of hazardous materials that we generate, we have determined that the cost to secure insurance coverage for environmental liability and toxic tort claims far exceeds the benefits. Accordingly, we do not maintain any insurance to cover pollution conditions or other extraordinary or unanticipated events relating to our use and disposal of hazardous materials. 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.

WE HAVE ADOPTED ANTI-TAKEOVER PROVISIONS THAT MAY FRUSTRATE ANY ATTEMPT TO REMOVE OR REPLACE OUR CURRENT MANAGEMENT.

Our corporate charter and by-law provisions and stockholder rights plan 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 stockholders, and certain provisions of the by-laws may be amended only with an 80% stockholder vote. Pursuant to our stockholder rights plan, each share of common stock has an associated preferred share purchase right. The rights will not trade separately from the common stock until, and are exercisable only upon, the acquisition or the potential acquisition through tender offer by a person or group of 15% or more of the outstanding common stock. We may issue shares of any class or series of preferred stock in the future without stockholder 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. As a result, stockholders or other parties may find it more difficult to remove or replace our current management.

OUR STOCK PRICE MAY FLUCTUATE BASED ON FACTORS BEYOND OUR CONTROL.

Market prices for securities of companies such as Vertex are highly volatile. Within the twelve months ended December 31, 2005, our common stock traded between $8.61 and $29.24 per share. The market for our stock, like that of other companies in the biotechnology field, has from time to time experienced significant price and volume fluctuations that are unrelated to our operating performance. The future market price of our securities could be significantly and adversely affected by factors such as:

- announcements of results of clinical trials or nonclinical studies;
- announcements of financial results and other operating performance measures, or capital structuring activities;
- technological innovations or the introduction of new products by our competitors;
- government regulatory action;
- public concern as to the safety of products developed by others;
- 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; and
- developments relating specifically to other companies and market conditions for pharmaceutical and biotechnology stocks in general.

OUR OUTSTANDING INDEBTEDNESS MAY MAKE IT MORE DIFFICULT TO OBTAIN ADDITIONAL FINANCING OR REDUCE OUR FLEXIBILITY TO ACT IN OUR BEST INTERESTS.

As of December 31, 2005, we had approximately $42.1 million in aggregate principal amount of 5% Convertible Subordinated Notes due in September 2007 ("2007 Notes") and approximately $118.0 million in aggregate principal amount of 5.75% Convertible Senior Subordinated Notes due in February 2011 ("2011 Notes") outstanding. The high level of our indebtedness will affect us by:

- exposing us to fixed rates of interest, which may be in excess of prevailing market rates;
- making it more difficult to obtain additional financing for working capital, capital expenditures, debt service requirements or other purposes;

- constraining our ability to react quickly in an unfavorable economic climate or to changes in our business or the pharmaceutical industry; and

- requiring the dedication of a substantial portion of our expected cash flow to service of our indebtedness, thereby reducing the amount of expected cash flow available for other purposes.

OUR ESTIMATES OF OUR LIABILITY UNDER OUR KENDALL SQUARE LEASE MAY BE INACCURATE.

We leased a 290,000 square foot facility in Kendall Square, Cambridge, Massachusetts in January 2003 for a 15-year term. Under the lease, we are required to complete certain build-outs and improvements of the facility. We currently expect to occupy approximately 120,000 square feet of the facility. We have sublease arrangements in place for the remaining rentable square footage of the facility. In determining our obligations under the lease for the portion of the facility that we do not expect to occupy, we have made certain assumptions relating to the costs that will be incurred to satisfy our build-out commitments under the lease, operating costs, the time necessary to sublease the space after the expiration of the initial subleases, projected future sublease rental rates and the anticipated durations of future subleases. Our estimates have changed in the past, and may change in the future, resulting in additional adjustments to the estimate of liability, and the effect of any such adjustments could be material.

GOVERNMENT INVESTIGATIONS OR LITIGATION AGAINST OUR COLLABORATORS COULD IMPACT OUR BUSINESS.

The federal government, certain state governments and private payors are investigating and have begun to file actions against numerous pharmaceutical and biotechnology companies alleging that the reporting of prices for pharmaceutical products has resulted in a false and overstated Average Wholesale Price, or AWP, which in turn is alleged to have improperly inflated the reimbursement paid by Medicare beneficiaries, insurers, state Medicaid programs, medical plans and others to health care providers who prescribed and administered those products. Some payors are also alleging that pharmaceutical and biotechnology companies are not reporting their "best price" to the states under the Medicaid program. In addition, recent government litigation against pharmaceutical companies has focused on allegations of off-label promotion in connection with the filing of false claims for government reimbursement. In any AWP cases or other cases brought by the government where our collaborators or licensees are named as defendants with respect to any products licensed from us, the outcome of the case could have a material adverse effect on our financial results.

SALES OF ADDITIONAL SHARES OF OUR COMMON STOCK COULD CAUSE THE PRICE OF OUR COMMON STOCK TO DECLINE.

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. In addition, the issuance of common stock upon exercise of any outstanding option or the conversion of any of our outstanding convertible debt would be dilutive, and may cause the market price for a share of our common stock to decline. As of December 31, 2005, we had 108,153,000 shares of common stock issued and outstanding. We also had outstanding options to purchase approximately 14,669,000 shares of common stock with exercise prices as set forth in Note N, "Common and Preferred Stock," to our consolidated financial statements included in this Annual Report on Form 10-K, and with a weighted average exercise price of $22.84 per share. Our outstanding notes were convertible into approximately 8,354,000 shares of common stock with a weighted average conversion price of $19.16 per share. Outstanding options and convertible notes may be exercised or converted, as the case may be, if the market price of our common stock exceeds the applicable exercise or conversion price.

ITEM 1B. UNRESOLVED STAFF COMMENTS

We have not received any written comments that have not been resolved from the Securities and Exchange Commission regarding our filings under the Securities Exchange Act of 1934, as amended.

ITEM 2. PROPERTIES

We lease an aggregate of approximately 624,000 square feet of laboratory and office space in six facilities in Cambridge, Massachusetts. The leases have expiration dates ranging from 2006 to 2018. We have the option to extend the lease for our headquarters facility at 130 Waverly Street, Cambridge, for one additional term of five years, ending in 2015, with respect to one portion of the building, and for up to two additional terms of five years, ending in 2019, for the other portion of the building. The lease for the laboratory and office building at 200 Sidney Street, located adjacent to our headquarters, will expire in 2010. We have the option to extend that lease for up to two additional consecutive ten-year terms.

The lease for our Kendall Square, Cambridge, Massachusetts facility will expire in 2018. We have the option to extend that lease for two consecutive terms of ten years each. We have subleased approximately 145,000 square feet of the facility, and we intend to begin using the balance of the facility in the first half of 2006. The subleases are for terms ending in 2011 and 2012 with extension options to 2015 and 2018. One of the subleases has certain termination provisions beginning in 2010.

We also lease approximately 81,200 square feet of laboratory and office space in San Diego, California. The lease for this space will expire on August 31, 2008. We have the option to extend this lease for up to two additional terms of five years each.

We lease approximately 22,000 square feet of laboratory and office space in Milton Park, Abingdon, England, for our United Kingdom business and research and development activities under a lease expiring in 2013 with a right of early termination exercisable by us in 2008.

We believe our facilities are adequate for our current needs.

ITEM 3. LEGAL PROCEEDINGS

We are not a party to any material legal proceedings. We are not a party to any litigation in any court with any governmental authority, and management is not aware of any contemplated proceeding by any governmental authority against the Company.

ITEM 4. SUBMISSION OF MATTERS TO A VOTE OF SECURITY HOLDERS

There were no matters submitted to a vote of security holders during the quarter ended December 31, 2005.

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 National 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:

Year Ended December 31, 2004:	High	Low
First quarter	$ 12.20	$ 8.82
Second quarter	10.00	8.00
Third quarter	11.19	8.06
Fourth quarter	12.05	9.79
Year Ended December 31, 2005:		
First quarter	$ 11.99	$ 9.20
Second quarter	17.06	8.61
Third quarter	22.68	15.33
Fourth quarter	29.24	20.31

As of March 14, 2006, there were 1,312 holders of record of our common stock (approximately 20,200 beneficial holders).

Dividends

We have never declared or paid any cash dividends on our common stock, and we currently expect that future earnings, if any, will be retained for use in our business.

Issuer Repurchases of Equity Securities

We did not repurchase any equity securities of the Company during the quarter ended December 31, 2005.

Unregistered Sales of Equity Securities

In December 2005, we issued an additional 781,000 shares of our common stock in connection with exchanges with certain existing holders of 2011 Notes. The exchanges were exempt from registration under the Securities Act of 1933, as amended, under Section 3(a)(9) thereof, as exchanges by the Company of securities with its existing holders exclusively in transactions in which no commission or other remuneration was paid.

ITEM 6. SELECTED CONSOLIDATED FINANCIAL DATA

The following unaudited selected financial data for each of the five years in the period ended December 31, 2005 are derived from our audited consolidated financial statements. These data should be read in conjunction with our audited consolidated financial statements and related notes which are included elsewhere in this Annual Report on Form 10-K and "Management's Discussion and Analysis of Financial Condition and Results of Operations" included in Item 7 below.

	Year Ended December 31,				
	2005	2004	2003	2002	2001(1)
	(In thousands, except per share amounts)				
Consolidated Statement of Operations Data:					
Revenues:					
Royalties	$ 32,829	$ 17,322	$ 9,002	$ 10,054	$ 10,783
Collaborative and other research and development revenues	128,061	85,395	60,139	84,716	74,514
Total revenues	160,890	102,717	69,141	94,770	85,297
Costs and expenses:					
Royalty payments	10,098	5,649	3,126	3,334	3,594
Research and development	248,540	192,162	199,636	198,338	141,988
Sales, general and administrative	43,990	42,139	39,082	41,056	31,856
Restructuring and other expense	8,134	17,574	91,824	—	—
Merger related costs	—	—	—	—	22,960
Total costs and expenses	310,762	257,524	333,668	242,728	200,398
Loss from operations	(149,872)	(154,807)	(264,527)	(147,958)	(115,101)
Other income/(expense), net	(5,332)	(7,994)	(1,886)	11,000	24,532
Loss on exchange of convertible subordinated notes(5)	(48,213)	—	—	—	—
Gain (loss) on retirement of convertible subordinated notes(4)	—	(3,446)	—	—	10,340
Loss from continuing operations before cumulative effect of changes in accounting principles	(203,417)	(166,247)	(266,413)	(136,958)	(80,229)
Income from discontinued operations(2):					
Gain on sales of assets	—	—	70,339	—	—
Income (loss) from discontinued operations	—	—	(693)	28,337	22,148
Total income from discontinued operations	—	—	69,646	28,337	22,148
Loss before cumulative effect of changes in accounting principles	$ (203,417)	$ (166,247)	$ (196,767)	$ (108,621)	$ (58,081)
Cumulative effect of change in accounting principle—revenue recognition(1)	—	—	—	—	(25,901)
Cumulative effect of change in accounting principle—derivatives(3)	—	—	—	—	17,749
Net loss	$ (203,417)	$ (166,247)	$ (196,767)	$ (108,621)	$ (66,233)
Basic and diluted net loss per common share	$ (2.28)	$ (2.12)	$ (2.56)	$ (1.43)	$ (0.89)
Basic and diluted weighted average number of common shares outstanding	89,241	78,571	77,004	75,749	74,464
Pro forma amounts assuming the 2001 accounting change relating to revenue recognition is applied retroactively(1)					
Net loss	$ (203,417)	$ (166,247)	$ (196,767)	$ (108,621)	$ (40,332)
Net loss per weighted common share — basic and diluted	$ (2.28)	$ (2.12)	$ (2.56)	$ (1.43)	$ (0.54)

	December 31,				
	2005	2004	2003	2002	2001
Consolidated Balance Sheets Data:					
Cash, cash equivalents and marketable securities	$ 407,510	$ 392,320	$ 583,164	$ 634,984	$ 743,202
Other current assets	23,898	14,392	10,642	21,588	32,890
Restricted cash	41,482	49,847	26,061	26,091	26,190
Property and equipment, net	54,533	64,225	80,083	95,991	80,377
Other non-current assets	21,575	24,669	24,461	37,066	42,472
Total assets	$ 548,998	$ 545,453	$ 724,411	$ 815,720	$ 925,131
Deferred revenue, current portion	$ 31,449	$ 47,741	$ 7,746	$ 11,888	$ 39,498
Accrued restructuring and other expense	42,982	55,843	69,526	—	—
Other current liabilities	54,443	50,161	47,795	52,709	52,055
Collaborator development loan (due 2008)	19,997	19,997	32,460	5,000	—
Other long-term obligations	—	2,925	7,268	5,944	8,026
Deferred revenue, excluding current portion	851	18,345	51,771	46,598	35,201
Convertible notes (due 2007)(4)(5)	42,102	82,552	315,000	315,000	315,000
Convertible notes (due 2011)(4)(5)	117,998	232,448	—	—	—
Stockholders' equity	239,176	35,441	192,845	378,581	475,351
Total liabilities and stockholders' equity	$ 548,998	$ 545,453	$ 724,411	$ 815,720	$ 925,131

On July 18, 2001, we completed a merger with Aurora Biosciences Corporation. The merger was accounted for as a pooling of interests. All prior period consolidated financial statements presented have been restated to include the consolidated results of operations, financial position and cash flows of Aurora as though the merger had been in effect on the dates indicated.

(1) In the third quarter of 2001, in connection with our overall review of accounting policies concurrent with our merger with Aurora, we elected to change our revenue recognition policy for collaborative and other research and development revenues from the Emerging Issues Task Force No. 91-6 ("EITF 91-6") method to the Substantive Milestone Method, adopted retroactive to January 1, 2001. We believe this method is preferable because it is reflective of our on-going business operations and is more consistent with industry practice following the implementation of the Securities and Exchange Commission's Staff Accounting Bulletin No. 101, "Revenue Recognition in Financial Statements" ("SAB 101") in 2000 throughout the biotechnology industry.

(2) We sold certain assets and liabilities of our Discovery Tools and Services business in two independent transactions in March and December 2003. In October 2001, the FASB issued FASB 144, "Accounting for the Impairment of Long-Lived Assets" ("SFAS 144"). Pursuant to SFAS 144, the Statement of Operations data shown above give effect to the disposition of the assets sold, accounting for such assets as discontinued operations. The results of discontinued operations prior to 2002 have been prepared using estimates and assumptions we deemed appropriate based upon information currently available and does not necessarily reflect the results that would have been achieved had the business operated on a stand-alone basis for the periods presented. Prior to 2002, the Discovery Tools and Services business was not separately managed, operationally or financially. Please refer to Note C, "Sale of Assets", in the notes to our consolidated financial statements included in this Annual Report on Form 10-K for further information.

(3) During 2001, we recorded a cumulative effect of change in accounting principle related to the adoption of Derivative Implementation Group Issue No. A17 ("DIG A17") in connection with the valuation of derivative instruments.

(4) During 2004, we issued approximately $232.4 million in aggregate principal amount of 5.75% Convertible Senior Subordinated Notes due in February 2011 ("2011 Notes") in exchange for an equal principal amount of our outstanding 5% Convertible Subordinated Notes due in September 2007 ("2007 Notes").

(5) In the third quarter of 2005, holders of 2007 Notes exchanged $40.5 million in aggregate principal amount of 2007 Notes, plus interest, for approximately 2.5 million shares of newly issued common stock. As a result of this exchange, a non-cash charge of approximately $36.3 million was incurred. In separate transactions, in the fourth quarter 2005, holders of 2011 Notes exchanged $114.5 million in aggregate principal amount of 2011 Notes, plus interest, for approximately 8.1 million shares of newly issued common stock. As a result of this exchange, a non-cash charge of approximately $11.9 million was incurred. These charges relate to the incremental shares issued in the transactions over the number of shares that would have been issued upon conversion of the notes at the conversion prices set forth therein.

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

Overview

We are a biotechnology company in the business of discovering, developing and commercializing small molecule drugs for the treatment of serious diseases. We have built a drug discovery capability that integrates biology, chemistry, biophysics, automation and information technologies, with a goal of making the drug discovery process more efficient and productive. We have a number of drug candidates in development, including compounds targeting HCV infection, RA, cystic fibrosis, cancer, pain and HIV infection. Our corporate strategy is to retain principal responsibility for the development and commercialization of some of our proprietary drug candidates in certain major markets, concentrating a significant part of our overall development and commercialization resources on those drug candidates once we select them. We intend to rely on collaborators to conduct development and commercialization of certain of our other drug candidates either worldwide or in markets upon which we are not currently focused. We are concentrating most of our drug development resources at the present time on three compounds: VX-950 for the treatment of HCV infection, VX-702 for the treatment of RA, and VX-770 for the treatment of cystic fibrosis.

Drug Discovery and Development

Discovery and development of a single new pharmaceutical product is a lengthy and resource-intensive process, which may take 10 to 15 years or more. Throughout this entire process, potential drug candidates are subjected to rigorous evaluation, driven in part by stringent regulatory considerations, designed to generate information concerning efficacy, proper dosage levels and a variety of other physical and chemical characteristics that are important in determining whether a proposed drug candidate should be approved for marketing. The toxicity characteristics and profile of drug candidates at varying dose levels administered for varying periods of time also are monitored continually and evaluated during the nonclinical and clinical development process. Most chemical compounds that are investigated as potential drug candidates never progress into formal development, and most drug candidates that do advance into formal development never become commercial products. A drug candidate's failure to progress or advance may be the result of any one or more of a wide range of adverse experimental outcomes including, for example, the lack of acceptable absorption characteristics or other physical properties, the lack of sufficient efficacy against the disease target, difficulties in developing a cost-effective manufacturing or formulation method, or the discovery of toxicities or side effects that are unacceptable for the disease indication being treated.

We have a variety of drug candidates in clinical development and a broad-based drug discovery effort. Given the uncertainties of the research and development process, it is not possible to predict with confidence which, if any, of these efforts will result in a marketable pharmaceutical product. We constantly monitor the results of our discovery research and our nonclinical and clinical trials and regularly evaluate our portfolio investments with the objective of balancing risk and potential return in light of new data and scientific, business and commercial insights. This process can result in relatively abrupt changes in focus and priority as new information becomes available and we gain additional insights into ongoing programs and potential new programs.

Business Strategy

We have elected to diversify our research and development activities across a relatively broad array of investment opportunities, due in part to the high risks associated with the biotechnology and pharmaceutical business. We plan to expend significant resources on development and commercialization of some of our drug product candidates in certain markets, and rely on collaborators to conduct development and commercialization of certain of our other drug candidates either worldwide or in markets upon which we are not currently focused. This diversification strategy requires more significant financial resources than would be required if we pursued a more limited approach.

Because we have incurred losses from our inception and expect to incur losses for the foreseeable future, we are dependent in large part on our continued ability to raise significant funding to finance our discovery and development operations and our overhead and to meet our long term contractual commitments and obligations. In the past, we have secured funds principally through capital market transactions, strategic collaborative agreements, proceeds from the disposition of assets, investment income and the issuance of stock under our employee benefit programs. At December 31, 2005, we had $407.5 million of cash, cash equivalents and available-for-sale securities, $42.1 million in principal amount of 5% Convertible Subordinated Notes due 2007 (the "2007 Notes") and $118.0 million in principal amount of 5.75% Convertible Senior Subordinated Notes due 2011 (the "2011 Notes"). During 2005, we took a number of steps that we believe reinforced our ability to implement our business strategy. In June 2005, we completed a public equity offering and issued approximately 13.5 million shares of our common stock, resulting in net proceeds to us of approximately $165.4 million. In September 2005, we exchanged approximately 2.5 million newly issued shares of common stock for approximately $40.5 million in aggregate principal amount of 2007 Notes, plus accrued interest, and in December 2005, we exchanged approximately 8.1 million newly issued shares of common stock for approximately $114.5 million in aggregate principal amount of 2011 Notes plus accrued interest, resulting in a net reduction by approximately $155 million of our outstanding indebtedness. During 2005, we also signed new discovery and development collaborations with GlaxoSmithKline and Avalon Pharmaceuticals.

Collaborations and Collaborative Revenues

Collaborations have been and will continue to be an important component of our business strategy. We entered into two new collaborative relationships in 2005, and extended the duration of our research collaboration with CFFT early in 2006. In February 2005, we licensed VX-944, an IMPDH inhibitor, to Avalon Pharmaceuticals, Inc. for development and commercialization in the treatment of cancer. Avalon has made an upfront payment and has committed to make milestone payments to us, to conduct further development of VX-944 and to pay royalties to us if VX-944 is successfully commercialized. In December 2005, we entered into a global collaboration with GlaxoSmithKline to develop and commercialize VX-409, our novel, subtype selective sodium channel modulator for the treatment of pain. Under that collaboration agreement, GlaxoSmithKline paid us a $20 million up-front license payment, and has committed to make milestone payments to us, conduct further development of VX-409 and any backup compounds that are selected for development, and pay us royalties on future sales of VX-409 and backup compounds. Early in 2006, we extended the period of our research collaboration with CFFT. The amended CFFT agreement provides for an additional $22 million in continued research funding through early 2008, to further investigate our "corrector" compounds to see if they act to restore the function of the CFTR protein. We retain the right to develop and commercialize any compounds discovered in the CFFT collaboration, and will pay royalties to CFFT upon the approval and commercialization of any compounds discovered under the collaboration.

Our financial guidance for 2006, as set forth below, reflects a significant increase in revenues over 2005 levels, an important part of which is anticipated revenue from new collaborations that we believe we could enter into this year. These anticipated new collaborative revenues will be important in offsetting the loss of revenues as certain of our existing collaborations expire in 2006. Our research collaborations with Novartis and Merck are scheduled to conclude, along with our research funding, in April and June 2006, respectively. Revenue recognized from our Merck and Novartis collaborations accounted for approximately 61% of our total collaborative research and development revenue in 2005. We may continue to realize revenue from these collaborations beyond their research term, in the form of milestone payments that may be earned if product candidates proceed successfully through development and royalties on sales of any resulting drugs. We also believe that the intellectual property rights we may retain from these collaborations, as well as the value we have built in our other research and development programs, may help us initiate other collaborative opportunities. Based on our perception of the level of interest in certain of our programs among some potential collaborators, we believe that we could enter into additional collaborative agreements in 2006 that would be material to

our business. Our business development priorities include new collaborations to support development and commercialization of VX-950 outside North America and to assist us with the development and commercialization of VX-702. Our product and development pipeline also includes drug candidates such as VX-692 and VX-883 (bacterial infection), VX-166 (sepsis), VX-765 and pralnacasan (inflammatory diseases) and VX-271 (cancer) that we may choose to develop with or through a collaborator, as we maintain focus on our core product candidates. We may also seek collaborators for our kinase, ion channels and other research programs.

Clinical Development Programs

We are focusing our 2006 preclinical and clinical development investment on VX-950, VX-702 and VX-770. We are projecting an increase in research and development expense for 2006 to a range of $350 million to $370 million. We expect this increase to be driven by increased clinical investment in these core programs. We believe that each of these programs requires comprehensive investment to realize its full clinical and commercial value. We also recognize that development investment at this stage is subject to the considerable risk that any one or more of these compounds will not advance to product registration. Each compound could fail to progress or advance due to a wide range of adverse experimental outcomes, placing our full investment in the compound at risk. While we attempt to stage our investments to mitigate these financial risks, drug discovery and development by its nature is a very risky undertaking. We expect to continue to evaluate and prioritize investment in our clinical development programs based on the emergence of new clinical and nonclinical data in each program in 2006 and in subsequent years.

Manufacturing and Supply Chain

We are focused on implementing the necessary infrastructure and procedures for manufacturing and supplying drug products containing VX-950, VX-702 and VX-770 for clinical trials and ultimately for the commercial market. We currently are making a significant investment in our supply chain management, to ensure timely delivery of drug product in accordance with all applicable regulatory guidelines. We do not currently plan to manufacture VX-950, VX-702 or VX-770 ourselves. We rely on networks of third party manufacturers and suppliers worldwide to provide raw materials and to synthesize, tablet, and package our drug candidates for clinical trials. We currently expect that we will continue to outsource for our commercial supply requirements for our potential products. We monitor our third party manufacturers' and suppliers' capabilities to assess their ability to meet our needs efficiently and economically. However, a delay in manufacture or supply of clinical trial material could delay the completion of a clinical trial or compromise its results, causing a delay in the anticipated launch of a commercial product. In addition, our significant supply chain investment could be at risk if we do not obtain favorable results in the clinical trials for any of VX-950, VX-702 or VX-770.

Financial Guidance

The key financial measures for which we have provided guidance are as follows:

Loss: We expect that the net loss for 2006 will be in the range of $205 to $225 million. This net loss estimate includes an estimated $34 million in stock-based compensation expense and an estimated $6 million of restructuring expense as a result of imputed interest charges relating to the restructuring accrual.

Revenues: We expect that the Company's revenue will be in the range of $210 to $235 million in 2006.

Research and Development ("R&D") Expense: We expect that R&D expense will be in the range of $350 to $370 million for 2006, including approximately $28 million of stock-based compensation expense.

Sales, General and Administrative ("SG&A") Expense: We expect our SG&A expense will be in the range of $55 to $60 million for 2006, including approximately $6 million of stock-based compensation expense.

Cash, Cash Equivalents and Available for Sale Securities: We expect cash, cash equivalents and marketable securities to be in excess of $300 million at the end of 2006.

The financial measures set forth above are forward-looking and are subject to risks and uncertainties that could cause our actual results to vary materially, including the risks and uncertainties that we describe in "Risk Factors" in Item 1A of this Annual Report on Form 10-K and in the section below entitled "Forward-Looking Statements."

Contractual Commitments and Obligations

The first part of the following table sets forth commitments and obligations that have been recorded on our consolidated balance sheets at December 31, 2005. Certain other obligations and commitments, while not required under generally accepted accounting principles in the United States ("GAAP") to be included in the consolidated balance sheets, may have a material impact on liquidity. We have presented these items, all of which we have entered into in the ordinary course of business, in the table below in order to present a more complete picture of our financial position and liquidity.

	2006	2007-2008	2009-2010	2011 and later	Total
			(in thousands)		
Commitments and Obligations Recorded on the Consolidated Balance Sheets at December 31, 2005:					
Collaborator development loans	$ —	$ 19,997	$ —	$ —	$ 19,997
Convertible subordinated notes	—	42,102	—	117,998	160,100
Off-Balance Sheet Commitments and Obligations at December 31, 2005:					
Facilities operating leases	46,715	76,781	69,014	195,667	388,177
Purchase obligation	3,000	—	—	—	3,000
Research and development and other commitments	1,035	75	—	—	1,110
Total contractual commitments and obligations	$ 50,750	$ 138,955	$ 69,014	$ 313,665	$ 572,384

Commitments and Obligations Recorded on the Consolidated Balance Sheets at December 31, 2005

The collaborator development loans in the table above represent indebtedness to Novartis in the amount of approximately $20.0 million that was advanced under a loan facility established pursuant to the original collaboration agreement with Novartis. Loans under the facility were intended to fund early clinical trials of kinase inhibitor compounds that we selected for early development. In February 2004, we amended the terms of the Novartis collaboration agreement. Under the amended agreement, Novartis assumed responsibility for all nonclinical and clinical development of drug candidates that it accepts for development. Consequently the loan facility providing funding for development activities by Vertex was terminated. Outstanding loans that funded amounts either spent or committed to be spent on development activities relating to compounds not selected by Novartis will be repayable without interest in May 2008. Please refer to Note O, "Significant Revenue Arrangements", to our consolidated financial statements included in this Annual Report on Form 10-K for additional information regarding these loans.

At December 31, 2005, we had $42.1 million in aggregate principal amount of 2007 Notes and $118.0 million in aggregate principal amount of 2011 Notes outstanding. We are required to make

semi-annual interest payments on the outstanding principal balance of both the 2007 and 2011 Notes. Our aggregate annual interest payment obligation is approximately $8.9 million.

Off-Balance Sheet Commitments and Obligations at December 31, 2005

At December 31, 2005, our future minimum commitments and contractual obligations included facilities operating leases, a purchase obligation and contractual commitments related to our research and development programs. These items are not required under GAAP to be recorded on our consolidated balance sheets. They are disclosed in the table presented above and described more fully in the following paragraphs in order to provide a more complete picture of our financial position and liquidity at December 31, 2005.

The term under our Kendall Square lease began January 1, 2003. We began making lease payments in May 2003. We have an obligation, staged over a number of years, to build out the leased space into finished laboratory and office space (the "Kendall Square Facility"). The lease will expire in 2018, and we have options to extend for two consecutive terms of ten years each. The Company's future minimum commitments under the Kendall Square lease for the period commencing January 1, 2006, including lease payments and a construction obligation, are $30.0 million for 2006, $45.5 for 2007 and 2008, $47.6 million for 2009 and 2010 and $195.7 million for the period thereafter. These amounts are included in the table above. We expect to occupy and use for our operations approximately 40% of the Kendall Square Facility. We have entered into two subleases for the remaining rentable square footage at the Kendall Square Facility to offset our on-going contractual lease obligations. The subleases will expire in 2011 and 2012 and contain options to extend through 2015 and 2018, respectively. One of the subleases has certain termination provisions beginning in 2010. The future minimum committed income from the subleases is $7.4 million for 2006, $16.3 million for 2007 and 2008, $16.3 million for 2009 and 2010 and $6.2 million for years thereafter. These amounts are not offset against our obligations set forth in the table above. See Note D, "Restructuring and Other Expense." to our consolidated financial statements included in this Annual Report on Form 10-K.

Commitments under research and development programs represent contractual commitments entered into for materials and services in the normal course of business.

The purchase obligation referred to above arises under our agreement to purchase a minimum of $3.0 million of products from Invitrogen Corporation annually for three years. We made this commitment in connection with the sale of certain assets of our former Discovery Tools and Services business on March 28, 2003.

Our table detailing contractual commitments and obligations does not include severance pay obligations to certain of our executive officers in the event of a not-for-cause termination under existing employment contracts. The cash amount for which the Company might be liable upon any such termination, based on current executive pay and bonus levels, could range from $0.4 to $1.4 million.

Liquidity and Capital Resources

We have incurred operating losses since our inception and historically have financed our operations principally through public and private offerings of our equity and debt securities, strategic collaborative agreements that include research and development funding, development milestones and royalties on the sales of products, proceeds from the disposition of assets of our Discovery Tools and Services business, investment income and proceeds from the issuance of stock under our employee benefit programs.

At December 31, 2005, we had cash, cash equivalents and marketable securities of $407.5 million, which is an increase of $15.2 million from $392.3 million at December 31, 2004. The increase reflects net proceeds of approximately $165.4 million from our public offering of common stock, which closed in June 2005, as well as $32.2 million from the issuance of common stock under our employee benefit

plans, offset by the net loss of $203.4 million. Expenditures for property and equipment during the 12 months ended December 31, 2005 were $17.0 million.

As part of our strategy to manage our long-term operating cash needs, we exchanged approximately $155.0 million in aggregate principal amount of our convertible subordinated notes, plus interest, in a series of transactions, for approximately 10.6 million shares of newly issued common stock. As a result of these exchanges, we incurred a non-cash charge of approximately $48.2 million. This charge is related to the incremental shares issued in the transactions over the number that would have been issued upon conversion of the notes under their original conversion prices. At December 31, 2005, we had approximately $42.1 million in aggregate principal amount of the 2007 Notes and approximately $118.0 million in aggregate principal amount of the 2011 Notes outstanding. The 2011 Notes are convertible into common stock at the option of the holder at a price equal to $14.94 per share, subject to adjustment under certain circumstances. The 2007 Notes are convertible into common stock at the option of the holder at a price equal to $92.26 per share, subject to adjustment under certain circumstances.

The restructuring accrual of $43.0 million at December 31, 2005 relates to the portion of the Kendall Square Facility that we do not intend to occupy, and includes build-out commitments and other lease obligations, recorded at net present value. In 2005, we made cash payments of $24.2 million against the accrual and received $3.2 million in sublease rental income. We expect to make net cash payments of approximately $14.4 million against the accrual in 2006. We review our estimates underlying the restructuring accrual on at least a quarterly basis, and the accrual, and consequently any expected future payment, could change with any change in our estimates.

The net decrease of $33.8 million in deferred revenue for the 12 months ended December 31, 2005 is a result of revenue recognized in 2005 related to cash payments received from collaborators, primarily Novartis and Merck, in previous periods, which were deferred and are being recognized over our period of performance in accordance with our revenue recognition policy. In connection with new collaborations in 2005, we received and recognized as revenue approximately $25.0 million up-front license payments. We also received $22.0 million in milestone payments from our collaborators during 2005. Consistent with our revenue recognition policy, we recognized approximately $10.0 million of this amount and have deferred recognition of the majority of these milestone payment amounts, which will be recognized over our remaining period of obligation.

In February 2004, we amended the terms of our collaboration agreement with Novartis. Under the amended agreement, Novartis assumed responsiblity for all nonclinical and clinical development of drug candidates that it accepts for development. Consequently, the loan facility established under the original agreement, which provided funding for development activities by Vertex, has been terminated. As permitted under the amended agreement, on June 22, 2004, we gave notice to Novartis of our election to develop VX-680 outside of our Novartis collaboration. As a result, we repaid to Novartis approximately $12.5 million of unspent and uncommitted loan amounts relating to VX-680. At December 31, 2004, we had approximately $20.0 million in remaining loans outstanding under the loan facility. Loans advanced by Novartis for the development of collaboration compounds under the original agreement will be forgiven on a compound-by-compound basis if any such compounds are selected by Novartis for development. All loans not forgiven under the facility will be repayable, without interest, in May 2008.

We expect to continue to make significant investments in our drug candidates, particularly in clinical trials of VX-950, VX-702 and VX-770, in our ion channel and kinase discovery efforts, in our effort to prepare for potential registration, regulatory approval and commercial launch of our product candidates and in supply chain management. Consequently, we expect to incur losses on a quarterly and annual basis for the foreseeable future. We also expect to incur substantial administrative expenditures in the future and expenses related to filing, prosecution, defense and enforcement of patent and other intellectual property rights.

In 2006 and in future periods, the adequacy of our available funds to meet our future operating and capital requirements, including repayment of the 2007 Notes and the 2011 Notes, will depend on many factors, including the number, breadth and prospects of our discovery and development programs, the costs and timing of obtaining regulatory approvals for any of our product candidates and our decisions regarding manufacturing and commercial investments. Collaborations have been and will continue to be an important component of our business strategy. We will continue to rely on cash receipts from our existing research and development collaborations, including research funding, development reimbursements and potential milestone payments, and from new collaborations, in order to help fund our research and development efforts.

As part of our strategy for managing our capital structure, we have from time to time adjusted the amount and maturity of our debt obligations through new issues, privately negotiated transactions and market purchases, depending on market conditions and our perceived needs at the time. During 2006 we expect to continue pursuing a general financial strategy that may lead us to undertake one or more additional capital transactions. Any such capital transactions may or may not be similar to transactions in which we have engaged in the past.

To the extent that our current cash and marketable securities, in addition to the above-mentioned sources, are not sufficient to fund our activities, it will be necessary to raise additional funds through public offerings or private placements of our securities or other methods of financing. We also will continue to manage our capital structure and consider all financing opportunities, whenever they may occur, that could strengthen our long-term liquidity profile. There can be no assurance that any such financing opportunities will be available on acceptable terms, if at all.

Critical Accounting Policies and Estimates

Our discussion and analysis of our financial condition and results of operations is based upon our consolidated financial statements prepared in accordance with GAAP. 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 revenue and expense during the reported periods. These items are constantly 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 recorded in the period in which they become known. 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 the application of the accounting policies for restructuring and other expense, revenue recognition, research and development expenses and investments, all of which are important to our financial condition and results of operations, require significant judgments and estimates on the part of management. Our accounting polices, including the ones discussed below, are more fully described in Note B, "Accounting Policies," to our consolidated financial statements included in this Annual Report on Form 10-K.

Restructuring and Other Expense

We record liabilities associated with restructuring activities based on estimates of fair value in the period the liabilities are incurred, in accordance with SFAS 146. As prescribed by SFAS 146, we use a probability-weighted discounted cash-flow analysis to calculate the amount of the liability. The probability-weighted discounted cash-flow analysis is based on management's assumptions and estimates of our ongoing lease obligations, including contractual rental commitments, build-out commitments and building operating costs, and estimates of income from subleases, based on the term and timing of such subleases. We discount the estimated cash flows using a discount rate of approximately 10%. These cash flow estimates are reviewed and may be adjusted in subsequent periods. Adjustments are based,

among other things, on management's assessment of changes in factors underlying the estimates. Because our estimate of the liability includes the application of a discount rate to reflect the time-value of money, the estimate will increase simply as a result of the passage of time, even if all other factors remain unchanged.

Our estimates of our restructuring liability have changed in the past, and it is possible that our assumptions and estimates will change in the future, resulting in additional adjustments to the amount of the estimated liability. The effect of any such adjustments could be material. For example, we currently have two subleases for portions of the Kendall Square Facility with terms of six and seven years, respectively, and we have made certain estimates and assumptions relating to future sublease terms following the expiration of the current subleases. As a result, we may be exposed to market variability in the future. We will review our assumptions and judgments related to the lease restructuring on at least a quarterly basis until the Kendall Square lease is terminated, and make whatever modifications we believe are necessary, based on our best judgment, to reflect any changed circumstances.

The accrual for restructuring expense of $43.0 million at December 31, 2005 is related to the portion of the Kendall Square Facility that we do not intend to occupy. This estimate represents our best judgment of the assumptions and estimates most appropriate in measuring the ongoing obligation.

Revenue Recognition

We recognize revenue in accordance with the SEC's Staff Accounting Bulletin No. 101, "Revenue Recognition in Financial Statements" ("SAB 101") as amended by SEC Staff Accounting Bulletin No. 104, "Revenue Recognition" ("SAB 104") and for revenue arrangements entered into after June 30, 2003, Emerging Issues Task Force Issue No. 00-21, "Revenue Arrangements with Multiple Deliverables" ("EITF 00-21").

Our revenues are generated primarily through collaborative research, development and commercialization agreements. The terms of the agreements typically include payment to Vertex of non-refundable up-front license fees, funding of research and development efforts, milestone payments and/or royalties on product sales.

Agreements containing multiple elements are divided into separate units of accounting if certain criteria are met, including whether the delivered element has stand-alone value to the customer and whether we have objective and reliable evidence of fair value of the undelivered obligation(s). The consideration received is allocated among the separate units based on their respective fair values or the residual method, and the applicable revenue recognition criteria are applied to each of the separate units.

We recognize revenues from non-refundable, up-front license fees on a straight-line basis over the contracted or estimated period of performance, which is typically the research or development term. Research and development funding is recognized as earned, ratably over the period of effort.

Substantive milestones are recognized as earned when the corresponding payment is reasonably assured and we have evidence of fair value for our remaining obligations. Substantive milestones are recognized over the period of performance when the corresponding payment is reasonably assured but we do not have fair value for our remaining obligations. This typically results in a portion of the milestone payment being recognized as revenue at the date the milestone is achieved, which portion is equal to the applicable percentage of the performance period that has elapsed as of the date the milestone is achieved, with the balance being deferred and recognized over the remaining period of performance. We evaluate whether milestones are substantive at the inception of the agreement based on the contingent nature of the milestone, specifically reviewing factors such as the technological and commercial risk that must be overcome as well as the level of effort and investment required to achieve the milestone. Milestones that are not considered substantive and do not meet the separation criteria are accounted for as license payments and recognized on a straight-line basis over the remaining period of performance.

Payments received after performance obligations are met completely are recognized when earned.

Royalty revenue on our products Agenerase and Lexiva/Telzir is recognized based upon actual and estimated net sales of licensed products in licensed territories, as provided by our collaborator GlaxoSmithKline, and is recognized in the period the sales occur. Differences between actual royalty revenues and estimated royalty revenues, which have not historically been significant, are reconciled and adjusted for in the quarter they become known.

