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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, 2004

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

(617) 444-6100

(Registrant's telephone number, including area code)

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 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. ☒

Indicate by check mark whether the registrant is an accelerated filer (as defined in Rule 12b-2 of the Act). Yes ☒ No o

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, 2004 was $503,370,650.

As of March 14, 2005, the registrant had 81,206,723 shares of common stock outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the definitive Proxy Statement for the 2005 Annual Meeting of Stockholders to be held on May 11, 2005 are incorporated by reference into Part III.

FORM 10-K INDEX

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.

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, among other things, statements relating to:

- our business strategy;
- our predicted development and commercial timelines;
- the selection, development and approval of our products;

- the establishment, development and maintenance of collaborative relationships;
- our ability to identify and develop new potential products;
- our ability to achieve commercial acceptance of our products;
- our ability to scale up our manufacturing capabilities and facilities;
- our estimates regarding obligations associated with a lease of a facility in Kendall Square, Cambridge, Massachusetts;
- the potential for the acquisition of new and complementary technologies, resources and products;
- our projected capital expenditures; and
- our liquidity.

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. Consequently, no forward-looking statement can be guaranteed. Actual future results may vary materially. A more detailed description of our forward-looking statements can be found under "Forward-looking Statements" in Item 7 of this Annual Report.

We also provide a cautionary discussion of risks and uncertainties under "Risk Factors" in Item 1 of this Annual Report. These 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.

PART I

ITEM 1. BUSINESS

Overview

We are a biotechnology company in the business of discovering, developing and commercializing small molecule drugs for serious diseases, including HIV infection, chronic hepatitis C virus (HCV) infection, inflammatory and autoimmune disorders, cancer, pain and bacterial infection, independently and with collaborators. Our principal focus at this time is on the development and commercialization of new treatments for viral diseases, inflammatory and autoimmune diseases and cancer. Two Vertex-discovered products for the treatment of HIV infection and AIDS have advanced to the market. Our pipeline of potential products includes several drug candidates targeting chronic HCV infection, inflammatory and autoimmune diseases such as rheumatoid arthritis and psoriasis, and cancer.

Our goal is to mature into a profitable pharmaceutical company with industry-leading capabilities in research, development and commercialization of products. Our strategy is to continue building these capabilities as we advance our product candidates to market. We focus our efforts both on programs that we expect to control throughout the development and commercialization phases, and programs that we expect will be conducted principally by a collaborator. We expect to retain control of the development of certain product candidates for the treatment of chronic HCV infection and inflammation. We believe that we can effectively commercialize products in these therapeutic areas, while expending comparatively fewer resources, through the use of a specialist-focused sales force. We have focused our Vertex-controlled commercialization efforts in North America, and we expect to concentrate on identifying collaborative relationships for development of our HCV infection and inflammation product candidates outside of North America. The most advanced product candidates for which we control North American development are:

- merimepodib, an oral IMPDH inhibitor for the treatment for chronic HCV infection;
- VX-950, an oral hepatitis C protease inhibitor for the treatment of chronic HCV infection;
- VX-702, an oral p38 MAP kinase inhibitor for the treatment of inflammatory diseases; and
- VX-765, an oral ICE inhibitor for the treatment of autoimmune diseases.

We expect to continue to invest in our research and development capabilities as we advance our product candidates to market.

Collaborations will continue to be a key component of our corporate strategy. We currently are collaborating with Novartis Pharma AG, GlaxoSmithKline plc, Merck & Co., Inc., Mitsubishi Pharma Corp., Kissei Pharmaceutical Co., Ltd., Cystic Fibrosis Foundation Therapeutics Incorporated 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 with GlaxoSmithKline plc that has resulted in our two marketed products to date, the HIV protease inhibitors Agenerase and Lexiva (marketed under the name Telzir in the European Union) and the advancement of a third HIV protease inhibitor, VX-385, into Phase II clinical development. Our collaboration with Eli Lilly and Company, now ended, produced VX-950, one of our HCV drug candidates, and our collaboration with Novartis produced the potential oncology therapeutics VX-680, now in Phase I clinical development by Merck, and VX-322, now in preclinical development by Novartis.

We plan to continue to add promising potential products to our development pipeline through our continuing commitment to discovery research. Our drug design approach integrates biology, chemistry, biophysics, automation and information technologies to make the drug discovery process more efficient and productive. We believe that our drug discovery expertise is one of our distinguishing features. In addition to our efforts to research and develop kinase inhibitors, we currently are conducting a productive research program in the area of ion channel modulation. We expect that future development

candidates from our programs will be focused on the treatment of a wide variety of diseases and conditions, including cancer, cystic fibrosis and pain.

We also 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.

The Company's internet address is www.vrtx.com. The Company's 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.

We were incorporated in Massachusetts in 1989, and our principal executive offices are located at 130 Waverly Street, Cambridge, Massachusetts 02139.

COMMERCIAL PRODUCTS AND CLINICAL DEVELOPMENT PROGRAMS

Our product pipeline is principally focused on viral diseases, inflammatory and autoimmune diseases, cancer, pain and bacterial infection.

Therapeutic Area and Product Candidate	Clinical Indications	Development Phase	Company With Marketing Rights (Region)
Viral Diseases			
Lexiva/Telzir (fosamprenavir calcium)*	HIV infection	Marketed	GlaxoSmithKline (Worldwide)**
Merimepodib (VX-497)	Chronic hepatitis C virus infection	Phase II	Vertex (Worldwide)
VX-950	Chronic hepatitis C virus infection	Phase I	Mitsubishi (Far East); Vertex (Rest of World)
VX-385	HIV infection	Phase II	Vertex (Far East); GlaxoSmithKline (Rest of World)
Inflammatory and Autoimmune Diseases			
VX-765	Psoriasis and other autoimmune diseases	Phase II	Vertex (Worldwide)
VX-702	Rheumatoid arthritis and other inflammatory diseases	Phase II	Kissei (Far East); Vertex (Rest of World; Co-exclusive in certain Far East countries)
Pralnacasan (VX-740)	Rheumatoid arthritis and other inflammatory and autoimmune diseases	Phase II	Sanofi-Aventis (Worldwide)†
Cancer			
VX-680	Oncology	Phase I	Merck (Worldwide)
VX-944	Oncology	Phase I	Avalon Pharmaceuticals (Worldwide)
VX-322	Oncology	Preclinical	Novartis (Worldwide)
Other			
VX-409	Pain	Preclinical	Vertex (Worldwide)
VX-692	Bacterial infection	Preclinical	Vertex (Worldwide)

* Fosamprenavir calcium is marketed under the trade names Lexiva in North America and Telzir in the European Union. Lexiva/Telzir, a prodrug of our first marketed HIV drug, Agenerase (amprenavir), also marketed by GlaxoSmithKline, is replacing Agenerase in world markets.

** Vertex has co-promotion rights in the United States and the European Union.

† Sanofi-Aventis has notified us that it intends to terminate our collaboration for the development of pralnacasan. Upon the effectiveness of that termination, all commercial and other rights to pralnacasan will revert to Vertex.

HIV Infection/AIDS

Background: Treatment of HIV Infection/AIDS

Infection with human immunodeficiency virus (HIV) leads to AIDS, a severe, life-threatening impairment of the immune system. The World Health Organization estimates that approximately 39.4 million individuals worldwide are infected with HIV. The U.S. Centers for Disease Control and Prevention (CDC) has estimated that there are between 850,000 and 950,000 patients 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 (NRTIs), such as AZT and 3TC; non-nucleoside reverse transcriptase inhibitors (NNRTIs), such as efavirenz; the fusion inhibitor enfuvirtide; and HIV protease inhibitors (PIs). PIs such as Lexiva commonly are used as part of combination regimens for the treatment of HIV. PIs block the cleavage of HIV polyproteins into active proteins, and result in the production of non-infectious viral particles. The PI ritonavir has been shown to significantly boost the levels of certain other PIs in the bloodstream and therefore co-administration of 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.

As of the end of 2004, over 206,000 patients in the United States receiving drug treatment for HIV infection were taking at least one PI. The market for HIV PIs is highly competitive, with seven different PIs vying for a share. We estimate that worldwide sales of HIV PIs exceeded $2.0 billion in 2004, and U.S. sales alone during the same period were estimated at more than $1.1 billion. We believe that trends in the demographics of HIV-infected patients and recently evolving approaches to the treatment regimen for HIV infection have resulted in a recent increase in the use of PIs generally, including Lexiva. We believe that, in 2004, there was an increase in both the number and the percentage (from 47% to 53%) of HIV infected patients in the U.S. being treated with a PI. We attribute this growth, in part, to the use of new PIs, such as Lexiva, that offer potent therapy combined with greater tolerability and convenience, as compared with first-generation PIs.

Vertex HIV Infection/AIDS Products

- ***Lexiva/Telzir***

Our second generation PI Lexiva, which is sold in the European Union under the name Telzir, was co-discovered by Vertex and GlaxoSmithKline plc ("GlaxoSmithKline") and has been developed by GlaxoSmithKline pursuant to our collaboration agreement. GlaxoSmithKline has worldwide marketing rights for Lexiva/Telzir, and we have the right to co-promote Lexiva/Telzir in the United States and the European Union. We also have the right to supply bulk drug substance to GlaxoSmithKline. We receive royalties on GlaxoSmithKline's sales of Lexiva/Telzir.

GlaxoSmithKline conducted an extensive Phase III clinical program for Lexiva, including trials in both treatment-naïve and treatment-experienced patients. The first study (NEAT) compared Lexiva to nelfinavir in treatment-naïve patients. The second study (SOLO) compared Lexiva in combination with ritonavir, administered once-daily, to nelfinavir in treatment-naïve patients. The third study (CONTEXT) evaluated both once-daily and twice-daily dosing of Lexiva in combination with ritonavir, compared to lopinavir/ritonavir, in treatment-experienced patients. In all of these studies, patients received NRTIs as part of the combination regimen.

In December 2002, GlaxoSmithKline filed a New Drug Application with the U.S. Food and Drug Administration (FDA) and a Marketing Authorization Application in the European Union for marketing approval of Lexiva/Telzir in the U.S. and the European Union. The registration submissions included data from more than 1,100 treatment-naïve and treatment-experienced patients who

participated in the Phase III trials. The FDA approved Lexiva on October 20, 2003. GlaxoSmithKline and Vertex launched Lexiva in the United States shortly thereafter. The European Commission granted marketing approval for Telzir in July 2004, and GlaxoSmithKline launched Telzir in certain European Union countries in the third quarter of 2004. Lexiva/Telzir currently is marketed in 17 countries. Lexiva currently holds a 9% share of the PI market in the United States, and is one of two HIV protease inhibitors that demonstrated an increase in the number of prescriptions written in the United States in 2004, compared to 2003.

We believe that the favorable properties of Lexiva/Telzir include:

* potent anti-viral activity;

* a half-life which allows for convenient twice-daily dosing and provides high levels of the drug in the bloodstream;

* ability to be dosed once daily when co-administered with ritonavir;

* ability to be dosed effectively with or without food, providing convenience for patients;

* good tolerability;

* ability to be co-administered with certain antacids and drugs such as ranitidine (Zantac);

* relatively low levels of cross-resistance to other protease inhibitors; and

* a favorable lipid profile.

Lexiva/Telzir is a prodrug of amprenavir, our first generation HIV protease inhibitor, which also was discovered and developed in collaboration with GlaxoSmithKline. A prodrug is an inactive compound that is metabolized by the body to become the active drug. Due to the physical properties of a prodrug, in particular cases it may be possible to achieve a higher effective dose of the active drug for each prodrug pill administered, resulting in a smaller pill burden for patients.

At the International AIDS conference held in July 2004, GSK presented data on the ability of patients taking PI regimens that included Lexiva to maintain viral suppression through nearly two years of therapy. At 96 weeks of therapy, of the 113 patients initially enrolled in the NEAT study for whom data were available, 109 (96%) had a viral load below 400 copies/ml HIV-RNA and 97 (86%) had a viral load below 50 copies/ml HIV-RNA. Also at 96 weeks of therapy, of the 60 patients initially enrolled in the SOLO study for whom data were available, 54 (90%) had a viral load below 400 copies/ml HIV-RNA and 51 (85%) had a viral load below 50 copies/ml HIV-RNA. The data presented also showed that after 96 weeks of treatment, no PI- resistance mutations were observed in patients. We believe that these data demonstrate that Lexiva-based regimens are durable, and support the use of Lexiva/Telzir as an element of both first-line therapies and second-line therapies for HIV infection.

- ***VX-385***

We have a third novel, orally available HIV protease inhibitor in clinical development, VX-385, which was co-discovered by Vertex and GlaxoSmithKline. VX-385 is chemically distinct from Agenerase, Lexiva/Telzir, and other currently marketed PIs. Preclinical results presented at medical meetings in 2003 demonstrate that VX-385 is a highly potent inhibitor that exhibits anti-HIV activity against HIV strains resistant to a number of currently marketed PIs. Phase I clinical results indicate that VX-385 is well-tolerated in single doses in healthy volunteers and achieves blood levels consistent with those believed to have an antiviral effect.

Our collaborator GlaxoSmithKline controls development of VX-385. In the fourth quarter of 2004, GlaxoSmithKline initiated a pilot Phase II study of VX-385. The open-label Phase II trial is designed for approximately 30 patients with HIV infection who will receive VX-385 for up to 48 weeks. The trial will assess the safety, efficacy and clinical activity of VX-385, and will use a planned interim analysis as a basis for designing larger, randomized clinical trials to support product registration. We expect that GlaxoSmithKline will report interim results from the pilot Phase II VX-385 trial in 2005.

Hepatitis C Virus Infection

Background: Treatment of Hepatitis C Virus Infection

Hepatitis C virus (HCV) infection causes chronic inflammation in the liver. In a majority of patients, HCV infection can persist for decades and eventually lead to cirrhosis, liver failure and liver cancer. HCV infection represents a significant medical problem worldwide. Sources at the Centers for Disease Control have estimated that approximately 2.7 million Americans are chronically infected with HCV, and the World Health Organization estimates that there are as many as 185 million chronic carriers of the virus worldwide.

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. Not only is this treatment regimen associated with significant side effects, including fatigue, flu-like symptoms, depression and anemia, but approximately 50% of patients infected with HCV genotype I, the most common HCV genotype in the United States, fail to show long-term sustained response to the therapy. As a result, new safe and effective treatment options for HCV infection are needed.

Vertex HCV Drug Candidates

We are developing two drug candidates targeting HCV infection through different mechanisms. Our most advanced compound is the IMPDH inhibitor merimepodib, which targets HCV indirectly and currently is in Phase IIb development. Vertex's second HCV drug candidate, VX-950, targets HCV directly, by inhibiting hepatitis C NS3-4A protease, an enzyme necessary for HCV replication. In 2004, we completed a Phase I clinical trial of VX-950 in healthy volunteers, and initiated a currently on-going Phase Ib clinical trial of VX-950 in both healthy volunteers and HCV-infected patients. In 2004, we were named a Business Leader in Medical Treatment by *Scientific American* magazine, based on our leadership in the search for new medicines for the treatment of HCV infection.

- ***Merimepodib***

Merimepodib is Vertex's most advanced orally available drug candidate for the treatment of HCV infection. Merimepodib targets HCV infection indirectly through inhibition of the human enzyme inosine 5'-monophosphate dehydrogenase (IMPDH). Merimepodib was discovered through Vertex's program to discover and develop novel orally administered IMPDH inhibitors. IMPDH inhibition selectively inhibits cell proliferation and/or the cycle of viral infection by interrupting the biosynthesis of guanine nucleotides and, indirectly, the synthesis of RNA and DNA in the cell, through one of two pathways available to cells for guanine synthesis. Accordingly, IMPDH is believed to be a target for inhibition of rapid cell proliferation and/or viral replication. In addition, IMPDH inhibitors appear to work additively or synergistically with other treatments for HCV, including ribavirin. The specific mechanism by which merimepodib enhances ribavirin activity is not known, but it has been suggested that merimepodib may increase the likelihood of ribavirin incorporation into viral RNA during replication, resulting either in decreased viral replication or in the production of immature or defective viral particles. We currently are conducting or planning a number of studies of merimepodib in order to position this compound as an additive anti-viral agent for use with evolving therapies to treat HCV infection.

In 2004, we initiated a Phase IIb, double-blind, placebo-controlled randomized triple combination study (the METRO study) of merimepodib with Pegasys® (peginterferon alfa-2a) and Copegus® (ribavirin) in patients who are non-responders to prior treatment with pegylated interferon and ribavirin. The goal of the METRO study is to evaluate the safety, pharmacokinetics and efficacy of merimepodib in combination with pegylated interferon and ribavirin. The primary endpoint of the study is to evaluate the antiviral activity of merimepodib 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 also plan to conduct an analysis of the antiviral activity of merimepodib-treated patients at 12, 24 and 48 weeks of treatment. The study is designed to enroll approximately 315

patients, and we expect to complete enrollment in the second quarter of 2005. Reaching our METRO enrollment goal will permit an interim analysis of data and, possibly, lead to discussions by the end of 2005 with the FDA about the registration path for triple combination treatment for patients who are non-responders to a combination of pegylated interferon and ribavirin alone.

In early 2005, we initiated a 28-day clinical virology study to evaluate the effects of a combination of merimepodib and ribavirin on hepatitis C viral load. We also plan an additional triple combination study of merimepodib, in this case involving treatment-naïve patients with HCV infection, for later in 2005.

In 2003, we completed the treatment arms of a triple combination Phase II study of merimepodib with pegylated interferon and ribavirin, to evaluate the safety of the triple combination, in 31 patients with genotype I HCV infection who did not respond to a previous course of alpha interferon in combination with ribavirin. The study provided for 24 weeks of treatment, with an optional 24 week extension phase for patients who responded to therapy. In 2003, we reported 24 weeks results from this study, indicating that merimepodib was well-tolerated and, in addition, that merimepodib treatment was associated with a statistically-significant, dose-dependent increase in the percentage of patients who had undetectable hepatitis C viral RNA after 24 weeks of treatment. With regard to the extension phase, eleven patients were eligible to participate, and ten of those patients completed the full 48 weeks of treatment. Of those completing the extension phase, one of three patients in the placebo group and three of seven patients in the merimepodib groups achieved a sustained viral response, measured 24 weeks after completing the 48 weeks of treatment. Vertex also has conducted experiments that demonstrate that merimepodib has an additive antiviral effect, *in vitro,* in combination with pegylated interferon and ribavirin.

In preclinical and early clinical studies, merimepodib demonstrated potent biological activity and oral bioavailability. Data from a Phase I trial in healthy volunteers showed that merimepodib was well-tolerated in single escalating doses and achieved blood levels well above those we believe to be necessary, based on *in vitro* studies, to achieve potent inhibition of IMPDH. Data from a Phase II clinical trial indicated that merimepodib, when given for 28 days as monotherapy to HCV patients who were unresponsive to prior treatment with alpha interferon, was well tolerated and appeared to reduce levels of serum alanine aminotransferase, a marker of liver inflammation.

We also have assessed the safety, tolerability and clinical activity of merimepodib combined with alpha interferon in another Phase II trial involving treatment-naïve patients with HCV infection. The viral load data from this study showed a trend toward enhanced antiviral activity in patients given one of two doses of merimepodib combined with alpha interferon, as compared to patients receiving alpha interferon alone. Merimepodib treatment was associated with statistically significant viral RNA decreases in this study when treatment-non-compliant patients were excluded from the analysis. These results are consistent with an additive antiviral effect mediated by merimepodib, when given in combination with alpha interferon.

Vertex holds all development and commercial rights to merimepodib.

- ***VX-950***

VX-950 is Vertex's lead oral HCV protease inhibitor, and one of the most advanced of a new class of antiviral treatments in development for HCV infection. VX-950 is designed to inhibit NS3-4A protease, an enzyme thought to be necessary for HCV replication. We believe that therapeutics that directly target viral replication, such as VX-950, may significantly increase the number of patients who achieve a complete viral response.

In 2004, we conducted and completed a Phase Ia placebo-controlled study of VX-950 in healthy volunteers. This study assessed safety, tolerability and pharmacokinetics in escalating, single oral doses of VX-950 ranging from 25 milligrams to 1250 milligrams. In this study, VX-950 was well-tolerated at all dose levels and was not associated with any serious adverse events. There did not seem to be an increase in adverse events with increasing dose levels. Pharmacokinetic assessments from this trial

showed that VX-950 is orally bioavailable and achieved desired blood concentrations at and above the middle range of the doses tested. The liver is the target organ for antiviral therapies directed against HCV infection. Using a combination of preclinical and clinical data, analyses by Vertex researchers suggest that average liver concentration values of VX-950 are predicted to be up to 57-fold above the 90% inhibitory concentration IC^{90} and up to 113-fold above the 50% inhibitory concentration IC^{50}, based on the antiviral activity of VX-950 in the replicon assay, a commonly used laboratory test of antiviral activity.

Later in 2004, we initiated a Phase Ib clinical study of VX-950 in HCV-infected patients. This Phase Ib study will investigate three doses of VX-950 for a period of 14 days in three serially-scheduled dose groups. The results from this study should provide Vertex with important information on the ability of VX-950 to reduce viral load. We plan to conduct the first interim analysis of the study results, which will include all on-treatment data from the three dose groups of HCV-infected patients, in the second quarter of 2005. If the study is successfully completed, we expect to file an IND in the United States in the second half of 2005 to support the start of Phase II clinical development of VX-950.

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 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.

Inflammatory and Autoimmune Diseases

Background: ICE Inhibitors for Inflammatory and Autoimmune Diseases

Interleukin-1b converting enzyme (ICE; caspase-1) is an enzyme that controls the release of active interleukin-1beta (IL-1b, one of two forms of IL-1) and interleukin-18 (IL-18) from white blood cells into the bloodstream and within tissues. IL-1b and IL-18 are cytokines that mediate a wide range of immune and inflammatory responses in many cell types. Early in the inflammatory process, IL-1b is released from white blood cells, initiating a complex cascade of events that results in inflammation and tissue damage. IL-18 is an important factor in the activation of lymphocytes, a type of white blood cell. Elevated IL-1b and IL-18 levels have been correlated with disease states in a number of acute and chronic inflammatory diseases.

In particular, we believe that small molecule ICE inhibitors have potential as a treatment for psoriasis. In patients with psoriasis, increased activity of IL-18 has been closely correlated with disease severity. In a clinical trial of healthy volunteers, our ICE inhibitor VX-765 appeared to lower serum levels of IL-18 by 50% or more after treatment for two weeks. We believe there are as many as 2.7 million people in the United States suffering from psoriasis, and that approximately 900,000 of them have moderate-to-severe psoriasis requiring drug treatment and/or phototherapy. Existing oral therapies for psoriasis are effective, but are associated with significant organ toxicities. Newer biological therapies also are effective and are not associated with these types of toxicities, but all are administered by injection. We believe the major unmet need for patients with moderate-to-severe psoriasis is for treatments that are active upon oral administration and that are not associated with significant organ toxicities.