Research and Development Costs

All research and development costs, including amounts funded by research and development collaborations, are expensed as incurred. Research and development expenses are comprised of costs incurred in performing research and development activities including salaries and benefits; laboratory supplies; contract services, including clinical trial costs; and infrastructure costs, including facilities costs and depreciation. To record clinical trial, contract services and other outside costs, we are required to make estimates of the costs incurred in a given accounting period and record accruals at period-end, because the third party service periods and billing terms do not always coincide with our period-end. We base our estimates on our knowledge of the research and development programs, services performed for the period, past history for related activities and the expected duration of the third party service contract, where applicable.

Altus Investment

We assess our investment in Altus Pharmaceuticals Inc., which we account for using the cost method, on a quarterly basis to determine if there has been any estimated decrease in the fair value of that investment below its $18.9 million carrying value that might require us to write down the cost basis of the asset. If any adjustment to the fair value of an investment reflects a decline in the value of that investment below its cost, we consider the evidence available to us, including the duration and extent to which the decline is other-than-temporary. If the decline is considered other-than-temporary, the cost basis of the investment is written down to fair value as a new cost basis and the amount of the write-down is included in the consolidated statements of operations. We have not identified facts or circumstances which would cause us to determine that the investment basis of our interest in Altus should be changed.

Altus completed an initial public offering in January 2006. We own 817,749 shares of common stock and warrants to purchase 1,962,494 shares of common stock. In addition, we hold 450,000 shares of redeemable preferred stock, which are not convertible into common stock and which are redeemable at our option on or after December 31, 2010, or by Altus at any time. We are restricted from trading Altus securities for a period of six months following the initial public offering. Due to the public offering, in 2006 we will classify the common stock as an available-for-sale investment and record it at fair value, based on quoted market prices, with unrealized gains and losses included as a component of accumulated other comprehensive income (loss), which is a separate component of stockholders' equity, until such gains and losses are realized. We will continue to account for the warrants under the cost method of accounting until the end of the restricted trading period, at which time the warrants will be classified as derivatives. Gains or losses on the fair market value of the warrants, as derivatives, will be included in the consolidated statements of operations. We will continue to account for the redeemable preferred stock under the cost method of accounting.

Results of Operations

The following discussion of revenues and expenses is based only on the results of our continuing operations. We sold the assets of our Discovery Tools and Services business in two independent transactions in March and December 2003. In accordance with SFAS No. 144, "Accounting for the Impairment of Long-Lived Assets" ("SFAS No. 144"), the results of operations associated with the assets sold have been reclassified in the Company's consolidated financial statements under the heading "discontinued operations" for the twelve months ended December 31, 2003. The reclassification of the amounts to discontinued operations was accomplished using estimates and assumptions we have

deemed appropriate based upon the information currently available. Amounts reclassified to discontinued operations are not necessarily indicative of the results that would have been achieved had the Discovery Tools and Services business operated on a stand-alone basis during the periods presented.

As a result of the disposition of these assets, we now operate in a single operating segment: Pharmaceuticals.

Year Ended December 31, 2005 Compared with Year Ended December 31, 2004

Our net loss for 2005 was $203,417,000, or $2.28 per basic and diluted common share, compared to a net loss for 2004 of $166,247,000, or $2.12 per basic and diluted common share. Our loss in 2005 includes restructuring expense of $8,134,000 and a charge of $48,213,000 for the exchange of newly issued common stock for a portion of our outstanding convertible notes. Our loss in 2004 includes restructuring expense of $17,574,000 and a charge for the retirement of convertible notes of $3,446,000.

Our net loss for 2005, as compared with our net loss for 2004, increased primarily as a result of increased development investment to advance our propriety drug candidates, which was partially offset by an increase in revenue.

Total revenues increased to $160,890,000 in 2005 compared to $102,717,000 in 2004. In 2005, revenue was comprised of $32,829,000 in royalties and $128,061,000 in collaborative and other research and development revenues, as compared with $17,322,000 in royalties and $85,395,000 in collaborative research and development revenue in 2004.

Royalties consist of Lexiva/Telzir (fosamprenavir calcium) and Agenerase (amprenavir) royalty revenue. Fosamprenavir calcium is marketed under the trade name Lexiva in the United States and Telzir in the European Union. Royalty revenue is based on actual and estimated worldwide net sales of Lexiva/Telzir and Agenerase. We began earning royalties on sales of Lexiva in the United States in the fourth quarter of 2003 and on Telzir in the European Union in third quarter of 2004. The increase in royalty revenue is due to the increase in Lexiva/Telzir sales. By the end of 2005, Lexiva had largely replaced Agenerase in worldwide markets. As a result, we expect that royalty revenue in the foreseeable future will consist primarily of Lexiva/Telzir royalty revenue. We pay a royalty to a third party on sales of Agenerase and Lexiva/Telzir.

Collaborative and other research and development revenues increased $42,666,000, or 50%, in 2005 as compared with 2004. The increase in collaborative and other research and development revenues is due to the execution of new collaboration agreements in 2004 and in 2005. In 2005 we entered into collaboration agreements with Avalon Pharmaceuticals (license, development and commercialization of VX-944) and GlaxoSmithKline (research, license, development and commercialization of VX-409). Under these new collaboration agreements, in 2005 we earned $5,000,000 in up-front license fees from Avalon and $20,000,000 in up-front license fees from GlaxoSmithKline. In 2004 we entered into collaboration agreements with CFFT (cystic fibrosis drug discovery), Mitsubishi Pharma Corporation (Far East development and commercialization of VX-950), and Merck (research, development and commercialization of Aurora kinase inhibitors, including VX-680 and VX-667). We recognized revenue of approximately $7,339,000 in 2005 from two milestone payments made by Merck in our Aurora kinase inhibitor collaboration, one made in connection with Merck's selection of VX-667 as a follow-on compound to VX-680, and one for demonstrating that administration of VX-680 to patients had an effect on a clinically relevant biomarker, in an aggregate amount of $19.5 million. We earned $2.5 million in milestone revenue from Kissei related to the completion of regulatory filings in preparation for Phase I clinical development of VX-702 in Japan.

The table presented below is a summary of revenue from collaborative arrangements for the year ended 2005 as compared with the year ended 2004.

	2005	2004
	(In thousands)	
Collaborative and other research and development revenues:		
Summary of revenues from collaborative arrangements:		
Novartis	$ 53,082	$ 50,497
Merck	24,428	8,367
GlaxoSmithKline	20,000	—
CFFT	14,490	6,792
Other	16,061	19,739
Total collaborative and other research and development revenues	$ 128,061	$ 85,395

We expect that collaborative and other research and development revenues will continue to be a significant component of our total revenues and we are seeking to enter into additional collaboration agreements in 2006 that could be material to our business.

Research and development expenses increased $56,378,000, or 29%, to $248,540,000 in 2005, from $192,162,000 in 2004. The increase in research and development expenses in 2005 as compared with 2004 is primarily a result of investment in our clinical development programs for VX-950 and VX-702. Development expenses accounted for 87%, or $48,875,000, of the aggregate increase in research and development expenses. In 2005 we incurred costs from Phase II-enabling activities for VX-950, we completed enrollment in a 315-patient Phase II clinical trial of VX-702 for the treatment of RA, and we continued a Phase IIb clinical trial (called the "METRO" trial) of merimepodib (VX-497) for the treatment of HCV infection. We initiated the METRO trial during 2004. During 2004 we also completed a Phase Ia trial of VX-950, and began a Phase Ib evaluation of VX-950 in patients with chronic HCV infection. During the fourth quarter of 2004 we commenced Phase II clinical development of VX-765 in psoriasis.

Research and development expenses consist primarily of salary and benefits, laboratory supplies, contractual services and infrastructure costs, including facilities costs and depreciation. Set forth below

is a summary that reconciles our total research and development expenses for the 12 months ended December 31, 2005 and 2004 (in thousands):

	2005	2004	$ Change	% Change
Research Expenses:				
Salary and benefits	$ 40,877	$ 36,772	$ 4,105	11.2%
Laboratory supplies and other direct expenses	20,877	19,052	1,825	9.6%
Contractual services	7,619	8,857	(1,238)	(14.0)%
Infrastructure costs	51,406	48,595	2,811	5.8%
Total research expenses	$ 120,779	$ 113,276	$ 7,503	
Development Expenses:				
Salary and benefits	$ 28,119	$ 20,493	$ 7,626	37.2%
Laboratory supplies and other direct expenses	11,674	7,600	4,074	53.6%
Contractual services	61,188	28,837	32,351	112.2%
Infrastructure costs	26,780	21,956	4,824	22.0%
Total development expenses	$ 127,761	$ 78,886	$ 48,875	
Total Research and Development Expenses:				
Salary and benefits	$ 68,996	$ 57,265	$ 11,731	20.5%
Laboratory supplies and other direct expenses	32,551	26,652	5,899	22.1%
Contractual services	68,807	37,694	31,113	82.5%
Infrastructure costs	78,186	70,551	7,635	10.8%
Total research and development expenses	$ 248,540	$ 192,162	$ 56,378	

To date we have incurred in excess of $1 billion in research and development costs associated with drug discovery and development. We expect research and development expenses in 2006 to be greater than in 2005 due to increased investment in clinical development as we advance our core programs. In 2006, we expect to focus our preclinical and clinical development investment on VX-950, VX-702 and VX-770. However, our anticipated 2006 research and development expenses could vary materially from our projections, depending on the occurrence and timing of clinical trials and actual clinical trial results. We expect that our combined research and development expenses will increase in future periods as we add personnel and capabilities to support the advancement of our lead drug candidates. We do not expect that our research expenses will increase significantly unless we obtain a significant amount of funding from new research collaborations.

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

Phase:	Objective:	Estimated Duration:
Discovery	Lead identification and target validation	2 to 4 years
Preclinical	Initial toxicology for preliminary identification of risks for humans; gather early pharmacokinetic data	1 to 2 years
Phase I	Evaluate safety in humans; study how the drug works, metabolizes and interacts with other drugs	1 to 2 years
Phase II	Establish effectiveness of the drug and its optimal dosage; continue safety evaluation	2 to 4 years
Phase III	Confirm efficacy, dosage regime and safety profile of the drug; submit New Drug Application	2 to 4 years
FDA approval	Approval by the FDA to sell and market the drug for the approved indication	6 months to 2 years

Animal and other nonclinical studies typically are conducted during each phase of human clinical trials.

The successful development of our products is highly uncertain and subject to a number of risk factors. The duration of clinical trials may vary substantially according to the type, complexity and novelty of the pharmaceutical product. 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 preclinical, nonclinical and clinical activities at any step in the testing process may be adverse and lead to discontinuation or redirection of development activity. Data obtained from these activities also are susceptible to varying interpretations, which could delay, limit or prevent regulatory approval. The duration and cost of discovery, preclinical, nonclinical 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. The most significant costs associated with drug discovery and development are those costs associated with Phase II and Phase III clinical trials. Given the uncertainties related to development, we are currently unable to reliably estimate when, if ever, our drug candidates will generate revenue and net cash inflows.

Sales, general and administrative expenses increased $1,851,000, or 4%, to $43,990,000 in 2005 from $42,139,000 in 2004.

For the twelve months ended December 31, 2005, we recorded net restructuring expense of $8.1 million. This net expense includes a $10.0 million credit to the restructuring accrual made when we decided in mid-2005 to occupy and use a portion of the Kendall Square Facility for our operations, which was offset by (i) the estimated incremental net ongoing lease obligations associated with the portion of the Kendall Square Facility that we do not intend to occupy and (ii) imputed interest costs relating to the restructuring liability.

The activity related to restructuring expense for the twelve months ended December 31, 2005 is as follows (in thousands):

	Accrual as of December 31, 2004	Cash Payments, twelve months ended Dec. 31, 2005	Cash received from subleases, twelve months ended Dec. 31, 2005	Credit for portion of facility Vertex expects to occupy, twelve months ended Dec. 31, 2005	Charge, twelve months ended Dec. 31, 2005	Accrual as of Dec. 31, 2005
Lease restructuring expense	$ 55,843	$ (24,229)	$ 3,234	$ (10,018)	$ 18,152	$ 42,982

In accordance with SFAS 146, we review our estimates and assumptions with respect to the Kendall Square lease on at least a quarterly basis, and will make whatever modifications we believe necessary until the termination of the lease, 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 liability, and the effect of any such adjustments could be material. Because our estimate of the liability includes the application of a discount rate to reflect the time-value of money, the estimate of the liability will increase each quarter simply as a result of the passage of time.

Interest income increased approximately $1,671,000 to $11,994,000 in 2005 from $10,323,000 in 2004. The increase is mainly the result of higher returns on invested funds.

Interest expense decreased $991,000 or 5% to $17,326,000 in 2005 from $18,317,000 in 2004 as a result of the exchange of newly issued stock for a portion of our outstanding convertible debt in the second half of 2005.

In addition, as a result of the issuance during 2005 of common stock in exhange for convertible subordinated notes, we recorded a non-cash charge of $48,213,000. This charge relates to the incremental shares issued in the transactions over the number of shares that would have been issued upon the conversion of the notes under their original terms.

Year Ended December 31, 2004 Compared with Year Ended December 31, 2003

Our net loss for 2004 was $166,247,000, or $2.12 per basic and diluted common share, compared to a net loss for 2003 of $196,767,000, or $2.56 per basic and diluted common share. Our loss in 2004 includes restructuring and other expense of $17,574,000 and a charge for the retirement of convertible notes of $3,446,000. Our loss in 2003 includes restructuring and other expense of $91,824,000 and income from discontinued operations of $69,646,000. Included in the income from discontinued operations is a gain from the sale of assets of $70,339,000.

Our net loss for 2004, as compared with our net loss for 2003, decreased primarily as a result of increased revenue, principally related to new collaboration agreements and increased royalties.

Total revenues increased to $102,717,000 in 2004 compared to $69,141,000 in 2003. In 2004, revenue was comprised of $17,322,000 in royalties and $85,395,000 in collaborative and other research and development revenues, as compared with $9,002,000 in royalties and $60,139,000 in collaborative research and development revenues in 2003.

Royalties consist of Lexiva/Telzir (fosamprenavir calcium) and Agenerase (amprenavir) royalty revenue. Fosamprenavir calcium is marketed under the trade name Lexiva in the United States and Telzir in the European Union. Royalty revenue is based on actual and estimated worldwide net sales of Lexiva/Telzir and Agenerase. We began earning royalties on sales of Lexiva in the United States in the fourth quarter of 2003 and on Telzir in the European Union in the third quarter of 2004.

Collaborative and other research and development revenues increased $25,256,000, or 42%, in 2004 as compared with 2003. The increase in collaborative and other research and development revenues is due to the execution of new collaboration agreements and recognition of revenue in the amount of approximately $4.1 million from a $10 million milestone payment made in connection with Novartis' selection of VX-322 for development. We also earned $2,500,000 in milestone revenue from GlaxoSmithKline relating to regulatory approval of Telzir in the European Union and the initiation of Phase II clinical trials for brecanavir (VX-385). The table presented below is a summary of revenue from collaborative arrangements for the year ended 2004 as compared with the year ended 2003.

	2004	2003
	(In thousands)	
Collaborative and other research and development revenue:		
Summary of revenue from collaborative arrangements:		
Novartis	$ 50,497	$ 44,502
Merck	8,367	—
CFFT	6,792	—
Mitsubishi Pharma	5,840	—
Other	13,899	15,637
Total collaborative and other research and development revenue	$ 85,395	$ 60,139

Research and development expenses decreased to $192,162,000 in 2004, from $199,636,000 in 2003. Research expenditures were $113,276,000 in 2004 compared with $113,435,000 in 2003. Development expenditures were $78,886,000 in 2004 compared with $86,201,000 in 2003. The decrease in research and development expenses in 2004 as compared with 2003 is a result of our decision to focus during

2004 on development activities aimed at new treatments for viral and inflammatory diseases. In 2003, we engaged in development activities with drug candidates targeting potential therapeutic indications other than viral and inflammatory diseases, including VX-944 (oncology), which is now licensed to Avalon and VX-680 (oncology), which is now licensed to Merck. During 2004, we initiated the METRO trial. We completed a Phase Ia trial of VX-950, also for the treatment of HCV infection, and began a Phase Ib evaluation of VX-950 in patients with chronic HCV infection. During the fourth quarter of 2004 we also commenced Phase II clinical development of VX-765 in psoriasis.

Research and development expenses consist primarily of salary and benefits, laboratory supplies, contractual services and infrastructure costs, including facilities costs and depreciation. Set forth below is a summary that reconciles our total research and development expenses for the 12 months ended December 31, 2004 and 2003 (in thousands):

	2004	2003	$ Change	% Change
Research Expenses:				
Salary and benefits	$ 36,772	$ 38,140	$ (1,368)	(3.6)%
Laboratory supplies and other direct expenses	19,052	20,025	(973)	(4.9)%
Contractual services	8,857	6,390	2,467	38.6%
Infrastructure costs	48,595	48,880	(285)	(0.6)%
Total research expenses	$ 113,276	$ 113,435	$ (159)	
Development Expenses:				
Salary and benefits	$ 20,493	$ 19,796	$ 697	3.5%
Laboratory supplies and other direct expenses	7,600	5,307	2,293	43.2%
Contractual services	28,837	42,594	(13,757)	(32.3)%
Infrastructure costs	21,956	18,504	3,452	18.7%
Total development expenses	$ 78,886	$ 86,201	$ (7,315)	
Total Research and Development Expenses:				
Salary and benefits	$ 57,265	$ 57,936	$ (671)	(1.2)%
Laboratory supplies and other direct expenses	26,652	25,332	1,320	5.2%
Contractual services	37,694	48,984	(11,290)	(23.0)%
Infrastructure costs	70,551	67,384	3,167	4.7%
Total research and development expenses	$ 192,162	$ 199,636	($ 7,474)	

Sales, general and administrative expenses increased $3,057,000, or 8%, to $42,139,000 in 2004 from $39,082,000 in 2003. The increase is partially attributable to increased professional consulting expenses incurred to comply with the Sarbanes-Oxley Act of 2002, as well as increased costs related to the further development of our patent portfolio and increased business development costs associated with the pursuit of new collaborative relationships.

Restructuring and other expense for the twelve months ended December 31, 2004 was $17.6 million. The expense recorded during 2004 reflects a revision of our key estimates and assumptions, specifically relating to the projected sublease rental rates and timing of subleases, as well as the imputed interest cost related to the restructuring accrual.

The activity related to restructuring and other expense for the twelve months ended December 31, 2004, in connection with the Kendall Square lease, is presented below (in thousands):

	Accrual as of December 31, 2003	Cash Payments in 2004	Cash received from sublease, net of operating costs	Additional Charge in 2004	Accrual as of December 31, 2004
Lease restructuring expense and other operating lease expense	$ 69,526	$ (31,550)	$ 293	$ 17,574	$ 55,843

Interest income decreased approximately $5,089,000 to $10,323,000 in 2004 from $15,412,000 in 2003. The decrease is the result of both a lower level of invested funds and lower portfolio yields due to a reduced interest rate environment.

In connection with the sale of the assets of our Discovery Tools and Services business in 2003 we recorded income from discontinued operations of $69,646,000. Included in this amount is a gain on the sale of those assets of $70,339,000.

Forward-looking Statements

Our disclosure in this Annual Report on Form 10-K contains forward-looking statements. Forward-looking statements give our current expectations or present forecasts of future events. You can identify these statements by the fact that they do not relate strictly to historical or current facts. Such statements may include words such as "anticipate," "estimate," "expect," "project," "intend," "plan," "believe" and other words and phrases of similar meaning in connection with any discussion of future operating or financial performance. In particular, these statements include forward-looking statements about our business, including our expectations that:

(1) we will continue to make progress toward our goal of becoming a profitable pharmaceutical company and advancing our product candidates to market;

(2) we will continue investing in, and building, industry-leading capabilities in research, development and commercialization of pharmaceutical products;

(3) we will retain principal responsibility for the development and commercialization of some of our proprietary compounds in certain major markets, and concentrate a significant part of our resources on those drug candidates;

(4) collaborations will continue to be a key component of our corporate strategy and we will rely on collaborators to conduct development and commercialization of certain of our drug candidates either worldwide or in markets upon which we currently are not focused;

(5) at the present time we will concentrate most of our drug development resources on three compounds: VX-950, VX-702 and VX-770;

(6) our losses will continue for the foreseeable future, and our net loss in 2006 will be in the range of $205 to $225 million, including an estimated $34 million in stock based compensation expense and $6 million of restructuring expense;

(7) our research and development expense for 2006 will be in the range of $350 to $370 million, including approximately $28 million of stock-based compensation expense;

(8) our revenues will be in the range of $210 to $235 million in 2006;

(9) our SG&A expense for 2006 will be in the range of $55 to $60 million, including approximately $6 million of stock-based compensation expense;

(10) our cash, cash equivalents and marketable securities will be in excess of $300 million at the end of 2006;

(11) we may enter into new collaborative arrangements in 2006 that could be material to our business including research collaboration agreements, a collaboration agreement for the development of VX-950 outside of North America, a collaboration agreement to assist us with development and commercialization of VX-702, and we may consider entering into collaborative relationships to further develop VX-692, VX-883, VX-271, VX-166, VX-765, pralnacasan and/or merimepodib;

(12) we will continue to add promising potential products to our development pipeline, which will be focused on a wide variety of diseases and conditions, including cancer, cystic fibrosis and pain;

(13) we will seek to opportunistically license and acquire technologies, resources and products that have the potential to strengthen our drug discovery platform, product pipeline and commercial capabilities;

(14) therapeutics such as VX-950 that target HCV viral replication may significantly increase the number of patients who achieve a sustained viral response to drug therapy;

(15) treatment with VX-950 could result in improved sustained virologic response rates and a more favorable adverse event profile;

(16) our completed toxicology studies will support clinical trials of VX-950 of up to three months' duration;

(17) it may be possible to achieve sustained virologic response by including VX-950 in a treatment regimen of approximately 12 weeks' duration and subject to FDA agreement, we will initiate a three-month Phase II clinical trial of VX-950 that will include a comparison to the current standard of care in HCV therapy in more than 200 HCV patients in the second quarter of 2006;

(18) we will initiate additional clinical trials of VX-950 in 2006, including a Phase II trial in patients that have failed prior therapy;

(19) data from the Phase Ib combination therapy trial of VX-950 will be presented at a medical conference in 2006;

(20) VX-702 may be a potent and attractive therapy for RA;

(21) we will file an IND application with the FDA in 2006 to support clinical trials of VX-702 in the United States;

(22) we will initiate clinical trials of VX-702 on a background of methotrexate, including a three-month dose-ranging Phase II clinical trial in more than 200 patients with RA by mid-2006;

(23) we will file an IND and initiate our first clinical trial of VX-770 in the first half of 2006;

(24) kinase inhibition may offer a therapeutic opportunity against a broad range of human tumors;

(25) data from nonclinical studies with pralnacasan will be presented at a medical conference in 2006;

(26) we will complete the METRO trial in 2006, but will not conduct additional merimepodib clinical trials after that;

(27) the results of GlaxoSmithKline's Phase IIa and IIb clinical trials of brecanavir will be made available in 2006;

(28) GlaxoSmithKline will commence a Phase III clinical trial program for brecanavir (VX-385) in 2006;

(29) Merck will report Phase I clinical data for VX-680 in 2006, and will also commence Phase II clinical development of VX-680 during 2006;

(30) GlaxoSmithKline will initiate Phase I clinical development of VX-409 early in 2007;

(31) our systematic drug discovery approach is increasing the speed and efficiency of drug design efforts directed at novel biological targets and is securing valuable intellectual property;

(32) our ongoing research programs, particularly those directed at the kinase and ion channel gene families, will continue to create potential value for Vertex by generating new product candidates in areas of significant unmet medical need;

(33) we will use our proprietary gene family based platform and experience in structure based drug design to pursue targets in other medically important gene families;

(34) funds from our anticipated sources will be adequate to fund our planned activities for at least the next eighteen months from the date of filing;

(35) we will significantly augment our manufacturing, logistics, supply chain and quality assurance resources;

(36) we will seek the benefits of the Drug Price Competition and Patent Term Restoration Act of 1984;

(37) our facilities are adequate for our future needs;

(38) the intellectual property rights that we will retain from our current research collaborations may help us initiate other collaborative opportunities;

(39) our increased research and development expense in 2006 will be driven by increased clinical investment in certain core programs;

(40) we will continue to evaluate and prioritize investment in our clinical development programs based on the emergence of new clinical and nonclinical data in each program in 2006 and in subsequent years;

(41) we will continue to outsource to meet the commercial supply requirements for our potential products and will enter into commercial relationships with multiple suppliers to reduce our supply chain disruption risk;

(42) our losses on a quarterly basis and annual basis will continue;

(43) royalty revenue in the foreseeable future will consist primarily of Lexiva/Telzir revenue;

(44) we will incur substantial expenditures relating to filing, prosecution, defense and enforcement of patent and other intellectual property rights;

(45) we will continue to rely on cash receipts from our existing research and development collaborations, including research funding, development reimbursements, and potential milestone payments, and from new collaborations to meet our future operating and capital requirements;

(46) our combined research and development expenses will increase in future periods as we add personnel and capabilities to support advancement of our lead drug candidates;

(47) our research expenses will not increase significantly unless we obtain a significant amount of funding from new research collaborations;

(48) it takes 10 to 15 years, or longer, to discover, develop and bring to market a new pharmaceutical product in the United States;

(49) during 2006 we will continue to pursue a general financial strategy that may lead us to undertake one or more capital transactions, which may or may not be similar to transactions in which we have engaged in the past;

(50) collaborative and other research and development revenues will continue to be a significant component of our total revenues; and

(51) our restructuring liability will be as we have estimated, and we will make net cash payments against the $43.0 million restructuring accrual in 2006 of approximately $14.4 million.

Any or all of our forward-looking statements in this Annual Report may turn out to be wrong. They can be affected by inaccurate assumptions we might make or by known or unknown risks and uncertainties. Many factors mentioned in our discussion in this Annual Report will be important in determining future results. While management makes its best efforts to be accurate in making forward- looking statements, such statements are subject to risks and uncertainties that could cause our actual results to vary materially, including the cautionary information set forth under the heading "Risk Factors" appearing in Item 1A of this Annual Report on Form 10-K, which are factors that we think could cause our actual results to differ materially from expected results. Other factors besides those listed there could also adversely affect us. Consequently, no forward-looking statement can be guaranteed. We disclaim any intention or obligation to update or revise any forward-looking statements, whether as a result of new information, future events or otherwise.

Recent Accounting Pronouncements

In December 2004, the Financial Accounting Standards Board ("FASB") issued FASB Statement No. 123(R), "Share-Based Payments" ("FASB 123(R)"). FASB 123(R) revises FASB Statement No. 123, "Accounting for Stock-Based Compensation" ("FASB 123"), supersedes APB Opinion No. 25, "Accounting for Stock Issued to Employees," ("APB 25") and amends FASB Statement No. 95, "Statement of Cash Flows." FASB 123(R) requires companies to expense the fair value of employee stock options and other forms of stock-based compensation over the employees' service periods. Compensation cost is measured at the fair value of the award at the grant date and is adjusted to reflect actual forfeitures and the outcome of certain conditions. The fair value of an award is not re-measured after its initial estimation on the grant date.

We are required to comply with FASB 123(R) beginning January 1, 2006 (the "Effective Date"). We will apply the Modified Prospective Method of adoption in our application of FASB 123(R). Under this method, compensation cost is recognized beginning with the Effective Date (a) based on application of the requirements of FASB 123(R) to all share-based payments granted after the effective date; and (b) based on application of the requirements of FASB 123 to all awards granted to employees prior to the Effective Date of FASB 123(R) that remain unvested on the Effective Date.

As permitted by FASB 123, we currently account for share-based payments to employees using APB 25's intrinsic value method, and therefore generally recognize no compensation cost for employee stock options. Accordingly, the adoption of FASB 123(R)'s fair value method will have a significant impact on our results of operations, although it will have no impact on our overall financial position. In 2006 we expect to record approximately $34 million in compensation expense in connection with the adoption of FASB 123(R). The impact of adoption of FASB 123(R) beyond fiscal 2006 cannot be predicted at this time because it will depend on our stock price and the amount of share-based awards granted in future periods, as well as a number of complex and subjective valuation assumptions, including, but not limited to, the volatility of our stock price and employee stock option exercise behaviors. However, had we adopted FASB 123(R) in prior periods, the impact would have approximated the effect of FASB 123 as described in "Stock-Based Compensation" found in Note B to our consolidated financial statements.

In May 2005, the FASB issued SFAS No. 154, "Accounting Changes and Error Corrections" ("SFAS 154"). SFAS No. 154 replaces APB Opinion No. 20, "Accounting Changes" and SFAS No. 3, "Reporting Accounting Changes in Interim Financial Statements." SFAS No. 154 requires retrospective application to prior periods' financial statements of changes in accounting principle, unless it is impractible to determine either the period-specific effects or the cumulative effect of the change. We do not expect the adoption of SFAS No. 154 on January 1, 2006 to have a material impact on our consolidated financial statements.

In November 2005, FASB issued FSP FAS 115-1 and FAS 124-1, "The Meaning of Other-Than-Temporary Impairment and Its Application to Certain Investments" ("FSP FAS 115-1"), which provides guidance on determining when investments in certain debt and equity securities are

considered impaired, whether an impairment is other-than-temporary, and on measuring such impairment loss. FSP FAS 115-1 also includes accounting considerations subsequent to the recognition of an other-than-temporary impairment and requires certain disclosures about unrealized losses that have not been recognized as other-than-temporary impairments. FSP FAS 115-1 is required to be applied to reporting periods beginning after December 15, 2005. We are required to adopt FSP FAS 115-1 in the first quarter of 2006. We do not expect the adoption of this statement to have a material impact on our consolidated results of operations or financial condition.

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 United States government and its agencies, investment grade corporate bonds and notes and money market instruments. These investments are denominated in United States 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 Vertex has implemented guidelines limiting the term-to-maturity of its investment instruments. Due to the conservative nature of these instruments, we do not believe that we have a material exposure to interest rate risk.

ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA

The information required by this Item 8 is contained on pages F-3 through F-39 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 Exchange Act Rule 13a-15(c)) 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 our 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 Vertex 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 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 detections 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, 2005. 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 (COSO). Based on our assessment, we have concluded that, as of December 31, 2005, the Company's internal control over financial reporting is effective based on those criteria.

Our management's assessment of the effectiveness of the Company's internal control over financial reporting as of December 31, 2005, has been audited by Ernst & Young LLP, an independent registered public accounting firm, as stated below.

(3) Changes in Internal Controls. In connection with our evaluation of internal control over financial reporting that occurred during the quarter ended December 31, 2005, we did not change such internal control in a manner that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

(4) Report of Independent Registered Public Accounting Firm

To the Board of Directors and Stockholders of Vertex Pharmaceuticals Incorporated

We have audited management's assessment, included in the accompanying Management's Annual Report on Internal Control over Financial Reporting, that Vertex Pharmaceuticals Incorporated maintained effective internal control over financial reporting as of December 31, 2005, based on criteria established in Internal Control—Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (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. Our responsibility is to express an opinion on management's assessment and an opinion on the effectiveness of 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, evaluating management's assessment, testing and evaluating the design and operating effectiveness of internal control, 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, management's assessment that Vertex Pharmaceuticals Incorporated maintained effective internal control over financial reporting as of December 31, 2005, is fairly stated, in all material respects, based on the COSO criteria. Also, in our opinion, Vertex Pharmaceuticals Incorporated maintained, in all material respects, effective internal control over financial reporting as of December 31, 2005, 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 sheet of Vertex Pharmaceuticals Incorporated as of December 31, 2005, and the related consolidated statements of operations, stockholders' equity and comprehensive loss, and cash flows for the year ended December 31, 2005 of Vertex Pharmaceuticals Incorporated and our report dated March 8, 2006 expressed an unqualified opinion thereon.

/s/ Ernst & Young LLP

Boston, Massachusetts
March 8, 2006

ITEM 9B. OTHER INFORMATION

Not applicable.

PART III

ITEM 10. DIRECTORS AND EXECUTIVE OFFICERS OF THE REGISTRANT

The information regarding directors required by this Item 10 is included in the definitive Proxy Statement for Vertex's 2006 Annual Meeting of Stockholders (the "2006 Proxy Statement"), under "Information Regarding the Board of Directors and its Committees" and is incorporated herein by reference. Other information required by this Item 10 is included in the 2006 Proxy Statement under "Section 16(a) Beneficial Ownership Reporting Compliance" and "Code of Conduct and Ethics" and is incorporated herein by reference. The information regarding executive officers required by this Item is included in Part I of this Annual Report on Form 10-K.

ITEM 11. EXECUTIVE COMPENSATION

The information required by this Item 11 is included in the 2006 Proxy Statement under "Executive Compensation" and is incorporated herein by reference (excluding, however, the "Report on Executive Compensation" and the Performance Graph contained in the 2006 Proxy Statement, which shall not be deemed incorporated herein).

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

The information required by this Item 12 is included in the 2006 Proxy Statement under "Security Ownership of Certain Beneficial Owners and Management" and "Equity Compensation Plan Information" and is incorporated herein by reference.

ITEM 13. CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS

The information required by this Item 13 is included in the 2006 Proxy Statement under "Employment Contracts and Change-in-Control Arrangements" and "Certain Relationships and Related Transactions" and is incorporated herein by reference.

ITEM 14. PRINCIPAL ACCOUNTING FEES AND SERVICES

The information required by this Item 14 is included in the 2006 Proxy Statement under "Independent Registered Public Accounting Firm" and is incorporated herein by reference.

PART IV

ITEM 15. EXHIBITS; 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.

(a)(3) **Exhibits.**

Exhibit Number	Exhibit Description
3.1	Restated Articles of Organization of Vertex, filed with the Secretary of State of The Commonwealth of Massachusetts on July 31, 1991 (filed as Exhibit 3.1 to Vertex's Annual Report on Form 10-K for the year ended December 31, 1997 [File No. 000-19319] and incorporated herein by reference).
3.2	Certificate of Vote of Directors Establishing a Series of a Class of Stock, filed with the Secretary of State of The Commonwealth of Massachusetts on July 31, 1991 (filed as Exhibit 3.3 to Vertex's Annual Report on Form 10-K for the year ended December 31, 1997 [File No. 000-19319] and incorporated herein by reference).
3.3	Articles of Amendment of the Articles of Organization of Vertex, filed with the Secretary of State of The Commonwealth of Massachusetts on May 17, 1995 (filed as Exhibit 3.2 to Vertex's Registration Statement on Form S-3 [Registration No. 333-123731] and incorporated herein by reference).
3.4	Articles of Amendment of the Articles of Organization of Vertex, filed with the Secretary of State of The Commonwealth of Massachusetts on June 4, 1997 (filed as Exhibit 3.2 to Vertex's Annual Report on Form 10-K for the year ended December 31, 1997 [File No. 000-19319] and incorporated herein by reference).
3.5	Articles of Amendment of the Articles of Organization of Vertex, filed with the Secretary of State of The Commonwealth of Massachusetts on May 21, 2001 (filed as Exhibit 3.4 to Vertex's Registration Statement on Form S-4 [Registration No. 333-61480] and incorporated herein by reference).
3.6	By-laws of Vertex, as amended and restated as of May 11, 2005 (filed as Exhibit 3.1 to Vertex's Quarterly Report on Form 10-Q for the quarter ended June 30, 2005 [File No. 000-19319] and incorporated herein by reference).
4.1	Specimen stock certificate (filed as Exhibit 4.1 to Vertex's Registration Statement on Form S-1 [Registration No. 33-40966] and incorporated herein by reference).
4.2	Rights Agreement, dated as of July 1, 1991 (filed as Exhibit 4.2 to Vertex's Registration Statement on Form S-1 [Registration No. 33-40966] and incorporated herein by reference).

4.3 First Amendment to Rights Agreement, dated as of February 21, 1997 (filed as Exhibit 4.3 to Vertex's Annual Report on Form 10-K for the year ended December 31, 1996 [File No. 000-19319] and incorporated herein by reference).

4.4 Second Amendment to Rights Agreement, dated as of June 30, 2001 (filed as Exhibit 4.4 to Vertex's Quarterly Report on Form 10-Q for the quarter ended June 30, 2001 [File No. 000-19319] and incorporated herein by reference).

4.5 Indenture, dated as of September 19, 2000, between Vertex and State Street Bank and Trust Company (filed as Exhibit 4.1 to Vertex's Quarterly Report on Form 10-Q for the quarter ended September 30, 2000 [File No. 000-19319] and incorporated herein by reference).

4.6 Supplemental Indenture, dated as of December 12, 2000, between Vertex and State Street Bank and Trust Company (filed as Exhibit 4.2 to the Registration Statement on Form S-3 [Registration No. 333-49844] and incorporated herein by reference).

4.7 Indenture, dated February 13, 2004, between Vertex and U.S. Bank National Association (filed as Exhibit 4.1 to Vertex's Current Report on Form 8-K dated February 23, 2004 [File No. 000-19319] and incorporated herein by reference).

4.8 Indenture, dated as of September 17, 2004, between Vertex and U.S. Bank National Association (filed as Exhibit 10.2 to Vertex's Current Report on Form 8-K dated September 17, 2004 [File No. 000-19319] and incorporated herein by reference).

10.1 Research and Development Agreement, dated April 13, 1993, between Vertex and Kissei Pharmaceutical Co., Ltd. (filed as Exhibit 10.1 to Vertex's Quarterly Report on Form 10-Q for the quarter ended March 31, 1993 [File No. 000-19319] and incorporated herein by reference).†

10.2 Research and Development Agreement, dated as of September 10, 1997, between Vertex and Kissei Pharmaceutical Co. Ltd. (filed as Exhibit 10.1 to Vertex's Quarterly Report on Form 10-Q for the quarter ended September 30, 1997 [File No. 000-19319] and incorporated herein by reference).†

10.3 Research Agreement and License Agreement, both dated December 16, 1993, between Vertex and Burroughs Wellcome Co. (filed as Exhibit 10.16 to Vertex's Annual Report on Form 10-K for the year ended December 31, 1993 [File No. 000-19319] and incorporated herein by reference).†

10.4 Research Agreement, dated as of August 24, 1998, between Vertex and Schering AG (filed as Exhibit 10.1 to Vertex's Quarterly Report on Form 10-Q for the quarter ended September 30, 1998 [File No. 000-19319] and incorporated herein by reference).†

10.5 License, Development and Commercialization Agreement, dated as of September 1, 1999, between Vertex and Hoechst Marion Roussel Deutschland GmbH (filed as Exhibit 10.1 to Vertex's Quarterly Report on Form 10-Q for the quarter ended September 30, 1999 [File No. 000-19319] and incorporated herein by reference).†

10.6 First Revised and Restated Research and Early Development Agreement, dated as of February 3, 2004, between Vertex and Novartis Pharma AG (filed as Exhibit 10.35 to Vertex's Annual Report on Form 10-K, as amended, for the year ended December 31, 2003 [File No. 000-19319] and incorporated herein by reference).†

10.7 License, Development and Commercialization Agreement, dated as of June 11, 2004, between Vertex and Mitsubishi Pharma Corporation (filed as Exhibit 99.2 to Vertex's Current Report on Form 8-K/A dated September 10, 2004 [File No. 000-19319] and incorporated herein by reference).†

10.8 Research, Development and Commercialization Agreement, dated as of May 24, 2004, between Vertex and Cystic Fibrosis Foundation Therapeutics Incorporated (filed as Exhibit 99.2 to Vertex's Current Report on Form 8-K/A dated September 10, 2004 [File No. 000-19319] and incorporated herein by reference).†

10.9	Amendment to Research, Development and Commercialization Agreement, dated as of January 6, 2006, between Vertex and Cystic Fibrosis Foundation Therapeutics Incorporated (filed herewith).†
10.10	Exclusive Research Collaboration, License and Commercialization Agreement, dated as of June 21, 2004, between Vertex Pharmaceuticals Incorporated and Merck & Co., Inc. (filed as Exhibit 99.4 to Vertex's Current Report on Form 8-K/A dated September 10, 2004 [File No. 000-19319] and incorporated herein by reference).†
10.11	Research, License and Commercialization Agreement, dated as of December 12, 2005, between Vertex and Glaxo Group Limited (filed herewith).†
10.12	Lease, dated as of March 3, 1995, between Fort Washington Realty Trust and Vertex (filed as Exhibit 10.15 to Vertex's Annual Report on Form 10-K for the year ended December 31, 1994 [File No. 000-19319] and incorporated herein by reference).
10.13	First Amendment to Lease, dated as of December 29, 1995, between Fort Washington Realty Trust and Vertex (filed as Exhibit 10.15 to Vertex's Annual Report on Form 10-K for the year ended December 31, 1995 [File No. 000-19319] and incorporated herein by reference).
10.14	Second Amendment to Lease, dated as of June 13, 1997, between Fort Washington Realty Trust and Vertex (filed as Exhibit 10.20 to Vertex's Annual Report on Form 10-K for the year ended December 31, 1999 [File No. 000-19319] and incorporated herein by reference).
10.15	Third, Fourth and Fifth Amendments to Lease between Fort Washington Realty Trust and Vertex (filed as Exhibit 10.14 to Vertex's Annual Report on Form 10-K for the year ended December 31, 2001 [File No. 000-19319] and incorporated herein by reference).†
10.16	Lease, dated as of September 17, 1999, between Trustees of Fort Washington Realty Trust and Vertex (filed as Exhibit 10.27 to Vertex's Quarterly Report on Form 10-Q for the quarter ended September 30, 1999 [File No. 000-19319] and incorporated herein by reference).†
10.17	Lease, dated as of January 18, 2001, between Kendall Square, LLC and Vertex (filed as Exhibit 10.16 to Vertex's Annual Report on Form 10-K for the year ended December 31, 2000 [File No. 000-19319] and incorporated herein by reference).†
10.18	Agreement for Lease, dated as of November 4, 1998, between Milton Park Limited, Vertex and Vertex Pharmaceuticals (Europe) Limited (filed as Exhibit 10.21 to Vertex's Annual Report on Form 10-K for the year ended December 31, 1999 [File No. 000-19319] and incorporated herein by reference).
10.19	1991 Stock Option Plan, as amended and restated as of September 14, 1999 (filed as Exhibit 10.1 to Vertex's Annual Report on Form 10-K for the year ended December 31, 1999 [File No. 000-19319] and incorporated herein by reference).*
10.20	1994 Stock and Option Plan, as amended and restated as of September 14, 1999 (filed as Exhibit 10.2 to Vertex's Annual Report on Form 10-K for the year ended December 31, 1999 [File No. 000-19319] and incorporated herein by reference).*
10.21	1996 Stock and Option Plan, as amended and restated as of March 14, 2005 (filed as Exhibit 10.3 to Vertex's Annual Report on Form 10-K for the year ended December 31, 2005 [File No. 000-19319] and incorporated herein by reference).*
10.22	Form of Stock Option Agreement under 1996 Stock and Option Plan (filed as Exhibit 10.1 to Vertex's Current Report on Form 8-K dated February 9, 2005 [File No. 000-19319] and incorporated herein by reference).*
10.23	Form of Restricted Stock Agreement under 1996 Stock and Option Plan—Annual Vesting (filed as Exhibit 10.2 to Vertex's Current Report on Form 8-K dated February 9, 2005 [File No. 000-19319] and incorporated herein by reference).*
10.24	Form of Restricted Stock Agreement under 1996 Stock and Option Plan—Performance Accelerated Restricted Stock (filed as Exhibit 10.3 to Vertex's Current Report on Form 8-K dated February 9, 2005 [File No. 000-19319] and incorporated herein by reference).*

10.26	Executive Employment Agreement, dated as of November 1, 1994, between Vertex and Joshua S. Boger (filed as Exhibit 10.6 to Vertex's Annual Report on Form 10-K for the year ended December 31, 1994 [File No. 000-19319] and incorporated herein by reference).*
10.27	Amendment to Employment Agreement, dated as of May 12, 1995, between Vertex and Joshua S. Boger (filed as Exhibit 10.1 to Vertex's Quarterly Report on Form 10-Q for the quarter ended June 30, 1995 [File No. 000-19319] and incorporated herein by reference).*
10.28	Second Amendment to Employment Agreement, dated as of November 8, 2004, between Vertex and Joshua S. Boger (filed as Exhibit 10.9 to Vertex's Quarterly Report on Form 10-Q for the quarter ended September 30, 2004 [File No. 000-19319] and incorporated herein by reference).*
10.29	Amended and Restated Employment Agreement, dated as of November 8, 2004, between Vertex and Ian F. Smith (filed as Exhibit 10.13 to Vertex's Quarterly Report on Form 10-Q for the quarter ended September 30, 2004 [File No. 000-19319] and incorporated herein by reference).*
10.30	Amended and Restated Employment Agreement, dated as of November 8, 2004, between Vertex and Kenneth S. Boger (filed as Exhibit 10.11 to Vertex's Quarterly Report on Form 10-Q for the quarter ended September 30, 2004 [File No. 000-19319] and incorporated herein by reference).*
10.31	Employment Agreement, dated as of February 15, 2005, between Vertex and Victor Hartmann (filed as Exhibit 10.2 to Vertex's Quarterly Report on Form 10-Q for the quarter ended March 31, 2005 [File No. 000-19319] and incorporated herein by reference).*
10.32	Form of Letter Agreement, dated as of March 7, 2003, between Vertex and each of John J. Alam; Lynne H. Brum; Peter Mueller; Mark Murcko; Steven Schmidt; John A. Thomson; and Jeffrey D. Wilson (filed as Exhibit 10.32 to Vertex's Annual Report on Form 10-K for the year ended December 31, 2002[File No. 000-19319] and incorporated herein by reference).*
10.33	Form of Amendment to Letter Agreement, dated as of November 8, 2004, between Vertex and each of John J. Alam; Lynne H. Brum; Peter Mueller; Mark Murcko; Steven Schmidt; John A. Thomson; and Jeffrey D. Wilson (filed as Exhibit 10.7 to Vertex's Quarterly Report on Form 10-Q for the quarter ended September 30, 2004 [File No. 000-19319] and incorporated herein by reference).*
10.34	Form of Restricted Stock Agreement between Vertex and each of the individuals listed on Schedule 1 thereto (filed as Exhibit 10.8 to Vertex's Quarterly Report on Form 10-Q for the quarter ended September 30, 2004 [File No. 000-19319] and incorporated herein by reference).*
10.35	Letter Agreement, dated as of December 5, 2005, between Vertex and Richard C. Garrison (filed herewith).*
10.36	Change of Control Letter Agreement, dated as of December 12, 2005, between Vertex and Richard C. Garrison (filed herewith).*
10.37	Amendment to Change of Control Letter Agreement, dated as of December 12, 2005, between Vertex and Richard C. Garrison (filed herewith).*
10.38	Salary Amendments to Employment Arrangements with certain Named Executive Officers (filed herewith).*
10.39	Form of Employee Non-Disclosure and Inventions Agreement (filed as Exhibit 10.4 to Vertex's Registration Statement on Form S-1 [Registration No. 33-40966] and incorporated herein by reference).*
10.40	Amendment to Non-employee Director Compensation Policy (filed herewith).*
21.1	Subsidiaries of Vertex (filed herewith).
23.1	Consent of Independent Registered Public Accounting Firm Ernst & Young LLP (filed herewith).

23.2	Consent of Independent Registered Public Accounting Firm PricewaterhouseCoopers LLP (filed herewith).
31.1	Certification of the Chief Executive Officer under Section 302 of the Sarbanes-Oxley Act of 2002 (filed herewith).
31.2	Certification of the Chief Financial Officer under Section 302 of the Sarbanes-Oxley Act of 2002 (filed herewith).
32.1	Certification of the Chief Executive Officer and the Chief Financial Officer under Section 906 of the Sarbanes-Oxley Act of 2002 (filed herewith).

* Management contract, compensatory plan or agreement.

† Confidential portions of these documents 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

March 16, 2006 By: /s/ JOSHUA S. BOGER

Joshua S. Boger
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/ JOSHUA S. BOGER Joshua S. Boger	Director, Chairman, President and Chief Executive Officer (Principal Executive Officer)	March 16, 2006
/s/ IAN F. SMITH Ian F. Smith	Executive Vice President and Chief Financial Officer (Principal Financial Officer)	March 16, 2006
/s/ JOHANNA MESSINA POWER Johanna Messina Power	Vice President and Corporate Controller (Principal Accounting Officer)	March 16, 2006
/s/ ERIC K. BRANDT Eric K. Brandt	Director	March 16, 2006
/s/ ROGER W. BRIMBLECOMBE Roger W. Brimblecombe	Director	March 16, 2006
/s/ STUART J. COLLINSON Stuart J. Collinson	Director	March 16, 2006
/s/ EUGENE H. CORDES Eugene H. Cordes	Director	March 16, 2006
/s/ MATTHEW W. EMMENS Matthew W. Emmens	Director	March 16, 2006
/s/ BRUCE I. SACHS Bruce I. Sachs	Director	March 16, 2006
/s/ CHARLES A. SANDERS Charles A. Sanders	Director	March 16, 2006
/s/ EVE E. SLATER Eve E. Slater	Director	March 16, 2006
/s/ ELAINE S. ULLIAN Elaine S. Ullian	Director	March 16, 2006

Report of Independent Registered Public Accounting Firm

The Board of Directors and Stockholders of
Vertex Pharmaceuticals Incorporated

We have audited the accompanying consolidated balance sheet of Vertex Pharmaceuticals Incorporated as of December 31, 2005 and the related consolidated statements of operations, stockholders' equity and comprehensive loss, and cash flows for the year ended December 31, 2005. 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 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 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 audit provides 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, 2005, and the consolidated results of its operations and its cash flows for the year ended December 31, 2005, 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), the effectiveness of Vertex Pharmaceuticals Incorporated's internal control over financial reporting as of December 31, 2005, based on criteria established in Internal Control-Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission and our report dated March 8, 2006 expressed an unqualified opinion thereon.

/s/ Ernst & Young LLP

Boston, Massachusetts
March 8, 2006

Report of Independent Registered Public Accounting Firm

To the Board of Directors and Stockholders of
Vertex Pharmaceuticals Incorporated:

In our opinion, the accompanying consolidated balance sheet as of December 31, 2004 and the related consolidated statements of operations, of stockholders' equity and comprehensive loss and of cash flows for the years ended December 31, 2004 and 2003 present fairly, in all material respects, the financial position of Vertex Pharmaceuticals Incorporated and its subsidiaries at December 31, 2004, and the results of their operations and their cash flows for the year ended December 31, 2004 and 2003 in conformity with accounting principles generally accepted in the United States of America. 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 of these statements 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, assessing the accounting principles used and significant estimates made by management, and evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

/s/ PricewaterhouseCoopers LLP

Boston, Massachusetts
March 15, 2005

VERTEX PHARMACEUTICALS INCORPORATED

Consolidated Balance Sheets

	December 31,	
	2005	2004
	(In thousands, except share and per share amounts)	
Assets		
Current assets:		
Cash and cash equivalents	$ 78,045	$ 55,006
Marketable securities, available for sale	283,112	331,240
Accounts receivable	20,595	11,891
Prepaid expenses	3,303	2,501
Total current assets	385,055	400,638
Marketable securities, available for sale	46,353	6,074
Restricted cash	41,482	49,847
Property and equipment, net	54,533	64,225
Investments	18,863	18,863
Other assets	2,712	5,806
Total assets	$ 548,998	$ 545,453
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	$ 6,210	$ 6,660
Accrued expenses and other current liabilities	42,061	32,951
Accrued interest	3,184	5,862
Deferred revenue	31,449	47,741
Accrued restructuring expense	14,351	55,843
Other obligations	2,988	4,688
Total current liabilities	100,243	153,745
Accrued restructuring expense	28,631	—
Collaborator development loan	19,997	19,997
Deferred revenue	851	18,345
Other obligations	—	2,925
Convertible subordinated notes (due September 2007)	42,102	82,552
Convertible subordinated notes (due February 2011)	117,998	232,448
Total liabilities	309,822	510,012
Commitments and contingencies (Note J and Note R)		
Stockholders' equity:		
Preferred stock, $0.01 par value; 1,000,000 shares authorized; none issued and outstanding at December 31, 2005 and 2004, respectively	—	—
Common stock, $0.01 par value; 200,000,000 shares authorized; 108,153,149 and 80,764,904 shares issued and outstanding at December 31, 2005 and 2004, respectively	1,081	807
Additional paid-in capital	1,243,960	833,832
Deferred compensation, net	(13,408)	(11,657)
Accumulated other comprehensive loss	(2,873)	(1,374)
Accumulated deficit	(989,584)	(786,167)
Total stockholders' equity	239,176	35,441
Total liabilities and stockholders' equity	$ 548,998	$ 545,453

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

VERTEX PHARMACEUTICALS INCORPORATED

Consolidated Statements of Operations

	Years Ended December 31,		
	2005	2004	2003
	(In thousands, except per share data)		
Revenues:			
Royalties	$ 32,829	$ 17,322	$ 9,002
Collaborative and other research and development revenues	128,061	85,395	60,139
Total revenues	160,890	102,717	69,141
Costs and expenses:			
Royalty payments	10,098	5,649	3,126
Research and development	248,540	192,162	199,636
Sales, general and administrative	43,990	42,139	39,082
Restructuring and other expense	8,134	17,574	91,824
Total costs and expenses	310,762	257,524	333,668
Loss from operations	(149,872)	(154,807)	(264,527)
Interest income	11,994	10,323	15,412
Interest expense	(17,326)	(18,317)	(17,298)
Loss on exchange of convertible subordinated notes	(48,213)	—	—
Loss on retirement of convertible subordinated notes	—	(3,446)	—
Loss from continuing operations	$ (203,417)	$ (166,247)	$ (266,413)
Income from discontinued operations:			
Gain on sales of assets	—	—	70,339
Loss from discontinued operations	—	—	(693)
Total income from discontinued operations	—	—	69,646
Net Loss	$ (203,417)	$ (166,247)	$ (196,767)
Basic and diluted loss per common share from:			
Continued operations	$ (2.28)	$ (2.12)	$ (3.46)
Discontinued operations	—	—	0.90
Basic and diluted net loss per common share	$ (2.28)	$ (2.12)	$ (2.56)
Basic and diluted weighted average number of common shares outstanding	89,241	78,571	77,004

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

VERTEX PHARMACEUTICALS INCORPORATED

Consolidated Statements of Stockholders' Equity and Comprehensive Loss

	Common Stock		Additional Paid-In Capital	Deferred Compensation	Accumulated Other Comprehensive Income (Loss)	Accumulated Deficit	Total Stockholders' Equity	Comprehensive Income (Loss)
	Shares	Amount						
					(in thousands)			
Balance, December 31, 2002	76,357	764	794,206	—	6,764	(423,153)	378,581	
Net change in unrealized holding gains/(losses) on marketable securities					(4,705)		(4,705)	$ (4,705)
Translation adjustments					631		631	631
Net loss						(196,767)	(196,767)	(196,767)
Comprehensive loss								$ (200,841)
Issuances of common stock:								
Benefit plans	1,668	16	16,039	(1,128)			14,927	
Equity compensation for services rendered			162				162	
Amortization of deferred compensation				16			16	
Balance, December 31, 2003	78,025	780	810,407	(1,112)	2,690	(619,920)	192,845	
Net change in unrealized holding gains/(losses) on marketable securities					(4,269)		(4,269)	$ (4,269)
Translation adjustments					205		205	205
Net loss						(166,247)	(166,247)	(166,247)
Comprehensive loss								$ (170,311)
Issuances of common stock:								
Benefit plans	2,740	27	23,425	(12,206)			11,246	
Amortization of deferred compensation				1,661			1,661	
Balance, December 31, 2004	80,765	807	833,832	(11,657)	(1,374)	(786,167)	35,441	
Net change in unrealized holding gains/(losses) on marketable securities					(868)		(868)	$ (868)
Translation adjustments					(631)		(631)	(631)
Net loss						(203,417)	(203,417)	(203,417)
Comprehensive loss								$ (204,916)
Issuances of common stock:								
Equity Offering	13,513	135	165,251				165,386	
Convertible Subordinated Notes exchanged	10,578	106	203,424				203,530	
Benefit plans	3,297	33	41,453	(6,172)			35,314	
Amortization of deferred compensation				4,421			4,421	
Balance, December 31, 2005	108,153	1,081	1,243,960	(13,408)	(2,873)	(989,584)	239,176	

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

VERTEX PHARMACEUTICALS INCORPORATED

Consolidated Statements of Cash Flows

	Years Ended December 31,		
	2005	2004	2003
	(In thousands)		
Cash flows from operating activities:			
Net loss	$ (203,417)	$ (166,247)	$ (196,767)
Net income from discontinued operations	—	—	(69,646)
Loss from continuing operations	$ (203,417)	$ (166,247)	(266,413)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization	27,289	29,640	23,438
Non-cash based compensation expense	7,530	4,165	3,146
Non-cash restructuring and other expense	—	—	4,395
Loss on disposal of property and equipment	344	43	116
Realized loss (gain) on marketable securities	60	(423)	(1,249)
Charge for exchange of convertible subordinated notes	48,213	—	—
Charge for retirement of a portion of 2007 convertible subordinated notes	—	3,446	—
Changes in operating assets and liabilities:			
Accounts receivable	(8,704)	(4,567)	1,574
Prepaid expenses and other current assets	(802)	817	594
Accounts payable	(450)	(5,646)	(2,151)
Accrued expenses and other current liabilities	4,262	2,362	(4,050)
Accrued restructuring and other expense	(12,861)	(13,683)	69,526
Accrued interest	268	1,407	—
Deferred revenue	(33,786)	6,569	4,683
Net cash used in operating activities from continuing operations	(172,054)	(142,117)	(166,391)
Net cash used in operating activities from discontinued operations	—	—	(1,232)
Net cash used in operating activities	(172,054)	(142,117)	(167,623)
Cash flows from investing activities:			
Purchases of marketable securities	(236,489)	(148,506)	(555,842)
Sales and maturities of marketable securities	243,410	292,351	593,998
Expenditures for property and equipment	(16,959)	(12,538)	(17,351)
Restricted cash	8,365	(23,786)	30
Investments and other assets	(59)	(136)	1,603
Net cash provided by investing activities from continuing operations	(1,732)	107,385	22,438
Net cash provided by investing activities from discontinued operations	—	—	97,147
Net cash provided by investing activities	(1,732)	107,385	119,585
Cash flows from financing activities:			
Issuances of common stock from employee benefit plans, net	32,205	8,742	11,959
Issuances of common stock from stock offering, net	165,386	—	—
Proceeds from notes payable, capital lease and loan obligations	—	—	27,460
Principal payments on capital leases and other obligations	—	(12,563)	(1,951)
Issuance costs related to 2011 notes	(16)	(4,805)	—
Exchange costs	(119)	—	—
Net cash provided by (used in) financing activities from continuing operations	197,456	(8,626)	37,468
Net cash used in financing activities from discontinued operations	—	—	—
Net cash provided by (used in) financing activities	197,456	(8,626)	37,468
Effect of changes in exchange rates on cash	(631)	205	631
Net increase (decrease) in cash and cash equivalents	23,039	(43,153)	(9,939)
Cash and cash equivalents — beginning of period	55,006	98,159	108,098
Cash and cash equivalents — end of period	$ 78,045	$ 55,006	$ 98,159
Supplemental disclosure of cash flow information:			
Cash paid for interest	$ 16,077	$ 15,597	$ 15,896
Cash paid for taxes	$ —	$ —	$ —

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

A. The Company

Vertex Pharmaceuticals Incorporated ("Vertex" or the "Company") is a biotechnology company in the business of discovering, developing and commercializing small molecule drugs for the treatment of serious diseases. The Company intends to continue investing in and building capabilities in research, development and commercialization of pharmaceutical products while it advances its product candidates to market. Vertex earns royalty revenues from the sale of Lexiva/Telzir (fosamprenavir calcium), a Vertex-discovered product for the treatment of HIV infection, and conducts certain educational activities for this product in collaboration with GlaxoSmithKline plc.

The Company's corporate strategy is to retain principal responsibility for the development and commercialization of some of its proprietary drug candidates in certain major markets, concentrating a significant part of its overall development and commercialization resources on those drug candidates. Vertex intends to rely on collaborators to conduct development and commercialization of certain of its other drug candidates either worldwide or in markets upon which the Company is not currently focused. The Company is concentrating most of its drug development resources at the present time on three compounds: VX-950 for the treatment of HCV infection; VX-702 for the treatment of RA; and VX-770 for the treatment of cystic fibrosis.

Collaborations are a key component of Vertex's corporate strategy. Collaborations provide Vertex with financial support and other valuable resources for its research programs, development resources for its clinical drug candidates, and marketing and sales support for its products and product candidates. Vertex currently has drug candidates in development under collaborations with GlaxoSmithKline plc, Merck & Co., Inc., Cystic Fibrosis Foundation Therapeutics Incorporated, Novartis Pharma AG, Mitsubishi Pharma Corp., Kissei Pharmaceutical Co., Ltd., and Avalon Pharmaceuticals, Inc.

Vertex is subject to risks common to companies in the biotechnology industry including, but not limited to, rapid technological change and competition, uncertain protection of proprietary technology, clinical trial uncertainty, dependence on collaborative relationships, share price volatility, the need to obtain additional funding, uncertainties relating to pharmaceutical pricing and reimbursement, limited experience in manufacturing, sales and marketing, potential product liability and the need to comply with government regulations. The Company expects to incur operating losses for the foreseeable future, as a result of expenditures for its research and development programs.

B. Accounting Policies

Basis of Presentation

The consolidated financial statements reflect the operations of the Company and its wholly owned subsidiaries.

The assets of the Company's Discovery Tools and Services business sold in March 2003 and December 2003 represent a component of Vertex's business that, beginning in 2002, had separately identifiable cash flows. As such, pursuant to SFAS No. 144, "Accounting for the Impairment of Long-Lived Assets" ("SFAS No. 144"), the consolidated statements of operations and of cash flows have been restated to show the results of operations and cash flows of the assets sold as discontinued operations for the twelve months ended December 31, 2003. Please refer to Note C, "Sale of Assets," for further information.

All significant intercompany balances and transactions have been eliminated.

The Company operates in one segment, Pharmaceuticals, and all revenues are from United States operations.

Reclassification in the Preparation of Financial Statements

Certain amounts in prior years' financial statements have been reclassified to conform to the current presentation. The Company reclassified certain marketable securities on the 2004 consolidated balance sheets as long-term assets to conform to the 2005 presentation. These reclassifications had no effect on the reported net loss.

Use of Estimates

The preparation of consolidated financial statements in conformity with accounting principles generally accepted in the United States of America 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 reported amounts of revenues and expenses during the reported periods. Significant estimates in these consolidated financial statements include restructuring and other expense, revenue recognition, research and development expenses and investments. Changes in estimates are recorded in the period in which they become known. The Company bases its estimates on historical experience and various other assumptions that management believes to be reasonable under the circumstances. Actual results could differ from those estimates.

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. Cash equivalents consist principally of money market funds, municipal bonds, and debt securities. Changes in cash and cash equivalents may be effected by shifts in investment portfolio maturities as well as by actual cash receipts and disbursements.

Marketable Securities

Marketable securities consist of investments in high-grade corporate bonds, asset-backed securities, municipal bond securities and U.S. government agency securities that are classified as available-for-sale. The Company classifies marketable securities available to fund current operations as current assets on the balance sheet. 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 to hold them (a) until the carrying value is recovered and (b) such holding period may be longer than one year. Marketable securities are stated at fair value with their unrealized gains and losses included as a component of accumulated other comprehensive loss, which is a separate component of stockholders' equity, until such gains and losses are realized. The fair value of these securities is based on quoted market prices. If a decline in the fair value is considered other-than-temporary, based on available evidence, the unrealized loss is transferred from other comprehensive loss to the consolidated statement of operations. There were no write-downs of marketable securities in 2005, 2004 or 2003. Realized gains and losses are determined on the specific identification method and are included in interest income.

Investments

Investments at December 31, 2005 and 2004 include long-term investments recorded using the cost method of accounting. When the Company holds an ownership interest of less than 20%, and does not have the ability to exercise significant influence over the investment entity's operating activities, the Company accounts for its investment using the cost method. If any adjustment to the fair value of an investment reflects a decline in the value of that investment below its cost, the Company considers the evidence available to it, including the duration and extent to which the market value of the investment has been less than cost, to evaluate the extent to which the decline is other-than-temporary. If the decline is considered other-than-temporary, the cost basis of the investment is written down to fair value as a new cost basis and the amount of the write-down is included in the Company's consolidated statements of operations. There were no write-downs of investment in 2005 or 2004.

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 in highly rated financial institutions, and, by policy, limits the amounts of credit exposure to any one financial institution. These amounts at times may exceed federally insured limits. The Company has not experienced any credit losses in these accounts and does not believe it is exposed to any significant credit risk on these funds. The Company has no foreign exchange contracts, option contracts or other foreign exchange hedging arrangements.

To date, the Company's revenue has been generated from a limited number of customers in the biotechnology and pharmaceuticals industries in the U.S., Europe and Japan. In 2005 the Company had significant revenue transactions with Novartis, GlaxoSmithKline and Merck which accounted for 33%, 33% and 15% respectively, of the Company's total revenue. In 2004, revenue transactions with Novartis and GlaxoSmithKline accounted for 49% and 19%, respectively, of the Company's total revenue. In 2003, revenue transactions with Novartis and GlaxoSmithKline represented 64% and 17%, respectively, of the Company's total revenue.

Receivables from GlaxoSmithKline and Novartis represented approximately 46% and 22%, respectively, of the Company's accounts receivable balance at December 31, 2005. Receivables from GlaxoSmithKline and Mitsubishi represented approximately 46% and 15%, respectively, of the Company's accounts receivable balance at December 31, 2004. Management believes that credit risks associated with these collaborators are not significant.

Property and Equipment

Property and equipment are recorded at cost. Depreciation and amortization are provided using the straight-line method over the lesser of the lease terms or the estimated useful lives of the related assets, generally four to seven years for furniture and equipment and three to five years for computers and software. Leasehold improvements are amortized over the lesser of the useful life of the improvements or the remaining life of the lease. Major additions and betterments are capitalized; maintenance and repairs, which do not improve or extend the life of the respective assets, are charged to operations. When assets are retired or otherwise disposed of, the assets and related allowances for depreciation and amortization are eliminated from the accounts and any resulting gain or loss is reflected in the Company's consolidated statements of operations.

Long-Lived Assets

The Company accounts for the impairment and disposition of long-lived assets in accordance with Statement of Financial Accounting Standards No. 144, "Accounting for the Impairment or Disposal of Long-Lived Assets" ("SFAS 144"). In accordance with SFAS No. 144, management assesses the potential impairments of its long-lived assets whenever events or changes in circumstances indicate that an asset's carrying value may not be recoverable. If the carrying value exceeds the undiscounted future cash flows estimated to result from the use and eventual disposition of the asset the Company writes down the asset to its estimated fair value.

Stock-Based Compensation

In accordance with Statements of Financial Accounting Standards No. 148, "Accounting for Stock-Based Compensation, Transition and Disclosure" ("SFAS 148"), for periods prior to January 1, 2006, the Company adopted the disclosure-only provisions of Statements of Financial Accounting Standards No. 123, "Accounting for Stock-Based Compensation" ("SFAS 123") and also applies Accounting Principles Board Opinion No. 25, "Accounting for Stock Issued to Employees" ("APB 25") and related interpretations in accounting for all stock awards granted to employees. Under APB 25, provided that other criteria are met, when the exercise price of options or the issue price of restricted shares granted to employees equals the market price of the common stock on the date of the grant, no compensation cost is required.

At December 31, 2005, the Company had one Employee Stock Purchase Plan ("ESPP") and three stock-based employee compensation plans, which are described more fully in Note N, "Common and Preferred Stock." For the years ended December 31, 2005, 2004 and 2003, the Company recorded $4,421,000, $1,661,000 and $16,000, respectively, in net compensation expense related to restricted shares issued to employees. The net expense of $4,421,000 for the twelve months ended December 31, 2005 included approximately $840,000 of expense related to the accelerated vesting of restricted stock awards in accordance with executives' severance agreements. Additionally, for the year ended December 31, 2005, the Company recorded $211,000 in compensation expense related to stock and option grants in accordance with executives' severance agreements. No additional stock-based employee compensation cost related to stock options is reflected in the Company's reported net loss, as all options granted under the plans had an exercise price equal to the market value of the underlying common stock on the date of grant. For stock options granted to non-employees, the Company recognizes compensation costs in accordance with the requirements of SFAS 123, which requires that companies recognize compensation expense for grants of stock, stock options and other equity instruments based on fair value.

The following table illustrates the effect on net loss and net loss per share if the fair value recognition of SFAS 123 had been applied to the Company's stock-based employee compensation. Employee stock-based compensation expense is amortized on a staight-line basis, as our valuation of options subject to SFAS 123 assumes a single weighted-average expected-life for each award.

Assumptions used to calculate the fair value of employee stock based compensation are detailed in Note N, "Common and Preferred Stock."

	Year Ended December 31,		
	2005	2004	2003
	(In thousands, except per share data)		
Net loss attributable to common shareholders, as reported	$ (203,417)	$ (166,247)	$ (196,767)
Add: Employee stock-based compensation expense included in net loss	4,632	1,661	16
Deduct: Total stock-based employee compensation expense determined under the fair value based method for all awards	(38,217)	(39,504)	(51,180)
Pro forma net loss	$ (237,002)	$ (204,090)	$ (247,931)
Basic and diluted net loss per common share, as reported	$ (2.28)	$ (2.12)	$ (2.56)
Basic and diluted net loss per common share, pro forma	$ (2.66)	$ (2.60)	$ (3.22)

Restructuring and Other Expense

The Company records costs and liabilities associated with exit and disposal activities, as defined in Statements of Financial Accounting Standards No. 146, "Accounting for Costs Associated with Exit or Disposal Activities" ("SFAS 146"), at fair value in the period the liability is incurred. In periods subsequent to initial measurement, changes to a liability are measured using the credit-adjusted risk-free discount rate applied in the initial period. In 2005, 2004 and 2003, the Company recorded costs and liabilities for exit and disposal activities related to a restructuring plan in accordance with SFAS 146. The liability is evaluated and adjusted as appropriate on at least a quarterly basis for changes in circumstances. Please refer to Note D, "Restructuring and Other Expense," for further information.

Revenue Recognition

The Company recognizes revenue in accordance with the Securities and Exchange Commission's ("SEC") Staff Accounting Bulletin No. 101, "Revenue Recognition in Financial Statements" ("SAB 101"), as amended by SEC Staff Accounting Bulletin No. 104, "Revenue Recognition," ("SAB 104") and for revenue arrangements entered into after June 30, 2003, Emerging Issues Task Force Issue No. 00-21, "Revenue Arrangements with Multiple Deliverables" ("EITF 00-21").

The Company's revenues are generated primarily through collaborative research, development and commercialization agreements. The terms of the agreements typically include payment to Vertex of non-refundable up-front license fees, funding of research and development efforts, milestone payments and/or royalties on product sales.

Agreements containing multiple elements are divided into separate units of accounting if certain criteria are met, including whether the delivered element has stand-alone value to the customer and whether there is objective and reliable evidence of fair value of the undelivered obligation(s). The consideration received is allocated among the separate units based on their respective fair values or the residual method, and the applicable revenue recognition criteria are applied to each of the separate units.

The Company recognizes revenues from non-refundable, up-front license fees on a straight-line basis over the contracted or estimated period of performance, which is typically the research or

development term. Research and development funding is recognized as earned, ratably over the period of effort.

Substantive milestones are recognized as earned when the corresponding payment is reasonably assured and the Company has evidence of fair value for its remaining obligations. Substantive milestones are recognized over the period of performance when the corresponding payment is reasonably assured but the Company does not have fair value for its remaining obligations. This typically results in a portion of the milestone payment being recognized as revenue at the date the milestone is achieved, which portion is equal to the applicable percentage of the performance period that has elapsed as of the date the milestone is achieved, with the balance being deferred and recognized over the remaining period of performance. The Company evaluates whether milestones are substantive at the inception of the agreement based on the contingent nature of the milestone, specifically reviewing factors such as the technological risk that must be overcome as well as the level of effort and investment required to achieve the milestone. Milestones that are not considered substantive and do not meet the separation criteria are accounted for as license payments and recognized on a straight-line basis over the remaining period of performance.

Payments received after performance obligations are met completely are recognized when earned.

Royalty revenue is recognized based upon actual and estimated net sales of licensed products in licensed territories as provided by the licensee and is recognized in the period the sales occur. Differences between actual royalty revenues and estimated royalty revenues, which have not historically been significant, are reconciled and adjusted for in the quarter they become known.

Research and Development Costs

All research and development costs, including amounts funded by research collaborators, are expensed as incurred. Research and development expenses are comprised of costs incurred in performing research and development activities, including salaries and benefits; laboratory supplies; contract services, including clinical trial costs; and infrastructure costs, including facilities costs and depreciation. The Company's collaborators have agreed to fund portions of the Company's research and development programs related to specific research targets and drug candidates, including, in 2005, VX-950, VX-702, kinases and certain cystic fibrosis research targets; in 2004, VX-950, kinases, caspase inhibitors, and certain cystic fibrosis research targets; and in 2003, VX-702, kinases, caspase inhibitors, and certain cystic fibrosis research targets. The following table details the aggregate amount of research and development expenses for the three years ended December 31, 2005, 2004, and 2003 (in thousands) for programs that are funded, in total or in part, by collaborators ("Collaborator-sponsored") and for programs that the Company funds entirely with its own resources ("Company-sponsored"):

	2005			2004			2003		
	Research	Development	Total	Research	Development	Total	Research	Development	Total
Collaborator-sponsored	$ 68,194	$ 72,101	$ 140,295	$ 62,181	$ 28,294	$ 90,475	$ 62,162	$ 19,935	$ 82,097
Company-sponsored	52,585	55,660	108,245	51,095	50,592	101,687	51,273	66,266	117,539
Total	$ 120,779	$ 127,761	$ 248,540	$ 113,276	$ 78,886	$ 192,162	$ 113,435	$ 86,201	$ 199,636

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 weighted available evidence, it is more likely than not that some or all of the deferred tax assets will not be realized.

Debt Issuance Costs

Debt issuance costs incurred to complete Vertex's convertible subordinated note offerings are deferred and included in other assets on the consolidated balance sheets. The costs are amortized based on the effective interest method over the term of the related debt issuance. The amortization expense is included in interest expense on the consolidated statements of operations. Unamortized costs related to exchanged debt is reversed from other assets to additional paid-in capital.

Stock Offering Costs

Expenses incurred in connection with common stock issuances are recorded as an offset to additional paid-in capital on the consolidated balance sheets.

Comprehensive Loss

Comprehensive loss consists of net loss and other comprehensive loss, which includes foreign currency translation adjustments and unrealized gains and losses on certain marketable securities. For purposes of comprehensive loss disclosures, the Company does not record tax provisions or benefits for the net changes in foreign currency translation adjustment, as the Company intends to permanently reinvest undistributed earnings in its foreign subsidiary.

Foreign Currency Translation

The functional currency of the Company's foreign subsidiary is the local currency. Assets and liabilities of the foreign subsidiary are re-measured into U.S. dollars at rates of exchange in effect at the end of the year. Revenue and expense amounts are re-measured using the average exchange rates for the period. Net unrealized gains and losses resulting from foreign currency translation are included in other comprehensive loss, which is a separate component of stockholders' equity. Included in other comprehensive loss is a net unrealized loss related to foreign currency translation of $18,000 at December 31, 2005 and a net unrealized gain related to foreign currency translation of $613,000 at December 31, 2004.

Basic and Diluted Net Loss per Common Share

Basic net loss per share is based upon the weighted average number of common shares outstanding during the period. Diluted net loss per share 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 not anti-dilutive. Common equivalent shares result from the 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), the assumed conversion of convertible notes and the vesting of unvested restricted shares of common stock. Common equivalent shares have not been included in the net loss per share calculations because their effect would have

been anti-dilutive. Total potential gross common equivalent shares consisted of the following (in thousands, except per share amounts):

	At December 31,		
	2005	2004	2003
Stock Options	14,669	15,820	16,802
Weighted-average exercise price (per share)	$ 22.84	$ 22.67	$ 23.42
Convertible Notes	8,354	16,454	3,414
Weighted-average conversion price (per share)	$ 19.16	$ 19.15	$ 92.26
Unvested restricted shares	1,521	1,399	125

New Accounting Pronouncements

In December 2004, the Financial Accounting Standards Board ("FASB") issued FASB Statement No. 123(R), "Share-Based Payments" ("FASB 123(R)"). FASB 123(R) revises FASB Statement No. 123, "Accounting for Stock-Based Compensation" ("FASB 123"), supersedes APB Opinion No. 25, "Accounting for Stock Issued to Employees," ("APB 25") and amends FASB Statement No. 95, "Statement of Cash Flows." FASB 123(R) requires companies to expense the fair value of employee stock options and other forms of stock-based compensation over the employees' service periods. Compensation cost is measured at the fair value of the award at the grant date and is adjusted to reflect actual forfeitures and the outcome of certain conditions. The fair value of an award is not re-measured after its initial estimation on the grant date.

Vertex is required to comply with FASB 123(R) beginning January 1, 2006 (the "Effective Date"). The Company will apply the Modified Prospective Method of adoption in its application of FASB 123(R). Under this method, compensation cost is recognized beginning with the Effective Date (a) based on application of the requirements of FASB 123(R) to all share-based payments granted after the Effective Date and (b) based on application of the requirements of FASB 123 to all awards granted to employees prior to the Effective Date of FASB 123(R) that remain unvested on the Effective Date.

As permitted by FASB 123, the Company currently accounts for share-based payments to employees using APB 25's intrinsic value method, and therefore generally recognize no compensation cost for employee stock options. Accordingly, the adoption of FASB 123(R)'s fair value method will have a significant impact on the result of operations, although it will have no impact on the overall financial position. In 2006 the Company expects to record approximately $34 million in compensation expense in connection with the adoption of FASB 123(R). The impact of adoption of FASB 123(R) beyond fiscal 2006 cannot be predicted at this time because it will depend on our stock price and the amount of share-based payments granted in future periods, as well as a number of complex and subjective valuation assumptions, including, but not limited to, the volatility of our stock price and employee stock option exercise behaviors. However, had the Company adopted FASB 123(R) in prior periods, the effect would have approximated the impact of FASB 123 as described in "Stock-Based Compensation", above, in this Note B.

In May 2005, the FASB issued SFAS No. 154, "Accounting Changes and Error Corrections ("SFAS 154")." SFAS No. 154 replaces APB Opinion No. 20, "Accounting Changes" and SFAS No. 3, "Reporting Accounting Changes in Interim Financial Statements." SFAS No. 154 requires retrospective application to prior periods' financial statements of changes in accounting principle, unless it is impractible to determine either the period-specific effects or the cumulative effect of the change. The

Company does not expect the adoption of SFAS No. 154 on January 1, 2006 to have a material impact on its consolidated financial statements.