Vertex ICE Inhibitors for Inflammatory and Autoimmune Diseases

We currently are developing our second generation ICE inhibitor, VX-765, in psoriasis. We also have collaborated with Sanofi-Aventis (successor to Aventis S.A.) in the development of our first generation ICE inhibitor, pralnacasan, which is chemically distinct from VX-765. Sanofi-Aventis has notified us that it intends to terminate our agreement to collaborate on the development of pralnacasan. Upon the effectiveness of that termination, we will hold worldwide rights to both VX-765 and pralnacasan. Depending upon outcomes from clinical and nonclinical studies currently underway for VX-765 and pralnacasan, respectively, we expect to move forward with development efforts relating to VX-765 or pralnacasan in the second half of 2005.

- ***VX-765***

VX-765 was selected for clinical development from our second generation ICE inhibitor research program. In late 2004, we initiated a four week Phase IIa safety and pharmacokinetic study of VX-765 in psoriasis. The results of this study, anticipated in the second half of 2005, could provide the basis for larger and longer term efficacy-based studies of VX-765 in psoriasis and potentially other autoimmune diseases.

In 2003, we completed Phase I clinical studies of VX-765 in healthy volunteers. Those studies demonstrated a dose-dependent decrease in levels of IL-18, the first time this has been demonstrated for any therapeutic agent. Preclinical data show that VX-765 reduces inflammation and cytokine levels in animal dermatitis and arthritis models.

- ***Pralnacasan***

Pralnacasan has been studied in both rheumatoid arthritis (RA) and osteoarthritis (OA), as well as in ongoing nonclinical toxicology studies. In 2003, Aventis (now Sanofi-Aventis) and Vertex voluntarily suspended the clinical development of pralnacasan pending full analysis of findings that had 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 are ongoing and will be completed in 2005. We believe that the results of these studies will assist us in determining a path forward with respect to our ICE inhibitor compounds. If the toxicology findings cannot be satisfactorily resolved, we may discontinue development of pralnacasan.

In 2002, Aventis completed a 284 patient Phase IIa study of pralnacasan in RA to evaluate clinical activity using standard measures of response to treatment, including the American College of Rheumatology (ACR) response criteria, which measure improvement in patient-reported and physician-assessed disease severity and activity. Data from the Phase IIa clinical trial demonstrated that treatment with pralnacasan was well tolerated and led to positive anti-inflammatory effects in patients with RA. Aventis previously had completed a Phase IIa 28-day clinical trial of pralnacasan in patients with RA to evaluate the safety and pharmacokinetics of multiple doses of pralnacasan. Results showed dose-dependent suppression of the production of interleukin-1b, a cytokine that plays a role in inflammation and tissue damage.

In 2003, Aventis completed a Phase II study of pralnacasan in OA. The purpose of this study was to enable Vertex and Aventis to evaluate the safety and efficacy of pralnacasan in OA patients. More than 500 patients were enrolled in the OA study, and each patient received one of three doses of pralnacasan or placebo for 12 weeks. Pralnacasan was well-tolerated across all three dosage groups. There was improvement (29 to 35%) in the primary endpoint, total WOMAC scores, for all four treatment groups during the 12 weeks of study. The WOMAC is the "Western Ontario and McMasters Universities" scale for measuring signs and symptoms in OA studies. There were no statistically significant differences in the change in total WOMAC score 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. Interpretation of these results in the context of modifying OA disease progression requires additional scientific understanding, which will require further clinical validation.

Background: p38 MAP Kinase Inhibitors for Inflammatory Diseases

The mitogen-activated protein (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 IL-1b, tumor necrosis factor-alpha (TNF-alpha), and interleukin-6 (IL-6). Excess levels of IL-1b 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 have the potential to be a powerful and broadly useful new class of oral anti-inflammatory drugs. The initial objective of our p38 MAP kinase program was to identify and evaluate compounds for the treatment of inflammatory diseases, such as rheumatoid arthritis, asthma, Crohn's disease, certain hematologic disorders, congestive heart failure and neurological diseases such as stroke. More recently, the central role of inflammation in many cardiovascular diseases has become well established. Inflammation increasingly is recognized as a key component of the overall process in the development of coronary artery disease and particularly, acute coronary syndromes (ACS). ACS is a broad term that includes unstable angina and certain types of myocardial infarctions.

- ***VX-702***

Study results from clinical and other trials of our p38 MAP kinase inhibitor, VX-702, indicate that VX-702 has the potential to be a very potent therapy in a variety of inflammatory disorders. We are currently planning to initiate a three-month Phase II study of VX-702 in 200 or more patients with rheumatoid arthritis (RA), to assess the safety and pharmacokinetics of VX-702 when dosed as a monotherapy in RA patients. The study also will be designed to evaluate clinical activity as measured by ACR20 and ACR50 responses and to provide us with important information about the general safety of administering VX-702 in a chronic indication such as RA.

Studies 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 the compound on liver enzymes. This study showed some transient elevations in liver enzymes in a small number of patients. However, the magnitude of those enzyme elevations did not reach clinical significance and did not require treatment discontinuation. The enzyme levels returned to normal during continued treatment. Using data from this study and other trials of VX-702, we have identified a dosing level for VX-702 that we expect will be both well-tolerated and therapeutically active in treatment of a chronic indication such as RA.

In 2004, we completed a Phase IIa double-blind, randomized, placebo-controlled, dose-escalation clinical trial of VX-702 in the treatment of patients with acute coronary syndromes (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. As a potential once-daily therapy for ACS addressing a novel target, a potent p38 MAP kinase inhibitor could provide an approach to complement current therapies for this disease, which affects nearly 1.9 million individuals in the United States each year.

The Phase IIa study of VX-702 was designed to evaluate the safety, tolerability and pharmacokinetics of VX-702 in 45 unstable angina patients with elevated CRP levels undergoing PCI. Preliminary results indicated that 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. The study also included an evaluation of the drug's anti-inflammatory activity, as measured by c-reactive protein (CRP) levels, a marker of inflammation measured in the blood. VX-702 significantly reduced serum levels of CRP in patients undergoing PCI. Assessment of the laboratory data indicated a potent and sustained anti-inflammatory effect as measured by CRP levels at multiple time points in the trial. For example, at 48 hours post-procedure, median CRP levels had decreased from baseline in a highly statistically significant, dose-dependent manner in all VX-702 treatment groups. CRP remained significantly lowered out to four weeks beyond the five-day dosing period. By contrast, in patients in the placebo group at 48 hours post-procedure, CRP had increased from baseline. Patients in this trial also underwent Holter (continuous ECG) monitoring for 72 hours to evaluate effects of VX-702 on silent ischemia. Asymptomatic ventricular ectopy (VE) (ventricular extra beats), which was observed in all treatment groups, was recorded during this monitoring at a higher incidence in the higher dose VX-702 treatment groups. In addition, during routine (non-continuous) ECG monitoring, 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. In view of the limited number of patients in the ACS trial, the high underlying variability in both VE and QT intervals, evaluation while undergoing an acute cardiac intervention, and variable past cardiac histories, the significance of both findings is at present unclear. In planning for any clinical RA study, we would expect to include further Holter monitoring and multiple routine ECG determinations, to allow assessments of VE and QT intervals in a more stable clinical setting.

We conducted a Phase I clinical study of VX-702 in June 2002. This double-blind, placebo-controlled, randomized clinical trial was designed to test the safety, tolerability, pharmacokinetics and pharmacodynamics of VX-702 in single and multiple doses in healthy volunteers. Results from this Phase I study supported further clinical development of VX-702. Another compound discovered by Vertex, VX-850, is in preclinical development and serves as a backup to VX-702.

Oncology

Vertex is developing three drug candidates targeting cancer, each by a different mechanism, in collaboration with three different pharmaceutical companies. The most advanced is VX-680, which targets the Aurora kinases and Flt-3 kinase, in Phase I clinical trials with Merck & Co., Inc. In collaboration with Novartis Pharma AG, we have advanced a dual inhibitor of the Flt-3 and c-kit kinases, VX-322, into pre-clinical development for the treatment of certain leukemias as well as other hematological malignancies and solid tumors. We also have an IMPDH inhibitor, VX-944, in development by our collaborator Avalon Pharmaceuticals, Inc. for the treatment of both hematological and solid tumor cancers.

- ***VX-680***

We are collaborating with Merck & Co., Inc. in the clinical development of VX-680. VX-680 is a potent inhibitor of Aurora kinases and of Flt-3 kinase. 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. Flt-3 is a receptor tyrosine kinase that is known to be inappropriately activated in several different types of leukemia. Inhibitors of Aurora kinases and Flt-3 kinase have the potential to be useful as highly targeted treatments for a range of oncology indications.

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 that indicate the potential of VX-680 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) inhibits tumor growth and induces 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.

VX-680 currently is in Phase I clinical development by Merck. The first Phase I clinical study, initiated early in 2005, is an open-label, dose-escalation study in patients with solid tumor cancers. This study is designed to evaluate the safety and tolerability of VX-680 when administered in multiple cycles to patients with solid tumors refractory to prior chemotherapy treatment. Merck and Vertex expect to initiate additional Phase I studies of VX-680 in 2005.

- ***VX-322***

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 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 as a 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). 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.

VX-322 was discovered in a joint effort by scientists in our San Diego and Cambridge research sites, taking advantage of expertise in protein biochemistry, structural biology, high throughput cell assays and medicinal chemistry. Our determination of the crystal structure of Flt-3 kinase in 2004 was a key scientific advance. It provided insight into the mechanism by which mutated forms of the Flt-3 receptor on a cell membrane can activate themselves, triggering uncontrolled proliferation of immature blood cells characteristic in several types of leukemia. 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%-80% of AML patients. Preclinical studies conducted at Vertex using cells isolated from AML patients suggested that dual Flt-3/c-kit inhibition provides more potent reduction in cell proliferation than is provided by inhibition of Flt-3 kinase or c-kit kinase alone.

- ***VX-944***

We are collaborating with Avalon Pharmaceuticals, Inc. in the clinical development and potential commercialization of VX-944, an oral IMPDH inhibitor, for the treatment of cancer. Recent reports in medical literature and presentations at scientific conferences provide a clinical rationale for the development of IMPDH inhibitors generally, and VX-944 specifically, 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 was shown to significantly prolong survival in a model of aggressive mouse leukemia. A single-dose, dose-escalation Phase I clinical study of VX-944 in healthy volunteers demonstrated that VX-944 was orally bioavailable and well-tolerated. We expect that Avalon Pharmaceuticals, Inc. will initiate a clinical study of VX-944 in a hematologic cancer indication in the second half of 2005.

Pain

The first compound to be selected for development from our ion channels research program is VX-409, a selective voltage-gated sodium channel (Na_V) inhibitor for the treatment of pain. Specific sodium channels in peripheral nerve cells are involved in transmitting pain signals to the central nervous system, making them novel and attractive targets for the treatment of pain. For example, a majority of patients suffering from neuropathic pain do not obtain adequate relief from any of the four classes of drugs currently approved in the United States for treatment of that indication. In addition to limited efficacy, many agents also have dose-limiting side effects. A highly selective Na_V inhibitory compound such as VX-409 may have the potential to be more efficacious with fewer side effects than currently available non-selective sodium channel inhibitors. Vertex holds worldwide development and commercial rights to VX-409. We are evaluating the possibility of entering into a collaborative relationship to advance development of VX-409.

Bacterial Infection

We are engaged in the discovery of novel antibiotics that target DNA gyrase B and topoisomerase IV, essential enzymes found in many bacteria. DNA gyrase and topoisomerase IV are utilized during the bacterial 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 infections in various treatment settings. Existing gyrase inhibitors work by interacting with the gyrase A subunit. In contrast, Vertex researchers have targeted the gyrase B subunit, and specifically the ATP-binding site that is common to multiple species of bacteria. We have discovered a class of molecules that also shows activity against the highly similar subunit of topoisomerase IV (GyrB/GrIB). These dual gyrase/topoisomerase IV inhibitors not only appear to be potent in preclinical testing, but may also be less susceptible than agents targeting only one of the enzymes to the development of drug resistance, a major and growing problem with marketed antibiotics.