In November 2005, FASB issued FSP FAS 115-1 and FAS 124-1, "The Meaning of Other-Than-Temporary Impairment and Its Application to Certain Investments" ("FSP FAS 115-1"), which provides guidance on determining when investments in certain debt and equity securities are considered impaired, whether an impairment is other-than-temporary, and on measuring such impairment loss. FSP FAS 115-1 also includes accounting considerations subsequent to the recognition of an other-than-temporary impairment and requires certain disclosures about unrealized losses that have not been recognized as other-than-temporary impairments. FSP FAS 115-1 is required to be applied to reporting periods beginning after December 15, 2005. The Company is required to adopt FSP FAS 115-1 in the first quarter of 2006. The Company does not expect the adoption of this statement to have a material impact on the Company's consolidated results of operations or financial condition.

C. Sale of Assets

In March and December 2003, in two independent transactions, the Company sold the assets of its Discovery Tools and Services business. The Discovery Tools and Services business specialized in assay development, screening services, instrumentation development and sales and the manufacture and sale of proteins, reagents and probes. As a result of these sales, the Company now operates in one operating segment, Pharmaceuticals.

On March 28, 2003, Vertex completed the sale of certain assets of the Discovery Tools and Services business, including certain proprietary reagents, probes and proteins and certain biochemical and cellular assay capabilities, to Invitrogen Corporation ("PanVera Asset Sale"). Substantially all of the assets sold were owned by Vertex's wholly-owned subsidiary, PanVera LLC ("PanVera"). In connection with the sale, Mirus Corporation ("Mirus") exercised a right of first refusal with respect to shares of Mirus owned by PanVera. Additionally, on the same date, Mirus acquired certain of PanVera's assets. The aggregate gross consideration received by PanVera for the assets conveyed to Invitrogen and Mirus was approximately $97 million in cash and assumption of certain liabilities.

In connection with the sale, Vertex obtained a license from Invitrogen to make and use the reagents and probes sold to Invitrogen, solely for its drug discovery activities, conducted independently and with collaborators, but has agreed that it will not engage in the business of providing reagents, probes or assay development services to third parties for a term of five years. Vertex also agreed to purchase a minimum of $3 million of specified products annually from Invitrogen for three years after the completion of the sale. The prices of the products within the purchase commitment approximate fair value. The sale did not include the instrumentation assets of the Discovery Tools and Services business, which were historically managed both financially and operationally together with the assets sold on March 28, 2003.

The Company recorded a gain on the PanVera Asset Sale of approximately $69 million. The gain was recorded net of transaction costs and certain accruals and receivables established for transaction bonuses payable by Vertex to former employees meeting certain employment requirements, an obligation in connection with certain annual contractual license fees under a customer agreement, estimated losses on the three-year purchase commitment for required payments in excess of the fair value of products expected to be purchased and an adjustment based upon the net book value of the assets sold on the closing date. Vertex has not recorded any income tax liability associated with the gain on the sale; operating losses were used to offset the taxable income generated from the sale. Accruals recorded in connection with the sale are included in other obligations, current, on the consolidated balance sheets.

On December 3, 2003, Vertex sold the remaining instrumentation assets of its Discovery Tools and Services business to Aurora Discovery, Inc., a new company formed by Telegraph Hill Partners, LP and certain former employees of Vertex, for approximately $4.3 million and the assumption of certain liabilities. The assets sold were used to develop and commercialize liquid and cell-dispensing instruments that are used in high-throughput drug discovery screening and large-scale, automated molecular biology. Vertex has retained non-exclusive licenses to use the instrumentation technologies sold in its drug discovery research. The Company recorded a $1.0 million gain on the sale. The gain was recorded net of transaction costs. The Company did not record any income tax liability associated with the sale in December 2003; operating losses were used to offset the taxable income generated from the sale.

The combination of the Discovery Tools and Services assets sold in March 2003 and in December 2003 represents a component of the Company's business that, beginning in 2002, was managed separately both financially and operationally.

In accordance with SFAS No. 144, "Accounting for the Impairment of Long-Lived Assets" ("SFAS No. 144"), the results of operations and cash flows of the assets sold have been reclassified in the consolidated financial statements under the heading "discontinued operations" for the twelve months ended December 31, 2003. The reclassification of the amounts to discontinued operations has been prepared using certain estimates and assumptions deemed appropriate based upon information available. Amounts reclassified to discontinued operations are not necessarily indicative of what revenues, expenses or income would have been had the business operated on a stand-alone basis.

Income from discontinued operations for the twelve months ended December 31, 2003 is comprised of the following revenue and expenses (in thousands):

	Year Ended December 31, 2003
Revenues from discontinued operations	$ 11,574
Expenses from discontinued operations	12,267
Gain from sale of discontinued operations	70,339
Income from discontinued operations	$ 69,646

D. Restructuring and Other Expense

On June 10, 2003, Vertex adopted a plan to restructure its operations to coincide with its increasing internal emphasis on advancing drug candidates through clinical development to

commercialization. The restructuring was designed to re-balance the Company's relative investments in research and development to better support the Company's long-term objective of becoming a profitable pharmaceutical company. 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. Based on developments in the Company's clinical pipeline in the second quarter of 2005, the Company revised its assessment of its real estate requirements. The Company now expects to occupy approximately 120,000 square feet of the facility subject to the Kendall Square lease (the "Kendall Square Facility") in the future. The Company currently has sublease arrangements in place for the remaining rentable square footage of the Kendall Square Facility.

For the twelve months ended December 31, 2005, the Company recorded net restructuring expense of $8.1 million. This net expense includes a $10.0 million credit to the restructuring accrual made when the Company decided to occupy and use a portion of the Kendall Square Facility, which was offset by (i) the estimated incremental net ongoing lease obligations associated with the portion of the Kendall Square that the Company does not intend to occupy and (ii) imputed interest costs relating to the restructuring liability. The portion of the $18.2 million additional charge in 2005 that was for incremental lease obligations was related to the revision of certain key estimates and assumptions about operating costs, including real estate taxes associated with the portion of the Kendall Square Facility that the Company does not intend to occupy.

The activity related to restructuring expense for the twelve months ended December 31, 2005 is as follows (in thousands):

	Accrual as of December 31, 2004	Cash Payments in 2005	Cash received from subleases in 2005	Credit for portion of facility Vertex expects to occupy in 2005	Additional Charge in 2005	Accrual as of December 31, 2005
Lease restructuring expense	$ 55,843	$ (24,229)	$ 3,234	$ (10,018)	$ 18,152	$ 42,982

During the twelve months ended December 31, 2004, the Company recorded $17.6 million of additional restructuring expense, which primarily resulted from the revision of estimates and assumptions about when subtenants would be identified and secured and imputing an interest charge for the related restructuring liability.

The activity related to restructuring expense for the twelve months ended December 31, 2004 is as follows (in thousands):

	Accrual as of December 31, 2003	Cash Payments in 2004	Cash received from sublease, net of operating costs	Additional Charge in 2004	Accrual as of December 31, 2004
Lease restructuring expense and other operating lease expense	$ 69,526	$ (31,550)	$ 293	$ 17,574	$ 55,843

The Company recorded restructuring and other related expenses of $91.8 million for the twelve months ended December 31, 2003. The $91.8 million includes $78.7 million of lease restructuring

expense, $6.0 million of lease operating expense incurred prior to the decision not to occupy the Kendall Square Facility, $2.6 million for severance and related employee transition benefits and $4.5 million for a write-off of leasehold improvements and other assets.

The activity related to restructuring and other expense for the twelve months ended December 31, 2003 is presented below (in thousands):

	Charge for the Twelve Months Ended December 31, 2003	Cash Payments in 2003	Non-cash Write-off in 2003	Accrual as of December 31, 2003
Lease restructuring expense 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 accordance with SFAS 146, the Company's initial estimate of its liability for its net ongoing costs associated with the Kendall Square Lease obligation was recorded in the second quarter of 2003 at fair value. The restructuring expense incurred from the second quarter of 2003 through the end of the first quarter of 2005 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 will continue to be estimated in accordance with SFAS 146, but will relate only to the portion of the building that the Company still does not intend to occupy. The lease obligations associated with the portion of the Kendall Square Facility that the Company expects to occupy and use for its operations are recorded as rental expense in the period incurred. The Company reviews its assumptions and estimates quarterly and updates its estimates of this liability as changes in circumstances require. As prescribed by SFAS 146, the expense and liability recorded is calculated using probability-weighted discounted cash-flows of the Company's estimated ongoing lease obligations, including contractual rental and build-out commitments, net of estimated sublease rentals, offset by related sublease costs.

In estimating the expense and liability under its Kendall Square lease obligation, the Company estimated the costs that would be incurred to satisfy its rental and build-out commitments under the lease (including operating costs), the time necessary to sublease the space, the projected sublease rental rates and the anticipated durations of subleases. The Company validates its estimates and assumptions through consultations with independent third parties having relevant expertise. The Company used a credit-adjusted risk-free rate of approximately 10% to discount the estimated cash flows. The Company will review its estimates and assumptions on at least a quarterly basis, until the termination of the Kendall Square lease, and will make whatever modifications management 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 liability, and the effect of any such adjustments could be material. Because the Company's estimate of the liability includes the application of a discount rate to reflect the time-value of money, the estimate of the liability will increase each quarter simply as a result of the passage of time. Changes to the Company's estimate of the liability are recorded as additional restructuring expense/(credit).

The severance, benefits and other related costs also were recorded in accordance with SFAS 146 in the second quarter of 2003. The Company specifically identified all employees whose employment was to be terminated and notified them prior to the end of the quarter in which the related charge was recorded. This restructuring plan resulted in a reduction of 111 employees, or 13% of the Company's

workforce, of which 66 were from the Cambridge site and 45 were from the San Diego site. Of the terminated employees, 59% were from research, 30% were from sales, general and administrative, who primarily supported research, and 11% were from development.

The restructuring accrual of $43.0 million at December 31, 2005 relates solely to the portion of the Kendall Square Facility that the Company does not intend to use for its operations and includes build-out commitments and other lease obligations, recorded at net present value.

Of the $43.0 million restructuring accrual at December 31, 2005, the Company classified $14.4 million as short-term and $28.6 million as long-term. The short-term portion of the accrual represents the amount the Company expects to pay out in 2006.

E. Marketable Securities

A summary of cash equivalents and marketable securities is shown below (in thousands):

December 31, 2005	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
Cash and cash equivalents				
Cash and money market funds	$ 73,288	1	—	$ 73,289
Corporate debt securities	4,757	—	1	4,756
Total cash and cash equivalents	$ 78,045	1	1	$ 78,045
Marketable securities				
Municipal bonds, due over 5 years	8,370	—	—	8,370
US government securities				
Due within 1 year	23,275	—	205	23,070
Due within 1 to 5 years	41,658	5	702	40,961
Total US government securities	64,933	5	907	64,031
Corporate debt securities				
Due within 1 year	184,841	10	753	184,098
Due within 1 to 5 years	72,622	5	1,212	71,415
Due over 5 years	1,553	—	2	1,551
Total corporate debt securities	259,016	15	1,967	257,064
Total marketable securities	$ 332,319	$ 20	$ 2,874	$ 329,465
Total cash, cash equivalents and marketable securities	$ 410,364	$ 21	$ 2,875	$ 407,510

December 31, 2004	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
Cash and cash equivalents				
Cash and money market funds	$ 55,006			$ 55,006
Total cash and cash equivalents	$ 55,006			$ 55,006
Marketable securities				
Municipal bond securities				
Due within 1 year	$ 2,016	$ —	$ 14	$ 2,002
US government securities				
Due within 1 year	15,854	—	73	15,781
Due within 1 to 5 years	47,899	34	472	47,461
Total US government securities	63,753	34	545	63,242
Corporate debt securities				
Due within 1 year	169,757	16	484	169,289
Due within 1 to 5 years	103,775	40	1,034	102,781
Total corporate debt securities	273,532	56	1,518	272,070
Total marketable securities	$ 339,301	$ 90	$ 2,077	$ 337,314
Total cash, cash equivalents and marketable securities	$ 394,307	$ 90	$ 2,077	$ 392,320

The Company has marketable securities of $283,112,000 and $331,240,000 classifed as current assets on the consolidated balance sheets as of December 31, 2005 and 2004, respectively, and $46,353,000 and $6,074,000, respectively, classified as long term assets on the consolidated balance sheets.

The Company reviews investments in municipal bond securities, US government securities, and corporate debt securities for other-than-temporary impairment whenever the fair value of an investment is less than 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 the ability and intent to hold the investment until a market price recovery and considers whether the evidence indicating the cost of the investment is recoverable outweighs evidence to the contrary. 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. The following table summarizes the fair value and gross unrealized losses related to marketable securities, aggregated by

investment category and length of time that individual securities have been in a continuous unrealized loss position as of December 31, (in thousands):

2005

	Less than 12 months		12 months or more		Total	
	Fair Value	Gross Unrealized Loss	Fair Value	Gross Unrealized Loss	Fair Value	Gross Unrealized Loss
U.S. government securities	$ 20,680	$ (180)	$ 40,916	$ (727)	$ 61,596	$ (907)
Corporate debt securities	151,521	(710)	94,573	(1,258)	246,094	(1,968)
Total	$ 172,201	$ (890)	$ 135,489	$ (1,985)	$ 307,690	$ (2,875)

2004

	Less than 12 months		12 months or more		Total	
	Fair Value	Gross Unrealized Loss	Fair Value	Gross Unrealized Loss	Fair Value	Gross Unrealized Loss
Municipal bond securities	—	—	$ 2,002	$ (14)	$ 2,002	$ (14)
U.S. government securities	57,894	(545)	—	—	57,894	(545)
Corporate debt securities	241,571	(1,414)	6,074	(104)	247,645	(1,518)
Total	$ 299,465	$ (1,959)	$ 8,076	$ (118)	$ 307,541	$ (2,077)

The Company owned 154 available-for-sale marketable securities at December 31, 2005. Of these 154 securities, there were 71 securities with losses for twelve months or more.

U.S. Government Securities

The unrealized losses on the investments in U.S. Treasury obligations and direct obligations of the U.S. Government agencies were caused by rising interest rates. Because the Company has the ability to hold these investments until a recovery of fair value, which may be maturity, the Company does not consider these investments to be other-than-temporarily impaired as of December 31, 2005 and 2004.

Corporate debt securities

The unrealized losses on the investments in corporate bonds were caused by rising interest rates. The corporate bonds held by the Company are high investment grade and there were no credit events on any of the corporate bonds held. Therefore, the Company does not believe that it is probable that it will be unable to collect all amounts due according to the contractual terms of the investments. It is expected that the corporate bonds will not be settled at a price less than the amortized cost of the investment. Because the Company has the ability to hold these investments until a recovery of fair

value, which may be maturity, the Company does not consider these investments to be other-than-temporarily impaired as of December 31, 2005 and 2004.

Gross realized gains and losses for 2005 were $15,000 and $75,000, respectively. Gross realized gains and losses for 2004 were $628,000 and $205,000, respectively. Gross realized gains for 2003 were $1,249,000. There were no gross realized losses for 2003. Maturities stated are effective maturities.

F. Restricted Cash

At December 31, 2005 and 2004, the Company held $41,482,000 and $49,847,000, respectively, in restricted cash. At December 31, 2005 and 2004 the balance was held in deposit with certain banks predominantly to collateralize conditional stand-by letters of credit in the names of the Company's landlords pursuant to certain operating lease agreements.

G. Property and Equipment

Property and equipment consist of the following at December 31 (in thousands):

	2005	2004
Furniture and equipment	$ 98,387	$ 90,893
Leasehold improvements	66,318	65,294
Computers	18,971	18,421
Software	18,683	16,411
Total property and equipment, gross	202,359	191,019
Less accumulated depreciation and amortization	147,826	126,794
Total property and equipment, net	$ 54,533	$ 64,225

Depreciation expense for the years ended December 31, 2005, 2004 and 2003 was $26,307,000, $28,353,000 and $27,988,000 respectively.

In 2005 and 2004, the Company wrote off certain assets that were fully depreciated and no longer utilized. There was no effect on the Company's net property and equipment. Additionally, the Company wrote off or sold certain assets that were not fully depreciated. The net loss on disposal of those assets was $344,000 for 2005 and $43,000 for 2004.

H. Investments

In accordance with the Company's policy, as outlined in Note B, "Accounting Policies," the Company assessed its investment in Altus Pharmaceuticals, Inc. ("Altus"), which it accounts for using the cost method, and determined that there had not been any adjustments to the fair values of that investment which would indicate a decrease in its fair value below the carrying value that would require the Company to write down the investment basis of the asset, as of December 31, 2005 and December 31, 2004. The Company's cost basis carrying value in its outstanding equity and warrants of Altus was $18,863,000 at December 31, 2005 and 2004.

Altus completed an initial public offering in January 2006. Vertex owns 817,749 shares of common stock and warrants to purchase 1,962,494 shares of common stock. In addition, the Company also holds 450,000 shares of redeemable preferred stock, which are not convertible into common stock and which are redeemable, at Vertex's option on or after December 31, 2010, or by Altus at any time. The Company is restricted from trading Altus securities for a period of six months following the initial public offering. Due to the public offering, in 2006 the Company will classify the common stock as an available-for-sale investment and record it at fair value, based on quoted market prices, with unrealized gains and losses included as a component of accumulated other comprehensive loss, which is a separate component of stockholders' equity, until such gains and losses are realized. The Company will continue to account for the warrants under the cost method of accounting until the end of the restricted trading period, at which time the warrants will be classified as derivatives with gains or losses based on the fair market value of the warrants included in the statement of operations. The Company will continue to account for the redeemable preferred stock under the cost method of accounting.

I. Accrued Expenses and Other Current Liabilities

Accrued expenses and other current liabilities consist of the following at December 31 (in thousands):

	2005	2004
Research and development contract costs	$ 20,098	$ 14,883
Payroll and benefits	15,832	11,114
Professional fees	4,816	5,658
Other	1,315	1,296
	$ 42,061	$ 32,951

J. Commitments

The Company leases its facilities and certain equipment under non-cancelable operating leases. The Company's leases have terms through April 2018. The term of the Kendall Square lease began January 1, 2003 and lease payments commenced in May 2003. The Company has an obligation, staged through 2006, to build-out the space into finished laboratory and office space. The lease will expire in 2018 and the Company has the option to extend the term for two consecutive terms of ten years each, ultimately expiring in 2038. The Company expects to occupy and use for its operations approximately 120,000 square feet of the Kendall Square Facility. The Company has sublease arrangements in place for the remaining rentable square footage of the Kendall Square Facility. See Note D, "Restructuring and Other Expense" for further information.

At December 31, 2005, future minimum commitments under facility operating leases with non-cancelable terms of more than one year (including commitments under the Kendall Square lease) are as follows (in thousands):

Year	Kendall Square Lease	Sublease income for Kendall Square Facility	Other Operating Leases	Total Operating Leases
2006	30,035	(7,418)	16,680	39,297
2007	21,794	(8,156)	16,052	29,690
2008	23,683	(8,156)	15,252	30,779
2009	23,748	(8,156)	11,488	27,080
2010	23,816	(8,156)	9,962	25,622
Thereafter	195,667	(6,213)	—	189,454
Total minimum lease payments	$ 318,743	$ (46,255)	$ 69,434	$ 341,922

Rental expense for the year ended December 31, 2005, was $20,427,000, which included $4,669,000 related to the space that the Company intends to occupy in the Kendall Square Facility. For the years ended December 31, 2004, and 2003, rental expense primarily related to facilities, excluding the Kendall Square lease, was $16,303,000, and $15,449,000, respectively.

The Company has future contractual commitments in connection with its research and development programs. For 2006 and 2007 the amount committed under these contracts is $1,035,000 and $75,000, respectively.

In connection with the PanVera Asset Sale in 2003 (see Note C, "Sale of Assets"), Vertex agreed to purchase a minimum of $3 million of certain specified products from Invitrogen annually for three years after the completion of the sale. The estimated losses on the three-year purchase commitment for anticipated payments in excess of the fair value of products expected to be purchased have been booked against the gain on the sale and recorded as a liability on the consolidated balance sheets.

K. Convertible Subordinated Notes

On February 13, 2004, the Company issued approximately $153.1 million in aggregate principal amount of 5.75% Convertible Senior Subordinated Notes due in February 2011 (the "February 2011 Notes") in exchange for an equal principal amount of its outstanding 5% Convertible Subordinated Notes due in September 2007 (the "2007 Notes"). On September 17, 2004, the Company issued approximately $79.3 million in aggregate principal amount of 5.75% Convertible Senior Subordinated Notes due in February 2011 (the "September 2011 Notes") in exchange for an equal principal amount of its 2007 Notes. The terms of the September 2011 Notes are identical to those of the February 2011 Notes (the February 2011 Notes and the September 2011 Notes are referred to together as the "2011 Notes").

The 2011 Notes are convertible, at the option of the holder, into common stock at a price equal to $14.94 per share, subject to adjustment under certain circumstances. The 2011 Notes bear interest at the rate of 5.75% per annum, and the Company is required to make semi-annual interest payments on the outstanding principal balance of the 2011 Notes on February 15 and August 15 of each year. On or after February 15, 2007, the Company may redeem the 2011 Notes at a redemption price equal to the principal amount plus accrued and unpaid interest, if any. The deferred issuance costs associated with

the issuance of the 2011 Notes, which are classified as long-term other assets, were approximately $3.0 million for the February 2011 Notes and $1.9 million for the September 2011 Notes.

The 2007 Notes are convertible, at the option of the holder, into common stock at a price equal to $92.26 per share, subject to adjustment under certain circumstances. The 2007 Notes bear interest at the rate of 5% per annum, and the Company is required to make semi-annual interest payments on the outstanding principal balance of the 2007 Notes on March 19 and September 19 of each year. The 2007 Notes are redeemable by the Company at any time at specific redemption prices if the closing price of the Company's common stock exceeds 120% of the conversion price for at least 20 trading days within a period of 30 consecutive trading days. The deferred issuance costs associated with the original sale of the 2007 Notes were $9.3 million.

As a result of the 2004 exchanges of the 2007 Notes for 2011 Notes, the Company recorded a charge on the retirement of $153.1 million in aggregate principal amount of the 2007 Notes in February 2004 in the amount of $2.5 million, and a charge on the retirement of $79.3 million in aggregate principal amount of the 2007 Notes in September 2004 in the amount of $1.0 million. These charges represent that portion of the unamortized deferred issuance costs applicable to the amount of 2007 Notes retired. For the year ended December 31, 2005, $1.0 million was amortized to interest expense for the issuance costs of the remaining 2007 Notes and the 2011 Notes. For the year ended December 31, 2004, $1.3 million was amortized to interest expense for the issuance costs of the 2007 Notes and the 2011 Notes. For the year ended December 31, 2003, $1.4 million was amortized to interest expense for the issuance costs associated with the 2007 Notes.

In September 2005, the Company issued approximately 2.5 million shares of common stock to certain holders of 2007 Notes in exchange for approximately $40.5 million in aggregate principal amount of those notes, plus accrued interest. As a result of the exchange, the Company incurred a non-cash charge of $36.3 million. This charge is related to the incremental shares issued in the transaction over the number that would have been issued upon conversion of the 2007 Notes under their original terms, at the original conversion price of $92.26. The following items related to the exchange were recorded as an offset to additional paid-in capital on the consolidated balance sheets: accrued interest of approximately $1.0 million; remaining unamortized issuance costs of the exchanged 2007 Notes of approximately $0.3 million; and $0.1 million of issuance costs of the common stock.

In the fourth quarter of 2005, the Company issued approximately 8.1 million shares of common stock to certain holders of 2011 Notes in exchange for approximately $114.5 million in aggregate principal amount of those notes, plus accrued interest. As a result of the exchange, the Company incurred a non-cash charge of $11.9 million. This charge is related to the incremental shares issued in the transaction over the number that would have been issued upon conversion of the 2011 Notes under their original terms, at the original conversion price of $14.94. The following items related to the exchange were recorded as an offset to additional paid-in capital on the consolidated balance sheets: accrued interest of approximately $2.0 million; remaining unamortized issuance costs of the exchanged 2011 Notes of approximately $1.8 million; and $0.2 million of issuance costs of the common stock.

At December 31, 2005, there was approximately $42.1 million in aggregate principal amount of the 2007 Notes and approximately $118.0 million in aggregate principal amount of the 2011 Notes outstanding. At December 31, 2005, the 2007 Notes and the 2011 Notes had a fair value of $40.5 million and $227.0 million, respectively, as obtained from a quoted market source.

L. Equity Offering

In June 2005, the Company completed a public offering of 13,512,500 shares of common stock, including the underwriters' over-allotment of 1,762,500 shares, at a price of $13.00 per share. This transaction resulted in net proceeds of approximately $165.4 million to the Company. The net proceeds include $10.3 million of stock offering costs which were recorded as an offset to additional paid-in capital on the consolidated balance sheets.

M. Income Taxes

For the years ended December 31, 2005, 2004 and 2003, there is no provision for income taxes included in the consolidated statements of operations.

The Company's federal statutory income tax rate for 2005, 2004, and 2003 was 34%. The Company has incurred losses from operations but has not recorded an income tax benefit for 2005, 2004, and 2003, as the Company has recorded a valuation allowance against its net operating losses and other net deferred tax assets due to uncertainties related to the realizability of these tax assets.

The difference between the Company's "expected" tax provision (benefit), as computed by applying the U.S federal corporate tax rate of 34% to (loss) before provision for income taxes, and actual tax is reconciled as follows (in thousands):

	2005	2004	2003
Loss before provision for income taxes	$ (203,417)	$ (166,247)	$ (196,767)
Expected tax benefit at 34%	$ (69,162)	$ (56,524)	$ (66,901)
State taxes, net of federal benefit	(12,754)	(10,424)	(12,337)
Unbenefited operating losses	64,262	66,983	78,730
Non-deductible expenses	17,450	40	36
Other	204	(75)	472
Income tax provision	$ —	$ —	$ —

For federal income tax purposes, as of December 31, 2005, the Company has net operating loss carryforwards of approximately $1,042,065,000, and $22,122,000 of tax credits, which may be used to offset future federal income and tax liability, respectively. For state income tax purposes, the Company has net operating loss carryforwards of approximately $576,315,000, and 8,819,000 of tax credits, which may be used to offset future state income and tax liability, respectively. These operating loss carryforwards began to expire in 2005, and the tax credit carryforwards began to expire in 2004. After consideration of all the evidence, both positive and negative, management has established a valuation allowance for the full amount of the 2005 net deferred tax asset since it is more likely than not that the net deferred tax asset will not be realized.

Deferred tax liabilities and assets 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 at December 31 were as follows (in thousands):

	2005	2004
Deferred Tax Assets:		
Net operating loss	$ 390,437	$ 303,332
Tax credit carryforwards	27,942	25,987
Property, plant and equipment	14,955	12,135
Deferred revenue	596	19,577
Capitalized R&D	21,471	27,351
Other	15,265	19,348
Gross Deferred Tax Asset	470,666	407,730
Valuation Allowance	(459,608)	(396,672)
Total Deferred Tax Asset	11,058	11,058
Deferred Tax Liabilities:		
Gain on Investment	(11,058)	(11,058)
Net Deferred Tax Asset/(Liability)	$ —	$ —

Of the $459,608,000 valuation allowance at December 31, 2005, $111,672,000 relates to deductions for nonqualified stock options, which will be credited to additional paid-in capital, if realized.

Ownership changes, as defined by Internal Revenue Code, may limit the amount of net operating losses and research and experimentation credit carryforwards that can be utilized annually to offset future taxable income and taxes payable.

N. Common and Preferred Stock

Common Stock

Stock and Option Plans

The Company has a 1991 Stock Option Plan (the "1991 Plan"), a 1994 Stock and Option Plan (the "1994 Plan") and a 1996 Stock and Option Plan (the "1996 Plan") (together, the "Plans"). Stock options may be granted under the Plans either as options intended to qualify as "incentive stock options" ("ISOs") under the Internal Revenue Code or as non-qualified stock options ("NQSOs"). Under the 1991 Plan, stock options may be granted to employees (including officers and directors who are employees) and to consultants of the Company (NQSOs only). Under the 1994 Plan and the 1996 Plan, stock rights, which may be (i) ISOs when Internal Revenue Code requirements are met, (ii) NQSOs, or (iii) shares of common stock or the opportunity to make a direct purchase of shares of common stock ("Stock Awards"), may be granted to employees (including officers and directors who are employees) and consultants, advisors and non-employee directors (NQSOs and stock awards only). Under the 1991 Plan and the 1994 Plan, ISOs may be granted at a price not less than the fair market value of the common stock on the date of the grant, and NQSOs may be granted at an exercise price established by the Management Development and Compensation Committee of the Board of Directors, which may be less than, equal to or greater than the fair value of the common stock on the date of the grant. Stock options granted under the 1996 Plan may not be granted at a price less than the fair market value of the common stock on the date of grant. Vesting is ratable over specified periods for all plans, is generally four or five years, and is determined by the Management Development and

Compensation Committee. ISOs granted under the Plans must expire not more than ten years from the date of grant.

The Company has reserved 8,000,000 shares under the 1991 Plan and 1994 Plan. The Company reserved 22,000,000 shares for issuance under the 1996 Plan, of which 5,500,000 were reserved during 2001 and 6,000,000 were reserved in 2002. At December 31, 2005, the Company had approximately 3,090,000 shares of common stock available for future grants under the 1996 Plan.

Consolidated stock option activity for the years ended December 31, 2005, 2004 and 2003 is as follows (shares in thousands):

	2005		2004		2003	
	Shares	Weighted Average Exercise Price	Shares	Weighted Average Exercise Price	Shares	Weighted Average Exercise Price
Outstanding at beginning of year	15,820	$ 22.67	16,802	$ 23.42	17,065	$ 25.73
Granted	2,054	14.11	1,554	10.35	3,465	14.59
Exercised	(2,198)	12.86	(732)	7.09	(914)	9.15
Canceled	(1,007)	24.07	(1,804)	25.37	(2,814)	31.00
Outstanding at end of year	14,669	$ 22.84	15,820	$ 22.67	16,802	$ 23.42
Options exercisable at year-end	10,347	$ 26.19	10,695	$ 24.34	10,205	$ 23.08
Weighted average fair value of options granted during the year		$ 7.11		$ 5.00		$ 9.46

The fair value of each option granted under the Plans during 2005, 2004 and 2003 was estimated on the date of grant using the Black-Scholes option pricing model with the following weighted average assumptions:

	2005	2004	2003
Expected life (years)	4.20	4.00	5.50
Expected volatility	60.00%	60.00%	75.00%
Risk-free interest rate	3.78%	2.95%	3.27%
Dividend yield	—	—	—

The following table summarizes information about stock options outstanding and exercisable at December 31, 2005 (shares in thousands):

Range of Exercise Prices	Options Outstanding			Options Exercisable	
	Number Outstanding	Weighted Average Remaining Contractual Life	Weighted Average Exercise Price	Number Exercisable	Weighted Average Exercise Price
$1.22–$10.19	1,567	6.30	$ 9.60	1,012	$ 9.68
10.28–11.40	1,608	8.71	$ 10.81	379	$ 10.84
11.53–13.63	1,803	4.10	$ 13.17	1,727	$ 13.20
13.67–15.60	2,821	4.57	$ 15.07	2,126	$ 14.92
15.66–17.16	2,056	7.44	$ 16.37	917	$ 16.04
17.19–22.75	826	5.96	$ 19.63	560	$ 19.20
22.93–24.66	1,477	5.91	$ 24.64	1,206	$ 24.64
24.69–70.75	2,352	5.11	$ 57.50	2,261	$ 58.61
71.62–132.26	155	4.68	$ 92.24	155	$ 92.24
135.49–135.49	4	4.15	$ 135.49	4	$ 135.49
$1.22–$135.49	14,669	5.85	$ 22.84	10,347	$ 26.19

Stock-Based Compensation

The Company grants restricted shares to employees, at a price per share equal to the par value of the Company's common stock, or $0.01 per share. In general, the restricted shares vest over four years in four equal annual installments.

During 2005, the Company issued approximately 616,000 restricted shares to employees. The shares had an average fair value on dates of grant of $13.77. At December 31, 2005, the Company had approximately 1,521,000 restricted shares unvested and outstanding.

During 2004, the Company issued approximately 1,369,000 restricted shares to employees. The shares had an average fair value on dates of grant of $9.39. Included in the total number of restricted shares issued is a one-time grant of approximately 923,000 shares to senior managers and executives on May 6, 2004. Under the terms of the one-time grant to senior managers and executives, the restricted shares vest in two increments: 50% on May 6, 2007 (the three year anniversary of the grant), and the balance on May 6, 2009 or earlier, upon the Company achieving profitability, as measured under specified criteria applied by the Board of Directors. At December 31, 2004, the Company had approximately 1,399,000 restricted shares unvested and outstanding.

The Company has recorded deferred compensation, net of cancellations, of approximately $6,172,000 and $12,206,000 related to the issuance of restricted shares during the twelve months ended December 31, 2005 and 2004, respectively. The Company recorded compensation expense of approximately $4,421,000, $1,661,000, and $16,000 for the twelve months ended December 31, 2005, 2004 and 2003 respectively, related to all restricted shares outstanding during those periods.

The Company records and amortizes over the related vesting periods deferred compensation representing the difference between the exercise price of stock options granted or the price per share of restricted stock issued, and the fair value of the Company's common stock at the date of grant or issuance. There was no deferred compensation expense related to stock options in 2005, 2004 and 2003.

For the year ended December 31, 2005 the Company recorded $211,000 in compensation expense related to stock and option grants in accordance with executives' severance agreements.

Compensation cost, calculated using a Black-Scholes option pricing model, recognized in connection with the issuance of stock options to nonemployees was $161,826 in 2003. There was no compensation cost recognized in 2005 and 2004 related to the issuance of stock options to nonemployees.

Employee Stock Purchase Plan

On July 1, 1992, Vertex adopted the Vertex Pharmaceuticals Incorporated Employee Stock Purchase Plan (the "Vertex Purchase Plan"), which has been subsequently amended to add additional shares to the pool of available shares under the plan, including an amendment in 2002 to add 600,000 shares and an amendment in 2004 to add 1,500,000 shares. The Vertex Purchase Plan 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.

During 2005, 2004, and 2003 the following shares were issued to employees under the Vertex Purchase Plan (shares in thousands):

	2005	2004	2003
Number of shares	439	468	379
Average price paid	$ 8.95	$ 7.60	$ 9.49

Had the Company adopted SFAS 123, the weighted average fair value of each purchase right granted during 2005, 2004 and 2003 would have been $6.42, $5.34, and $5.86, respectively. The fair value was estimated at the beginning of the withholding period using the Black-Scholes option-pricing model with the following weighted average assumptions:

	2005	2004	2003
Expected life (years)	.43	.80	.80
Expected volatility	59.00%	65.00%	75.00%
Risk-free interest rate	3.59%	1.35%	1.17%
Dividend yield	—	—	—

Rights

Each Vertex shareholder also holds one share purchase right (a "Right") for each share of common stock owned. Each Right entitles the holder to purchase from the Company one half of one-hundredth of a share of Series A junior participating preferred stock, $0.01 par value (the "Junior Preferred Shares"), of the Company at a price of $135 per one half of one-hundredth of a Junior Preferred Share subject to adjustment (the "Purchase Price"). The Rights are not exercisable until after the acquisition by a person or group of 15% or more of the outstanding common stock (an "Acquiring Person"), or after the announcement of an intention to make or commencement of a tender offer or exchange offer, the consummation of which would result in the beneficial ownership by a person or group of 15% or more of the outstanding common stock (the earlier of such dates being called the

"Distribution Date"). Until the Distribution Date (or earlier redemption or expiration of the Rights), the Rights will be traded with, and only with, the common stock. Until a Right is exercised, the Right will not entitle the holder thereof to any rights as a stockholder.

If any person or group becomes an Acquiring Person, each holder of a Right, other than Rights beneficially owned by the Acquiring Person, will thereafter have the right to receive upon exercise and payment of the Purchase Price that number of shares of common stock having a market value of two times the Purchase Price and, if the Company is acquired in a business combination transaction or 50% or more of its assets are sold, each holder of a Right will thereafter have the right to receive upon exercise and payment of the Purchase Price that number of shares of common stock of the acquiring company which at the time of the transaction will have a market value of two times the Purchase Price.

At any time after any person becomes an acquiring person and prior to the acquisition by such person or group of 50% or more of the outstanding common stock, the Board of Directors of the Company may cause the Rights (other than Rights owned by such person or group) to be exchanged, in whole or in part, for common stock or Junior Preferred Shares, at an exchange rate of one share of common stock per Right or one half of one-hundredth of a Junior Preferred Share per Right.

At any time prior to the acquisition by a person or group of beneficial ownership of 15% or more of the outstanding common stock, the Board of Directors of the Company may redeem the Rights at a price of $0.01 per Right.

The Rights have certain anti-takeover effects, in that they will cause substantial dilution to a person or group that attempts to acquire a significant interest in Vertex on terms not approved by the Board of Directors.

Common Stock Reserved for Future Issuance

At December 31, 2005, the Company has reserved shares of common stock for future issuance under all equity compensation plans as follows (shares in thousands):

Common stock under stock and option plans	17,739
Common stock under the Vertex Purchase Plan	842
Common stock under the Vertex 401(k) Plan	270
Total	18,851

O. Significant Revenue Arrangements

The Company has formed strategic collaborations with pharmaceutical companies and other organizations in the areas of drug discovery, development, and commercialization. Research, development and commercialization agreements provide the Company with financial support and other valuable resources for its research programs and for the development of clinical drug candidates, and the marketing and sales of products.

Collaborative Research, Development and Commercialization Agreements

In the Company's collaborative research, development and commercialization programs the Company seeks to discover, develop and commercialize pharmaceutical products in conjunction with and supported by the Company's collaborators. Collaborative research and development arrangements may provide research funding over an initial contract period with renewal and termination options that

vary by agreement. The agreements may also include milestone payments based on the achievement of a pre-agreed objective or the occurrence of a designated event. The agreements may also contain development reimbursement provisions, royalty rights or profit sharing rights and manufacturing options. The Company has entered into significant research and development collaborations under terms which vary from agreement to agreement.

Novartis

In May 2000, the Company entered into an agreement with Novartis Pharma AG ("Novartis") to collaborate on the discovery, development and commercialization of small molecule drugs directed at protein kinases. The agreement was amended in February 2004. Under the original agreement, the Company was responsible for drug discovery and clinical proof-of-concept testing of all drug candidates. Novartis agreed to pay the Company up to $200 million in research funding through April 2006, and to loan the Company up to $200 million on a non-interest-bearing basis to support clinical proof-of-concept studies. Development loans with respect to any drug candidates accepted by Novartis for development would be forgiven. Under the amended agreement, Vertex will continue to receive research funding through April 2006 along with development milestone payments and royalties with respect to any drug candidates selected by Novartis for development. Novartis holds an option to develop drug candidates meeting certain pre-agreed criteria. The option is exercisable with respect to each development candidate at the pre-development stage, at which point a $10 million milestone payment will be due from Novartis, with up to $25 million in additional pre-commercial milestone payments. Following completion of the six-year research term in April 2006, Novartis' development option with respect to all compounds discovered in the research program will terminate no later than the end of a specified period following delivery by Vertex to Novartis of a final research report. Vertex retains all rights to any candidate not selected by Novartis, as well as to all of the intellectual property it generates under the collaboration that is not specific to candidates selected by Novartis for development. As part of the amended agreement, restrictions under the original agreement that limited Novartis' right to pursue kinase research and development outside the collaboration were removed, and the development loan facility was terminated. In November 2004, Novartis accepted VX-322 for preclinical development and made a $10 million milestone payment to Vertex that is being recognized as revenue over the term of the contract. Novartis will have exclusive worldwide development, manufacturing and commercialization rights to VX-322 and any other drug candidates that it accepts from the Company for development. The Company will receive royalties on any products that are marketed as part of the collaboration. In 2005, 2004, and 2003, the Company recognized approximately $53.1 million, $50.5 million and $44.5 million, respectively, in revenue under this agreement.

Under the amended agreement, the Company retained the right either to develop VX-680 to proof-of-concept under the terms of the original agreement, or to elect to remove VX-680, and the Aurora kinases it targets, from the collaboration. On June 22, 2004, the Company exercised its election to develop VX-680 outside the Novartis collaboration and repaid approximately $12.5 million of unspent and uncommitted development loans previously advanced on account of VX-680. Loans advanced under the original agreement for the early development of certain other compounds will be forgiven on a compound-by-compound basis if any of those compounds are selected by Novartis for development. All loans not forgiven under the facility will be repayable, without interest, in May 2008. At December 31, 2005, there were approximately $20 million in remaining loans outstanding under the loan facility.

GlaxoSmithKline

In December 1993, the Company and GlaxoSmithKline entered into a collaborative agreement to research, develop and commercialize HIV protease inhibitors, including Agenerase (amprenavir), Lexiva/Telzir (fosamprenavir calcium) and brecanavir (VX-385). Under the collaborative agreement, GlaxoSmithKline agreed to pay the Company up to $42 million, comprised of a $15 million up-front license payment made in 1993, $14 million of product research funding over five years and $13 million of development and commercialization milestone payments for an initial drug candidate. Research funding under this agreement ended on December 31, 1998 and Vertex has received the entire $42 million referenced above plus additional milestones for the second and third generation drug candidates Lexiva/Telzir and brecanavir. Vertex is also entitled to royalties on sales of its HIV protease inhibitors by GlaxoSmithKline. The Company began earning a royalty from GlaxoSmithKline in 1999 on sales of Agenerase, in the fourth quarter of 2003 on sales of Lexiva, and in the third quarter of 2004 on sales of Telzir. GlaxoSmithKline is also obligated to pay additional development and commercialization milestone payments for subsequent drug candidates, including brecanavir.

In the fourth quarter of 2004, GlaxoSmithKline paid the Company a milestone payment of $1 million based on the initiation of Phase II clinical trials for brecanavir. In the third quarter of 2004, GlaxoSmithKline paid the Company a milestone payment of $1.5 million in connection with the regulatory approval of Telzir in the European Union. In the fourth quarter of 2003, GlaxoSmithKline paid the Company a milestone payment of $2.5 million upon FDA approval of Lexiva in the United States. In the fourth quarter of 2002, GlaxoSmithKline paid the Company a milestone payment of $1.5 million in connection with the submission of a new drug application for marketing approval of Lexiva/Telzir in the United States and the European Union.

GlaxoSmithKline is required to bear the costs of developing drug candidates in its territory under the collaboration. Under the original agreement, GlaxoSmithKline had exclusive rights to develop and commercialize Vertex's HIV protease inhibitors in all parts of the world except the Far East. In 2003, the Company amended the agreement to add the Far East to GlaxoSmithKline's territory for development and commercialization of Lexiva/Telzir. The Company has retained certain bulk drug manufacturing rights and certain product educational rights in territories licensed to GlaxoSmithKline. GlaxoSmithKline has the right to terminate its arrangement with the Company without cause upon twelve months' notice. Termination of the agreement by GlaxoSmithKline will relieve it of its obligation to make further commercialization and development milestone and royalty payments and will end any license granted to GlaxoSmithKline by Vertex under the agreement.

In June 1996, the Company and GlaxoSmithKline obtained a worldwide, non-exclusive license under certain G.D. Searle & Co. ("Searle," now owned by Pharmacia/Pfizer) patents in the area of HIV protease inhibition. The Company pays Searle a royalty based on sales of Agenerase and Lexiva/Telzir.

In the fourth quarter of 2005, GlaxoSmithKline and the Company entered into a collaborative agreement to develop and commercialize VX-409, Vertex's novel, subtype selective sodium channel modulator for the treatment of pain. Under the terms of the agreement, GlaxoSmithKline has the exclusive right and license to develop and commercialize VX-409 and certain back-up compounds worldwide. Vertex received a $20 million up-front license payment and could receive up to $385 million in additional development and commercial milestone payments based on the development of VX-409 and back-up compounds in major pharmaceutical markets across a range of indications. GlaxoSmithKline will also pay Vertex royalties on annual sales.

Revenues and royalties earned from GlaxoSmithKline under both agreements were $52.8 million, $19.8 million, and $11.5 million, in 2005, 2004 and 2003, respectively.

Cystic Fibrosis Foundation Therapeutics Incorporated (CFFT)

In May 2004, Vertex entered into an agreement with Cystic Fibrosis Foundation Therapeutics Incorporated ("CFFT") that provided funding through December 31, 2005 for Vertex's late-stage cystic fibrosis drug discovery effort. Under this agreement, Vertex will retain the right to develop and commercialize any compounds discovered in the course of the research collaboration. For the twelve months ended December 31, 2005 and 2004, Vertex recognized $14.5 million and $6.8 million in revenue related to this agreement. During the first quarter of 2004, under an earlier agreement, Vertex earned revenue of $1.9 million.

In January 2006, Vertex and CFFT extended the duration of their research collaboration. Under the extended agreement, CFFT has agreed to provide an additional $22 million to Vertex for continued research funding through early 2008 directed toward CFTR corrector compounds. CFFT has the right to terminate the agreement without cause, effective on June 30, 2006 and June 30, 2007, upon 60 days' prior written notice.

Mitsubishi Pharma Corporation

In June 2004, Vertex entered into a collaboration agreement with Mitsubishi Pharma Corporation, which will provide financial and other support for the development of VX-950, the Company's oral hepatitis C virus protease inhibitor. Under the terms of the agreement, Mitsubishi has the right to develop and commercialize VX-950 in Japan and certain other Far East countries, while Vertex has retained exclusive development and marketing rights to VX-950 in the rest of the world, including North America and Europe. The agreement provides for up to $33 million in payments by Mitsubishi to Vertex through Phase II clinical development, including an up-front license fee, development stage milestone payments and contributions to certain drug development costs for VX-950. Further cost sharing beyond Phase II clinical development will be determined by Mitsubishi and Vertex based on the design of registration studies for VX-950. The agreement also provides Vertex with royalties on any sales of VX-950 in the Mitsubishi territory. Mitsubishi may terminate the agreement at any time without cause upon 60 days' prior written notice. In the fourth quarter of 2004, Mitsubishi paid the Company a milestone payment of $4 million for first dosing of VX-950 in a patient in the Phase Ib clinical trial in the United States. Vertex recognized $3.4 million and $1.8 million of non-milestone revenue in 2005 and 2004, respectively, under the Mitsubishi agreement, primarily for reimbursement of Vertex's expenses incurred in VX-950 development.

Merck & Co., Inc.

In June 2004, Vertex entered into a global collaboration with Merck & Co., Inc. to develop and commercialize VX-680, Vertex's lead Aurora kinase inhibitor, and possibly additional follow-on compound(s), for the treatment of cancer. The Merck collaboration provides for an up-front license payment of $20 million, which was made in June 2004, and for research funding of $14 million over two years, ending in June 2006. In addition, Vertex could receive as much as $350 million in milestone payments, including up to $130 million for the successful development of VX-680 in the first oncology indication and additional milestone payments for development of VX-680 and follow-on compounds in subsequent major oncology indications. Merck is responsible for worldwide clinical development and commercialization of VX-680 and any other Aurora kinase inhibitors discovered during the research program and will pay Vertex royalties on product sales. Merck may terminate the agreement without cause at any time upon 90 days' advance written notice, except that six months' advance written notice

is required for termination during the second year of the research term (ending June 2006) or at any time when a product has marketing approval in a major market and the termination is not the result of a safety issue. Vertex recognized $17.1 million and $8.4 million of revenue related to research support and the up-front license payment for this collaboration in 2005 and 2004, respectively.

In the fourth quarter of 2005, Vertex received a $7.5 million milestone payment from Merck upon the demonstration of activity by VX-680 on a clinically relevant biomarker during a Phase I clinical trial. Vertex recognized revenue of $5.6 million in 2005 related to this milestone. The remainder will be recognized over the remaining contract term.

In addition, in the fourth quarter of 2005, Merck selected a follow-on compound (VX-667) for development. Merck paid the Company a milestone payment of $12 million upon the selection of the follow-on compound. Vertex recognized revenue of $1.7 million in 2005 related to this milestone. The remainder will be recognized over the remaining contract term.

Kissei Pharmaceutical Co., Ltd.

The Company and Kissei Pharmaceutical Co., Ltd. ("Kissei") are parties to an agreement to collaborate on the identification of inhibitors of p38 MAP kinase and the development of those compounds as novel, orally active drugs for the treatment of inflammatory and neurological diseases. Under the terms of the agreement, Kissei agreed to pay the Company up to $22 million comprised of a $4 million up-front license payment, $11 million of product research funding over three years and $7 million of development and commercialization milestone payments. Additionally, Kissei agreed to reimburse the Company for certain development costs, including a portion of costs for Phase II trials of VX-702. Research funding ended under this program on June 30, 2000 and the Company has received the full amount of research funding specified under the agreement. Kissei has exclusive rights to develop and commercialize VX-702 in Japan and certain Far East countries and co-exclusive rights in China, Taiwan and South Korea. The Company retains exclusive marketing rights outside the Far East and co-exclusive rights in China, Taiwan and South Korea. In addition, the Company will have the right to supply bulk drug material to Kissei for sale in its territory and will receive royalties or drug supply payments on future product sales, if any. In 2005, 2004 and 2003, approximately $7.3 million, $3.5 million, and $0.3 million, respectively, was recognized as revenue under the p38 MAP kinase research and development program. The $7.3 million of revenue recognized in 2005 includes a $2.5 million milestone paid upon Kissei's completion of regulatory filings in preparation for Phase I clinical development of VX-702 in Japan.

P. Employee Benefits

The Company has a 401(k) retirement plan (the "Vertex 401(k) Plan") in which substantially all of its permanent 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 that are payable in the form of Vertex common stock. The match is paid in the form of fully vested interests in a Vertex common stock

fund. Employees have the ability to transfer funds from the Company stock fund as they choose. The Company declared matching contributions to the Vertex 401(k) Plan as follows (in thousands):

	2005	2004	2003
Discretionary matching contributions for the year ended December 31,	$ 2,894	$ 2,492	$ 2,237
Shares issued for the year ended December 31,	215	239	185
Shares issuable as of the year ended December 31,	19	57	61

Q. Related Party Transactions

As of December 31, 2005 and 2004, the Company had an interest-free loan outstanding to an officer in the amount of $36,000 and $97,000, respectively, which was initially advanced in April 2002. The loan balance is included in other assets on the consolidated balance sheets.

In 2001, the Company entered into a four year consulting agreement with a director of the Company for the provision of part-time consulting services over a period of four years, at the rate of $80,000 per year commencing in January 2002 and terminating in January 2006.

R. Contingencies

The Company has certain contingent liabilities that arise in the ordinary course of its business activities. The Company accrues contingent liabilities when it is probable that future expenditures will be made and such expenditures can be reasonably estimated.

On December 17, 2003, a purported class action, *Marguerite Sacchetti v. James C. Blair et al.*, was filed in the Superior Court of the State of California, County of San Diego, naming as defendants all of the directors of Aurora who approved the merger of Aurora and Vertex, which closed in July 2001. The plaintiffs claim that Aurora's directors breached their fiduciary duty to Aurora by, among other things, negligently conducting a due diligence examination of Vertex by failing to discover alleged problems with VX-745, a Vertex drug candidate that was the subject of a development program which was terminated by Vertex in September 2001. Vertex has certain indemnity obligations to Aurora's directors under the terms of the merger agreement between Vertex and Aurora, which could result in Vertex liability for attorney's fees and costs in connection with this action, as well as for any ultimate judgment that might be awarded. There is an outstanding directors' and officers' liability policy which may cover a significant portion of any such liability. The defendants are vigorously defending this suit. The Company believes this suit will be settled without any significant liability to Vertex or the former Aurora directors.

S. Guarantees

As permitted under Massachusetts law, Vertex's Articles of Organization and Bylaws 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 certain directors' and officers' liability insurance policies that reduce its monetary exposure and enable it to recover a portion of any future amounts paid. The Company believes the estimated fair value of these indemnification arrangements is minimal.

Vertex customarily agrees in the ordinary course of its business to indemnification provisions in agreements with clinical trials investigators and sites in its drug development programs, in sponsored research agreements with academic and not-for-profit institutions, in various comparable agreements involving parties performing services for the Company in the ordinary course of business, and in its real estate leases. The Company also customarily agrees to certain indemnification provisions in its drug discovery and development 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, 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 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 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.

Effective on March 28, 2003 the Company sold certain assets of PanVera LLC to Invitrogen Corporation for approximately $97 million. The agreement with Invitrogen requires the Company to indemnify Invitrogen against any loss it may suffer by reason of Vertex's breach of certain representations and warranties, or failure to perform certain covenants, contained in the agreement. The representations, warranties and covenants are of a type customary in agreements of this sort. The Company's aggregate obligations under the indemnity are, with a few exceptions which the Company believes are not material, capped at one-half of the purchase price, and apply to claims under representations and warranties made within fifteen months after closing (which period has ended) although there is no corresponding time limit for claims made based on breaches of covenants. Invitrogen has made no claims to date under this indemnity, and the Company believes that the estimated fair value of the remaining indemnification obligation is minimal.

Effective on December 3, 2003, the Company sold certain instrumentation assets to Aurora Discovery, Inc. for approximately $4.3 million. The agreement with Aurora Discovery, Inc. requires the Company to indemnify Aurora Discovery, Inc. against any loss it may suffer by reason of the Company's breach of certain representations and warranties, or failure to perform certain covenants, contained in the agreement. The representations, warranties and covenants are of a type customary in agreements of this sort. The Company's aggregate obligations under the indemnity are capped at one-half of the purchase price, and apply to claims under representations and warranties made within fifteen months after closing (which period has ended) although there is no corresponding time limit for claims made based on breaches of covenants. Aurora Discovery, Inc. has made no claims to date under

this indemnity, and the Company believes that the estimated fair value of the remaining indemnification obligation is minimal.

On February 10, 2004, Vertex entered into a Dealer Manager Agreement with UBS Securities LLC in connection with the exchange of approximately $153.1 million of the February 2011 Notes for approximately $153.1 million of 2007 Notes. On September 13, 2004, the Company entered into a second Dealer Manager Agreement with UBS Securities in connection with the exchange of approximately $79.3 million of the September 2004 Notes for approximately $79.3 million of 2007 Notes. Each of the Dealer Manager Agreements requires the Company to indemnify UBS Securities against any loss UBS Securities may suffer by reason of the Company's breach of representations and warranties relating to the exchanges of the convertible notes, the Companies failure to perform certain covenants in those agreements, the inclusion of any untrue statement of material fact in the materials provided to potential investors in the 2011 Notes, the omission of any material fact needed to make those materials not misleading, and any actions taken by the Company or its representatives in connection with the exchanges. The representations, warranties and covenants in the Dealer Manager Agreements are of a type customary in agreements of this sort. The Company believes the estimated fair value of these indemnification obligations is minimal.

On June 7, 2005, the Company entered into a Purchase Agreement with Merrill Lynch, Pierce, Fenner & Smith Incorporated, as the representative of the several underwriters named therein, relating to the public offering and sale of shares of the Company's common stock. The Purchase Agreement requires the Company to indemnify the underwriters against any loss they may suffer by reason of the Company's breach of representations and warranties relating to that public offering, the Company's failure to perform certain covenants in those agreements, the inclusion of any untrue statement of material fact in the prospectus used in connection with that offering, the omission of any material fact needed to make those materials not misleading, and any actions taken by the Company or its representatives in connection with the offering. The representations, warranties and covenants in the Purchase Agreement are of a type customary in agreements of this sort. The Company believes the estimated fair value of these indemnification obligations is minimal.

T. Quarterly Financial Data (unaudited)

(in thousands, except per share data)

	Three Months Ended			
	March 31, 2005	June 30, 2005	Sept. 30, 2005	Dec. 31, 2005
Revenues:				
Royalties	$ 6,153	$ 7,467	$ 9,466	$ 9,743
Collaborative and other research and development revenues	22,453	24,854	26,741	54,013
Total revenues	28,606	32,321	36,207	63,756
Costs and expenses:				
Royalty payments	2,030	2,489	2,796	2,783
Research and development	57,435	59,357	63,590	68,158
Sales, general and administrative	9,627	10,814	10,738	12,811
Restructuring expense	1,914	(1,743)	1,565	6,398
Total costs and expenses	71,006	70,917	78,689	90,150
Loss from operations	(42,400)	(38,596)	(42,482)	(26,394)
Interest income	2,319	2,247	3,733	3,695
Interest expense	(4,639)	(4,639)	(4,505)	(3,543)
Loss on exchange of convertible subordinated notes	—	—	(36,324)	(11,889)
Net loss	$ (44,720)	$ (40,988)	$ (79,578)	$ (38,131)
Basic and diluted net loss per common share	$ (0.56)	$ (0.50)	$ (0.84)	$ (0.38)
Basic and diluted weighted average number of common shares outstanding	79,428	82,274	94,590	100,535

	Three Months Ended			
	March 31, 2004	June 30, 2004	Sept. 30, 2004	Dec. 31, 2004
Revenues:				
Royalties	$ 2,582	$ 4,011	$ 4,403	$ 6,326
Collaborative and other research and development revenues	14,931	14,530	22,425	33,509
Total revenues	17,513	18,541	26,828	39,835
Costs and expenses:				
Royalty payments	846	1,328	1,466	2,009
Research and development	41,675	47,450	48,790	54,247
Sales, general and administrative	9,722	10,160	10,600	11,657
Restructuring expense	1,818	1,837	1,561	12,358
Total costs and expenses	54,061	60,775	62,417	80,271
Loss from operations	(36,548)	(42,234)	(35,589)	(40,436)
Interest income	2,990	2,546	2,445	2,342
Interest expense	(4,427)	(4,581)	(4,634)	(4,675)
Loss on retirement of convertible subordinated notes	(2,453)	—	(993)	—
Net loss	$ (40,438)	$ (44,269)	$ (38,771)	$ (42,769)
Basic and diluted net loss per common share	$ (0.52)	$ (0.56)	$ (0.49)	$ (0.54)
Basic and diluted weighted average number of common shares outstanding	78,094	78,807	78,742	79,073

QuickLinks

AMENDMENT NO. 1
TO
RESEARCH, DEVELOPMENT AND
COMMECIALIZATION AGREEMENT (the "Existing Agreement")
DATED MAY 24, 2004 BY AND BETWEEN VERTEX PHARMACEUTICALS
INCORPORATED ("Vertex") and CYSTIC FIBROSIS FOUNDATION
THERAPEUTICS INCORPORATED ("CFFT")

This Amendment No. 1 (the "Amendment") is made this 6th day of January, 2006 (the "Effective Date") between Vertex, a Massachusetts corporation with principal offices at 130 Waverly Street, Cambridge, MA 02139-4242 and CFFT, a Delaware corporation with principal offices at 6931 Arlington Road, Bethesda, Maryland 20814. Vertex and CFFT are referred to hereinafter collectively as the Parties.

INTRODUCTION

In 1998, CFFT made an award to Aurora Biosciences to do a feasibility study using high throughput screening for cf targets. On May 19, 2000, CFFT selected and provided support for Aurora Biosciences to conduct high throughput screening with respect to the CFTR target identified by CFFT. Since that time, Aurora Biosciences, and then after its merger into Vertex, Vertex, have been conducting a Research Program with CFFT's support aimed at identification and design of Potentiator and Corrector Compounds, both of which are directed as a principal mode of therapeutic action at modulation of the biological effect of CFTR in different ways and with different anticipated results. The Existing Agreement contemplated that during the course of the Research Program, Vertex, with CFFT's agreement, would select either the Potentiator or the Corrector approaches as its Primary Program, to which a majority of resources under the Research Program would be directed, and the other approach would be designated as an Alternative Program, to which the balance of resources would be directed.

Vertex has selected the Potentiator approach as the Primary Program, with the concurrence of CFFT, and expects to designate a Potentiator Compound as a Development Candidate on or before December 31, 2005.

The Parties continue to believe that it may be possible to create Corrector Compounds of significant potential value as therapeutics in the Field. To further this effort, CFFT and Vertex agree hereinafter to provide additional funding and Vertex intends to continue its research efforts with respect to Correctors beyond the current Research Termination Date of December 31, 2005. The purpose of this Amendment is to modify the terms of the Existing Agreement to reflect the progress made in the Research Program during its current term and to set forth the terms of the extended Corrector Research Program.

Capitalized terms not otherwise defined in this Amendment shall have the meaning ascribed to them in the Existing Agreement. If specific provisions of this Amendment are inconsistent with specific provisions of the Existing Agreement, the provisions of this Amendment shall control.

In consideration of the mutual covenants set forth in this Amendment, and other good and valuable consideration, the receipt of which is hereby acknowledged, the Parties agree as follows:

1. General.

1.1. Vertex and CFFT acknowledge that the "Primary Program" under the Existing Agreement refers to research activities relating to Potentiator Compounds. CFFT has no further right to request under Section 2.5 of the Existing Agreement that Vertex designate Correctors as the Primary Program, or to terminate the Existing Agreement under Section 10.5.1 thereof.

1.2. After December 31, 2005, the "Research Program" will refer to research undertaken under the Existing Agreement, as amended hereby, with respect only to Corrector Compounds (except for the Potentiator research funded during 2006 as specified in the attached Research Plan). The "Research Plan" under Section 2.4 of the Existing Agreement will mean, after December 31, 2005, the initial plan for conduct of the Research Program focused on Correctors (and to a limited extent, Potentiators, as provided in the Research Plan), subject to applicable provisions of Section 2.4.1 of the Existing Agreement regarding modifications to that Research Plan. A copy of the initial Research Plan for continuing Corrector research (the "Initial Corrector Research Plan") is attached to this Amendment as *Exhibit 1.2*. The concepts of Primary Subplan and Alternative Subplan as referenced in Section 2.4.3 of the Existing Agreement will no longer apply to activities undertaken under the Research Program after December 31, 2005. The terms of the Existing Agreement that provide for the allocation of resources between the Primary and the Alternative Programs will not be applicable to the Research Program after December 31, 2005.

1.3. The budget for the Research Program under the Existing Agreement for the one year period ending December 31, 2005 (the "Current Budget") is attached hereto as *Exhibit 1.3*, has been approved by both Parties hereto and represents an agreed allocation of funding between the Primary and the Alternative Programs for the period ending December 31, 2005. The Parties have agreed on a separate budget (the "Initial Corrector Budget") representing an agreed allocation of additional Corrector research funding to be provided under this Amendment, as referenced in Section 4.1 below, for the period commencing on the Effective Date of this Amendment and ending on the Research Termination Date referenced in Section 1.4 below.

1.4. The Research Termination Date shall mean the end of the revised Research Program directed at the identification and design of Corrector Drug Product Candidates (the "Corrector Research Program") which shall be March 31, 2008, unless the Research Program under the Existing Agreement as amended hereby is otherwise extended or terminated in accordance with its terms.

1.5. The term "Drug Product[s]" is amended to mean a finished dosage form that is prepared from Bulk Drug Substance covered by Vertex CF Technology and is ready for administration to the ultimate consumer as a pharmaceutical.

1.6. The term "Vertex CF Technology" as defined in the Existing Agreement shall also be deemed to refer to data, technical information, know-how, inventions (whether or not patented), trade secrets, processes and methods discovered or developed, and Controlled by Vertex or its Affiliates, in the course of the performance of the Research Program under this Amendment, but shall not refer to Vertex's general drug design technology whether in hardware or software form, tangible or intangible.

Information redacted pursuant to a confidential treatment request. An unredacted version of this exhibit has been filed separately with the Commission.

1.7. The provisions of Section 6.3 of the Existing Agreement shall apply to this Amendment as if it were being entered into as part of the Existing Agreement. The Parties will agree on the timing and content of a press release relating to this Amendment.

2. Termination Provisions.

2.1. On the Effective Date of this Amendment, CFFT shall no longer have the right to terminate the Existing Agreement under Section 10.5.1 (relating to a disagreement over the choice of Primary and Alternative Programs) or Section 10.6.3 (relating to termination of the Alternative Program). Therefore, those sections of the Existing Agreement are hereby deleted.

2.2. Section 10.5.2 of the Existing Agreement is hereby amended to read as follows:

> "At its sole discretion, CFFT may terminate the Research Program effective June 30, 2006 or June 30, 2007, upon not less than sixty (60) days prior written notice to Vertex (an "Early Termination Notice")."

2.3. Sections 10.5.4, 10.5.6 and 10.7 of the Existing Agreement are hereby deleted.

2.4. Section 10.6.1 of the Existing Agreement is hereby amended by substituting the word "if" for the word "unless" in the fourth-to-last line of that section.

3. Other CFTR Research.

During the period for which funding is provided to Vertex by CFFT under the Existing Agreement (as amended herein or subsequently from time to time), and under a separate agreement providing for continued Potentiator funding (the "Potentiator Funding Agreement"), if such funding is provided in other than in the Existing Agreement, all of Vertex's research efforts directed at the identification, development and commercialization of pharmaceutical products that have as their principal mode of action the modulation of CFTR shall be conducted under the Existing Agreement (as amended herein or subsequently from time to time) and under the Potentiator Funding Agreement. During the **[***]** period following the later of the last date upon which CFFT provides funding to Vertex under the Existing Agreement (as amended herein or subsequently from time to time), or the last date upon which CFFT provides continuing Potentiator funding under the Potentiator Funding Agreement, if such funding is provided for other than in the Existing Agreement, Vertex shall not enter into any research, development or commercialization agreement (a "Third Party Agreement") with a third party directed toward the eventual commercialization (including the acquisition and sale of a marketed product) of a pharmaceutical product that has as its principal mode of action the modulation of CFTR and is not a Drug Product (the "New Product"), unless CFFT will receive the same royalty rate from Vertex or the third party under the Third Party Agreement as is provided under Section 5.3.1 of the Existing Agreement (as it may be subsequently amended), on account of any Net Sales of the New Product. An agreement between Vertex and a third party for the conduct of research activities, under which that third party does not then (or by subsequent agreement with such third party) receive any license rights to, or compensation with respect to the development or sale of, any pharmaceutical product that has CFTR modulation as its principal mode of action, shall not be deemed a Third Party Agreement for the purposes of the foregoing restriction. The foregoing provisions of this Section 3 shall not apply to any Third Party Agreement relating to a New Product that is a Corrector from and after the date upon which CFFT exercises its termination rights under section 10.5.2 of the Existing Agreement (as amended pursuant to this Amendment No. 1). In the event of an Interruption under Section 10.6.2 of the Existing Agreement with respect to either Potentiator or Corrector research programs, Vertex shall not enter into any agreement with a third party for commercial purposes, for a period of **[***]** after such Interruption, relating to the program to which the Interruption related.

Information redacted pursuant to a confidential treatment request. An unredacted version of this exhibit has been filed separately with the Commission.

4. Budget and Funding.

From and after the Effective Date of this Amendment, the following provisions shall apply to any incremental funding for Corrector research in 2005, and to the budget and funding for all Corrector research thereafter under the Research Plan, in lieu of the provisions in Sections 4.1, 4.2 and 4.3 of the Existing Agreement.

4.1. The initial budget for incremental funding of the Corrector Research Program, relating to discovery, optimization and IND-enabling activities for Corrector Compounds, is attached hereto as *Exhibit 4.1* (the "Initial Corrector Budget"). The Initial Corrector Budget includes only amounts that are incremental to the funding currently provided for Corrector research in the "Alternative Program" under the Current Budget. Any material revisions to the Initial Corrector Budget which would result in an increase in total funding for the Corrector Research Program beyond the amount provided under this Amendment will require the prior approval of CFFT. Any other adjustments to the Initial Corrector Budget may be undertaken by Vertex with prior notice to, but without prior approval from, CFFT. Vertex will provide CFFT with **[***]** reports within **[***]** showing expenses incurred under the Corrector Research Program during the quarter just ended against budgeted expenses for that quarter. For **[***]**, the report will cover the period from the Effective Date of this Amendment through the end of that quarter.

4.2. CFFT will fund **[***]** of the Initial Corrector Budget and Vertex will fund **[***]** of the Initial Corrector Budget. Based on the approved Initial Corrector Budget of **[***]**, CFFT will make the payments to Vertex specified below during the specified periods.

	INITIAL CORRECTOR BUDGET (millions $)	
Research Period	**Aggregate Budget Amount**	**CFFT Financial Commitment**
January 1, 2006—December 31, 2006	[***]	[***]
January 1, 2007—March 31, 2008	[***]	[***]

Payments due under the Initial Corrector Budget on account of internal FTEs shall be made by CFFT **[***]**. Payments due under the Initial Corrector Budget on account of external costs shall be made by CFFT to Vertex **[***]** within **[***]** following **[***]** . All payments shall be made without deduction for withholding or similar taxes in United States dollars to the credit of such bank account as may be designated in writing to CFFT. Any payments which fall due on a date that is a legal holiday in The Commonwealth of Massachusetts may be made on the next following day that is not a legal holiday in The Commonwealth. On or before January 31 of 2006, 2007, 2008 and 2009, Vertex will provide CFFT with an accounting of all internal FTE costs and external Research costs (including documentary evidence of such external costs) incurred under the Research Program during the most recently concluded calendar year. Internal FTE costs will be calculated at an annual rate of **[***]** per FTE.

4.3. If CFFT's contribution for any reporting period is in excess of its agreed portion of the total expense incurred by Vertex (internal and external) for the Corrector Research Program for that period, the excess amount will be carried over and applied as a credit against CFFT's required contribution in future periods, except that any aggregate excess contributions provided by CFFT as of the end of the Research Program Term will be refunded to CFFT within **[***]**thereafter. To the extent not inconsistent with the provisions of this Amendment, the provisions of Section 4.5 will apply to the Corrector Research Program.

Information redacted pursuant to a confidential treatment request. An unredacted version of this exhibit has been filed separately with the Commission.

4.4. Vertex will dedicate a minimum average of **[***]** FTE scientists (on an annualized basis) to the Corrector Research Program during its term, **[***]**.

5. Royalties Outside the Field

Section 5.3.2 of the Existing Agreement is amended as follows:

"5.3.2 Net Sales outside the Field. Vertex shall pay CFFT a royalty of **[***]**."

[Signature Page Follows]

Information redacted pursuant to a confidential treatment request. An unredacted version of this exhibit has been filed separately with the Commission.

IN WITNESS WHEREOF, the Parties hereto have executed this Agreement the day and year first above written.

VERTEX PHARMACEUTICALS INCORPORATED	CYSTIC FIBROSIS FOUNDATION THERAPEUTICS, INCORPORATED
By: /s/ KENNETH S. BOGER	By: /s/ ROBERT J. BEALL, PH.D.
Senior Vice President and General Counsel	President and Chief Executive Officer

Information redacted pursuant to a confidential treatment request. An unredacted version of this exhibit has been filed separately with the Commission.

Exhibit 1.2
Corrector Research Plan

[***]

Information redacted pursuant to a confidential treatment request. An unredacted version of this exhibit has been filed separately with the Commission.

Exhibit 1.3
Current Budget

[***]

Information redacted pursuant to a confidential treatment request. An unredacted version of this exhibit has been filed separately with the Commission.

Exhibit 4.1
Initial Corrector Budget

[***]

Information redacted pursuant to a confidential treatment request. An unredacted version of this exhibit has been filed separately with the Commission.

Exhibit 10.11

Execution version

Confidential Treatment Requested. Confidential portions of this document have been redacted and have been separately filed with the Commission.

RESEARCH, LICENSE AND COMMERCIALIZATION AGREEMENT

between

GLAXO GROUP LIMITED

and

VERTEX PHARMACEUTICALS INCORPORATED

CONFIDENTIAL TREATMENT REQUESTED

RESEARCH, LICENSE AND COMMERCIALIZATION AGREEMENT

This RESEARCH, LICENSE AND COMMERCIALIZATION AGREEMENT (this "Agreement") is effective as of December 12, 2005, (the "Effective Date") and is entered into by and between Glaxo Group Limited, a corporation organized under the laws of England, with offices at Glaxo Wellcome House, Berkeley Avenue, Greenford, Middlesex, UB6 0NN, United Kingdom ("GSK"), and Vertex Pharmaceuticals Incorporated, a Massachusetts corporation with corporate offices at 130 Waverly Street, Cambridge, MA 02139-4242, United States of America ("Vertex").

Background:

A. GSK is interested in developing and commercializing drugs selectively targeting the **[***]** ion channel.

B. Vertex has undertaken a broad drug discovery program relating to the **[***]** ion channel, and has exclusive rights to VX-409, a small-molecule **[***]** ion channel inhibitor. GSK desires to obtain a license to VX-409 and Vertex is willing to grant such a license, in each case on the terms set out in this Agreement.

C. Vertex also has an ongoing Back-up Program directed toward the identification of one or more additional **[***]** ion channel inhibitors as back-ups to VX-409. Vertex is willing to provide GSK with rights to Back-up Compounds generated in that program, on the terms set out in this Agreement.

NOW, THEREFORE, in consideration of the foregoing premises and the mutual covenants herein contained, the receipt and sufficiency of which are hereby acknowledged, the Parties agree as follows:

ARTICLE 1: DEFINITIONS

Unless specifically set forth to the contrary herein, the following terms, whether used in the singular or plural, shall have the respective meanings set forth below.

1.1 **"Affiliate"** shall mean, with respect to any Person, any other Person that directly or indirectly controls, is controlled by or is under direct or indirect common control with, such Person. For purposes of this Section 1.1, the term "control" means the possession, direct or indirect, of the power to direct or cause the direction of the management and policies of a Person, whether through the ownership of voting securities, by contract or otherwise. Control of any Person by another Person will be presumed if fifty percent (50%) or more of the securities or other ownership interests representing the equity, the voting stock or general partnership interest of the first Person are owned, controlled or held, directly or indirectly, by the other Person, or by an Affiliate of the other Person.

1.2 **"Back-up Compound"** means a Compound other than VX-409 that will be the subject of the Back-up Program, all of which are identified in *Schedule 1.2* hereto.

1.3 **"Back-up Program"** means the research activities undertaken by Vertex relative to the Back-up Compounds as set forth in Article 2.

1.4 **"Back-up Program Term"** means the period commencing on the Effective Date and ending on December 31, 2005, or such other date as may be agreed by the Parties pursuant to Section 2.2.

1.5 **"Calendar Year"** means each successive period of twelve (12) months commencing on January 1 and ending on December 31.

1.6 **"Change of Control"** means a transaction or series of related transactions that results in (a) the holders of outstanding voting securities of a Party immediately prior to such transaction ceasing to represent at least fifty percent (50%) of the combined outstanding voting power of the surviving entity immediately after such transaction; (b) any Third Party (other than a trustee or other

fiduciary holding securities under an employee benefit plan) becoming the beneficial owner of fifty percent (50%) or more of the combined voting power of the outstanding securities of a Party; or (c) a sale or other disposition to a Third Party of all or substantially all of a Party's assets or business.

1.7 **"Clinical Trial"** means a Phase I Clinical Trial, a Phase IIa Clinical Trial, a Phase IIb Clinical Trial or a Phase III Clinical Trial.

1.8 **"Combination Product"** means a single product that includes one or more therapeutically active ingredients other than a Product Candidate or a Product, in combination with a Product Candidate or Product. All references to Product in this Agreement shall be deemed to include a Combination Product unless otherwise specifically noted.

1.9 **"Commercial Failure or Technical Failure"** means the suspension or discontinuation of the development or commercialization of a Product Candidate or Product, based on the good faith determination by GSK that development or commercialization of that Product Candidate or Product is no longer commercially reasonable, **[***].**

1.10 **"Commercial Milestone Payment"** means a payment required under the provisions of Section 8.5 hereof.

1.11 **"Commercially Reasonable Efforts"** means efforts and resources, with respect to a particular Party, and with respect to a referenced Product Candidate or Product, that are comparable to those generally used by that Party in the exercise of its reasonable business judgment relating to other prescription pharmaceutical products owned or licensed by it or to which it has exclusive rights, which have market potential and are at a stage of development or product life similar to the referenced Product Candidate or Product, taking into account measures of relative safety and efficacy, product profile, the competitiveness of the marketplace, the proprietary position of the compound or product, the regulatory structure involved, the relative profitability of the products, and other relevant factors, including without limitation comparative technical, legal, scientific, and/or medical factors.

1.12. **"Competing Product"** shall mean a small molecule chemical compound (other than a Product Candidate or Product) that is either being marketed or is in clinical development **[***].**

1.13 **"Compound"** means each of (1) VX-409, (2) the Back-up Compounds and (3) any compounds included in this Agreement as provided in Sections 2.9(b) and 2.9(c), in each case including with respect to any such compound, all of its prodrugs and metabolites, its stereo-isomers and tautomers, and all of its and their esters, salts, hydrates, solvates and polymorphs.

1.14 **"Control"** or **"Controlled by"** means the ownership or other legal authority or right of a Party to grant a license or sublicense of intellectual property to another Party without breaching the terms of any agreement with a Third Party, infringing the intellectual property rights of a Third Party, or misappropriating the proprietary or trade secret information of a Third Party.

1.15 **"Development Candidate Criteria"** means the criteria set out in *Schedule 1.15*, as such criteria may subsequently be revised by the Parties as an amendment to this Agreement.

1.16 **"Development Milestone Event"** is defined in Section 8.4.

1.17 **"Development Milestone Payment"** is defined in Section 8.4.

1.18 **"Development Plan"** is described in Section 3.4.1.

1.19 **"Development Program"** means all activities associated with the clinical and nonclinical development, testing, manufacture and Regulatory Approval of Product Candidates and Products pursuant to a Development Plan.

1.20 **"Exclusivity Period"** means the **[***]** period commencing on the day following the end of the Back-up Program Term.

1.21 **"FDA"** means the United States Food and Drug Administration, or any successor U.S. governmental agency that is responsible for approving the sale of pharmaceuticals in the United States.

1.22 **"Field"** means all human therapeutic, prophylactic and diagnostic uses of Product Candidates and Products.

1.23 **"Filing"** of an NDA means the acceptance of the NDA filing by a Regulatory Authority.

1.24 **"Final Back-up Report"** is defined in Section 2.5.

1.25 **"First Commercial Sale"** means, with respect to any Product, the first sale of that Product in a country of the Territory for use or consumption by the general public in such country (rather than, *e.g.*, in so-called "Phase IV" clinical trials) after Marketing Authorization for such Product has been obtained in such country. For the avoidance of doubt, sales prior to receipt of all marketing approvals necessary to commence regular commercial sales, such as so-called "treatment IND sales", "named patient sales" and "compassionate use sales", shall not be construed as a First Commercial Sale. Such sales shall however constitute Net Sales.

1.26 **"GMP"** means current good manufacturing practices as required by the FDA under the provisions of 21 C.F.R. parts 210 and 211 (as the same may be amended) and all applicable FDA rules, regulations, orders and guidances.

1.27 **"GSK Information and Inventions"** means all discoveries, Improvements, processes, methods, protocols, formulas, data, Inventions, know-how and trade secrets, patentable or otherwise, Controlled by GSK or its Affiliates and discovered, created or developed by employees of GSK, or by other persons not employed or retained by Vertex and acting on behalf of GSK, directly related to the research, development, utilization, manufacture or sale of Product Candidates or Products.

1.28 **"Improvement"** means any enhancement, whether or not patentable, in the formulation, preparation, presentation, means of delivery, or dosage of a Product Candidate or Product, that is discovered or developed by Vertex during the Back-up Program Term, or by GSK or its Related Parties in connection with any activities conducted under this Agreement, relative to a Product Candidate or Product.