In 2004, Vertex advanced VX-692, a novel inhibitor of the ATPase of both gyrase and topoisomerase IV, to preclinical development for the treatment of bacterial infection. VX-692 is active against both Gram-positive and select Gram-negative pathogens prevalent in both community and hospital settings. We hold worldwide development and commercial rights to VX-692. We are evaluating the possibility of entering into a collaborative relationship to advance development of VX-692.

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 in genomic research. We believe that our approach has been validated through our collaborations and 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. Vertex has pioneered a novel approach to drug discovery in target-rich gene families. Our approach organizes and prioritizes targets within gene families, which are groups of genes with similar sequences that code for structurally similar proteins. This approach essentially clusters targets according to how they interact with chemical inhibitors, and 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. In concert 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

Our integrated technology platform employs a variety of technologies and uses information from a number of different scientific disciplines. 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.

Pharmacology. We employ a number of approaches to obtain predictive information on the bioavailability and pharmacokinetic profile 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 assay development and screening techniques, built upon a number of gene reporter technologies such as green fluorescent protein (GFP) and beta lactamase, to rapidly generate large numbers of lead compounds and drug candidates across certain gene families. We also are utilizing our assay development capabilities to develop novel proprietary assays to 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 approaches integrate compound management, plate replication with miniaturized screening, hit (potential lead) identification and follow-up.

Instrumentation. 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. We can use E-VIPR to study both fast and slow channel activity and state dependence, a phenomenon in which compounds bind preferentially to certain conformations of channels. With respect to voltage-gated channels, electrical stimulation eliminates the need for the addition of liquids and pharmacological modifiers that often distort the native conformation and activity of ion channels.

Current Research Programs

Our past drug discovery efforts have produced a variety of drug candidates for development by Vertex or its collaborators. 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.

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 most major diseases, including cancer and autoimmune, inflammatory, cardiovascular, metabolic, and neurological diseases. As a result, kinases can be ideal targets for therapeutic intervention. The clinical success of the oncology drugs Gleevec (Novartis) and Tarceva (OSI Pharmaceuticals) offer examples of how small molecule kinase inhibitors can be tailored to address specific diseases.

In May 2000 we 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. We expect the research effort under this agreement to continue through April 2006. The support provided by Novartis is enabling us to conduct extensive parallel drug design efforts within the kinase target family.

In 2004, Novartis selected VX-322, a novel dual Flt-3/c-kit kinase inhibitor, for preclinical development. Over the remaining period of the Novartis collaboration, we expect to advance additional kinase inhibitors as development candidates targeting multiple therapeutic areas.

Also in 2004, we entered into a collaboration agreement with Merck and Co., Inc. 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 this joint research effort to continue until June 2006.

Vertex has drug discovery efforts underway targeting several other kinases, including those that play a role in the development and progression of cancer, inflammation and autoimmune disease.

The prosecution of drug discovery over numerous targets in the kinase gene family continues to refine our understanding of kinase biology and the design of kinase inhibitors. Our researchers have determined the atomic structure of more than 20 kinase drug targets and hundreds of kinase/inhibitor co-complexes. This information continues to be of critical importance in the design of selective inhibitors for ongoing research projects. Vertex has designed a diverse library of proprietary kinase inhibitors and we continue to expand our chemical library. Using this foundation, we expect to continue to optimize a number of chemical scaffolds against targets of interest in the area of kinase inhibition, which is a competitive area in the field of drug discovery.

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 target family contains numerous druggable targets representing potential therapeutic intervention points for indications including cystic fibrosis, pain and inflammatory, cardio-vascular, and metabolic diseases. Existing therapies such as amlodipine and nifedipine, which are calcium channel blockers for the treatment of hypertension, and lamotrigine and carbamezepine, 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 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. Ion channel modulators also could be important therapeutic agents for cystic fibrosis, a chronic, progressive genetic disorder. We have an ongoing research collaboration with Cystic Fibrosis Foundation Therapeutics Incorporated targeting the cystic fibrosis regulator protein (CFTR). The symptoms of cystic fibrosis, particularly the development of thick mucous that causes lung tissue inflammation and damage, are caused by a defect in CFTR. A CFTR channel modulator potentially may slow or halt the progression of cystic fibrosis.

We are utilizing our expertise in assay development and screening to advance discovery efforts within the ion channel family. Our capabilities are augmented by the use of E-VIPR, our proprietary ion channel screening technology. E-VIPR uses fluorescent probes and waves of electrical stimulation to study ion channels in an automated high-throughput platform, enabling the collection of high quality data at speeds up to a thousand times faster than patch-clamping.

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 exploratory efforts underway targeting g-protein coupled receptors (GPCRs) and nuclear receptors, among other things, as well as a program directed toward back-up hepatitis C protease inhibitors and gyrase inhibitors.

Corporate Collaborations

We have entered into corporate collaborations with pharmaceutical companies 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:

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. Originally, Novartis agreed to pay us up to $200 million in product 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 due if the candidate progresses in development. 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 marketing 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 below, 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, 2004 we had approximately $20 million in remaining loans outstanding under the loan facility.

GlaxoSmithKline plc

In December 1993, we entered into a collaboration with GlaxoSmithKline plc ("GlaxoSmithKline") covering the research, development and commercialization of HIV protease inhibitors, including Agenerase (amprenavir), Lexiva/Telzir (fosamprenavir calcium) and VX-385. Under the original agreement, GlaxoSmithKline had exclusive rights to develop and commercialize our HIV protease inhibitors 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 protease inhibitors 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 us 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. We have received the entire $42 million for the initial drug candidate, and additional milestones totalling $7.5 million for Lexiva/Telzir and VX-385. We began receiving royalties on sales of Agenerase in 1999 and on Lexiva/Telzir in 2003. GlaxoSmithKline is also obligated to pay us additional development and commercialization milestone payments for any subsequent drug candidates, including VX-385. 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 Agenerase and Lexiva/Telzir.

Merck & Co., Inc.

In June 2004, we entered into a global collaboration with Merck & Co., Inc. ("Merck") to develop and commercialize VX-680, our lead Aurora kinase inhibitor, for the treatment of cancer. The Merck collaboration agreement provides for an up-front payment of $20 million, which was paid in June 2004, and 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. Under the agreement, Merck is responsible for clinical development and commercialization of VX-680 worldwide and will pay us royalties on product sales. Merck may terminate the agreement at any time without cause after June 30, 2005 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 (beginning June 2005), or at any time when a product has marketing approval in a major market and the termination is not for a valid safety reason.

Mitsubishi Pharma Corp.

In June 2004, we entered into a license, development and commercialization agreement with Mitsubishi Pharma Corp. ("Mitsubishi") for the development and commercialization of VX-950, our 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. The agreement provides that Mitsubishi will make up to $33 million in pre-commercial payments to us, including an up-front license fee, development stage milestone payments and contributions to certain drug development costs incurred by us for VX-950 through Phase II clinical development. We will also be entitled to royalties on sales of VX-950 in Mitsubishi's territory. Further cost sharing, beyond Phase II clinical development, will be determined by Mitsubishi and us based on the design of registration studies for VX-950. Mitsubishi may terminate the agreement at any time without cause upon 60 days' prior written notice.

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 through December 31, 2005. Under this agreement, we will retain the right to develop and commercialize any compounds discovered in the course of the research collaboration. The agreement provides that CFFT will make up to $21 million of research payments through December 31, 2005 and, potentially, a milestone payment 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, 2005, upon 60 days' prior written notice.

Other Collaborations

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 exclusive worldwide right and sole responsibility to develop and commercialize VX-944 for the treatment of cancer. The agreement provides that Avalon will make up to $73 million in up-front license fees and milestone payments to Vertex 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.

Sanofi-Aventis. In September 1999, we entered into an expanded agreement with Aventis S.A., formerly Hoechst Marion Roussel Deutschland GmbH (HMR) and now Sanofi-Aventis, covering the development of pralnacasan. Sanofi-Aventis has notified us that it intends to terminate that agreement. We expect that the in-life portion of certain nonclinical studies now being conducted by Sanofi-Aventis, relating to certain animal toxicology findings by Aventis in 2003, will be completed on or before the termination date. Upon termination of the collaboration agreement, all rights to pralnacasan will revert to us.

Schering AG. In August 1998, we entered into a collaboration with Schering AG ("Schering") covering the research, development and commercialization of novel, orally-active neurophilin ligand compounds to promote nerve regeneration for the treatment of a number of neurological diseases. Research funding under this agreement has concluded. At Schering's request, we have agreed to extend until September 2005 Schering's option to designate a compound or compounds for development under the agreement. In North America, we will have manufacturing rights to, and we will share equally with Schering in the marketing expenses and profits from, any compounds which may be selected for development and commercialization. Schering will have the right to manufacture and market any commercialized compounds in Europe, the Middle East and Africa, and will pay us a royalty on any product sales.

Kissei Pharmaceutical Co., Ltd. Kissei Pharmaceuticals Co., Ltd. ("Kissei") launched amprenavir (Agenerase), our HIV protease inhibitor, in Japan under the name Prozei® in 1999. Kissei pays us a royalty on all sales of Prozei. In September 1997, we entered into a collaboration 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, a novel, orally-active p38 MAP kinase inhibitor, discovered during our p38 MAP kinase research program, for the treatment of rheumatoid arthritis and other inflammatory diseases. Kissei has exclusive rights to develop and commercialize VX-702 in Japan and certain Far East countries, and co-exclusive rights (with Vertex) in China, Taiwan and South Korea. We retain exclusive marketing rights outside the Far East. Kissei is providing a portion of the funding for our planned clinical trials of VX-702 in rheumatoid arthritis. We will have the right to supply bulk drug material to Kissei for any resulting drug product, for sale in its territory, and will receive royalties and drug supply payments on any product sales.

Eli Lilly and Company. In June 1997, we entered into a collaboration with Eli Lilly and Company ("Eli Lilly") covering the development of novel small molecule compounds to treat HCV infection, including VX-950. In December 2001, together with Eli Lilly, we selected VX-950 for development. In December 2002, we restructured our agreement with Eli Lilly, ending the research collaboration approximately six months early and providing us with worldwide rights to compounds identified during the collaboration. We will owe Eli Lilly a royalty on any future sales of VX-950 and certain other HCV protease inhibitors.

Serono S.A. In December 2000, we entered into a collaboration with Serono S.A. ("Serono") to discover, develop, and market certain types of caspase inhibitors. In May 2004, Serono terminated that agreement in accordance with its terms, effective September 30, 2004. We will hold worldwide rights to all intellectual property generated by us in the course of our collaboration with Serono, other than rights to any compounds that Serono selects on or before April 15, 2005, for development.

OTHER MATTERS

Intellectual Property

We actively seek, when appropriate, protection for our products and proprietary information by means of United States and foreign patents, trademarks, and copyrights. In addition, we rely upon trade secrets 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. These include patent applications claiming our e-VIPR platform that enables optical membrane potential assays for detecting activity of rapidly-gating ion channels, and methods of using our e-VIPR platform for high-throughput screening of voltage-gated ion channels.

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.

Patents and Pending Patent Applications

We have 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 most advanced research, development, and commercial programs. These include:

- issued United States patents that cover classes of chemical compounds, pharmaceutical formulations and/or uses of the same for treating HIV infection and AIDS. The 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 Searle patent applications claiming HIV protease inhibitors. 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 VX-385.

- 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 and VX-944, their combination with certain other therapeutic agents and their use thereof for treating HCV infection and other IMPDH-mediated diseases.

- issued United States patents covering pralnacasan, the active metabolite of pralnacasan, and 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 and related compounds.

- an issued United States patent that covers a class of chemical compounds that includes VX-702 as well as compositions comprising this and similar compounds and the use of those compounds to treat p38 MAP kinase related disorders.

- issued United States patents and pending applications covering assays useful to evaluate potential inhibitors of hepatitis C protease and covering the X-ray crystal structures of hepatitis C protease and hepatitis C helicase, including the use of those structures to develop hepatitis C protease inhibitors and hepatitis C helicase inhibitors, respectively. Other United States and worldwide pending applications cover VX-950, additional hepatitis C protease inhibitors and hepatitis C helicase inhibitors.

- 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 and the Flt-3/c-kit kinase inhibitor VX-322.

- 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 and the use of these compounds for the treatment of bacterial infections including the compound VX-692.

Manufacturing

We rely on third party manufacturers and collaborators to produce our compounds for clinical purposes and may do so for commercial production of any drug candidates that are approved for marketing. Commercial manufacturing of Lexiva/Telzir and Agenerase is being done by GlaxoSmithKline. We retain the option to manufacture a portion of GlaxoSmithKline's requirements for bulk drug substance for Lexiva/Telzir and Agenerase. 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.

We have established a quality assurance program intended to ensure that third party manufacturers under contract produce our compounds in accordance with the FDA's current Good Manufacturing Practices, or cGMP, and other applicable regulations.

We believe that all of our clinical drug candidates can be produced using established manufacturing methods, primarily through standard techniques of pharmaceutical synthesis. We believe that we will be able to continue to negotiate third party manufacturing arrangements on commercially reasonable terms and that it will not be necessary for us to develop an internal manufacturing capability in order to successfully commercialize our products. Our objective is to maintain flexibility in deciding if we should develop internal manufacturing capabilities for certain of our potential products. However, if we are unable to obtain contract manufacturing, or unable to obtain such manufacturing on commercially reasonable terms, we may not be able to commercialize our products as planned. We have limited experience in manufacturing pharmaceutical or other products or in conducting manufacturing testing programs required to obtain FDA and other regulatory approvals, and there can be no assurance that we will further develop those capabilities successfully.

Since most of our potential products are at an early stage of development, we will need to improve or modify our existing manufacturing processes and capabilities to produce commercial quantities of any drug product economically. We cannot quantify the time or expense that may ultimately be

required to improve or modify our existing process technologies, but it is possible that such time or expense could be substantial.

The production of our drug candidates is based in part on technology that we believe to be proprietary. We may license this technology to contract manufacturers to enable them to manufacture drug candidates for us. In addition, 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.

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. In order for us to compete successfully, we must demonstrate improved safety, efficacy, ease of manufacturing and market acceptance of our products over those of our competitors who have received regulatory approval and currently are marketing their drugs. For example, in the field of HIV protease inhibition, Abbott Laboratories, Bristol-Myers Squibb Company, Roche, Merck & Co., Inc., and Pfizer Inc., among others, have other HIV protease inhibitor drugs in development or on the market. Similarly, a variety of companies are attempting to develop new treatments for HCV infection. Many of our competitors have substantially greater financial, technical and human resources than ours and are more experienced in the development of new drugs.

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 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, preclinical studies typically are conducted in animals to identify potential safety problems. For certain diseases, animal models exist that are believed to be predictive of human efficacy. For such diseases, a drug candidate is tested in an animal model. The results of the studies are submitted to the FDA as a part of the Investigational New Drug application (IND) which is filed to comply with FDA regulations prior to commencement of human clinical testing in the United States. For diseases for which no appropriately predictive animal model exists, no such results can be filed. For several of our drug candidates, no appropriately predictive 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 trials 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. In Phase I, which frequently begins with the initial introduction of the drug candidate into healthy human subjects prior to introduction into patients, the drug candidate is tested 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 and duration 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 study, the parameters to be used to monitor safety and the efficacy criteria to be evaluated. In the United States, each protocol must be submitted to the FDA as part of the IND. Further, each clinical study must be evaluated by an independent Institutional Review Board at the institution at which the study will be conducted. The Institutional Review Board 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 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.

Timing to Approval

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 under approved labeling	6 months to 2 years

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

Post-approval Studies

Even after initial FDA approval has been obtained, further studies, including post-approval studies, may be required to provide additional data on safety and will be required to gain approval for the use of a product as a treatment for clinical indications other than those for which the product initially was tested. 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 further marketing of the drug product. Further, if there are any modifications to the drug, including changes in indication, manufacturing process, labeling or manufacturing facilities, an NDA supplement 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 New Drug Application, 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, 2004, we had 736 employees (approximately 727 full time, 9 part time), including approximately 487 in research and development and 249 in general and administrative functions. Approximately 81 of these employees were located at our U.K. research and development facility, 147 were located at our facility in San Diego and approximately 500 were based at our Cambridge, Massachusetts headquarters. Our scientific staff members (264 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.	53	Chairman and Chief Executive Officer
Vicki L. Sato, Ph.D.	56	President
Victor A. Hartmann, M.D.	55	Executive Vice President, Strategic and Corporate Development
John J. Alam, M.D.	43	Senior Vice President of Drug Evaluation and Approval
Kenneth S. Boger	58	Senior Vice President and General Counsel
N. Anthony Coles, M.D.	44	Senior Vice President, Commercial Operations
Peter Mueller, Ph.D.	48	Chief Scientific Officer and Senior Vice President, Drug Discovery and Innovation
Ian F. Smith, CPA, ACA	39	Senior Vice President and Chief Financial Officer
Lynne H. Brum	41	Vice President, Corporate Communications and Financial Planning
Eric K. Brandt	42	Director
Roger W. Brimblecombe, Ph.D., D.Sc.	75	Director
Stuart J.M. Collinson, Ph.D.	45	Director
Matthew W. Emmens	53	Director
Bruce I. Sachs	45	Director
Charles A. Sanders, M.D.	73	Director
Eve E. Slater, M.D., F.A.C.C.	59	Director
Elaine S. Ullian	57	Director

All executive officers are elected by the Board of Directors to serve in their respective capacities until their successors are elected and qualified or until their earlier resignation or removal. Pursuant to a Severance Agreement and Release between the Company and Dr. Vicki Sato, Dr. Sato's employment as the Company's President will terminate effective on May 11, 2005. Dr. Joshua Boger will assume Dr. Sato's title of President of the Company.

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 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. Sato joined Vertex in September 1992 as Vice President of Research and Chief Scientific Officer. She was appointed Senior Vice President of Research and Development in September 1994 and became President of Vertex in December 2000. She served as Chair of the Scientific Advisory Board from 1992 until December 2000. Previously, she was Vice President, Research and a member of the Scientific Board of Biogen, Inc. As research head at Biogen, she directed research programs in the fields of inflammation, immunology, AIDS therapy and cardiovascular therapy from early research into advanced product development. Dr. Sato received an A.B. in biology from Radcliffe College and an A.M. and a Ph.D. in biology from Harvard University. Following postdoctoral work in chemistry and immunology at the University of California at Berkeley and Stanford Medical School, she was appointed to the faculty of Harvard University in the Department of Biology.

Dr. Hartmann joined Vertex in February 2005 as Executive Vice President, Strategic and Corporate Development. From 2000 through 2005, Dr. Hartmann served as the Senior Vice President, Global Business Development and Licensing for Novartis Pharma AG. Prior to that, he served as Vice President, Head of Scientific and Business Evaluation of Novartis from 1999 to 2000. Dr. Hartmann

received his medical degree from the University of Bonn, Germany, and a bachelor's degree from Macalester College.

Dr. Alam served as Vice President of Clinical Development of the Company from October 1997 until January 2001, when he was appointed Senior Vice President of Drug Evaluation and Approval. Dr. Alam came to Vertex from Biogen, Inc., where he held a variety of positions from 1991 to 1997, 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 had 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.

Mr. Kenneth Boger joined Vertex as Senior Vice President and General Counsel in September 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 the 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 and Chief Executive Officer.

Dr. Coles joined Vertex as Senior Vice President, Commercial Operations-Pharmaceutical Products in March 2002. He came to Vertex from Bristol-Myers Squibb, where he served in a variety of positions beginning in 1996, including Senior Vice President of Strategy and Policy, Senior Vice President, Marketing and Medical Affairs for the Neuroscience, Infectious Disease, and Dermatology Division, Vice President, West Area Sales—Cardiovascular and Metabolic Business Unit for U.S. Primary Care, and Vice President, Cardiovascular Global Marketing. Prior to joining BMS, Dr. Coles was Vice-President of the Hypertension and Heart Failure Business Group at Merck. Dr. Coles holds an M.D. from Duke University, a Masters Degree in Public Health from Harvard University and a B.S. from Johns Hopkins University.

Dr. Mueller joined Vertex as Chief Scientific Officer and Senior Vice President, Drug Discovery and Innovation in July 2003. Dr. Mueller came to Vertex from Boehringer Ingelheim Pharmaceuticals, Inc., where he had served since 1997 as Senior Vice President, Research and Development, 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, inflammation, 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 joined Vertex as Vice President and Chief Financial Officer in October 2001, and was promoted to Senior Vice President and Chief Financial Officer in November 2003. Mr. Smith came to Vertex from Ernst & Young, LLP, an accounting firm, where he had served as a partner in its Life Science and Technology Practice since 1999. He had various responsibilities in E&Y's accounting, auditing and mergers and acquisitions groups. Mr. Smith initially joined E&Y's U.K. firm in 1987, and then joined its Boston office in 1995. 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.

Ms. Brum joined Vertex as Director, Corporate Communications in 1994 and was Vice President of Corporate Communications of the Company from 1998 until January 2001, when she was appointed Vice President of Corporate Communications and Market Development. In December 2001, she was appointed Vice President, Corporate Development and Communications, and in November 2003 she was appointed Vice President, Corporate Communications and Financial Planning. 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.

Mr. Brandt joined us as a member of the Board of Directors in May 2003. He has been the Executive Vice President, Finance, Strategy and Business Development, and Chief Financial Officer of Allergan Inc. since 2003, and was Corporate Vice President and Chief Financial Officer of Allergan from May 1999 until 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 holds a B.S. in chemical engineering from the Massachusetts Institute of Technology, and an M.B.A. from Harvard University. He currently serves as a director of Dentsply International Inc.

Dr. Brimblecombe has served as our director 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 (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 joined us as a member of the Board of Directors in 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. Before joining Aurora, Dr. Collinson served as a consultant to Aurora from December 1998 to May 1999 and as Chief Executive Officer of Andaris, Ltd., a privately held biopharmaceutical company, from June 1998 to November 1998. Prior to joining Andaris, Dr. Collinson held senior management positions with Glaxo Wellcome from December 1994 through 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.

Mr. Emmens was elected to the Vertex Board of Directors in July 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, the company's U.S. 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 served as our director since 1998. He currently serves as 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.

Dr. Sanders has served as our director since 1996. 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 currently a director of Biopure Corporation, Cephalon Corporation, Genentech, Inc., Icagen, Inc., Trimeris Inc., and Fisher Scientific International.

Dr. Slater was elected to the Vertex Board of Directors in May 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, U.S. Department of Health and Human Services 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., a Canadian company.

Ms. Ullian has served as our director 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.

SCIENTIFIC ADVISORY BOARD

Vertex's 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
Vicki L. Sato, Ph.D.	President, Vertex Pharmaceuticals Incorporated
Peter Mueller, Ph.D.	Chief Scientific Officer and Senior Vice President, Drug Discovery and Innovation, 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
Eugene H. Cordes, Ph.D.	Retired Professor of Medicinal Chemistry, 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, Dr. Mueller and Dr. Sato, 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 conflict or compete with their obligations to us. 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. Dr. Sato, will resign from the Scientific Advisory Board upon her resignation as the Company's President on May 11, 2005.

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 2005. We believe that operating losses will continue beyond 2005, 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 and developing our potential products. 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.

WE DO NOT KNOW WHETHER LEXIVA/TELZIR WILL CONTINUE TO BE COMPETITIVE IN THE MARKET FOR HIV PROTEASE INHIBITORS.