1.29 **"Indication"** means a separate and distinct disease or medical condition in humans (i) that a Product Candidate which is in Clinical Trial(s) is being evaluated to treat or prevent, or (ii) for which a Product has received Marketing Authorization, meaning that the disease or medical condition is contained in the Product's labeling as part of the Marketing Authorization for such Product. **[***].**

1.30 **"Information"** means any and all information and data, including all scientific, pre-clinical, clinical, regulatory, manufacturing, marketing, financial and commercial information or data, whether communicated in writing, electronically or orally or by any other method, which is provided by one Party to the other Party in connection with this Agreement.

1.31 **"Initiation"** means, with respect to a particular Clinical Trial, the administration of the first dose of a Product Candidate or Product to a human in that Clinical Trial.

1.32 **"Invention"** means any process, method, use, composition of matter, article of manufacture, discovery or finding that is conceived and/or reduced to practice (whether or not patentable) (i) in the course of the Back-up Program, or (ii) during the Development Program with respect to activities conducted under this Agreement, relating to a particular Product Candidate or Product.

1.33 **"Joint Development Team"** and **"JDT"** are defined in Section 3.3.

1.34 **"Joint Information and Inventions"** means all Information, Improvements and Inventions created, developed or invented jointly by employees of GSK and Vertex, or by others acting on behalf of GSK and Vertex, in the course of activities undertaken under this Agreement.

1.35 **"Joint Patent Rights"** means all national, regional and international patents and patent applications, certificates of invention and applications for certificates of invention, including divisions, continuations, continuations-in-part, additions, reissues, renewals, extensions, substitutions, re-examinations or restorations, registrations and revalidations, and supplementary protection certificates or the like or any of the foregoing and all foreign equivalents thereof, that, when granted, recite a claim directed to Joint Information and Inventions.

1.36 **"Joint Steering Committee"** and **"JSC"** are defined in Section 3.2.

1.37 **"Know-How"** means Vertex Know-How.

1.38 **"Lead Compound"** means, at any time, that Product Candidate that is in the most advanced stage of development. VX-409 is the Lead Compound as of the Effective Date. If at any time there is no Product Candidate in development, then the Lead Compound shall mean the next Product Candidate selected for development.

1.39 **"Major Market Country"** shall mean any one of the following countries: **[***].**

1.40 **"Marketing Authorization"** means all approvals from the relevant Regulatory Authority necessary to market and sell a Product in a particular country for the prevention or treatment of any one or more Indications. For countries where governmental approval is required for pricing or reimbursement for the Product, "Marketing Authorization" shall not be deemed to occur until such pricing or reimbursement approval is obtained.

1.41 **"[***] Ion Channel"** means **[***].**

1.42 **"NDA"** means a New Drug Application, Worldwide Marketing Application, Marketing Application Authorization, or similar application or submission for Marketing Authorization of a Product, that is filed with a Regulatory Authority to obtain marketing approval for a pharmaceutical product in a particular country or group of countries.

1.43 **"Net Sales"** means the gross amount billed or invoiced by GSK or its Related Parties on arms-length sales of a Product to a Third Party, less Permitted Deductions. "Permitted Deductions" includes only the following, and, with the exception of (vii) below, only to the extent specifically related to the gross amount billed or invoiced:

(i) customary transportation charges relating to the Product, including handling charge and insurance premium relating thereto;

(ii) sales taxes, excise taxes and duties paid by and not refunded to the selling Party and directly related to sale of the Product, and any other equivalent governmental charges imposed upon the importation, use or sale of the Product, but excluding income and similar taxes;

(iii) government-mandated and other rebates (such as those in respect of any state or federal Medicare, Medicaid or similar programs);

(iv) customary trade, quantity and cash discounts allowed on Product;

(v) allowances or credits to customers on account of retrospective price reductions affecting Product;

(vi) customary Product rebates and Product charge backs including those customarily granted to managed care entities; and

[***]

[***]

1.44 **"Party"** means GSK or Vertex, and **"Parties"** means GSK and Vertex.

1.45 **"Person"** means any individual, corporation, partnership, association, joint-stock company, trust, unincorporated organization or government or political subdivision thereof.

1.46 **"Phase I Clinical Trial"** means a human clinical trial for a Product Candidate or Product, in any country, that would satisfy the requirements of 21 CFR §312.21(a).

1.47 **"Phase IIa Clinical Trial"** means a human clinical trial in any country that would satisfy the requirements of 21 CFR §312.21(b) and is intended to explore a variety of doses, dose response, and duration of effect, and to generate initial evidence of clinical activity and safety, for a Product Candidate or Product in the target patient population.

1.48 **"Phase IIb Clinical Trial"** means a human clinical trial in any country that would satisfy the requirements of 21 CFR §312.21(b), and is a controlled dose-ranging study designed to further evaluate the efficacy and safety of a Product Candidate or Product in the target patient population, beyond the scope of any initial Phase II evaluation.

1.49 **"Phase III Clinical Trial"** means a human clinical trial, performed after preliminary evidence suggesting effectiveness of the Product Candidate or Product has been obtained, conducted for inclusion in (i) that portion of the FDA submission and approval process which provides for the continued trials of a Product Candidate on sufficient numbers of human patients to confirm with statistical significance the safety and efficacy of a Product sufficient to support Marketing Authorization in the proposed Indication, as more fully defined in 21 CFR §312.21(c), or (ii) equivalent Regulatory Agency submissions with similar requirements in a country other than the United States.

1.50 **"Product"** means any pharmaceutical preparation in final form containing a Product Candidate, for sale by prescription, over-the-counter or any other method, and including without limitation any Combination Product. For purposes of the definition of "Net Sales" hereunder, a "Product" shall include a Compound being used for any human therapeutic, prophylactic or diagnostic purposes.

1.51 **"Product Candidate"** means a Compound which GSK has the rights, pursuant to Section 2, to include within the Development Program. For the avoidance of doubt, VX-409 shall be deemed to be a Product Candidate.

1.52 **"Region"** means any one of (a) the United States of America, its territories and/or possessions, and Canada (the "North American Region"); (b) Europe (the "European Region," being the current member countries of the European Union and any additional member countries of the European Union or any successor to the European Union at the relevant date); or (c) Japan.

1.53 **"Regulatory Approval"** means, with respect to any country or region, all authorizations by the appropriate governmental entity or entities necessary for commercial sale of a Product in that country or region (not including pricing or reimbursement approval). "Regulatory Approval" in the United States shall mean final approval of a new drug application pursuant to 21 CFR §314 (or any successor regulation having the same purpose or effect), permitting marketing of a Product in interstate commerce in the United States. "Regulatory Approval" in the European Union shall mean final approval of a Marketing Authorization Application ("MAA") pursuant to Council

Directive 75/319/EEC, as amended, or Council Regulation 2309/93/EEC, as amended, or pursuant to any successor regulation having the same purpose or effect.

1.54 **"Regulatory Authority"** shall mean any applicable government regulatory authority involved in granting approvals for the manufacturing, marketing and sale of a Product in the Territory, including, in the United States, the United States Food and Drug Administration, and any successor governmental authority having substantially the same function.

1.55 **"Related Party"** shall mean each of GSK's Affiliates and permitted sublicensees.

1.56 **"Selectivity Assay"** shall mean

[***].

1.57 **"Specifications"** means the specifications for supplies of VX-409 to be provided pursuant to Section 5.2, as agreed and detailed on *Schedule 1.57*.

1.58 **"Territory"** means all of the countries in the world, and their territories and possessions.

1.59 **"Third Party"** means an entity other than GSK and its Related Parties, and Vertex and its Affiliates.

1.60 **"Unit Direct Cost of Goods"** is defined on *Schedule 1.60*.

1.61 **"U.S."** and **"United States"** and **"United States of America"** shall mean the United States of America and its territories and possessions.

1.62 **"Valid Patent Claim"** means a claim of an issued and unexpired patent included within the Vertex Patent Rights which (a) claims a Product as a composition of matter, or the formulation, method of manufacture or use of the Product and (b) has not been revoked or held unenforceable, unpatentable or invalid by a decision of a court or other governmental agency of competent jurisdiction (which decision is not appealable or has not been appealed within the time allowed for appeal), nor has been disclaimed, denied or admitted to be invalid or unenforceable through reissue, re-examination or disclaimer or otherwise.

1.63 **"Valid Safety Issue"** is defined in Section 11.2.

1.64 **"Vertex Information and Inventions"** shall mean all Vertex Know-How and all other discoveries, Improvements, processes, methods, protocols, formulas, data, Inventions and trade secrets, patentable or otherwise, discovered, created or developed, and Controlled by Vertex or its Affiliates as of the Effective Date or generated by Vertex or its Affiliates in the course of Vertex's performance of the Back-up Program under this Agreement, and related to the research, development, utilization, manufacture or sale of any Product Candidate or Product. Notwithstanding the foregoing, the term "Vertex Information and Inventions" shall not apply to Vertex's general drug design technology whether in hardware or software form, tangible or intangible.

1.65 **"Vertex Know-How**" means all information and materials, including discoveries, Improvements, processes, methods, protocols, formulas, data, inventions and trade secrets, patentable or otherwise, that do not fall within the Vertex Patent Rights and that are Controlled by Vertex or its Affiliates as of the Effective Date or are discovered, developed, used or applied by Vertex or its Affiliates in the course of Vertex's performance of the Back-up Program, and which are useful in the research, development, utilization, manufacture or sale of any Product Candidate or Product; provided, however, that the term "Vertex Know-How" shall not apply to Vertex's general drug design technology whether in hardware or software form, tangible or intangible, including its e-VIPR technology.

1.66 **"Vertex Patent Rights"** means all patents and patent applications that are Controlled by Vertex on the Effective Date or during the Back-up Program Term (or, with respect only to any Compounds which fall under this Agreement by reason of Sections 2.9(b) or 2.9(c), during the Exclusivity Period) which generically or specifically claim (i) a Compound, a Product Candidate or a Product; (ii) a process for manufacturing a Compound, a Product Candidate or a Product, or an intermediate used in such process; or (iii) a use of a Compound, a Product Candidate or a Product. Included within the definition of Vertex Patent Rights are all continuations, continuations-in-part, divisions, patents of addition, reissues, renewals or extensions, substitutions, re-examinations or restorations, registrations and revalidations thereof, and all supplementary protection certificates and the like. The current list of patent applications and patents encompassed within Vertex Patent Rights is set forth on *Schedule 1.66* attached hereto.

1.67 **"VX-409"** means the chemical compound, referred to by Vertex as VX-409, having the chemical structure referenced on *Schedule 1.67.*

ARTICLE 2: BACK-UP PROGRAM

2.1 **Back-up Program—General.** Vertex will, at its own cost, engage in the Back-up Program upon the terms set out in this Agreement. Vertex's objective in conducting the Back-up Program is to produce, by the end of the Back-up Program Term, Back-up Compounds which meet the Development Candidate Criteria. GSK shall have the exclusive option (as further defined within this Article 2), in its sole discretion, to develop and commercialize each Back-up Compound.

2.2 **Back-up Program Term.** The initial term of the Back-up Program shall be the period commencing on the Effective Date and ending on December 31, 2005. At any time during the initial period of the Back-up Program, the Parties may mutually agree to extend the Back-up Program beyond the initial period for an additional period not to exceed six (6) months. Any such extension shall only be deemed to be agreed when documented by a written instrument duly executed by authorized representatives of both Parties.

2.3 **Conduct of Back-up Program.** Vertex shall use Commercially Reasonable Efforts to conduct the Back-up Program in a manner to achieve the objectives of the Back-up Program efficiently and expeditiously. Vertex will conduct the Back-up Program in good scientific manner, and in compliance in all respects with all requirements of applicable laws, rules and regulations and all applicable good laboratory practices.

2.4 **GSK Access during Back-up Program.** Immediately following the Effective Date, Vertex shall provide GSK with full details of the chemical structures of each of the Back-up Compounds and samples of the Back-up Compounds (if Vertex determines that such quantities are available) to enable GSK to undertake initial evaluation of the Back-up Compounds.

2.5 **Final Back-up Report.** On or before the end of the Back-up Program Term, Vertex will provide GSK with a final report (the "Final Back-up Report") detailing for each of the Back-up Compounds the data generated in respect of each of the Development Candidate Criteria, and further containing all information and data known to Vertex concerning each of the Back-up Compounds, together with a statement of Vertex's opinion whether any Back-up Compounds satisfy the Development Candidate Criteria as of the last day of the Back-up Program Term.

2.6 **Product Candidates [***].** From and after the date of provision of the Final Back-up Report to GSK, each of the Back-up Compounds shall be deemed Product Candidates. **[***]

2.7 **Disputes as to whether the Development Candidate Criteria have been met.** GSK shall notify Vertex within **[***]** after receipt of the Final Back-up Report if GSK disputes whether any

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Back-up Compound satisfies the Development Candidate Criteria (a "Disputed Back-up Compound"), and at such time shall explain why it has given such notification. Within **[***]** following such notification, the Joint Steering Committee shall meet to consider whether any such Disputed Back-up Compound has met the Development Candidate Criteria.

(a) [***]

(b) [***]

(c) If the Joint Steering Committee is unable to agree on whether the Disputed Back-up Compound has been shown to satisfy the Development Candidate Criteria, the issue shall be referred to the Chief Executive Officer of Vertex (or to the Head of Research or to the Head of Development, as the CEO of Vertex shall determine) and to the Chairman of R&D of GSK (or to such other senior manager of GSK as the Chairman of R&D of GSK shall determine), who shall, as soon as practicable, attempt in good faith to resolve the dispute. If they are unable to resolve the dispute within **[***]** of referral, the dispute will be referred to an independent expert who will be appointed by agreement of the Parties. The expert shall act as an expert and not an arbitrator and his or her decision shall be final and binding on the Parties. The Parties will comply with any procedure established by the expert for making his or her decision and the expert's costs shall be paid by the party against whom the expert rules. Sections 2.7(a) or (b), as appropriate, shall apply depending on whether the expert determines that the Back-up Compound satisfies the Development Candidate Criteria.

2.8 **Back-up Program Information and Inventions.** The entire right, title and interest in:

2.8.1 Vertex Information and Inventions and Vertex Patent Rights discovered or developed during the Back-up Program shall be owned solely by Vertex.

2.8.2 Joint Information and Inventions and Joint Patent Rights discovered or developed during the Back-up Program shall be owned jointly by Vertex and GSK. Except as expressly provided in this Agreement, each joint owner may make, use, sell, keep, license, assign, or mortgage such jointly owned inventions, discoveries and know-how, and otherwise undertake all activities a sole owner might undertake (other than assigning or transferring exclusive rights in or exclusive ownership of any such Joint Information and Inventions and Joint Patent Rights), with respect to such inventions, discoveries and know-how, without the consent of and without accounting to the other joint owner.

2.8.3 GSK Information and Inventions discovered or developed during the Back-up Program shall be owned solely by GSK.

Inventorship will be determined in accordance with the United States laws of inventorship.

2.9 **Exclusive Efforts.**

(a) During the Exclusivity Period, Vertex and GSK agree that they and their Affiliates will develop (i) Compounds; **[***]**, exclusively pursuant to the terms of this Agreement, including, but not limited to, Sections 2.9(b) and 2.9(c).

(b) In the event that during the Exclusivity Period, either Party commences clinical development of any compounds, other than VX-409 or the Back-up Compounds, that fall within the provisions of Section 2.9(a)(ii) above, such compounds shall automatically be deemed Compounds under this Agreement and all of the provisions of this Agreement shall thereafter apply to those compounds as if they were originally Compounds hereunder, irrespective of whether they were invented by Vertex or GSK. With respect to any such Compounds Controlled by Vertex, the scope of the licenses granted pursuant to Sections 6.1.1, 6.1.2 and

6.1.6 shall automatically be extended to permit GSK to develop, make, have made, use, offer to sell, sell or import such compounds. With respect to any such Compounds Controlled by GSK, the license referenced in Section 11.5(c) shall become applicable to such Compounds under the circumstances outlined in Section 11.5. Any decision as to whether any such additional compound should be developed as a Product Candidate shall be made by the JSC.

(c) In the event that one or more Back-up Compounds does not meet the Development Candidate Criteria at the end of the Back-up Program, during the Exclusivity Period **[***].** GSK shall be entitled during the Exclusivity Period to research and develop such Alternate Compounds with the objective of producing Alternate Compounds meeting the Development Candidate Criteria which could be developed as Product Candidates and Products. **[***].** The intellectual property embodied in any Alternate Compound shall belong to Vertex, but may become subject to the licenses provided to GSK hereunder if the compound is substituted for one of the existing Compounds during the Exclusivity Period in accordance with the following paragraph. GSK will inform Vertex of any **[***]** directed at producing Alternate Compounds, and will provide to Vertex, as soon as practicable, any chemical or biological information generated with respect to any such Alternate Compound. The objective of any modification will be to produce Alternate Compounds meeting the Development Candidate Criteria which could be developed as Product Candidates and Products.

At any time during the Exclusivity Period, by giving written notice to Vertex, GSK may substitute, one-for-one, one or more of the Alternate Compounds which meet the Development Candidate Criteria for VX-409 or any of the Back-up Compounds. From the date of provision of written notice, each substituted Alternate Compound shall be deemed a Compound under this Agreement, and the Compound for which that Alternate Compound was substituted (a "Substituted Compound," being either VX-409 or a Back-up Compound) shall no longer be considered a Compound under this Agreement. The licenses granted under Sections 6.1.1, 6.1.2 and 6.1.3 hereof shall no longer apply to any such Substituted Compound.

ARTICLE 3: DEVELOPMENT

3.1 **Commencement of Development Program.** GSK shall use Commercially Reasonable Efforts to pursue a Development Program with respect to the Product Candidates in accordance with the provisions of this Agreement. The Development Program shall proceed in accordance with a Development Plan that provides for development of one or more Product Candidates or Products in the Territory. An initial summary Development Plan, currently focused on VX-409, is attached to this Agreement as *Schedule 3.1.* A completed Development Plan, as described in Section 3.4.1, shall be prepared by GSK and reviewed by the JSC, within **[***]** after the Effective Date (or such longer period as mutually agreed), and shall be modified and updated by GSK on a regular basis, with input from the JSC and the JDT as provided below.

3.2 **Joint Steering Committee.** Promptly after the Effective Date, the Parties will establish a Joint Steering Committee (the "Joint Steering Committee" or "JSC"), as more fully described in this Section 3.2, to review and oversee all research, development, manufacture and commercialization activities being conducted by the Parties under this Agreement, including the Back-up Program; *provided, however,* that the Joint Steering Committee shall have no authority to amend this Agreement. Each Party agrees to keep the Joint Steering Committee reasonably informed of its progress and activities performed under this Agreement.

3.2.1 **Membership.** The Joint Steering Committee shall be comprised of **[***].**

Each Party shall provide the other with a list of its initial members of the Joint Steering Committee within **[***]** after the Effective Date. Notwithstanding that each Party shall use all reasonable endeavors to maintain the continuity of its representation, each Party may replace or substitute any or all of its representatives and/or appoint a proxy at any time. Each Party may, in its reasonable discretion, invite non-member representatives of such Party to attend meetings of the Joint Steering Committee.

[***]

A meeting shall be quorate (i.e. deemed to have formed a quorum) if **[***].** If there are fewer than **[***].**

3.2.2 **Chair.** The chair of the Joint Steering Committee shall be designated by GSK.

3.2.3 **Meetings.** During the Term, the Joint Steering Committee shall meet at least **[***]** and as otherwise agreed by the Parties, on such dates, and at such places and times, as provided herein or as the Parties shall agree. Meetings of the Joint Steering Committee that are held in person shall alternate between the offices of the Parties, or such other place as the Parties may agree.

3.2.4 **Minutes.** The chair of the Joint Steering Committee shall be responsible for scheduling each meeting, and issuing appropriate minutes of each meeting of the Joint Steering Committee within **[***]**of the date of such meeting. The minutes shall be considered as accepted if, within **[***]**from receipt, no one has objected in a traceable form to the chair.

3.2.5 **Responsibilities.** The JSC shall oversee the collaborative relationship between GSK and Vertex. To that end, the JSC shall also be responsible, without limitation, for the following:

(a) coordination and review of Back-up Program activities and interactions between GSK and Vertex;

(b) review of the Final Back-up Report from Vertex;

(c) oversight of all development activities; all process development and manufacturing activities undertaken with respect to any Product Candidate or Product hereunder; core commercial activities to be undertaken by GSK; and all other activities contemplated under this Agreement related to the development, manufacture and commercialization of Product Candidates and Products;

(d) ensuring the exchange of relevant information and materials relating to each activity undertaken or contemplated under this Agreement;

(e) such other responsibilities as may be assigned to the Joint Steering Committee pursuant to this Agreement or as may be mutually agreed upon by the Parties in writing from time to time.

3.2.6 **Decision Making.[***]** The members of the JSC will attempt in good faith to reach consensus on all matters brought before the JSC. If agreement cannot be reached after a good faith discussion among the members of the JSC, **[***].**

3.2.7 **Alternatives to meeting.** Any decision required or permitted to be taken by the Joint Steering Committee may be taken without a meeting in person taking place, if a consent in writing, setting forth the decision so taken, is signed by all designated members of the JSC.

3.2.8 **Expenses.** Each Party will be responsible for its representatives' expenses incurred in attending meetings of the JSC.

3.2.9 **Alliance Managers.** Promptly after the Effective Date, each Party shall appoint an individual(s) to act as the alliance manager(s) for such Party (the "Alliance Managers"). Each Alliance Manager

who is not otherwise a member of the JSC shall thereafter be permitted to attend meetings of the Joint Steering Committee. The Alliance Managers shall be the primary point of contact for the Parties regarding the activities contemplated by this Agreement and shall facilitate all such activities hereunder.

3.3 **Joint Development Team.** Promptly after the Effective Date, the JSC will establish a Joint Development Team ("JDT"), which shall include, at Vertex's option, **[***].**

During the course of the Development Program, GSK shall provide the JDT (or Vertex, if Vertex has no representative on the JDT or the JSC) at least every **[***]** with the planning information listed under "Development" and "CMC" on Schedule 3.3, in GKS's standard format, as and when that information is generated and becomes available within GSK, updated to reflect ongoing activities. GSK will also provide summaries of results of all non-clinical and clinical trials. One purpose of the information is to allow the JDT (or Vertex) to review the progress and anticipated direction of the Development Program, propose amendments, where appropriate, to the Development Plan and provide comments for consideration regarding the future direction of the Development Program. Consequently information will be supplied to the JDT (or Vertex) at a time sufficiently prior to finalization of each Development Plan to accommodate any suggestions and comments by Vertex which are deemed by GSK, in its sole discretion, to be worth incorporating in the planning process for each Product Candidate and Product.

Following any Product Candidate entering into Phase III Clinical Trials, GSK shall provide the JDT at least every **[***]** with the planning information listed under "Commercialization" on Schedule 3.3, in GSK's standard format, as and when that information is generated and becomes available within GSK, updated to reflect ongoing activities, so that the JDT can review the preparation and implementation of the Global Marketing Plan and where appropriate propose for consideration amendments to it.

For the avoidance of doubt, the JDT shall act in an advisory capacity only and shall have no authority to require any amendments to either the Development Plan or the Global Marketing Plan.

During the Term, the Joint Development Team shall meet quarterly, or as otherwise agreed by the Parties, either in person or by teleconference or by videoconference, on such dates and at times as the Parties shall agree. Meetings of the JDT that are held in person shall alternate between the offices of the Parties, or such other places as the Parties may agree. Each party will be responsible for its representatives' expenses incurred in attending meetings of the JDT.

If at any time, Vertex is not represented at any JDT meeting by at least **[***].** GSK may thereafter suspend all meetings of the JDT until such time as Vertex notifies GSK of its intent to ensure representation at future JDT meetings.

3.4 **Development.**

3.4.1 **Development Plan.** Subject to the terms of this Agreement, GSK shall promptly prepare and oversee the implementation of an overall Development Plan for the Product Candidates. The Development Plan shall have as a principal objective the development of one or more Product Candidates for commercialization in each Region in the Territory. The Development Plan shall be presented promptly to the JDT and then the JSC, and shall be supplemented, modified and updated regularly by GSK as and when additional relevant data and information become available during the course of the Development Program (but in any event not less frequently than annually). Any such significant supplements, modifications or updates shall be promptly reported to the JDT and then to the JSC. The Development Plan shall, among other things, detail, schedule and fully describe the proposed toxicology and other nonclinical studies, Clinical Trials, regulatory

plans, manufacturing plans and material requirements and annual budget, and will outline the key elements involved in obtaining Regulatory Approval in each Region in the Territory.

3.4.2 **Development Responsibility and Costs.** GSK shall have sole responsibility for, and bear the cost of implementing, the Development Program and the Development Plan.

3.4.3 **Regulatory Approvals.** GSK shall be solely responsible for preparing and submitting registration dossiers for Regulatory Approval of Products and Product Candidates in the Territory. All Regulatory Approvals shall be held by and in the name of GSK, and GSK shall own all submissions in connection therewith. GSK shall have sole discretion as to the regulatory strategy and decision making for any Product Candidate or Product; provided, however, that GSK shall provide Vertex with an opportunity to review GSK's general regulatory strategy at the JSC and JDT.

3.5 **Due Diligence.** GSK shall use Commercially Reasonable Efforts to develop Product Candidates and Products in accordance with the provisions of the Development Plan, which shall be directed toward obtaining Regulatory Approval for commercial sale of one or more Products in each Region in the Territory. GSK will promptly notify Vertex through the JSC if it should determine that continued development of a Product Candidate or Product is not technically feasible or commercially reasonable, or if it determines that the continued development of a Product Candidate or Product should be suspended for a period of time, specifying the reasons for its decision or determination.

3.6 **Reporting.** During the Development Program GSK shall, at least every **[***]**, inform Vertex about the status of the Development Program, and will keep Vertex currently advised as and when any Development Milestone Events, in respect of which payments become due pursuant to Section 8.4, are achieved. For the avoidance of doubt, the obligation hereunder to inform Vertex about the status of the Development Program shall be deemed met if Vertex is attending the JDT during the relevant period, and GSK has met its obligations under Section 3.3.

ARTICLE 4: COMMERCIALIZATION

4.1 **Marketing and Promotion.** GSK shall have the exclusive right to market, sell and distribute all Products in the Territory (which may include sublicensing marketing rights as set forth in Section 6.2 below) subject to the other provisions of this Article 4. GSK shall bear all costs associated with marketing, sale and distribution of Products.

4.2 **Global Marketing Plan.** GSK shall have sole responsibility for the preparation and implementation of the Global Marketing Plan for Product Candidates and Products. GSK shall inform Vertex, through the JSC and JDT, about the status of the Global Marketing Plan (including product launches in the USA, Japan and the Major Market Countries) taking in good faith any comments made by Vertex at the JSC and JDT. For the avoidance of doubt, the obligation hereunder to inform Vertex about the status of the Global Marketing Plan shall be deemed met if Vertex is attending the JDT during the relevant period, and GSK has met its obligations under Section 3.3.

4.3 **Due Diligence.** GSK shall use Commercially Reasonable Efforts to commercialize one or more Products in each Region in the Territory in accordance with the provisions of the Global Marketing Plan. GSK will promptly notify Vertex if it should determine that commercialization of a Product is not technically feasible or commercially reasonable in any particular Region, specifying in detail the reasons for its decision or determination.

Information redacted pursuant to a confidential treatment request. An unredacted version of the exhibit has been filed separately with the Commission.

ARTICLE 5: MANUFACTURING AND SUPPLY

5.1 **Clinical and Commercial Supply.** GSK shall be responsible, at its sole expense, for manufacture and supply of all Product Candidates and Products hereunder for all purposes.

5.2 **Purchase of Inventory.**

(a) As soon as reasonably practicable following the Effective Date, and in any event before December 31, 2005, Vertex shall deliver FCA Facility (IncoTerms 2000) to a carrier designated by GSK all of its existing inventory of VX-409 bulk drug substance that in Vertex's opinion meets the Specifications (the "Transferring Inventory"). GSK shall accept and pay for all of such Transferring Inventory which meets the Specifications, has been manufactured to GMP standards, as documented by a corresponding Certificate of Analysis in accordance with ICH Guidance Q7A, Manufacturing Practice Guidance for Active Pharmaceutical Ingredients, and meets the requirements of ICH Guidance Q3C (together, "the Necessary Standard"). GSK shall have no obligation to pay for any inventory which does not meet the Necessary Standard as set out in this Section 5.2(a), though it may, in its sole discretion, waive the requirement to meet the Necessary Standard in respect of all or part of the Transferring Inventory. At Vertex's request GSK shall return to Vertex any inventory that it does not accept, FCA Facility (IncoTerms 2000) to a carrier designated by Vertex.

(b) Within **[***]** of receipt of the Transferring Inventory GSK shall notify Vertex if GSK does not accept that all of the Transferring Inventory meets the Necessary Standard. Failure to provide such notification shall be deemed acceptance of the Transferring Inventory. In the event that the Parties disagree as to whether or how much of the Transferring Inventory meets the Necessary Standard, such dispute shall be resolved pursuant to Section 12.7.

(c) The price payable by GSK for the Transferring Inventory shall be an amount equal to Vertex's Manufacturing Cost multiplied by the percentage of Transferring Inventory which meets the Necessary Standard or has otherwise been accepted by GSK, payable within **[***]** after receipt of an invoice by GSK detailing the Transferring Inventory and Vertex's Manufacturing Cost. For purposes of this section, "Vertex's Manufacturing Cost" means the **[***].** The volume of Transferring Inventory and an estimate of Vertex's Manufacturing Cost thereof is set forth in *Schedule 5.2* to this Agreement.

5.3 **Technology Transfer.** On or before December 31, 2005, Vertex at its own cost shall transfer (or cause to be transferred) to GSK all information and materials Controlled by Vertex (including information from any relevant Third Party contract manufacturer) relating to VX-409 and the Back-up Compounds and/or necessary for the conduct of the Development Program, including any applicable Vertex Know-How and any relevant information and materials listed in *Schedule 5.3.* Vertex will further provide such technical assistance as GSK may reasonably require in order to effect such technology transfer.

5.4 **Use of Vertex Logo.** Where not prohibited by law or regulation, and subject to any required Regulatory Approval, which GSK shall use reasonable efforts to obtain, Vertex's name and logo will be carried on all Product packaging, packaging inserts, labels, and containers, and on all printed, electronic and digital material related thereto, with a prominence substantially equivalent to that of GSK's name and logo.

ARTICLE 6: LICENSES; EXCHANGE OF INFORMATION

6.1 License Grants.

6.1.1 Vertex hereby grants to GSK an exclusive license (even as to Vertex) in the Territory in the Field under Vertex Patent Rights and Vertex's rights under Joint Patent Rights: (i) to discharge GSK's obligations and exercise its rights under this Agreement; and (ii) to make, have made, use, offer to sell, sell and import Product Candidates and Products.

6.1.2 Vertex hereby grants to GSK an exclusive license in the Territory in the Field under all Vertex Know-How insofar as it relates to Product Candidates and Products, solely to: (i) discharge GSK's obligations and exercise its rights under this Agreement; and (ii) make, have made, use, offer to sell, sell and import Product Candidates and Products.

6.1.3 Vertex hereby grants to GSK a sole license in the Territory in the Field under Vertex Patent Rights and all Vertex Know-How insofar as they relate to the Back-up Compounds to undertake research and development activities in relation to the Back-up Compounds during the Back-up Program Term.

6.1.4 Notwithstanding the foregoing, Vertex shall retain rights under the Vertex Patent Rights and the Joint Patent Rights to the extent necessary or useful for the Back-up Program Term, to discharge its obligations and exercise its rights under this Agreement.

6.1.5 GSK hereby grants to Vertex a fully-paid, non-exclusive license, without the right to sub-license, under all GSK Information and Inventions, and GSK's rights under the Joint Patent Rights for the sole purpose of the Back-up Program during the Back-up Program Term, to enable Vertex to discharge Vertex's obligations and exercise its rights under this Agreement. Such license shall terminate upon the termination of the Back-up Program Term and Vertex shall not use such GSK Information and Inventions for any reason whatsoever thereafter except as otherwise provided in this Agreement.

6.1.6 Vertex hereby grants to GSK a non-exclusive license under patents or patent applications Controlled by Vertex that do not constitute Vertex Patent Rights hereunder but which, in the absence of the license provided in this Section 6.1.6, would necessarily be infringed by GSK's practice of the licenses granted in Sections 6.1.1, 6.1.2 and 6.1.3, including but not limited to patents or patent applications encompassing claims to methods of use of any Compound. This non-exclusive license shall apply only to the exercise by GSK of its rights and the discharge by GSK of its obligations under this Agreement with respect to Product Candidates and Products.

6.2 **Right to Sublicense.** GSK shall have the right to grant sublicenses under the rights and licenses granted to it in this Article 6, *provided that* any such sublicense obliges the sublicensee to comply with all relevant terms of this Agreement and that GSK remains liable to Vertex for all material acts and omissions of any such sublicensee.

In addition, if GSK wishes to grant a sublicense to a Third Party of its development or commercialization rights in the **[***]** or in any of the Major Market Countries, **[***].**

6.3 **No Implied Licenses.** Except as specifically set forth in this Agreement, neither Party shall acquire any license or other intellectual property interest, by implication or otherwise, in any Information disclosed to it under this Agreement or under any patents or patent applications owned or Controlled by the other Party or its Affiliates.

ARTICLE 7: CONFIDENTIALITY AND PUBLICATION

7.1 **Nondisclosure Obligation.** All Information disclosed by one Party to the other Party shall be maintained in confidence by the receiving Party and shall not be disclosed to a Third Party or used

for any purpose except as set forth herein without the prior written consent of the disclosing Party, except to the extent that such Information:

7.1.1 is known by the receiving Party at the time of its receipt, and not through a prior disclosure by the disclosing Party, as documented by the receiving Party's contemporaneous business records;

7.1.2 is in the public domain through no breach of this Agreement by the receiving Party;

7.1.3 is subsequently disclosed to the receiving Party by a Third Party who may lawfully do so and is not to the best of the receiving Party's knowledge under an obligation of confidentiality to the disclosing Party;

7.1.4 is developed by the receiving Party independently of Information received from the disclosing Party, as documented by the receiving Party's contemporaneous business records;

7.1.5 is disclosed to governmental or other regulatory agencies to comply with applicable law or regulations, provided the receiving Party provides to the disclosing Party prompt prior written notice of its obligation to make such disclosure and takes reasonable and lawful actions to avoid or minimize the degree of such disclosure; or

7.1.6 is deemed necessary by GSK in the reasonable exercise of its judgment to be disclosed to any Third Party, to the extent GSK deems necessary or advisable, in connection with the research and development, manufacturing and/or marketing of a Product or Product Candidate (or for such entities to determine their interest in performing such activities) in accordance with this Agreement, on the condition that any such Third Parties agree to be bound by confidentiality and non-use obligations that are no less stringent than those confidentiality and non-use provisions contained in this Agreement.

Any combination of features or disclosures shall not be deemed to fall within the foregoing exclusions merely because individual features are published or available to the general public or in the rightful possession of the receiving Party unless the combination itself and principle of operation are published or available to the general public or in the rightful possession of the receiving Party.

If a Party is required by judicial or administrative process to disclose Information that is subject to the non-disclosure provisions of this Section 7.1, such Party shall promptly inform the other Party of the disclosure that is being sought in order to provide the other Party an opportunity to challenge or limit the disclosure obligations. Information that is disclosed by judicial or administrative process shall remain otherwise subject to the confidentiality and non-use provisions of this Section 7.1, and the receiving Party shall co-operate with any reasonable attempts of the disclosing Party to limit such disclosure required by law, including without limitation by way of obtaining an order of confidentiality, to ensure the continued confidential treatment of such Information.

7.2 Publication.

(a) GSK and Vertex each acknowledge the other Party's interest in publishing in a scientific journal or a scientific conference or through a similar medium the results of its research in order to obtain recognition within the scientific community and to advance the state of scientific knowledge. Each Party also recognizes the mutual interest in obtaining valid patent protection and in protecting business interests and trade secret information. Consequently, except for disclosures permitted pursuant to Section 7.1 and under subsections (b) and (c) below, if either Party, its employees or consultants wishes to publish or publicly present results of the Back-up Program or any information about a Product Candidate or a Product,

or the results of any activities to discover or develop any of the above, it shall deliver to the other Party a copy of the proposed written publication or an outline of an oral disclosure **[***]** prior to submission for publication or presentation. The reviewing Party shall notify the other Party **[***]**of receipt of such proposed publication whether such draft publication contains (i) Information that is confidential to the reviewing Party, or (ii) information that if published would have an adverse effect on a patent application covering the subject matter of this Agreement. The reviewing Party shall have the right to (a) propose modifications to the publication or presentation for patent reasons, trade secret reasons, confidentiality reasons or to protect proprietary business interests, or (b) request a reasonable delay in publication or presentation in order to protect patentable information. If the reviewing Party requests a delay to protect patentable information, the publishing Party shall delay submission or presentation for a period not to exceed **[***]** to enable patent applications protecting each Party's rights in such information to be filed. Upon expiration of such **[***]**, the publishing Party shall be free to proceed with the publication or presentation. If the reviewing Party reasonably requests modifications to the publication or presentation to prevent disclosure of trade secret or proprietary business information, the publishing Party shall edit such publication to prevent the disclosure of such information prior to submission of the publication or presentation.

(b) After the expiration of a **[***]** period following the end of the Back-up Program Term, intellectual property that is the subject of an exclusive license provided by Vertex to GSK shall be considered Information that is not confidential to Vertex, but rather is Information that is confidential to GSK, for purposes of Section 7.1 and this subsection (b), so long as any such license is in effect.

(c) For the avoidance of doubt, and without limiting in any way the above, GSK may post summaries on the GSK Clinical Trial Register of the results of any Clinical Trials conducted with respect to a Product Candidate or a Product pursuant to this Agreement without further approval from Vertex under subsection (a) above, provided:

(i) it notifies Vertex in writing not less than **[***]** prior to any such posting;

(ii) the posting of clinical trial summaries is the usual and customary practice of GSK;

(iii) by written notice to GSK prior to the end of the **[***]** period referenced in (i) above, Vertex may request a delay in any posting, in order to protect patentable information, and in such event GSK shall delay posting for up to **[***]**, as may be requested by Vertex to enable the prior filing of appropriate patent applications.

(d) Authorship of any publication shall be determined based on the accepted standards used in peer-reviewed, academic journals at the time of the proposed publication, and the contribution of each Party to the subject matter of each publication will be appropriately acknowledged.

7.3 **Publicity/Use of Names.** GSK and Vertex shall agree upon the timing and content of an initial press release relating to the execution of this Agreement and its terms. Except to the extent already disclosed in that initial press release, no disclosure of the existence of this Agreement or its terms may be made by either Party, and no Party shall use the name, trademark, trade name or logo of the other Party or its employees in any publicity, news release or promotional materials relating to this Agreement or its subject matter, without the prior express written permission of the other Party, except as may be required by applicable laws, regulations, or judicial order. The Party desiring to make any such public announcement shall provide the other Party with a written copy of the proposed announcement in sufficient time prior to public release to allow such other Party to comment upon such announcement, prior to public release.

In addition to the foregoing restrictions on public disclosure, if either Party concludes that a copy of this Agreement must be filed with a securities exchange or regulatory or governmental body to which that Party is subject wherever situated, such Party shall provide the other Party with a copy of this Agreement showing any sections as to which the filing Party proposes to request confidential treatment, will provide the other Party with an opportunity and a reasonable time period to comment on any such proposal and to suggest additional portions of the Agreement for confidential treatment and will take such Party's reasonable comments into consideration before filing the Agreement. If the filing Party disagrees with the other Party's additional confidential treatment request, the Parties shall have an opportunity to discuss the matter in good faith before the Agreement is filed.

7.4 **Survival.** Section 7.2(a) & (b) shall terminate with the termination of this Agreement, but the provisions of Section 7.1 shall continue to govern the disclosure by one Party, by publication or otherwise, of Information of the other, during the period set forth in Section 11.8.