We currently receive royalties from sales of Lexiva/Telzir and Agenerase, two HIV protease inhibitors discovered in our collaboration with GlaxoSmithKline. Agenerase sales have decreased, which we attribute to the availability and acceptance of Lexiva/Telzir, and we anticipate that this trend will continue until Agenerase is largely replaced by Lexiva/Telzir in the market. Lexiva/Telzir's share of the worldwide protease inhibitor market may decrease due to competitive forces and market dynamics. Other HIV protease inhibitors and a number of other products, including Gilead Science's Viread®, Dupont's Sustiva® and GlaxoSmithKline's Ziagen®, 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 and Boehringer Ingelheim, which may have better efficacy, fewer side effects, easier administration and/or lower costs than Lexiva/Telzir. Moreover, the growth in the worldwide market for HIV protease inhibitors 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 protease inhibitors. In addition, the clinical benefit of strategies used by clinicians to boost drug levels of Lexiva/Telzir by co-administering other antiretroviral agents may not prove to be effective, or may not result in increased revenues. As a result, the total market for protease inhibitors may decline, decreasing the sales potential of Lexiva/Telzir. Further, although we co-promote Lexiva/Telzir in the U.S. 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 will 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 upon any such termination.

WE MAY NOT SUCCESSFULLY DEVELOP OUR DRUG PIPELINE.

All of the products that we are pursuing independently and with collaborators will require extensive additional development, testing and investment, as well as regulatory approvals, prior to commercialization. Our product research and development efforts may not be successful. Our drug candidates may not enter preclinical, nonclinical or clinical studies as or when anticipated and may not receive required regulatory approvals. Moreover, our products, if introduced, may not be commercially successful. The results of nonclinical and initial clinical trials of products under development by us are not necessarily predictive of results that will be obtained from large-scale clinical testing. Clinical trials of products under development may not demonstrate the safety and efficacy of the products being tested or result in a marketable product. Findings in nonclinical studies conducted concurrently with clinical studies could adversely effect the development of our products. In addition, the administration, alone or in combination with other drugs, of any product developed by us may produce undesirable side effects in humans.

The failure to demonstrate adequately the safety and efficacy of a therapeutic drug under development, for the disease indication being targeted, could delay or prevent regulatory approval of the product and could have a material adverse effect on us. In addition, the FDA or regulatory authorities in other jurisdictions may require additional clinical or nonclinical studies, which could result in increased costs and significant delays in obtaining required marketing approvals and commercialization of a product. 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.

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 is 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 constantly monitor the results of our discovery research and our nonclinical 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.

IF DELAYS IN PATIENT ENROLLMENT SLOW OUR DEVELOPMENT PROGRESS, WE MAY LOSE COMPETITIVE ADVANTAGE OR BE UNABLE TO BRING OUR DRUGS TO MARKET.

The rate of completion of clinical trials of our products is dependent upon, among other factors, the rate of patient accrual. Patient accrual is a function of many factors, including the size of the patient population, the proximity of patients to clinical sites, the eligibility criteria for the trial, the level of compliance by the clinical sites to clinical trial protocols, and the availability of clinical trial material. Delays in patient enrollment in clinical trials may result in increased costs, program delays, or both, which could have a material adverse effect on us. 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 that are not licensed to a collaborator. If our clinical trials are not completed, we may not be able to submit a new drug application. If we are able to file a new drug application, such application may not be reviewed and approved in a timely manner, if at all.

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 independently developing products 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 collaborations 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.

IF WE DO NOT OBTAIN REGULATORY APPROVAL FOR OUR PRODUCTS ON A TIMELY BASIS, OR AT ALL, OUR REVENUES WILL BE NEGATIVELY IMPACTED.

The United States FDA and comparable agencies in foreign countries impose substantial requirements on the introduction of therapeutic pharmaceutical products through lengthy and detailed laboratory and clinical testing procedures, sampling activities and other costly and time-consuming procedures. Satisfaction of these requirements typically can take many years and may vary substantially based upon the type, complexity and novelty of the pharmaceutical product. Data obtained from preclinical, nonclinical and clinical activities are susceptible to varying interpretations, which could delay, limit or prevent regulatory approval. In addition, delays or rejections may be encountered based on changes in, or additions to, regulatory policies for drug approval during the period of product development and regulatory review. The effect of government regulation may be to delay or prevent the commencement of planned clinical trials for our drug candidates in clinical development. These regulations may also cause us to engage in complex and costly procedures that could result in a competitive advantage to companies more experienced in regulatory affairs that compete with us. Moreover, even if approval is granted, such approval may entail limitations on the indicated uses for which a product may be marketed.

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 AND DEVELOPMENT 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 products. In exchange, we have given them technology, product and marketing rights relating to those products. Some of our corporate collaborators, including GlaxoSmithKline, Merck and Novartis, 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 GlaxoSmithKline, Merck or Novartis were to terminate its relationship with us, or fail to meet its contractual obligations, it 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, Merck and CFFT, all of which are scheduled to conclude in the period between December 2005 and June 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.

Even if we are able to establish acceptable collaborative arrangements in the future, they may not be successful.

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.

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 have received regulatory approval and currently are marketed. Many of our competitors, including major pharmaceutical companies such as Abbott Laboratories, GlaxoSmithKline, Merck, and Novartis, 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.

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 products are highly technical in nature, we require the services of highly qualified and trained scientists who have the skills necessary to develop our products. 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 the Company. 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 movement 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, in particular the Novartis, Merck and CFFT collaborations, 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 WE FAIL TO 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.

WE DEPEND ON THIRD PARTY MANUFACTURERS, AND IF WE ARE UNABLE TO OBTAIN CONTRACT MANUFACTURING ON REASONABLE TERMS, WE MAY NOT BE ABLE TO DEVELOP OR COMMERCIALIZE OUR PRODUCTS.

Our ability to conduct clinical trials and our ability to commercialize our potential products will depend, in part, on our ability to manufacture our products on a large scale, either directly or through third parties, at a competitive cost and in accordance with regulatory requirements. We have no experience in manufacturing pharmaceuticals or other products, and we may not be able to develop such capabilities in the foreseeable future. In addition, some of our current corporate collaborators have manufacturing rights with respect to our products under development. We are, therefore, dependent on third party manufacturers and our collaborators for the production of our drug candidates for preclinical and nonclinical research, clinical trial purposes and commercial production. Accordingly, if we are not able to obtain contract manufacturing from these third parties on commercially reasonable terms, we may not be able to conduct or complete clinical trials or commercialize our products as planned. Further, commercial formulation and manufacturing processes have yet to be developed for our drug candidates other than Agenerase and Lexiva/Telzir. As a result, we or our collaborators may encounter difficulties developing commercial formulations and manufacturing processes for our drug candidates, which could result in delays in clinical trials, regulatory submissions, regulatory approvals and commercialization of our products.

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 competing 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, even in those instances in which 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 consolidated financial position.

IF WE ARE NOT ABLE TO SUBLET OUR KENDALL SQUARE FACILITY ON ACCEPTABLE TERMS, OR AT ALL, WE COULD BE OBLIGATED TO PAY AS MUCH AS THE FULL AMOUNT DUE UNDER THE LEASE, AS AND WHEN DUE UNDER THE LEASE AGREEMENT.

We have decided not to occupy a facility located in Kendall Square, Cambridge, Massachusetts that we lease under a 15-year agreement expiring in 2018. We have estimated our net ongoing obligations under this lease to be $55,843,000 as of December 31, 2004. This estimate is based on underlying estimates of the timing for executing subleases of the remaining space, the sublease rental terms we might expect to receive, and other assumptions and estimates we consider appropriate given current market conditions and other factors. To date, we have subleased 45,000 square feet of the 290,000 square foot facility. If we are unable to find a tenant or tenants willing to sublease the balance of the facility on the terms we have incorporated into our estimate, including the rental rate, timing and term of any such sublease(s), or if the market for specialized laboratory space in Cambridge, Massachusetts or other real estate fundamentals should change before we are able to sublease the remaining unoccupied space, or if any of our other assumptions or estimates are inaccurate or circumstances bearing upon the potential restructuring should change before we are able to sublease the facility, our estimated obligations could increase to as much as the full amount due under the lease. Our future obligations under the lease could be as much as $312 million, as set forth in "Off-Balance Sheet Commitments and Obligations at December 31, 2004" below.

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 and undertake clinical trials of potential drugs resulting from such compounds. 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 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. 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.

OUR SALES AND MARKETING EXPERIENCE IS LIMITED.

We have little 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. If 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 Agenerase and Lexiva/Telzir to GlaxoSmithKline worldwide (except for amprenavir in Japan, where Kissei holds rights under the name Prozei), for VX-702 to Kissei in certain countries in the Far East and for VX-680 and VX-322 to Merck and Novartis, respectively, worldwide. 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. Even though we retain some co-promotion rights, 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.

IF WE INCUR PRODUCT LIABILITY EXPENSES, OUR EARNINGS COULD BE NEGATIVELY IMPACTED.

Our business will expose us to potential product liability risks that arise from the testing, manufacturing and sales of our products. In addition to direct expenditures for damages, settlement and defense costs, there is the possibility of adverse publicity as a result of product liability claims. These risks will increase as our products receive regulatory approval and are commercialized. We currently carry $15 million of product liability insurance. This level of insurance may not be sufficient and it may not cover, in any event, all of the risks to which we are exposed in the course of conducting or sponsoring clinical trials. Moreover, we may not be able to maintain our existing levels of insurance or be able to obtain or maintain additional insurance that we may need in the future on acceptable terms.

In addition, our research and development activities may from time to time involve the controlled use of hazardous materials, including hazardous chemicals and radioactive materials. Accordingly, we are subject to federal, state and local laws governing the use, handling and disposal of these materials. Although we believe that our safety procedures for handling and disposing of hazardous materials comply with regulatory requirements, we cannot completely eliminate the risk that accidental contamination or injury from these materials could expose us to significant liability.

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 the Company or its 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, 2004, our common stock traded between $8.00 and $12.20. 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 or nonclinical trials;
- 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, 2004, we had approximately $82.6 million in aggregate principal amount of 5% Convertible Subordinated Notes due in September 2007 and approximately $232.4 million in aggregate principal amount of 5.75% Convertible Senior Subordinated Notes due in February 2011 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 REVENUE DEPENDS, AND WILL LIKELY CONTINUE TO DEPEND, ON A LIMITED NUMBER OF PRODUCTS.

We derive a portion of our revenue from royalties earned from the sale of our two marketed products. Accordingly, any factor either adversely affecting product sales or adversely affecting our expected royalties from product sales could also have a material adverse effect on our business, financial condition and results of operations.

MARKET ACCEPTANCE OF OUR PRODUCTS WILL BE LIMITED IF USERS OF OUR PRODUCTS ARE UNABLE TO OBTAIN ADEQUATE REIMBURSEMENT FROM THIRD-PARTY PAYORS.

The commercial success of Lexiva/Telzir will depend in part on the availability of reimbursement from third-party payors, including government health administrators, managed care providers and private health insurers. Third-party payors are increasingly challenging the pricing of pharmaceutical products. Additionally, third-party payors may conclude that Lexiva/Telzir is less safe, less effective or less cost-effective than existing products. We cannot assure you that third-party payors will provide reimbursement for Lexiva/Telzir, in whole or in part. If third-party payors do not provide adequate reimbursement for Lexiva/Telzir, the sale of that product may not be profitable to GlaxoSmithKline, which may stop selling Lexiva/Telzir, thus terminating the royalties we receive on sales of these products.

THE RECENT MEDICARE PRESCRIPTION DRUG COVERAGE LEGISLATION AND FUTURE LEGISLATIVE OR REGULATORY REFORM OF THE HEALTHCARE SYSTEM MAY AFFECT OUR COLLABORATOR'S ABILITY TO SELL AGENERASE OR LEXIVA PROFITABLY.

In the United States, there have been a number of legislative and regulatory proposals to change the healthcare system in ways that could affect our collaborator's ability to market and sell Lexiva profitably. The Centers for Medicare and Medicaid Services, or CMS, the agency within the Department of Health and Human Services that administers Medicare and is responsible for reimbursement of the cost of drugs, has asserted the authority of Medicare to elect not to cover particular drugs if CMS determines that the drugs are not "reasonable and necessary" for Medicare beneficiaries, or to elect to cover a drug at a lower reimbursement rate similar to that of drugs that CMS considers to be "therapeutically comparable." Further federal and state proposals and healthcare reforms are likely and legislation and regulations affecting the pricing of pharmaceuticals may change in ways adverse to us. For example, the potential for importation of lower-priced drugs from foreign sources may limit or erode sales of Lexiva, negatively affecting the amount of royalties we receive.

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 any AWP cases where our collaborators or licensees are named as defendants, the outcome of the case could have an 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, 2004, we had approximately 80,765,000 shares of common stock issued and outstanding, together with outstanding options to purchase approximately 15,820,000 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 $22.67 per share, and notes convertible into approximately 16,454,000 shares of common stock with conversion prices of $14.94 and $92.26 per share and a weighted average conversion price of $19.15 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 2. PROPERTIES

We lease an aggregate of approximately 624,000 square feet of laboratory and office space in seven 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 up to two additional terms, ending in 2015 with respect to one portion of the building, and in 2019 for the other portion of the building. The lease for the laboratory and office building adjacent to our headquarters will expire in 2010 with the option to extend the lease for up to two additional consecutive ten-year terms.

The lease for our Kendall Square, Cambridge, Massachusetts facility will expire in 2018, with the option to extend the lease for two consecutive terms of ten years each. We have decided not to occupy the Kendall Square facility. We have subleased 45,000 square feet of the facility, and are actively seeking to sublease the remaining unoccupied space. See Management's Discussion and Analysis—Overview—Kendall Square Lease, for a discussion of our estimated ongoing obligations under this lease.

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, with an option to extend 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, under a lease expiring in 2013, with a right of early termination in 2008, for our United Kingdom business and research and development activities.

We believe our facilities are adequate for our current needs.

ITEM 3. LEGAL PROCEEDINGS

We are not a party to any material legal proceedings. On February 23, 2005, the United States District Court for the District of Massachusetts entered judgment in favor of Vertex pursuant to an order of the trial judge granting our motion to dismiss a purported class action lawsuit against the Company and certain of its officers and a former employee. In the lawsuit, the plaintiffs claimed that the defendants made material misrepresentations and/or omissions of material fact regarding VX-745, an investigational agent with potential in the treatment of inflammatory and neurological diseases, in violation of Sections 10(b) and 20(a) of the Securities Exchange Act and Rule 10(b)(5). The plaintiffs

sought certification as a class action, compensatory damages in an unspecified amount, and unspecified equitable or injunctive relief. The plaintiffs have the right to appeal the judgment by filing a notice of appeal on or before March 25, 2005.

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 fourth quarter of the fiscal year ended December 31, 2004.

PART II

ITEM 5. MARKET FOR REGISTRANT'S COMMON EQUITY, RELATED STOCKHOLDER MATTERS AND ISSUER PURCHASES OF EQUITY SECURITIES

Market Information

Our common stock trades on the NASDAQ Stock Market ("NASDAQ") under the symbol "VRTX." The following table sets forth for the periods indicated the high and low sale prices per share of the common stock as reported by NASDAQ:

Year Ended December 31, 2003:	High	Low
First quarter	$ 16.50	$ 9.59
Second quarter	18.75	9.94
Third quarter	16.77	11.73
Fourth quarter	14.19	7.83
Year Ended December 31, 2004:		
First quarter	$ 12.20	$ 8.82
Second quarter	10.00	8.00
Third quarter	11.19	8.06
Fourth quarter	12.05	9.79

Stockholders

As of March 14, 2005, there were 1,172 holders of record of our common stock (approximately 19,000 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 fourth quarter of 2004.

ITEM 6. SELECTED CONSOLIDATED FINANCIAL DATA

The following unaudited selected financial data for each of the five years in the period ended December 31, 2004 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,				
	2004	2003	2002	2001(1)	2000(2)
	(In thousands, except per share amounts)				
Consolidated Statement of Operations Data:					
Revenues:					
Royalties	$ 17,322	$ 9,002	$ 10,054	$ 10,783	$ 12,036
Collaborative and other research and development revenues	85,395	60,139	84,716	74,514	70,459
Total revenues	102,717	69,141	94,770	85,297	82,495
Costs and expenses:					
Royalty payments	5,649	3,126	3,334	3,594	3,965
Research and development	192,162	199,636	198,338	141,988	96,308
Sales, general and administrative	42,139	39,082	41,056	31,856	30,006
Restructuring and other expense	17,574	91,824	—	—	—
Merger related costs	—	—	—	22,960	—
Total costs and expenses	257,524	333,668	242,728	200,398	130,279
Loss from operations	(154,807)	(264,527)	(147,958)	(115,101)	(47,784)
Other income/(expense), net	(7,994)	(1,886)	11,000	24,532	20,239
Debt conversion expense	—	—	—	—	(14,375)
Gain (loss) on retirement of convertible subordinated notes	(3,446)	—	—	10,340	—
Loss from continuing operations before cumulative effect of changes in accounting principles	(166,247)	(266,413)	(136,958)	(80,229)	(41,920)
Income from discontinued operations(3):					
Gain on sales of assets	—	70,339	—	—	—
Income (loss) from discontinued operations	—	(693)	28,337	22,148	10,341
Total income from discontinued operations	—	69,646	28,337	22,148	10,341
Loss before cumulative effect of changes in accounting principles	$ (166,247)	$ (196,767)	$ (108,621)	$ (58,081)	$ (31,579)
Cumulative effect of change in accounting principle—revenue recognition	—	—	—	(25,901)	(3,161)
Cumulative effect of change in accounting principle—derivatives(4)	—	—	—	17,749	—
Net loss	$ (166,247)	$ (196,767)	$ (108,621)	$ (66,233)	$ (34,740)
Basic and diluted net loss per common share	$ (2.12)	$ (2.56)	$ (1.43)	$ (0.89)	$ (0.51)
Basic and diluted weighted average number of common shares outstanding	78,571	77,004	75,749	74,464	67,682
Pro forma amounts assuming the 2001 accounting change relating to revenue recognition is applied retroactively(1)					
Net loss	$ (166,247)	$ (196,767)	$ (108,621)	$ (40,332)	$ (45,860)
Net loss per weighted common share—basic and diluted	$ (2.12)	$ (2.56)	$ (1.43)	$ (0.54)	$ (0.68)

	December 31,				
	2004	2003	2002	2001	2000
Consolidated Balance Sheet Data:					
Cash, cash equivalents and marketable securities	$ 392,320	$ 583,164	$ 634,984	$ 743,202	$ 814,061
Other current assets	14,392	10,642	21,588	32,890	43,370
Restricted cash	49,847	26,061	26,091	26,190	14,713
Property and equipment, net	64,225	80,083	95,991	80,377	43,961
Other non-current assets	24,669	24,461	37,066	42,472	25,031
Total assets	$ 545,453	$ 724,411	$ 815,720	$ 925,131	$ 941,136
Deferred revenue, current portion	$ 47,741	$ 7,746	$ 11,888	$ 39,498	$ 28,329
Accrued restructuring and other expense	55,843	69,526	—	—	—
Other current liabilities	50,161	47,795	52,709	52,055	41,527
Collaborator development loan (due 2008)	19,997	32,460	5,000	—	—
Other long-term obligations	2,925	7,268	5,944	8,026	12,269
Deferred revenue, excluding current portion	18,345	51,771	46,598	35,201	—
Convertible notes (due 2007)(5)	82,552	315,000	315,000	315,000	345,000
Convertible notes (due 2011)(5)	232,448	—	—	—	—
Stockholder's equity	35,441	192,845	378,581	475,351	514,011
Total liabilities and stockholder's equity	$ 545,453	$ 724,411	$ 815,720	$ 925,131	$ 941,136

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 Biosciences Corporation 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 Biosciences Corporation, 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 SEC's Staff Accounting Bulletin No. 101, "Revenue Recognition in Financial Statements" ("SAB 101") in 2000 throughout the biotechnology industry.

(2) In the fourth quarter of 2000, we changed our method of accounting for revenue recognition in conjunction with our adoption of SAB 101, which was retroactive to January 1, 2000.

(3) 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.

(4) 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.

(5) During 2004 the Company 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 its outstanding 5% Convertible Subordinated Notes due in September 2007 ("2007 Notes"). The total issuance of $232.4 million in aggregate principal amount of 2011 Notes resulted from two separate transactions, a February 2004 issuance of approximately $153.1 million in aggregate principal amount of 2011 Notes, and a September 2004 issuance of $79.3 million in aggregate principal amount of 2011 Notes. At December 31, 2004, the Company had $232.4 million in aggregate principal amount of 2011 Notes and $82.6 million in aggregate principal amount of 2007 Notes outstanding.

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 serious diseases, including HIV infection, chronic hepatitis C virus (HCV) infection, inflammatory and autoimmune disorders, cancer, pain and bacterial infection. We earn a royalty on the sales of two Vertex-discovered products for the treatment of HIV infection, Lexiva/Telzir and Agenerase, and co-promote these products in collaboration with GlaxoSmithKline plc. Our drug candidate pipeline is principally focused at present on the development and commercialization of new treatments for viral diseases, inflammatory and autoimmune diseases and cancer. 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.

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 are also continually monitored 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, lack of sufficient efficacy against the disease target, difficulties in developing a cost-effective manufacturing or formulation method, or the discovery of toxicities 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 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.

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 focus our efforts both on programs that we expect to control throughout the development and commercialization process, and programs that we expect will be conducted principally by a collaborator. This 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, 2004 we had $392.3 million of cash, cash equivalents and marketable securities, $82.6 million in principal amount of 5% Convertible Subordinated Notes due 2007 (the "2007 Notes") and $232.4 million in principal amount of 5.75% Convertible Senior Subordinated Notes due 2011 (the "2011 Notes"). During 2004 and early 2005, we took a number of steps that we believe reinforced our ability to implement our business strategy, including closing two debt exchange transactions, modifying our kinase collaboration, and signing new discovery and development collaborations.

Debt Exchange. On February 13, 2004, we exchanged approximately $153.1 million in aggregate principal amount of newly issued 2011 Notes for approximately $153.1 million in aggregate principal amount of outstanding 2007 Notes. On September 17, 2004, we exchanged a further $79.3 million in principal amount of newly issued 2011 Notes for an equal amount of 2007 Notes. As a result of these transactions, we deferred from 2007 until 2011 the repayment date for almost 75% of our outstanding debt. We incurred certain charges relating to the early retirement of the 2007 Notes and incremental costs in connection with the exchange transactions, and we expect our annual interest charge to be slightly higher due to the higher interest rate on the 2011 Notes. Since the conversion price for the 2011 Notes is significantly lower than the conversion price for the 2007 Notes, we have enhanced the equity characteristics of our debt and consequently increased the likelihood that the noteholders will convert the 2011 Notes to common stock at some point in the future.

Kinase Collaborations. In February 2004, we amended our collaboration agreement with Novartis. Under the amended agreement, we will continue to receive research funding through April 2006, and up to $35 million in pre-commercial payments for each preclinical drug candidate that we propose, and Novartis accepts, for development. Under the original agreement, we were responsible for early development of each drug candidate through proof-of-concept (generally Phase Ib or IIa), funded through a development loan from Novartis. That loan would be forgiven if Novartis accepted the drug candidate for further development, but was repayable if Novartis elected not to develop that candidate. Under the amended agreement, 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 is due from Novartis, with up to $25 million in additional pre-commercial milestone payments due if the candidate progresses in development. 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. 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.