ARTICLE 8: PAYMENTS; ROYALTIES AND REPORTS

8.1 **Consideration for License.** In consideration of the licenses granted pursuant to Article 6 and Section 2.9(c), GSK shall pay to Vertex a one-time non-refundable, non-creditable payment of Twenty Million Dollars (US $20,000,000) within five (5) business days of the Effective Date. On the Effective Date, Vertex will provide GSK with an invoice for the amount of this payment.

8.2 **[***] Payment.** In consideration of the licenses granted pursuant to Article 6 and Section 2.9(c), GSK shall make an additional non-refundable, non-creditable milestone payment to Vertex in the amount of **[***]** for the **[***]** ; provided, however, that if one or more **[***]**, but no **[***]** is completed on or before **[***]**, then the **[***]** Payment provided in this section shall be due and payable in any event, notwithstanding the results of any Qualifying Study thereafter conducted. Any payment due under this Section 8.2 shall be made within **[***]** after receipt by GSK of an invoice. The **[***]** payable under this Section 8.2 shall not be required with respect to more than **[***].** All **[***]**, regardless of whether they **[***]**, shall be deemed Product Candidates under this Agreement, irrespective of whether any **[***]** is earned under this Section 8.2.

8.3 **First Product Candidate Milestone Payment.** In further consideration of the licenses granted pursuant to Article 6, GSK shall make a non-refundable, non-creditable payment to Vertex in the amount of**[***]** payable upon **[***].**

8.4 **Development Milestone Payment.** In further consideration of the licenses granted pursuant to Article 6, GSK shall also pay each of the amounts set forth in the table below (each, a "Development Milestone Payment") if and when the corresponding development milestone event (each, a "Development Milestone Event") is achieved with respect to the first two Indications for which one or more Product Candidates or Products are being investigated.

	[***]	**[***]**
[***]	[***]	[***]
[***]	[***]	[***]
[***]	[***]	[***]
[***]	[***]	[***]
[***]	[***]	[***]
[***]	[***]	[***]
[***]	[***]	[***]
[***]	[***]	[***]
[***]	[***]	[***]

Information redacted pursuant to a confidential treatment request. An unredacted version of the exhibit has been filed separately with the Commission.

(a) Each Development Milestone Payment shall be payable only once upon the initial achievement of the associated Development Milestone Event. For the avoidance of doubt the maximum cumulative payments under Section 8.4 will not exceed **[***].** GSK shall notify Vertex in writing not later than **[***]** after the occurrence (or deemed occurrence) of a Development Milestone Event, and shall pay the appropriate Development Milestone Payment within **[***]** of receipt of an invoice thereafter from Vertex.

(b) In the event that the Development Milestone Payment triggered on **[***].** Any Development Milestone Payments deemed to have been earned under this provision that have not been previously paid, shall be paid by GSK within **[***]** of receipt of an invoice thereafter from Vertex.

(c) For the avoidance of doubt, if a Back-up Compound becomes the Lead Compound by reason of the termination or suspension of development of the prior Lead Compound and the "new" Lead Compound subsequently achieves the same Development Milestone Event for the same Indication as the prior Lead Compound, then payment of the Development Milestone Payment which would otherwise be due with respect to attainment of that Development Milestone Event by the "new" Lead Compound shall not be required.

(d) For the avoidance of doubt, *Schedule 8.4(d)* sets forth some examples of scenarios under which the Development Milestone Payments shall be payable hereunder.

8.5 **Commercial Milestone Payments.** In further consideration of the licenses granted pursuant to Article 6, GSK will pay Vertex each of the Commercial Milestone Payments set forth in the table below, within **[***]** after receipt of an invoice from Vertex following the occurrence of the associated Commercial Milestone Event. Each of the Commercial Milestone Payments shall be payable only once, regardless of the number of Product Candidates which are commercialized.

Commercial Milestone Event (US$)	Commercial Milestone Payment (US$ million)
[***]	
[***]	[***]
[***]	[***]
[***]	[***]

8.6 **Royalties.**

8.6.1 **Royalties Payable By GSK.** In further consideration of the licenses granted pursuant to Article 6, GSK shall pay to Vertex royalties on the Net Sales of each Product as set out in this Section 8.6.

8.6.2 **Patent Royalties.** The royalty rate payable in respect of Products shall be determined according to the following table containing staggered royalty rates:

[***]	[***]
[***]	
[***]	[***]
[***]	[***]
[***]	[***]

Royalties on sales of Product, at the Patent royalty rates determined as set forth above with reference to aggregate Net Sales, shall be payable on a country-by-country basis until, with respect to a particular country, the expiration of the last-to-expire Valid Patent Claim in effect in that country claiming the manufacture, use, sale or importation of the Product. For purposes of determining aggregate Calendar Year Net Sales under this Section 8.6.2, Net Sales shall include sales in a country whether or not those sales would infringe a Valid Patent Claim.

8.6.3 Special Know-How Royalties.

(a) In the event that there are Valid Patent Claims in any **[***]** of the Major Market Countries, which claim the manufacture, use, sale or importation of a Product in such Major Market Country, GSK shall pay royalties to Vertex on account of Net Sales of the Product in **[***]** even if in one or more countries (each, a "**[***]**") at the time of the First Commercial Sale of that Product in the **[***]**, there is no Valid Patent Claim claiming the manufacture, use, sale or importation of the Product in such **[***].** The royalty payable in the **[***]**, shall be payable for **[***]** from the date of First Commercial Sale of the Product in that Country (a "Special Know-How License Term"), at the applicable royalty rates determined according to Section 8.6.2. If during the Special Know-How License Term a Valid Patent Claim is established in that **[***]** with respect to that Product, then that Country shall no longer be considered a **[***]** and royalties shall be paid thereafter in accordance with, and at the rate and for the term set forth in, Section 8.6.2. For the purpose of this provision, "**[***]**" shall have the meaning assigned to it in **[***].**

(b) Notwithstanding (a) above, if at any time during the Special Know-How License Term applicable to a particular Product being sold in a **[***]**, then royalties shall cease to be payable pursuant to Section 8.6.3(a) above and royalties will instead become payable pursuant to Section 8.6.4 below. For purposes of this subsection (b), **[***].** This subsection 8.6.3(b) shall not be applicable if GSK or its Related Parties has granted the Third Party a sub-license hereunder.

8.6.4 Know How Royalties

In the event that there is no Valid Patent Claim claiming the manufacture, use, sale or importation of the Product in a particular country and therefore patent royalties would not be payable under Section 8.6.2, and if royalties shall also not be payable in that country under Section 8.6.3 above, **[***].** Royalties under this Section 8.6.4 on account of Net Sales of that Product in a country shall be paid for a period of **[***]** from the First Commercial Sale of the Product in such country.

8.6.5 Other Provisions.

All royalties are subject to the following conditions:

(a) only one royalty shall be due with respect to the same unit of Product. No multiple royalty shall be payable because the manufacture, use or sale of a Product Candidate or Product is claimed by more than one Valid Patent Claim;

(b) no royalties shall be due upon the sale or other transfer among GSK or its Related Parties, but in such cases the royalty shall be due and calculated upon GSK's or its Related Party's Net Sales to the first independent Third Party; and

(c) no royalties shall accrue on the disposition of Product without consideration in reasonable quantities by GSK or its Related Parties as samples (promotion or otherwise) or as donations (for example, to non-profit institutions or government agencies for a non-commercial purpose) and without direct or indirect consideration.

8.7 **Third Party Licenses.** If, during the term of this Agreement, GSK, in its sole discretion, deems it necessary to seek or exercise a license from any Third Party**[***]** of any royalties or other fees paid to such Third Party under such license may be deducted from royalties otherwise due to Vertex under this Agreement. In no event, however, shall such deduction reduce the royalties otherwise payable to Vertex in respect of any particular Product during any Calendar Year by more than **[***]** provided that any "unused' deduction may be carried over into subsequent years of the Agreement until the full deduction has been taken. For the avoidance of doubt, GSK shall not be entitled to deduct royalties or fees payable under licenses **[***].**

[**[***]**, the issue shall be referred to the Chief Executive Officer of Vertex (or to the Head of Research or to the Head of Development, as the CEO of Vertex shall determine) and to the Chairman of R&D of GSK (or to such other senior manager of GSK as the Chairman of R&D of GSK shall determine), who shall, as soon as practicable, attempt in good faith to resolve the dispute. If they are unable to resolve the dispute within **[***]** of referral, the dispute will be referred to an independent expert who will be appointed by agreement of the Parties. The expert shall act as an expert and not an arbitrator and his or her decision shall be final and binding on the Parties. The Parties will comply with any procedure established by the expert for making his or her decision and the expert's costs shall be paid by the party against whom the expert rules.

8.8 [**[***].**

[***]

[***]

8.9 [***]

8.9.1 No later than **[***]** of each year, GSK will calculate actual Unit Direct Cost of Goods for each Product in the Territory sold during the preceding fiscal year, in order to enable GSK to undertake the analysis set forth in Section 8.9.2 below.

8.9.2 Subject to the provisions of Section 8.9.3, if in any particular GSK fiscal year during the term of this Agreement, **[***].** GSK shall notify Vertex in writing on or before April 15 of any such following year of its entitlement to apply any offset during that year relating to the prior year providing Vertex with a summary showing the breakdown into direct materials, direct labour, direct service cost and other product specific cost per unit, in accordance with Schedule 1.60. **[***].**

8.9.3 In the first GSK fiscal year that the Direct Cost of Goods of a Product (calculated pursuant to Section 8.9.2) sold in such fiscal year plus royalties payable to Vertex on account of Net Sales of such Product during that fiscal year are greater than **[***]** of GSK's Net Sales of such Product sold in such fiscal year, then GSK will solicit bona fide bids with respect to the performance of the manufacturing function for the Product for the Territory on terms of supply customarily used by GSK with such preferred contract manufacturers (as reported to Vertex and not inconsistent with the provisions of this Agreement), as follows:

[***]. All of the bids will be reviewed by the Joint Steering Committee, such review to consider the following criteria, among others, with respect to provision of manufacturing services for the Product in the Territory:

[***]

[***]

[***]

[***]

The JSC will review and evaluate such **[***].**

At the end of the period for which supply was sought under the tender process, if the Direct Cost of Goods of a Product (calculated pursuant to Section 8.9.2) sold in any fiscal year plus royalties payable to Vertex on account of Net Sales of such Product during that year are greater than **[***]** of GSK's Net Sales of such Product sold in such year, GSK will continue to evaluate and consider alternate, lower cost Third Party manufacturing sources as provided above.

8.9.4 In the event that GSK decides to out-source at any time the manufacture of the Product to a Third Party, GSK will **[***].** All of the bids will be reviewed by the Joint Steering Committee, such review to consider the following criteria, among others, with respect to provision of manufacturing services for the Product in the Territory:

[***]

[***]

[***]

[***]

Information redacted pursuant to a confidential treatment request. An unredacted version of the exhibit has been filed separately with the Commission.

[***]

At the end of the period for which supply was sought under the tender process, if GSK decides to continue to out-source the manufacture of the Product, GSK will continue to evaluate and consider alternate, lower cost Third Party manufacturing sources as provided above.

8.10 **Combination Products.** For the purposes of determining royalty rates and the royalties payable on Combination Products, Net Sales of Product shall be calculated as follows: Net Sales of such Combination Product shall be **[***].**

8.11 **Reports; Payment of Royalty.** During the term of this Agreement following the First Commercial Sale of a Product, GSK shall furnish to Vertex a **[***]**, at the end of each **[***]**, showing (i) the Net Sales of each Product in each country in the world during the reporting period (ii) the royalties payable under this Agreement on account of those Net Sales and the basis for calculating those royalties; (iii) the exchange rates and other methodology used in converting into U.S. dollars, from the currencies in which sales were made, any payments due which are based on Net Sales; and (iv) dispositions of Products other than pursuant to sale for cash. Net Sales in countries invoiced in currency other than U.S. Dollars shall be translated to U.S. Dollars using GSK's then-current standard exchange rate methodology for the translation of foreign currency into U.S. dollars, as employed on a consistent basis throughout GSK's operations. Should GSK change its foreign currency translation methodology, the new methodology will be disclosed in writing to Vertex. All payments to be made by GSK to Vertex under this Agreement shall be made in United States dollars and shall be paid by bank wire transfer in immediately available funds to such bank account in the United States or elsewhere as may be designated in writing by Vertex from time to time. **[***]** GSK shall keep complete and accurate records in sufficient detail to enable the royalties payable hereunder to be determined and the information provided hereunder to be verified by Vertex's accounting firm pursuant to Section 8.12.

8.12 **Audits.** Upon the written request of Vertex, with **[***]** prior written notice to GSK, **[***]**, GSK shall permit an independent certified public accounting firm of nationally recognized standing selected by Vertex and reasonably acceptable to GSK, at Vertex's expense, to have access during normal business hours to such of the records of GSK and its Affiliates as may be reasonably necessary to verify the accuracy of the royalty reports hereunder for any **[***].** Those records shall include, without limitation, gross sales of each Product or Product Candidate on a country-by-country basis, as well as all deductions taken from gross sales in that country to arrive at Net Sales in that country, though it is acknowledged by Vertex that, depending upon GSK's then-current reporting practices for financial information, country-by-country data may only be accessible on an in-country basis from GSK's Affiliates. The accounting firm shall disclose to Vertex only whether the royalty reports are correct or incorrect and the specific details concerning any discrepancies. The audit rights provided in this paragraph shall also extend to audit of GSK's basis for and calculation of Unit Direct Cost of Goods and actual Unit Direct Cost of Goods for any Product.

Information redacted pursuant to a confidential treatment request. An unredacted version of the exhibit has been filed separately with the Commission.

If such independent accountant's review of GSK's royalty reports shows an underpayment, GSK shall remit or cause its Related Parties to remit to Vertex within **[***]** after GSK's receipt of such report: (i) the amount of such underpayment, and (ii) if such underpayment exceeds **[***]** of the total amount owed for the period being audited, the reasonable and necessary fees and expenses of the independent accountant performing the audit. Any overpayments shall be fully creditable against amounts payable in subsequent payment periods. Upon prior written notice to GSK as provided above, Vertex shall have a further right, exercisable not more frequently than once every **[***]**, to audit Net Sales, deductions taken from gross sales, and royalties earned by Vertex in any country in which a prior audit has shown an understatement of royalties due of at least **[***].**

GSK shall include in each sublicense granted by it pursuant to this Agreement a provision requiring the sublicensee to make reports to GSK, to keep and maintain records of sales made pursuant to such sublicense and to grant access to such records by Vertex's independent accountant to the same extent required of GSK under this Agreement.

Upon the expiration of **[***]** following **[***]**, the calculation of royalties payable with respect to such year shall be binding and conclusive upon the Parties, and GSK and its Related Parties shall be released from any liability or accountability with respect to royalties for such Calendar Year.

Vertex shall treat all financial information subject to review under this Section 8.12 or under any sublicense agreement in accordance with the confidentiality and non-use provisions of this Agreement, and shall cause its accounting firm to enter into an acceptable confidentiality agreement with GSK and/or its Related Parties obligating it to retain all such information in confidence pursuant to such confidentiality agreement.

8.13 **Income Tax Withholding.** Any tax required by law to be withheld and paid by GSK for the benefit of Vertex on account of any royalties or other payments payable to Vertex under this Agreement shall be deducted from the amount of royalties or other payments otherwise due, to the extent so paid or payable by GSK. GSK shall secure and send to Vertex proof of any such taxes withheld and paid or payable by GSK for the benefit of Vertex, and shall, at Vertex's request, provide reasonable assistance to Vertex in recovering such taxes.

Vertex warrants that Vertex is resident for tax purposes in the United States of America and that Vertex is entitled to relief from United Kingdom income tax under the terms of the double tax agreement between the UK and the United States of America. Vertex shall notify GSK immediately in writing in the event that Vertex ceases to be entitled to such relief.

Pending receipt of formal certification from the UK Inland Revenue GSK may pay royalty income and any other payments under this Agreement to Vertex by deducting tax at a rate specified in the double tax treaty between the UK and the United States of America. Vertex agrees to indemnify and hold harmless GSK against any loss, damage, expense or liability arising in any way from a breach of the above warranties or any future claim by a UK tax authority or other similar body alleging that GSK was not entitled to deduct withholding tax on such payments at source at the treaty rate.

8.14 **Currency Restrictions.** If restrictions on the transfer of currency exist in any country such as to prevent GSK from making the payments in the currency required under Section 8.11, GSK shall take all reasonable steps to obtain a waiver of such restrictions or otherwise enable GSK to make such payments, failing which GSK may make the royalty payments due upon sales in such country in local currency and deposit such payments in a local bank or other depository designated by Vertex.

Information redacted pursuant to a confidential treatment request. An unredacted version of the exhibit has been filed separately with the Commission.

8.15 **Substantial Competition.** If, during the term of this Agreement, substantial competition occurs in a country of the Territory between a Product and one or more Third Party products containing the same Compound as an active pharmaceutical ingredient and having the same or a similar Indication, and for so long as such substantial competition is continuing, **[***].** For the purposes of this Section 8.15, "substantial competition" shall mean **[***].** The royalty reduction provided in this Section 8.15 shall not be applied to any Net Sales in respect of which a royalty report has already been provided pursuant to Section 8.11 prior to the receipt by Vertex from GSK of written notice of any such substantial competition, with suitable supporting documentation, which might include, for example, copies of market survey reports, Third Party bid activities, competitive promotional materials, and internal financial statements. GSK shall bear the burden of establishing its entitlement to any reduction in the royalty under this Section 8.15 and any such reduction shall be available to GSK only during the period such competition remains substantial.

8.16 **Expiry of Royalty Obligations.** Following expiry of royalty obligations in respect of any Product GSK shall retain a perpetual non-exclusive, fully paid, right and license, with the right to grant sublicenses under the Vertex Know-How licensed hereunder solely to continue to make, have made, use, sell, offer for sale and import the Product, for so long as it continues so to do.

8.17 **Interest Penalty.** In case of any delay in payment by GSK to Vertex not occasioned by Force Majeure (as described in Section 12.2), interest at the annual rate of **[***]** above **[***]**, assessed from the **[***]** after the due date of the payment, shall be due from GSK.

8.18 **Over-The-Counter.** In the event that GSK is considering at any time developing and commercializing any Product Candidate and/or Product as an "Over-The-Counter" medicine, i.e. as a product that may be sold without prescription, the Parties agree to meet and discuss whether the royalty rates payable hereunder in respect of sales of such Product Candidate and/or Product should be adjusted, or whether any other terms and conditions of this Agreement should be modified or amended. No such adjustments, modifications or amendments shall be made without the prior written consent of both Parties.

ARTICLE 9: REPRESENTATIONS AND WARRANTIES

9.1 **Representations and Warranties of Vertex.** Vertex represents and warrants to GSK that as of the Effective Date:

9.1.1 **Authorization.** This Agreement has been duly executed and delivered by Vertex and constitutes the valid and binding obligation of Vertex, enforceable against Vertex in accordance with its terms except as enforceability may be limited by bankruptcy, fraudulent conveyance, insolvency, reorganization, moratorium and other laws relating to or affecting creditors' rights generally and by general equitable principles. The execution, delivery and performance of this Agreement have been duly authorized by all necessary action on the part of Vertex, its officers and directors.

9.1.2 **Ownership of Intellectual Property.** Vertex has full right and interest in all Vertex Information and Inventions, Vertex Know-How and Vertex Patent Rights. However Vertex makes no warranty or representation with respect to the validity of Vertex Information and Inventions, Vertex Know-How and Vertex Patent Rights or except as set forth in Section 9.1.3, the presence or absence of any infringement of or conflict with any Third Party right or patent.

9.1.3 **No Third Party Patents.** To Vertex's knowledge, except as disclosed in *Schedule 9.1.3*, the development, manufacture, use or sale of VX-409 and any Back-up Compounds pursuant to this Agreement does not infringe or conflict with any Third Party right or patent, and Vertex is not aware of any pending patent application that, if issued, would be infringed by the development,

manufacture, use or sale of VX-409 or any Back-up Compounds pursuant to this Agreement. Vertex has informed GSK that Vertex has not conducted an extensive review of Third Party intellectual property relative to the Back-up Compounds.

9.1.4 **No Interference.** The Vertex Patent Rights are not the subject of any interference known to Vertex and Vertex is not aware of any pending or threatened action, suit, proceeding or claim by a Third Party challenging Vertex's ownership rights in, or the validity or scope of, such Vertex Patent Rights.

9.1.5 **No Regulatory Authority Actions.** Vertex has not applied for or received any grant of rights of any kind from any Regulatory Authority with respect to a Compound, Product Candidate or Product.

9.1.6 **Back-up Compounds.** The Back-up Compounds listed in *Schedule 1.2* constitute all of the lead compounds which are or have been, at the Effective Date, under investigation by Vertex, which **[***].**

9.1.7 **Provision of Information.** Vertex has not failed to furnish GSK with any information requested by GSK, or intentionally concealed from GSK any information in its possession, including but not limited to information concerning VX-409, which Vertex reasonably believes would be material to GSK's decision to enter into this Agreement and undertake the commitments and obligations set forth herein.

9.1.8 **Schedule 1.66.** *Schedule 1.66* contains a complete list of all patents and patent applications Controlled by Vertex, as of the Effective Date, that cover the Compounds, processes for making the Compounds, use of the Compounds, and compositions containing the Compounds.

9.2 **Representation and Warranty of GSK.** GSK represents and warrants to Vertex that, as of the Effective Date, this Agreement has been duly executed and delivered by GSK and constitutes the valid and binding obligation of GSK, enforceable against GSK in accordance with its terms, except as enforceability may be limited by bankruptcy, fraudulent conveyance, insolvency, reorganization, moratorium and other laws relating to creditors' rights generally and by general equitable principles. The execution, delivery and performance of this Agreement have been duly authorized by all necessary action on the part of GSK, its officers and directors.

ARTICLE 10: PATENT PROVISIONS

10.1 **Filing, Prosecution and Maintenance of Vertex Patent Rights.** Vertex shall have the exclusive right and the obligation (subject to Vertex's election not to file, prosecute, or maintain pursuant to Section 10.3), **[***]**, to diligently file, prosecute and maintain (by timely paying all maintenance fees, renewal fees, and other such fees and costs required under applicable laws) in the Territory the Vertex Patent Rights, and to conduct any interference, oppositions and re-examinations or other similar proceeding with respect thereto, in all such countries as is customary for Vertex to file, prosecute and maintain patent rights covering pharmaceutical products. If GSK notifies Vertex that it wants Vertex to apply for registration in any country or countries in which it is not customary for Vertex to do so, or to conduct any interference, oppositions and re-examinations or other similar proceedings with respect to the Vertex Patent Rights, **[***].** Vertex shall keep GSK advised of the status of the actual and prospective patent filings and upon the request of GSK, provide advance copies of any papers related to the filing, prosecution and maintenance of such patent filings. Vertex shall promptly give reasonable advance notice to GSK of the grant, lapse, revocation, surrender, invalidation or abandonment of any Vertex Patent Rights for which Vertex is responsible for the filing, prosecution and maintenance. Vertex shall solicit GSK's advice and review of the nature and text of such patent applications and important prosecution matters

related thereto in reasonably sufficient time prior to filing thereof, and Vertex shall take into account GSK's reasonable comments related thereto.

10.2 **Filing, Prosecution and Maintenance of Joint Patent Rights.** In respect of any Joint Information and Inventions, the Parties shall agree, without prejudice to ownership, which Party shall have the right and/or obligation to prepare and file a priority patent application, and prosecute such application(s) and maintain any patents derived therefrom, with the Parties equally sharing the reasonable out-of-pocket costs for the preparation, filing, prosecution and maintenance of such priority patent application. Should the agreed upon Party elect not to prepare and/or file any such priority patent application, it shall (i) provide the other Party with written notice as soon as reasonably possible after making such election but in any event no later than **[***]** before the other Party would be faced with a possible loss of rights, (ii) give the other Party the right, at the other Party's discretion and sole expense, to prepare and file the priority application(s), and (iii) offer reasonable assistance in connection with such preparation and filing at no cost to the other Party except for reimbursement of reasonable out-of-pocket expenses incurred by the agreed upon Party in rendering such assistance. The other Party, at its discretion and cost, may prosecute such application(s) and maintain any patents derived therefrom.

10.3 **Option to Prosecute and Maintain Patents.** Vertex shall give notice to GSK of any desire to cease prosecution and/or maintenance of Vertex Patent Rights or Joint Patent Rights on a country by country basis in the Territory and, in such case, shall permit GSK, at its sole discretion, to continue prosecution or maintenance of such Vertex Patent Rights at its own expense. If GSK elects to continue prosecution or maintenance or to file based on Vertex's election not to file pursuant to Section 10.1, Vertex shall execute such documents and perform such acts at Vertex's expense as may be reasonably necessary to allow GSK to initiate or continue such filing, prosecution or maintenance.

10.4 **Interference, Opposition, Re-examination and Re-issue.**

10.4.1 Vertex shall promptly, but in any case within **[***]** of learning of such event, inform GSK of any request for, or filing or declaration of, any interference, opposition, or re-examination relating to Vertex Patent Rights or Joint Patent Rights for which Vertex is responsible. GSK and Vertex shall thereafter consult and cooperate fully to determine a course of action with respect to any such proceeding. GSK shall have the right to review and approve any submission to be made in connection with such proceeding.

10.4.2 Vertex shall not initiate any re-examination, interference or re-issue proceeding relating to Vertex Patent Rights or Joint Patent Rights without the prior written consent of GSK, which consent shall not be unreasonably withheld.

10.4.3 In connection with any interference, opposition, re-issue, or re-examination proceeding relating to Vertex Patent Rights or Joint Patent Rights, GSK and Vertex will cooperate fully and will provide each other with any information or assistance that either may reasonably request. Vertex shall keep GSK informed of developments in any such action or proceeding, including, to the extent permissible by law, consultation and approval of any settlement, the status of any settlement negotiations and the terms of any offer related thereto.

10.4.4 The expense of any interference, re-examination or re-issue proceeding shall, **[***].**

10.5 **Enforcement and Defense.**

10.5.1 Each Party shall promptly give the other Party notice of (i) any infringement of Vertex Patent Rights or Joint Patent Rights, or (ii) any misappropriation or misuse of Vertex Know-How, that

may come to the first Party's attention. GSK and Vertex shall thereafter consult and cooperate fully to determine a course of action, including but not limited to the commencement of legal action by either or both GSK and Vertex, to terminate any infringement of Vertex Patent Rights or Joint Patent Rights or any misappropriation or misuse of Vertex Know-How. Vertex, upon notice to GSK, shall have the first right to initiate and prosecute any such legal action at its own expense and in the name of Vertex and GSK, or to control the defense of any declaratory judgment action relating to Vertex Patent Rights, Joint Patent Rights or Vertex Know-How. **[***]** Vertex shall promptly inform GSK if it elects not to exercise that first right and GSK shall thereafter have the right to either initiate and prosecute such action or to control the defense of such declaratory judgment action in the name of GSK and, if necessary, Vertex. Each Party shall have the right to be represented by counsel of its own choice.

10.5.2 If Vertex elects not to initiate and prosecute an action as provided in Section 10.5.1, and GSK elects to do so, **[***].**

10.5.3 For any action to terminate any infringement of Vertex Patent Rights or Joint Patent Rights or any misappropriation or misuse of Vertex Know-How, in the event that GSK is unable to initiate or prosecute such action solely in its own name, Vertex will join such action voluntarily and will execute and cause its Affiliates to execute all documents necessary for GSK to initiate litigation to prosecute and maintain such action. In connection with any action, GSK and Vertex will cooperate fully and will provide each other with any information or assistance that either may reasonably request. Each Party shall keep the other informed of developments in any action or proceeding, including, to the extent permissible by law, the consultation and approval of any settlement negotiations and the terms of any offer related thereto.

Information redacted pursuant to a confidential treatment request. An unredacted version of the exhibit has been filed separately with the Commission.

10.5.4 Any recovery obtained by either or both GSK and Vertex in connection with or as a result of any action contemplated by this Section, whether by settlement or otherwise, shall be shared in order as follows:

[***]

[***]

[***]

10.5.5 Vertex shall inform GSK of any certification regarding any Vertex Patent Rights it has received pursuant to either 21 U.S.C. §§355(b)(2)(A)(iv) or (j)(2)(A)(vii)(IV) or its successor provisions or any similar provisions in a country in the Territory other than the United States and shall provide GSK with a copy of such certification within **[***].** Vertex's and GSK's rights with respect to the initiation and prosecution of any legal action as a result of such certification or any recovery obtained as a result of such legal action shall be as defined in subsections 10.5.1 through 10.5.4; *provided*, *however*, that Vertex shall have the first right to initiate and prosecute any action and shall inform GSK of such decision within thirty (30) days of receipt of the certification, after which time GSK shall have the right to initiate and prosecute such action.

10.5.6 **Patent Term Restoration.** The Parties hereto shall cooperate with each other in obtaining patent term restoration or supplemental protection certificates or their equivalents in any country in the Territory where applicable to Vertex Patent Rights and Joint Patent Rights. In the event that elections with respect to obtaining such patent term restoration are to be made, GSK shall have the right to make the election and Vertex agrees to abide by such election.

10.5.7 **Third Party Claims.**

(i) Without prejudice to Section 12.1(b), in the event that any action, suit or proceeding is brought against GSK or Vertex or any Affiliate or sublicensee of either Party alleging the infringement of the intellectual property rights of a Third Party by reason of the discovery, development, manufacture, use, sale, importation or offer for sale of a Product Candidate or Product, GSK shall have the sole right but not the obligation to defend itself and Vertex in such action, suit or proceeding **[***].** The Parties shall cooperate with each other in any defense of any such suit, action or proceeding. The Parties will give each other prompt written notice of the commencement of any such suit, action or proceeding, or receipt of any claim of infringement, and will furnish each other a copy of each communication relating to the alleged infringement. Neither Party shall compromise, litigate, settle or otherwise dispose of any such suit, action or proceeding without the other Party's advice and prior consent, provided that the Party not having the right to defend the suit shall not unreasonably withhold its consent to any settlement which does not have a material adverse effect on its rights, obligations or benefits, either under this Agreement or otherwise.

(ii) The Party first having actual notice of any claim, action or proceeding referenced in subsections (i) or (ii) above shall promptly notify the other Party in writing, setting forth in reasonable detail, to its knowledge, the facts related to any such claim, action or proceeding. The Parties shall promptly discuss proposed responses to any such matters.

10.5.8 **Trademarks.** GSK shall be responsible for the selection of all trademarks which it employs in connection with Product in the Territory and shall own and control such trademarks. GSK shall be responsible for registration and maintenance of all such trademarks. Nothing in this Agreement shall be construed as a grant of rights, by license or otherwise, to Vertex to use such trademarks or

any other trademarks owned by GSK for any purpose. GSK shall own such trademarks and shall retain such ownership upon termination or expiration of this Agreement.

ARTICLE 11: TERM AND TERMINATION

11.1 **Term and Expiration.** This Agreement shall be effective as of the Effective Date and unless terminated earlier pursuant to Sections 11.2, 11.3, 11.6 or 11.7, this Agreement shall continue in effect until expiration of all royalty obligations under Article 8.

11.2 **Termination by GSK Without Cause.** Notwithstanding anything contained herein to the contrary, after the end of the Back-up Program Term GSK shall have the right to terminate this Agreement at any time in its sole discretion by giving **[***]** advance written notice to Vertex; provided, however, if a Product has received a Marketing Authorization in the **[***]** advance written notice shall be required, unless such termination is for a reason other than a Valid Safety Issue, in which case termination may be with immediate effect. For the purposes of this Agreement, a "Valid Safety Issue" **[***].**

Following any delivery by GSK of notice of termination pursuant to this Section 11.2, GSK and Vertex will co-operate in good faith to agree and implement a transition plan, in order to give effect to Sections 11.5 (b)-(d). During the period between GSK's notice of termination pursuant to this Section 11.2 and the effective date of such termination, provided that GSK uses all reasonable efforts to agree and implement a transition plan, GSK shall be deemed to have met its due diligence obligations pursuant to Sections 3.5 and 4.3. For the avoidance of doubt, during the period of notice until the effective date of termination, GSK shall not be required to initiate any new clinical or non-clinical studies, make any further filings for Regulatory Approval other than as related to the prompt and complete transfer of regulatory authorizations and development and commercial rights to Vertex, or launch the Product in any further countries in order to meet its due diligence obligations pursuant to Sections 3.5 and 4.3.

Notwithstanding termination of this Agreement, for the avoidance of doubt, Section 11.5(b) shall remain in effect until the completion by GSK of all actions which are required by it to enable a full transfer to Vertex of all filings for Regulatory Approvals and all Marketing Authorizations relating to the Product.

11.3 **Termination for Cause.** This Agreement may be terminated at any time during the term of this Agreement:

11.3.1 upon written notice by either Party if the other Party is in breach of its material obligations hereunder and has not cured such breach after notice from the terminating Party requesting cure of the breach; *provided*, *however*, in the event of a good faith dispute with respect to the existence of a material breach, the cure period shall be tolled until such time as the dispute is resolved pursuant to Section 12.7; and provided that the terminating Party has given the defaulting Party the following opportunities to remedy any breach:

(i) the written notice of breach referenced above shall detail the specific obligation under this Agreement which is alleged to have been breached; the manner of such alleged breach; and the steps which must be taken in order to remedy such breach; and

(ii) the terminating Party has provided the defaulting Party with a reasonable amount of time (but no more than **[***]**) in which (x) to complete any steps which might be taken to remedy the breach, as stated in the notification of breach, or (y) if completion of those steps is not possible within a **[***]**, to commence those steps required as stated in the notification of

breach, on the condition that the defaulting Party continues to perform those steps with due diligence and the breach can be cured within a mutually agreeable period of time;

11.3.2 by either Party upon the filing or institution of bankruptcy, reorganization, liquidation or receivership proceedings, or upon an assignment of a substantial portion of the assets for the benefit of creditors by the other Party; *provided*, *however*, in the case of any involuntary bankruptcy proceeding such right to terminate shall only become effective if the Party consents to the involuntary bankruptcy or such proceeding is not dismissed within **[***]** after the filing thereof.

11.4 Effect on License of Termination by GSK for Cause.

11.4.1 If GSK terminates this Agreement under Section 11.3.1, then (i) GSK's licenses pursuant to Sections 6.1 and 6.2 shall become perpetual, exclusive licenses subject to the financial provisions of Article 8; and (ii) GSK shall have the right to offset against any monies owed to Vertex (pursuant to Article 8 of this Agreement) all of its direct costs, losses and expenses incurred as a result of Vertex's breach. In addition to any other provisions which may survive termination pursuant to Section 11.8, Article 10 shall survive such termination.

11.4.2 If this Agreement is terminated by GSK pursuant to subsection 11.3.2, all licenses and rights to licenses granted under or pursuant to this Agreement by Vertex to GSK are, and shall otherwise be deemed to be, for purposes of Section 365(n) of the United States Bankruptcy Code (the "Code"), licenses of rights to "intellectual property" as defined under Section 101(35A) of the Code. The Parties agree that GSK, as a licensee of such rights under this Agreement, shall retain and may fully exercise all of its rights and elections under the Code, and that upon commencement of a bankruptcy proceeding by Vertex under the Code, or against Vertex if such proceeding is not dismissed within **[***]** of its initial filing, GSK shall be entitled to a complete duplicate of or complete access to (as GSK deems appropriate), any such intellectual property and all embodiments of such intellectual property. Such intellectual property and all embodiments thereof shall be promptly delivered to GSK (i) upon any such commencement of a bankruptcy proceeding upon written request therefore by GSK, unless Vertex elects to continue to perform all of its obligations under this Agreement or (ii) if not delivered under (i) above, upon the rejection of this Agreement by or on behalf of Vertex upon written request therefore by GSK.

11.5 Effect of Termination by Vertex For Cause or by GSK Without Cause.

If Vertex terminates this Agreement under Sections 11.3, 11.6 or 11.7, or GSK terminates this Agreement under Section 11.2:

(a) GSK's licenses pursuant to Article 6 shall terminate as of such termination date and GSK shall, within **[***]** after such termination, return or cause to be returned to Vertex all Vertex Information in tangible form, and all substances or compositions delivered or provided by Vertex, as well as any other material provided by Vertex in any medium, except that GSK may retain one copy in its confidential files for records purposes.

(b) All filings with Regulatory Authorities concerning Product Candidates or Products will be assigned or otherwise transferred to Vertex as soon as practicable and at GSK's expense, and any reports required to be made to any Regulatory Authority covering any periods prior to the effective date of termination of the Agreement will be prepared promptly and filed at Vertex's direction with the appropriate Regulatory Authority or, at Vertex's discretion, made available to Vertex for filing by Vertex. GSK will also promptly deliver to Vertex all data and information (and including all information relative to any technology which is the subject of a non-exclusive license under Subsection 11.5(c)) generated in the course of any Clinical Trials and non-clinical studies of Product Candidates and Products. Notwithstanding Section 7.1,

Vertex shall be able to disclose any such data and information as is necessary to exercise its rights of development and commercialization (including usual and customary publication activities) of the Product Candidates and Products granted under this Agreement.

(c) **[***]**

(d) Vertex will be solely responsible for and, should it elect to exercise its supply option under (i) or (ii) below, will use commercially reasonable efforts to obtain an approved (by Regulatory Authorities, as required) alternate source of supply for Product Candidates and Products as soon as reasonably practicable.

(i) In respect of each Product Candidate that is not being marketed at the date of delivery by GSK or Vertex of notice of termination under Section 11.2, 11.3, 11.6 or 11.7 respectively, of this Agreement (the "Termination Notice Date"), GSK and Vertex shall negotiate in good faith, following the Termination Notice Date, regarding transfer of clinical and non-clinical supplies existing at such time **[***].**

(ii) In respect of each Product that is being marketed by GSK at the Termination Notice Date, at Vertex's option and for a period ending at the earlier of **[***]** following the Termination Notice Date or the date upon which Vertex has established an approved source of supply, GSK will supply Vertex with all of Vertex's requirements for commercial supplies of each Product in a maximum annual amount equal to: **[***].** GSK and Vertex shall, following the Termination Notice Date, negotiate in good faith a Supply Agreement under which Products will be supplied **[***]**, to the then current specifications, and in accordance with GSK's existing quality and compliance standards.

(e) In the event that Vertex shall subsequently commercialize any Product Candidates or Products, Vertex shall pay GSK **[***]** until, with respect to a particular country, the expiration of the last-to-expire valid patent claim in that country under any Vertex Patent Rights, Joint Patent Rights or patents Controlled by GSK and licensed under this Section 11.5 that would be infringed by the sale of the Product.

11.6. Suspension or Termination of Development.

11.6.1 At any time during the Development Program, GSK shall have the right to suspend or terminate the development, in whole or in part, of a Product Candidate or Product upon the occurrence of a Commercial Failure or Technical Failure with respect to that Product Candidate or Product (in which case the details of that Commercial Failure or Technical Failure shall be promptly shared with the JSC), or because another Product Candidate is demonstrating a better safety/efficacy profile, or because another Product Candidate is being progressed in development as the Lead Compound, promptly following communication to, and assessment of such proposed termination by, the Joint Steering Committee.

11.6.2 In the event that the Development Program is terminated in relation to any Region, or has been suspended in relation to any Region for any reason for a period of **[***]** or more, including but not limited to, reasons of **[***]**, and GSK is not diligently commercializing a Product in such Region, then Vertex may terminate the licenses granted to GSK hereunder in respect of such Region by giving written notice to GSK. The Development Program shall be deemed terminated or suspended in relation to the **[***]** if development activities are terminated or suspended in relation to the **[***]** for a period of **[***]** or more. If Vertex terminates the licenses granted to GSK in respect of such Region pursuant to this Section 11.6.2, the terms of Section 11.5 shall apply in relation to such Region. Vertex's right to terminate the licenses in relation to the Region under the circumstances specified above shall not apply during any period in which GSK's failure

to actively develop, market or sell a Product Candidate or Product under this Agreement is the direct result of circumstances beyond GSK's reasonable control (such as, but not limited to, where the suspension has been required or advised by a Regulatory Authority or independent ethics committee), so long as GSK, with the advice and participation of the JSC, has promptly established a plan which reasonably addresses the issues giving rise to the suspension or termination, with the objective of commencing development or commercialization of a Product Candidate or Product as soon as reasonably practicable, and is diligently executing such plan.

11.6.3 In the event that the Development Program is terminated in its entirety for all Regions for any reason, or has been suspended in its entirety for all Regions for any reason for a period of **[***]** or more, including but not limited to, **[***]**, and GSK is not diligently commercializing a Product, then Vertex may terminate this Agreement by giving written notice to GSK. If Vertex terminates this Agreement pursuant to this Section 11.6.3, the terms of Section 11.5 shall apply. Vertex's right to terminate this Agreement under the circumstances specified above shall not apply during any period in which GSK's failure to actively develop, market or sell a Product Candidate or Product under this Agreement is the direct result of circumstances beyond GSK's reasonable control (such as, but not limited to, where the suspension has been required or advised by a Regulatory Authority or independent ethics committee), so long as GSK, with the advice and participation of the JSC, has promptly established a plan which reasonably addresses the issues giving rise to the suspension or termination, with the objective of commencing development or commercialization of a Product Candidate or Product as soon as reasonably practicable, and is diligently executing such plan.

11.7 Termination of Product Commercialization.

11.7.1 At any time after First Commercial Sale of a Product in a country, GSK shall have the right to terminate commercialization of such Product on a country-by-country basis upon the occurrence of Commercial Failure or Technical Failure (upon the provision of **[***]** written notice unless there is a Valid Safety Issue, in which case termination may occur with immediate effect) and following communication to, and assessment of such proposed termination by, the Joint Steering Committee, which communication shall include the relevant details underlying any determination of Commercial Failure or Technical Failure or Valid Safety Issue.

11.7.2 In the event that GSK decides to terminate all commercialization of Products in a Region, and at such time GSK is not engaged in a Development Program which has as a principal objective the development of one or more Product Candidates for commercialization in such Region, then Vertex, upon **[***]** written notice to GSK may terminate GSK's rights and licenses under this Agreement with respect to such Region, and the terms of Section 11.5 shall apply to such Region on such termination by Vertex. GSK shall be deemed to have terminated all commercialization of Products in the North American Region if it has terminated all commercialization of Products in the United States.

11.8 Survival

Any expiration or termination of this Agreement shall be without prejudice to the rights of either Party against the other accrued or accruing under this Agreement prior to expiration or termination, including without limitation the obligation to pay royalties for Product(s) sold prior to such expiration or termination. The provisions of Section 7.1 shall survive the expiration or termination of this Agreement and shall continue in effect for ten (10) years. In addition, the provisions of Sections 1, 7.1, 7.2(c), 7.3, 7.4, 8.11, 8.12, 8.13, 8.17, 11.4, 11.5, 11.6.2, 11.6.3, 11.7.2, 11.8, 12.1, 12.5, 12.6 and 12.7 shall indefinitely survive any expiration or termination of this Agreement.

Information redacted pursuant to a confidential treatment request. An unredacted version of the exhibit has been filed separately with the Commission.

11.9 Effect of Vertex Change of Control.

If (a) a Change of Control of Vertex occurs and (b) as an immediate result another company (the "Change of Control Party") controls Vertex, as the term "control" is used in Section 1.1 hereof, and (c) the Change of Control Party or an Affiliate of the Change of Control Party at the time of the Change of Control or subsequently during the term of this Agreement, is developing or commercializing a Competing Product, then:

(a) the financial provisions of Article 8 shall continue and be payable to the Change of Control party; and

(b) **[***]**

(i) **[***]**

(ii) **[***]**

11.10 Effect of GSK Change of Control. If during the Exclusivity Period a Change of Control of GSK occurs and as an immediate result another company, or group of companies acting in concert, controls GSK (as the term "control" is used in Section 1.1 hereof), and that company or group of companies at the time of the Change of Control or subsequently during the term of this Agreement, is developing a Competing Product, then at Vertex's written request delivered within **[***]** after (a) the later of the public announcement of the Change of Control transaction or the closing of that transaction, or (b) the disclosure to Vertex by GSK of the commencement of development of a Competing Product, GSK or its successor shall, at GSK's discretion, within **[***]** of receipt of such written request either:

(i) [**[***]**; or

(ii) **[***]**

11.11 Acquisition of Company with a Competing Product.

The provisions of Sections 11.9 and 11.10 shall apply, *mutatis mutandis*, if Vertex or GSK acquire the control of a Third Party (as the term "control" is used in Section 1.1 hereof) that is developing or commercializing Competing Product(s), as appropriate.

ARTICLE 12: MISCELLANEOUS

12.1 Indemnification.

(a) Except to the extent due to the negligence or willful misconduct of GSK, Vertex shall indemnify, defend and hold GSK and its Affiliates, and their respective directors, officers, employees and agents, harmless from and against any claims of damages (except to the extent arising from any claims of intellectual property infringement), bodily injury, death, or property damage made by a Third Party (a "Third Party Claim") to the extent arising from: (i) the negligence or willful misconduct of Vertex under this Agreement; (ii) the material breach by Vertex of any warranty, representation or obligation of Vertex under this Agreement; or (iii) the development, synthesis, testing, use, storage or handling by Vertex or its representatives or agents under this Agreement of VX-409, or any Back-up Compound, Product Candidate or Product.

(b) Except to the extent due to the negligence or willful misconduct of Vertex, GSK shall indemnify, defend and hold Vertex and its Affiliates, and their respective directors, officers, employees and agents, harmless from and against any Third Party Claim resulting from (i) the

negligence or willful misconduct of GSK under this Agreement; (ii) the material breach by GSK of any warranty, representation or obligation of GSK under this Agreement; or (iii) the development, testing, synthesis, use, storage, handling, manufacture or commercialization by GSK or its representatives or agents under this Agreement of VX-409, or any Back-up Compound, Product Candidate or Product.

(c) If a Party (the "Indemnitee") intends to claim indemnification under this Section, it shall promptly notify the other Party (the "Indemnitor") in writing of any Third Party Claim for which the Indemnitee intends to claim such indemnification. The failure of the Indemnitee to deliver written notice to the Indemnitor within a reasonable time after the commencement of any such action shall relieve the Indemnitor of any obligation to the Indemnitee under this Section with respect to any such action, insofar as the failure prejudices the Indemnitor's ability to defend a Third Party Claim. The Indemnitee shall permit the Indemnitor to control the litigation and/or settlement of such Third Party Claim, and cooperate fully with Indemnitor in all matters related thereto, provided that unless agreed by Indemnitee (i) counsel appointed by Indemnitor to defend Indemnitee shall not take any position which if sustained would cause Indemnitee not to be indemnified by Indemnitor and (ii) no settlement will involve any terms binding on Indemnitee except payment of money to by paid by Indemnitor.

(d) Neither Party shall be liable to the other for indirect, consequential, special or punitive damages under this Agreement.

12.2 **Force Majeure.** Neither Party shall be held liable to the other Party nor be deemed to have defaulted under or breached this Agreement for failure or delay in performing any obligation under this Agreement when such failure or delay is caused by or results from causes beyond the reasonable control of the affected Party including, but not limited to, embargoes, war, acts of war (whether war be declared or not), insurrections, riots, civil commotions, strikes, lockouts or other labor disturbances, fire, floods, or other acts of God, or acts, omissions or delays in acting by any governmental authority or the other Party. The affected Party shall notify the other Party of such force majeure circumstances as soon as reasonably practical, and shall promptly undertake all reasonable efforts necessary to cure such force majeure circumstances.

12.3 **Assignment.** Except as provided in this Section 12.3, this Agreement may not be assigned or otherwise transferred, nor may any right or obligation hereunder be assigned or transferred, by either Party without the consent of the other Party. Either Party may, without the other Party's consent, assign this Agreement and its rights and obligations hereunder in whole or in part to an Affiliate, if that Party guarantees the full performance of its Affiliate's obligations hereunder. Any permitted assignee shall assume all obligations of its assignor under this Agreement and shall be subject to all of the provisions of this Agreement. Any attempted assignment not in accordance with this Section shall be void. Notwithstanding the above, Vertex or GSK may, without the other's consent, assign this Agreement and all rights and obligations hereunder, in the event it experiences a Change of Control, to the Change of Control party, subject to the other provisions of this Agreement.

12.4 **Severability.** If any one or more of the provisions contained in this Agreement is held invalid, illegal or unenforceable in any respect, the validity, legality and enforceability of the remaining provisions contained herein shall not in any way be affected or impaired thereby, unless the absence of the invalidated provision(s) adversely affects the substantive rights of the Parties. The Parties shall in such an instance use their best efforts to replace the invalid, illegal or

unenforceable provision(s) with valid, legal and enforceable provision(s) which, insofar as practical, implement the purposes of this Agreement.

12.5 **Notices.** All notices that are required or permitted hereunder shall be in writing and will be sufficient if delivered personally, sent by facsimile (and promptly confirmed by personal delivery, registered or certified mail or overnight courier), sent by internationally-recognized courier or sent by registered or certified mail, postage prepaid, addressed as follows:if to Vertex, to:

if to Vertex, to:	Vertex Pharmaceuticals Incorporated 130 Waverly Street Cambridge, MA 02139 USA **Attn:** Office of Business Development **Facsimile No.:** (617) 444-6632
and:	**Attn:** General Counsel **Facsimile No.:** (617) 444-7117
if to GSK, to:	GlaxoSmithKline Greenford Road Greenford Middlesex UB6 0HE UK **Attn:** Vice-President Transactions and Commercial Alliances **Facsimile No.:** (44) 20 8966 5371
And	GlaxoSmithKline 980 Great West Road Brentford Middlesex TW8 9GS UK **Attn:** Senior Counsel, R&D Legal Transactions **Facsimile No.:** (44) 20 8047 6897

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. 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 next business day after dispatch if sent by facsimile or by internationally-recognized overnight courier; and/or (c) on the fifth (5th) business day following the date of mailing if sent by mail or other internationally-recognized courier. Notices hereunder will not be deemed sufficient if provided only between or among each Party's representatives on the JSC.

12.6 **Applicable Law.** This Agreement shall be governed by and construed in accordance with the laws of The Commonwealth of Massachusetts without reference to any rules of conflict of laws. The United Nations Convention on the Sale of Goods shall not apply.

12.7 **Dispute Resolution.**

12.7.1 The Parties shall negotiate in good faith and use reasonable efforts to settle any dispute, controversy or claim arising from or related to this Agreement or the breach thereof. If the Parties are initially unable to resolve a dispute, despite using reasonable efforts to do so, either Party may,

by written notice to the other, have such dispute referred to their respective senior management designated below or their respective successors, for attempted resolution by negotiation in good faith. Such attempted resolution shall take place no later than twenty one (21) days following receipt of such notice. The designated management are as follows:

For GSK:

Chairman of Research and Development (for a dispute principally involving research or development)

or

Chief Operations Officer (for dispute principally involving commercialization)

For Vertex:

the Chief Executive Officer, or at the CEO's option:

the Head of Research or Development (for a dispute principally involving research or development)

or

the Head of Commercial Operations (for dispute principally involving commercialization)

12.7.2. If the Parties are unable to resolve the dispute, controversy or claim within **[***]** following the day on which one Party provides written notice of the dispute to the other in accordance with Clause 12.7.1, and a Party wishes to pursue the matter, each such dispute, controversy or claim that is not an "Excluded Claim" as defined in Section 12.7.7 below, shall be finally resolved by binding arbitration in accordance with the Commercial Arbitration Rules and Supplementary Procedures for Large Complex Disputes of the American Arbitration Association ("AAA"), and judgment on the arbitration award may be entered in any court having jurisdiction thereof.

12.7.3 The arbitration shall be conducted by a panel of three persons experienced in the pharmaceutical business. Within **[***]** after initiation of arbitration, each Party shall select one person to act as arbitrator and the two Party-selected arbitrators shall select a third arbitrator within **[***]**of their appointment. If the arbitrators selected by the Parties are unable or fail to agree upon the third arbitrator, the third arbitrator shall be appointed by the AAA. **[***].**All proceedings and communications shall be in English. The decision of the arbitrators shall be final and binding upon the Parties and their respective Affiliates and the Parties hereby waive their respective rights to any form of appeal therefrom. The decision shall be rendered no later than sixty (60) days following commencement of the arbitration.

12.7.4 Either Party may apply to the arbitrators for interim injunctive relief until the arbitration award is rendered or the controversy is otherwise resolved. Either Party also may, without waiving any remedy under this Agreement, seek from any court having jurisdiction any injunctive or provisional relief necessary to protect the rights or property of that Party pending the arbitration award. The arbitrators shall have no authority to award punitive or any other type of damages not measured by a Party's compensatory damages. In addition to dealing with the merits of the case, the Arbitration award shall fix the costs of the Arbitration and decide which of the parties shall bear such costs or in which proportion such costs shall be borne by the parties.

12.7.5 Except to the extent necessary to confirm an award or as may be required by law, neither a Party nor an arbitrator may disclose the existence, content, or results of an arbitration without the prior written consent of both Parties. In no event shall an arbitration be initiated after the date when

commencement of a legal or equitable proceeding based on the dispute, controversy or claim would be barred by the applicable Massachusetts statute of limitations.

12.7.6 The Parties agree that, in the event of a dispute over the nature or quality of performance under this Agreement, neither Party may terminate this Agreement until final resolution of the dispute through arbitration or other judicial determination. The Parties further agree that any payments made pursuant to this Agreement pending resolution of the dispute shall be refunded if an arbitrator or court determines that such payments are not due.

12.7.7 As used in this Section, the term "Excluded Claim" shall mean a dispute, controversy or claim that concerns **[***].**

12.7.8 Notwithstanding anything to the contrary in the foregoing, to the extent that the Parties have a dispute about whether or not a Back-up Compound satisfies the Development Candidate Criteria, the Parties shall resolve that dispute as set forth in Section 2.7.

12.7.9 Notwithstanding anything to the contrary in the foregoing, to the extent that the Parties have a dispute about whether a Third Party license can reasonably be expected to materially increase Net Sales, the Parties shall resolve that dispute as set forth in Section 8.7.

12.8 **Entire Agreement; Amendments.** This Agreement, together with the Schedules hereto, contains the entire understanding of the Parties with respect to the subject matter hereof and supercedes and cancels all previous express or implied agreements and understandings, negotiations, writings and commitments, either oral or written, in respect to the subject matter hereof. The Schedules to this Agreement are incorporated herein by reference and shall be deemed a part of this Agreement. This Agreement may be amended, or any term hereof modified, only by a written instrument duly executed by authorized representatives of both Parties. If the provisions of the Development Plan or the Global Marketing Plan are inconsistent with this Agreement, the provisions of this Agreement shall control.

12.9 **Headings.** The captions to the several articles, sections and subsections hereof are not a part of this Agreement, but are merely for convenience to assist in locating and reading the several articles and sections hereof.

12.10 **Independent Contractors.** It is expressly agreed that Vertex and GSK shall be independent contractors and that the relationship between the two Parties shall not constitute a partnership, joint venture or agency. Neither Vertex nor GSK shall have the authority to make any statements, representations or commitments of any kind, or to take any action, which shall be binding on the other Party, without the prior written consent of the other Party.

12.11 **Waiver.** The waiver by either Party hereto of any right hereunder, or the failure of the other Party to perform, or a breach by the other Party, shall not be deemed a waiver of any other right hereunder or of any other breach or failure by such other Party whether of a similar nature or otherwise.

12.12 **Cumulative Remedies.** No remedy referred to in this Agreement is intended to be exclusive, but each shall be cumulative and in addition to any other remedy referred to in this Agreement or otherwise available under law.

12.13 **Waiver of Rule of Construction.** Each Party has had the opportunity to consult with counsel in connection with the review, drafting and negotiation of this Agreement. Accordingly, the rule of construction that any ambiguity in this Agreement shall be construed against the drafting Party shall not apply.

Information redacted pursuant to a confidential treatment request. An unredacted version of the exhibit has been filed separately with the Commission.

12.14 **Certain Conventions.** Any reference in this Agreement to an Article, Section, subsection, paragraph, clause, Schedule or Exhibit shall be deemed to be a reference to an Article, Section, subsection, paragraph, clause, Schedule or Exhibit, of or to, as the case may be, this Agreement, unless otherwise indicated. Unless the context of this Agreement otherwise requires, (a) words of any gender include each other gender, (b) words such as "herein", "hereof", and "hereunder" refer to this Agreement as a whole and not merely to the particular provision in which such words appear, (c) words using the singular shall include the plural, and vice versa, and (d) the words "include," "includes" and "including" shall be deemed to be followed by the phrase "but not limited to", "without limitation", "inter alia" or words of similar import.

12.15 **Counterparts.** This Agreement may be executed in two or more counterparts, each of which shall be deemed an original, but all of which together shall constitute one and the same instrument.

12.16 **Pharmacovigilence.**

12.16.1 GSK shall be responsible for the timely reporting of product quality complaints, adverse events and product safety data related to Product Candidates or Products to the appropriate Regulatory Agency or other health authorities. GSK shall maintain a global adverse event database for Product Candidates and Products. GSK shall respond effectively in a timely manner to all safety issues with respect to a Product Candidate or a Product, and to all requests made by any Regulatory Authority in the Territory.

12.16.2 Not later than **[***]** after the first filing of an NDA for each Product, the Parties will agree on terms to facilitate the management of safety for the Product in accordance with standards which are no less stringent than those contained in the ICH Guidelines.

The agreed terms will ensure that:

(i) The Parties will be able to comply with regulatory requirements for the reporting of safety data in accordance with standards stipulated in the ICH Guidelines, and all applicable regulatory and legal requirements regarding the management of safety data; and

(ii) The Parties will exchange relevant safety data within appropriate timeframes and in an appropriate format to enable them to meet both expedited and periodic regulatory reporting requirements.

[Signature Page Follows]

Information redacted pursuant to a confidential treatment request. An unredacted version of the exhibit has been filed separately with the Commission.

IN WITNESS WHEREOF, the Parties have executed this Agreement as of the date first set forth above.

GLAXO GROUP LIMITED	**VERTEX PHARMACEUTICALS INCORPORATED**
By: /s/ VICTORIA LLEWELLYN	By: /s/ JOSHUA S. BOGER
Name:	Name: Joshua Boger
Title: Assistant Company Secretary	Title: Chairman, President and Chief Executive Officer
December 17, 2005	December 17, 2005
Date	Date

Information redacted pursuant to a confidential treatment request. An unredacted version of the exhibit has been filed separately with the Commission.

Schedule 1.2
Back-up Compounds

[***]

[***]

[***]

[***]

Information redacted pursuant to a confidential treatment request. An unredacted version of this exhibit has been filed separately with the Commission.

Schedule 1.15
Development Candidate Criteria

[***]

[***]

Information redacted pursuant to a confidential treatment request. An unredacted version of this exhibit has been filed separately with the Commission.

Schedule 1.57
VX-409 Specification

[***]

Information redacted pursuant to a confidential treatment request. An unredacted version of this exhibit has been filed separately with the Commission.

Schedule 1.60
Unit Direct Cost of Goods of GSK or Third Party contract manufacturer (as appropriate)

[***]

Information redacted pursuant to a confidential treatment request. An unredacted version of this exhibit has been filed separately with the Commission.

Schedule 1.66
Vertex Patent Rights

[***]

[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]
VPI/02-138BR	Brazil	PI0408026-2	PUBLISHED
[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]
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[***]	[***]	[***]	[***]
VPI/02-138PE	Peru	2362004	PUBLISHED
[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]
VPI/02-138PROV	US	60/451,458	EXPIRED
VPI/02-138PROV	US	60/463,797	EXPIRED
VPI/02-138	US	10,792,688	PUBLISHED
[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]

[***]

Information redacted pursuant to a confidential treatment request. An unredacted version of this exhibit has been filed separately with the Commission.

Schedule 1.67
VX-409 Chemical Structure

[***]

Information redacted pursuant to a confidential treatment request. An unredacted version of this exhibit has been filed separately with the Commission.

Schedule 3.1
Development Plan as of the Effective Date

[***]

Information redacted pursuant to a confidential treatment request. An unredacted version of this exhibit has been filed separately with the Commission.

Schedule 3.3
Planning Information

[***]

Information redacted pursuant to a confidential treatment request. An unredacted version of this exhibit has been filed separately with the Commission.

Schedule 5.2
Inventory and Manufacturing Cost

[***]

Information redacted pursuant to a confidential treatment request. An unredacted version of this exhibit has been filed separately with the Commission.

QuickLinks

QuickLinks -- Click here to rapidly navigate through this document

EXHIBIT 10.35

December 5, 2005

VIA FEDEX

Mr. Richard C. ("Bink") Garrison
337 Marlborough Street, Apt. 3
Boston, MA 02115

RE: Vertex Pharmaceuticals Incorporated/Richard C. ("Bink") Garrison
Offer Letter

Dear Bink:

On behalf of Vertex Pharmaceuticals Incorporated (the "Company"), I am pleased to extend an offer to you for a position with the Company as follows:

- *Job Title:* Senior Vice President, Organizational Development, reporting to Joshua Boger, Ph.D., Chairman, President & Chief Executive Officer.

- *Employment Term:* Four year term commencing on December 12, 2005 (your "start date"), terminable by either party, with or without "Cause," on thirty (30) days' notice. Severance benefits will be available as described below.

- *Duties:* As requested by the Chief Executive Officer, but generally will include the following:

  - contribute as a member of the senior management team (currently referred to as the "Executive Team" or the "ET") which sets strategy and oversees operations for the pharmaceutical business worldwide, and as a member of the group of managers who coordinate the Company's functional activities worldwide (currently referred to as the "Operating Council" or the "OC");

  - develop and implement processes to increase the group effectiveness of the ET and the OC and the individual effectiveness of each of its members;

  - establish sustainable mechanisms to preserve and embed the Company's values and culture, enhance the performance capabilities of the Company's human capital assets, and improve the Company's ability to grow its human capital base;

  - develop messages, mechanisms and modalities to enhance communication of the Company's corporate image, mission and values, both within and outside the Company; and

  - work closely with the leaders of the human resources function, the investor relations function, and the other functional leaders to achieve the foregoing objectives.

- *Sign-On Bonus:* You will receive a sign-on bonus in the amount of $80,000, payable on the first regular payroll date following commencement of employment. During the first twelve months after your start date, if you terminate your employment or if your employment is terminated by the Company for Cause, you will be required to repay the sign-on bonus to the Company.

- *Compensation:* Annualized salary of $320,000, subject to review and adjustment (upward) by the Company's Board of Directors as part of the normal annual senior executive review process in effect from time to time, to be paid in accordance with the Company's customary payroll practices.

- *Initial Equity Grant:* As an important part of this offer, we will grant to you the following initial amounts of restricted shares and stock options. These restricted shares and stock options will be issued under, and subject to, the general terms and conditions of the Company's 1996 Stock and Option plan.

  Restricted Shares: You will be granted restricted shares at a nominal price, which will vest in four equal annual installments on the anniversary of your start date. Unvested shares will be

subject to repurchase by the Company upon termination of your employment, for a price equal to the price for which you purchased them. The number of shares to be issued will be calculated by dividing $200,000 by the Company's average stock price over the ten trading days immediately prior to your start date, rounded up to the nearest 100 shares *(e.g.*, 9,090 shares would become 9,100).

Stock Option: You will be granted an initial option to purchase shares of the Company's common stock, which will vest and become exercisable with respect to equal amounts of the underlying option stock at the end of each quarter during the 4-year period commencing on the Start Date. The exercise price of the shares subject to the initial stock option (the "Initial Exercise Price") will be the average market price of the Company's shares on your start date. The number of shares subject to the purchase option will be calculated by dividing $750,000 by the Initial Exercise Price, rounded up to the nearest 1,000 shares (*e.g.*, 27,300 option shares would become 28,000 option shares).

- *Employment Benefits:* Major medical and dental coverage, three weeks vacation, 401(k) plan with a matching Company contribution, long term disability, company-paid life insurance and other benefits, all as in effect from time to time. We have previously provided you with a summary description of the benefits currently offered by the Company. In addition, the Company will promptly reimburse you for all business expenses reasonably incurred by you in connection with your employment, provided that you supply receipts for or other proof of the expenses and your claim for reimbursement is otherwise in accordance with general Company policy.

- *Participation in Bonus Program:* You will be eligible to participate in the Company's cash bonus programs in effect from time to time and applicable to the Company's senior executives, as determined by the Board. The Company's current plan contemplates an annual cash bonus of up to 40% of a senior executive's annual base salary, depending on both individual and Company performance.

- *Long Term Incentive Compensation Plans:* You will be eligible to participate in the Company's long-term incentive compensation plans, including the Company's option and restricted stock plans, in effect from time to time and available to the Company's senior executives, as determined by the Board.

- *Change of Control Benefit:* The Company will provide you with a "change of control" benefit on the same terms and conditions extended generally to other senior executives. A copy of the "*Change of Control Agreement"* is enclosed herewith for your review.

- *Outside Interests:* The position you are being offered is for full-time employment with the Company. We expect that your outside interests (*e.g.*, directorships and similar activities) will in general contribute to your skills and job performance at the Company and will require only reasonably amounts of time away from the Company (as determined by the Chief Executive Officer), and will, in all cases, be subject to prior approval by the Chief Executive Officer.

- *Confidentiality and Inventions Agreement:* As a condition of your employment, you will be required to sign a copy of our "Employee Non-Disclosure, Non-Competition and Inventions Agreement" in the form included with this letter.

- *Severance Benefits:* In the event you terminate your employment for "Good Reason" or if your employment is terminated by the Company without "Cause" during the during the 4-year contract term, you will receive:

(i) 12 months' salary plus bonus, payable monthly in equal installments (ceasing upon death, but in no event less than six months of benefit);

(ii) all stock options and time-vesting restricted stock held on the date of your termination will be deemed to have been held, for vesting purposes, an additional 18 months, and all vested options as of the termination date will remain exercisable for 12 months; and

(iii) continued participation in the Company's medical insurance plan until the earlier of the end of the severance pay period specified in (i) above, or the date you receive equivalent coverage from a subsequent employer.

- *"Cause":* For purposes of the severance benefit described above, "Cause" shall mean

(a) your conviction of a felony crime of 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 thirty (30) days to correct any problems and *further provided* if you correct the problem(s) you may not be terminated for Cause in that instance;

(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.

- *"Good Reason":* For purposes of the severance benefit described above, "Good Reason" shall mean that without your consent, one or more of the following events occurs and you terminate your employment by notice in writing to the Chief Executive Officer of the Company within 90 days after the first occurrence of the event:

(i) You are assigned to any duties or responsibilities that are inconsistent, in any significant respect, with the scope of duties and responsibilities currently performed in your positions and offices as described under "Job Title" and "Duties" above, provided that such reassignment of duties or responsibilities is not due to your Disability or performance, nor is at your request or with your prior agreement;

(ii) You suffer a reduction in the authorities, duties, and responsibilities associated with your positions and offices as described under "Job Title" and "Duties" above, on the basis of which you make a determination in good faith that you can no longer carry out such positions or offices in the manner contemplated at the time this Agreement was entered into, provided that such reassignment of duties or responsibilities is not due to your Disability or your performance, and is not at your request or with your prior agreement;

(iii) Your base salary, as determined under "Compensation" above, is decreased;

(iv) Your own office location as assigned to you by the Company is relocated thirty-five (35) or more miles from Cambridge, Massachusetts; or

(v) Failure of any entity, in the event of a Change of Control, as defined in your "Change of Control Agreement" referenced above, to assume all obligations and liabilities of this Agreement.

- *"Disability":* For purposes of the foregoing, a "Disability" is 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 Internal Revenue Code Section 22(e)(3).

Although you are being hired for your particular expertise, we are counting on the fact that the Company's management team will be highly interactive, with people who are interested not in building and maintaining artificial barriers around disciplines and skills, but in breaking down those barriers and applying new insights and initiatives across related fields. The position to which you have been hired is an important position in the Company, and we know it will be a challenging and exciting one.

Please note that this offer is conditional on approval of the terms and conditions set forth herein by the Board and your ability to commence employment with the Company on or before December 12, 2005.

Pending that approval, we are pleased to extend this offer to you and look forward to your acceptance. Please sign and return this offer letter and the additional documents enclosed herewith as soon as possible to indicate your agreement with the terms of this offer. We look forward to having your confirming response.

Once signed by you, this letter and its attachments will constitute the complete agreement between you and the Company regarding your employment and will supersede all prior written or oral agreements or understandings on these matters.

We believe you will be able to make an immediate contribution to the Company's efforts, and I think you will enjoy the rewards of working for an innovative, fast-paced company. One of the keys to our accomplishments is good people. We hope you accept our offer to be one of those people.

Sincerely yours,

/s/ JOSHUA BOGER

Joshua Boger, Ph.D.
Chairman, President & CEO

I accept the terms of employment as described in this offer letter dated December 5, 2005, and will start my employment on or before December 12, 2005. I confirm that by my start date at the Company I will be under no contract or agreement with any other entity which would in any way restrict my ability to work at the Company or perform the functions of my job for the Company, including, but not limited to, any employment agreement and/or non-compete agreement.

/s/ RICHARD C. GARRISON *Date* 12/6/05

Richard C. Garrison

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EXHIBIT 10.36

December 12, 2005

Mr. Richard C. ("Bink") Garrison
337 Marlborough Street, Apt. 3
Boston, MA 02115

RE: Vertex Pharmaceuticals Incorporated
Change of Control Agreement

Dear Bink:

Your expertise, reputation and position will make you 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" benefit to help ensure that in the event 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 Agreement, capitalized terms shall have the following meaning:

1. "*Base Salary*" shall mean your annual base salary in effect immediately prior to a Change of Control (as such term is defined in Section I.4 below).

2. "*Cause*" shall mean:

(e) your conviction of a felony crime of moral turpitude;

(f) 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 thirty (30) days to correct any problems and further provided if you correct the problem(s) you may not be terminated for Cause in that instance;

(g) 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

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

3. "*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 fifty percent (50%) of the combined voting power of the outstanding securities of the Company, as the case may be, having the right to vote in the election of directors; or

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.

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 under Internal Revenue Code Section 22(e)(3).

5. "*Good Reason*" shall mean that within ninety (90) days prior to a Change of Control, or within twelve (12) months after a Change of Control, one of the following events occurs without your consent:

(a) You are assigned to material duties or responsibilities that are inconsistent, in any significant respect, with the scope of duties and responsibilities associated with your position and office immediately prior to the Change of Control (provided that such reassignment of duties or responsibilities is not for Cause, due to your Disability or at your request);

(b) You suffer a material reduction in the authorities, duties, or job title and responsibilities associated with your position and office immediately prior to the Change of Control, on the basis of which you make a good faith determination that you can no longer carry out your position or office in the manner contemplated before the Change of Control (*provided* that such reduction in the authorities, duties, or job title and responsibilities is not for Cause, due to your Disability or at your request);

(c) your annual base salary is decreased below the Base Salary;

(d) the principal offices of the Company, or the location of the office to which you are assigned at the time this Agreement is entered into, is relocated to a place thirty-five (35) or more miles away, without your agreement; or

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

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

II. *Severance Benefits upon Change of Control*. In the event your employment is terminated (*except* for termination for Cause or due to a Disability) within ninety (90) days prior to a Change of Control or within twelve (12) months after a Change of Control; or if you, of your own initiative, terminate your employment within ninety (90) days prior to a Change of Control or within twelve (12) months after a Change of Control for Good Reason, in exchange for a general release of all claims, you shall receive the following benefits:

1. *Severance Payment*—The Company shall make a lump sum payment to you equal to:

(a) Your annual Base Salary (*provided, however,* that in the event you terminate your 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); and

(b) any unpaid portion of a bonus award actually awarded but not yet paid to you under any bonus program applicable to the Company's senior executives and in effect prior to the Change of Control, pro rated in the event the Termination Date is prior to the end of the bonus plan year.

The Severance Payment shall be made in cash within ten (10) days of the execution of a general release and expiration without revocation of any applicable revocation periods under the general release.

2. *Accelerated Vesting*—Stock options for the purchase of the Company's securities held by you as of the Termination Date and not then exercisable shall be deemed to have been held by you

for an additional 18-months, for purposes of calculating the number of options which are exercisable on the Termination Date. 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 Termination Date, or (b) the date the stock option(s) would otherwise expire.

3. *Continued Insurance Coverage*—If COBRA coverage is elected by you, the Company shall pay the cost of COBRA continuation premiums on your behalf to continue standard medical, dental and life insurance coverage for you (or the cash equivalent of same in the event you are ineligible for continued coverage) for a period of 18-months from the Termination Date.

You shall not be required to mitigate the amount of the Severance Payment or any other benefit provide 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 by any compensation earned by you as the result of other employment, by retirement benefits, or by offset against any amount claimed to be owed by you to the Company or otherwise.

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 be 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, the "*Employee Non-Disclosure, Non-Competition & Inventions Agreement*" executed by you and the Company effective as of December 12, 2005 and the offer letter previously signed by you and the Company, cover the entire understanding of the parties as to your rights and obligations in the event of a Change of Control, superseding all prior understandings and agreements related thereto. 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.

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. 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 forgoing 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/ KENNETH S. BOGER

Kenneth S. Boger
Sr. Vice President and General Counsel

ACCEPTED AND AGREED:

/s/ RICHARD C. GARRISON

Richard C. Garrison
December 12, 2005

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EXHIBIT 10.37

December 12, 2005

Mr. Richard C. ("Bink") Garrison
337 Marlborough Street, Apt. 3
Boston, MA 02115

Re: Amendment to Change of Control Agreement

Dear Bink:

The Change of Control Agreement dated as of December 12, 2005 between you and Vertex Pharmaceuticals Incorporated (the "*Agreement*") hereby is amended, effective as of the date set forth above, as follows:

1. Insert a new Section I.7, which shall state in its entirety:

I.7 "*Pro-Rata Share of Restricted Stock*" shall mean, for any grant of restricted stock as to which the Company's repurchase right lapses ratably over a specified period (e.g. in equal annual increments over four years), that number of shares as to which the Company's repurchase right with respect to those shares would have lapsed if the Executive's employment by the Company had continued an additional 18 month period. For any other shares of restricted stock, "Pro-Rata Share of Restricted Stock" shall mean, as to any shares of restricted stock which were granted on the same date and as to which the Company's repurchase right lapses on the same date, that portion of such shares calculated by multiplying the number of shares by a fraction, the numerator of which is the number of days that have passed since the date of grant, plus the number of days in 18 months, and the denominator of which is the total number of days from the date of the grant until the date (without regard to any provisions for earlier vesting upon achievement of a specified goal) on which the Company's repurchase right would lapse under the terms of the grant.

2. Delete Section 2, "Accelerated Vesting," in its entirety, and substitute the following therefor:

2. *Accelerated Vesting*

(a) Stock options for the purchase of the Company's securities held by you as of the Termination Date and not then exercisable shall be deemed to have been held by you for an additional 18 months, for purposes of calculating the number of options which are exercisable on the Termination Date. 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 Termination Date, or (b) the date the stock option(s) would otherwise expire; and

(b) the Company's lapsing repurchase right with respect to shares of restricted stock held by you shall lapse with respect to the Pro-Rata Share of Restricted Stock.

(c) 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, as applicable, except to the extent that the terms of this agreement are more favorable to you.

As so amended, the Change of Control Agreement shall remain in full force and effect.

If you agree to the foregoing amendment, please so indicate by signing and returning the enclosed copy of this letter.

Vertex Pharmaceuticals Incorporated

By: /s/ KENNETH S. BOGER

Kenneth S. Boger
Senior Vice President and General Counsel

Accepted and Agreed:

/s/ RICHARD C. GARRISON

Richard C. Garrison

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Exhibit 10.38

Salary Amendments to Employment Agreements with Named Executive Officers

Named Executive Officer	2006 Annual Base Salary Effective as of February 2, 2006
Joshua S. Boger	$600,000
Victor A. Hartmann	$452,434
Peter Mueller	$432,387
Ian F. Smith	$400,504
Kenneth S. Boger	$377,228

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Exhibit 10.40

AMENDMENT TO NON-EMPLOYEE DIRECTOR COMPENSATION POLICY

In the first quarter of 2006, the Board of Directors amended the Company's non-employee director compensation policy. Prior to the amendment, the Chair of the Audit Committee received a $15,000 annual retainer, and the Chair of the Management Development and Compensation Committee received a $10,000 annual retainer. Under the amended policy, the Chair of the Audit Committee will receive a $20,000 annual retainer, and the Chair of the Management Development and Compensation Committee will receive a $14,000 annual retainer.

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EXHIBIT 21

SUBSIDIARIES OF VERTEX PHARMACEUTICALS INCORPORATED

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

VSD Sub I LLC, a Delaware limited liability company(1)

VSD Sub II LLC, a Delaware limited liability company(2)

Vertex Holdings, Inc., a Delaware corporation

Vertex Securities Trust, a Massachusetts business trust(3)

Vertex Pharmaceuticals (Europe) Ltd., a United Kingdom limited liability company(4)

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(1) a subsidiary of Vertex Pharmaceuticals (San Diego) LLC

(2) a subsidiary of VSD Sub I LLC

(3) a subsidiary of Vertex Holdings, Inc.

(4) jointly held by Vertex Securities Trust and Vertex Holdings, Inc.

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Exhibit 23.1

Consent of Independent Registered Public Accounting Firm

We consent to the incorporation by reference in the following Registration Statements: Form S-8 (Nos. 33-48030, 33-48348, 33-65472, 33-93224, 333-12325, 333-27011, 333-56179, 333-65664, 333-79549, 333-104362 and 333-115458) and Form S-3 (Nos. 333-37794, 333-49844, 333-116376, 333-120055, 333-123731, 333-130179 and 333-130665) of our reports dated March 8, 2006, with respect to the consolidated financial statements of Vertex Pharmaceuticals Incorporated, Vertex Pharmaceuticals Incorporated's management's assessment of the effectiveness of internal control over financial reporting, and the effectiveness of internal control over financial reporting of Vertex Pharmaceuticals Incorporated, included in the Annual Report (Form 10-K) for the year ended December 31, 2005.

/s/ Ernst & Young LLP

Boston, Massachusetts
March 16, 2006

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Exhibit 23.2

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We hereby consent to the incorporation by reference in the Registration Statements on Form S-8 (Nos. 33-48030, 33-48348, 33-65472, 33-93224, 333-12325, 333-27011, 333-56179, 333-65664, 333-79549, 333-104362 and 333-115458) and Form S-3 (Nos. 333-37794, 333-49844, 333-116376 and 333-120055, 333-123731, 333-130179 and 333-130665) of Vertex Pharmaceuticals Incorporated of our report dated March 15, 2005 relating to the consolidated financial statements, which appears in this Annual Report on Form 10-K.

/s/ PricewaterhouseCoopers LLP

Boston, Massachusetts
March 16, 2006

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Exhibit 31.1

CERTIFICATION

I, Joshua S. Boger, 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: March 16, 2006

/s/ JOSHUA S. BOGER

Joshua S. Boger
Chairman, President and Chief Executive Officer

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Exhibit 31.2

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(s) 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: March 16, 2006

/s/ IAN F. SMITH

Ian F. Smith
Executive Vice President and Chief Financial Officer

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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, 2005 (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: March 16, 2006

/s/ JOSHUA S. BOGER

Joshua S. Boger
Chairman, President and Chief Executive Officer

Date: March 16, 2006

/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.

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