The Novartis amendment reduced our financial risk in connection with proof-of-concept development of kinase inhibitors, potentially accelerated the timing of payments associated with the selection of development candidates by Novartis, and strengthened the intellectual property position that we will have in the kinase field after the current research collaboration ends in April 2006. We believe these changes will improve our ability to generate further collaborations in the field of kinase inhibition in late 2006, which may be important for us because our Novartis collaboration accounted for approximately 49% of our total revenue in 2004.

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 collaboration. We exercised this election in June 2004, as part of our collaboration with Merck described below, and repaid to Novartis approximately $12.5 million in unspent and uncommitted development loans previously advanced on account of VX-680.

New Collaborations. We entered into four new collaborative relationships in 2004 and early 2005, covering programs in which we expect to retain control over development, and programs where we

expect our collaborator to control development. In May 2004 we expanded our collaboration with Cystic Fibrosis Foundation Therapeutics Incorporated ("CFFT") to provide for $21 million in research support payments in 2004 and 2005. In June 2004, we entered into a new collaboration with Mitsubishi Pharma Corp. ("Mitsubishi") granting Mitsubishi the right to develop and commercialize VX-950, our oral hepatitis C protease inhibitor, in Japan and certain Far East countries. Under that collaboration, Mitsubishi also will provide us with financial and other support for our development of VX-950, which is currently in Phase Ib clinical development. Also in June 2004, we entered into a global collaboration with Merck & Co., Inc. ("Merck") to develop and commercialize VX-680, our lead Aurora kinase inhibitor, for the treatment of cancer. The Merck agreement provides us with research funding in the amount of $14 million over two years, and an up-front payment of $20 million. In February 2005, we licensed VX-944, an IMPDH inhibitor, to Avalon Pharmaceuticals, Inc. ("Avalon"), for development and commercialization in the treatment of cancer. Avalon has committed to make up-front and milestone payments to us, conduct further development of VX-944 and pay royalties to us if VX-944 is successfully commercialized.

Balancing of Research and Development

During 2003 and 2004, we elected to focus our internal development and commercialization activity on two principal areas for the intermediate term: viral diseases and inflammatory and autoimmune diseases. Our most advanced drug candidates in these areas are merimepodib (HCV infection), VX-950 (HCV infection), VX-702 (rheumatoid arthritis) and VX-765 (psoriasis). In preparation for advancing these and other Vertex-controlled drug candidates, we restructured our operations in the second quarter of 2003 to rebalance our relative investment in research and development. Our investment in Company-sponsored research declined during 2003 approximately 22% from 2002 levels, while our investment in Company-sponsored development during 2003 increased over 2002 levels by approximately 57%. During 2004 we entered collaborations with Merck and CFFT that had significant research funding components, and we expect to enter into additional research-based collaborations in 2005. These collaborations provide revenue to partially offset our continuing research investment and better enable us to focus our research and development spending, net of collaborator-supported costs, on compounds and development candidates for which we retain significant commercial rights. We expect our Vertex-controlled development activities and related expense to increase significantly during 2005, depending on the progress of our current development candidates, both in absolute terms and in comparison with our investment in research, which should remain relatively constant over 2004 levels. To offset this spending increase we expect to enter new collaborations that will provide additional funding for our research and development efforts in areas where sharing development efforts and commercial returns is consistent with our overall business strategy.

Collaborative Revenue

Collaborations have been and will continue to be an important component of our business strategy. A significant portion of our total research effort is being conducted under our research collaborations with Novartis, Merck and CFFT, all of which are scheduled to conclude, along with our research funding, in the period between December 2005 and June 2006. Funding from our Novartis collaboration, the research portion of which is scheduled to conclude in April 2006, accounted for approximately 55% of our total collaborative research and development revenue in 2004. Our two-year research collaboration with Merck, for discovery of Aurora kinase inhibitors to serve as back-ups and/or follow-on candidates for VX-680, is scheduled to conclude in June 2006. In addition, our research collaboration with CFFT provides research funding ending on December 31, 2005. We believe that the intellectual property rights we may retain from some or all of these collaborations may help us initiate other collaborative opportunities if our existing collaborations are not extended. We will need to pursue those opportunities as well as other collaborations or financing alternatives in order to maintain our research effort at its existing level. It is not possible to predict at present whether any of those collaborations or other financing alternatives will be available in 2006 and beyond.

Based on the value that we believe we have built through research and development investments in certain of our drug discovery and development programs, and 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 2005 that would be material to our business. Our business development priorities include new collaborations to support development and commercialization of our HCV infection clinical candidates, and our oral cytokine inhibitors. Our product development pipeline also includes drug candidates such as VX-409 (pain) and VX-692 (bacterial infection) that we may choose to develop with a collaborator. In 2005 and future periods we expect to identify collaborative development and commercialization opportunities for some or all of these drug candidates in order to continue their clinical advancement, as we maintain focus on controlling clinical development of certain drug candidates in the United States. We may also seek collaborators for our ion channels and other research programs.

Kendall Square Lease

We currently lease approximately 290,000 square feet of office and laboratory space in Kendall Square, Cambridge, Massachusetts (the "Kendall Square Lease"), which we have decided not to occupy. We have subleased 45,000 square feet of that space and are seeking subtenants for the unoccupied portion. For the twelve months ended December 31, 2004, we recorded restructuring and other expense relating to the Kendall Square Lease of $17.6 million. Our estimate of the net ongoing obligation under the Kendall Square Lease at December 31, 2004 was approximately $55.8 million on a discounted net present-value basis, and relates to the remaining Kendall Square lease obligations net of estimated sublease revenue. This estimate represents our best judgment of the assumptions and estimates most appropriate in measuring the ongoing obligation. Our estimates in this regard have changed in the past, and may change in the future, resulting in additional adjustments to the estimate of liability. Also, 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. Please refer to Note D, "Restructuring and Other Expense," to the consolidated financial statements included in this Annual Report on Form 10-K, for a more complete discussion of the Kendall Square Lease liability.

Financial Guidance

The key financial measures for which we have provided guidance in 2005 are as follows:

- **Loss:** We expect that the Company's full year loss in 2005 will be in the range of $125 to $135 million, before certain charges and gains. We expect a loss for the first quarter of 2005 in the range of $44 to $47 million, before certain charges and gains. For purposes of these estimates, excluded charges and gains will include certain types of stock-based compensation expense incurred as a result of the adoption of Financial Accounting Standards Board Statement No. 123(R), "Share-Based Payments," in July 2005 as well as any additional credits or charges associated with the Kendall Square Lease.

- **Revenues:** We expect that total revenue will be in the range of $150 to $160 million in 2005. This is expected to be comprised of approximately $100 million of collaborative R&D revenues from existing collaborations, including $90 million in contracted collaborative R&D funding and approximately $10 million of revenue from milestone payments under existing collaborations, $25 million to $29 million from HIV product royalties, and an anticipated additional $20 million to $30 million from new research and product development agreements.

- **Research and Development (R&D) Expense:** We project that R&D expense will be in the range of $225 million to $240 million for 2005. The forecasted increase over the 2004 R&D expense level of $192 million is driven by increased clinical development investment in our Vertex-controlled programs.

- **Sales, General and Administrative (SG&A) Expense:** We expect SG&A expense to be in the range of $42 to $46 million for 2005.

- **Cash, Cash Equivalents and Available for Sale Securities:** We expect cash, cash equivalents and marketable securities to be in excess of $250 million at the end of 2005.

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 1 of this Annual Report on Form 10-K and in the section below entitled "Forward-Looking Statements." In this Annual Report on Form 10-K, we provide our expected financial results using certain financial measures that are not in accordance with generally accepted accounting principles in the United States ("GAAP"). In particular, our guidance for full year and first quarter 2005 loss, excluding certain charges or gains, are non-GAAP financial measures. These measures are provided because we believe they help indicate underlying trends in our business, and we use these non-GAAP financial measures to establish budgets and operational goals that are communicated internally and externally to manage the Company's business and to evaluate its performance.

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 as of December 31, 2004. Certain other obligations and commitments, while not required under GAAP to be included in the consolidated balance sheets, may have a material impact on liquidity. We have presented these items, all of which have been 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.

December 31, 2004	2005	2006-2007	2008-2009	2010 and later	Total
			(in thousands)		
Commitments and Obligations Recorded on the Consolidated Balance Sheets at December 31, 2004:					
Collaborator development loans	$ —	$ —	$ 19,997	$ —	$ 19,997
Convertible subordinated notes	—	82,552	—	232,448	315,000
Off-Balance Sheet Commitments and Obligations at December 31, 2004:					
Facilities operating leases	45,623	73,228	67,571	205,651	392,073
Purchase obligations	3,000	3,000	—	—	6,000
Research and development and other commitments	2,115	750	—	—	2,865
Total contractual obligations and commitments	$ 50,738	$ 159,530	$ 87,568	$ 438,099	$ 735,935

Commitments and Obligations Recorded on the Consolidated Balance Sheets at December 31, 2004:

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 studies of kinase inhibitor compounds that we selected for early development. In February 2004, we amended the terms of the Novartis collaboration agreement. We will continue to be responsible for drug discovery and Novartis will continue to provide research funding through the balance of the research term ending in April 2006, as provided in the original agreement. However, Novartis will now be responsible for all nonclinical and clinical development of drug candidates that it accepts for development, and consequently the loan facility providing funding for development activities by Vertex has been terminated. Outstanding loans that funded amounts either spent or committed to be spent on

development activities relating to a particular compound will be forgiven if that compound is selected by Novartis for development. If the compound is not selected by Novartis, the related loan 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, 2004, we had $82.6 million in aggregate principal amount of 2007 Notes and $232.4 million in aggregate principal amount of 2011 Notes outstanding. For both the 2007 and 2011 Notes, we are required to make semi-annual interest payments on the outstanding principal balance of the notes. Our aggregate annual interest payment obligation is approximately $17.5 million.

Off-Balance Sheet Commitments and Obligations at December 31, 2004:

At December 31, 2004, 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 to be recorded on our consolidated balance sheets under GAAP. 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, 2004.

Our Kendall Square Lease term began January 1, 2003 and 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 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 each year commencing January 1, 2005, including lease payments and a construction obligation, are $29.9 million for 2005, $43.1 million for 2006 and 2007, $42.9 million for 2008 and 2009 and $196.2 million for all of the years thereafter and are included in the table above. In June 2003, we decided not to occupy the space under this lease and to seek to sublease the space to third parties to minimize our on-going lease obligations. 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 obligations referred to above include an agreement to purchase a minimum of $3 million of certain specified products from Invitrogen Corporation annually for three years, to which we agreed in connection with the sale of certain assets of our former Discovery Tools and Services business on March 28, 2003. The purchase obligations referred to above do not include severance pay obligations to each of five executive officers of the Company 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 $467,000 to $1,185,000.

Liquidity and Capital Resources

We have incurred operating losses since our inception and historically have financed our operations principally through public stock offerings, private placements 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, 2004, we had cash, cash equivalents and marketable securities of $392,320,000, which is a decrease of $190,844,000 from $583,164,000 at December 31, 2003. The decrease of $190,844,000 is primarily due to the net cash used in operations of $142,160,000, which included cash payments of $31,550,000 made in connection with the restructuring and other expense accrual. In

addition, restricted cash increased $23,786,000 due to the issuance of stand-by letters of credit pursuant to the Kendall Square Lease agreement. Repayments under our loan facility with Novartis were $12,463,000 for the twelve months ended December 31, 2004, bringing the balance outstanding under the loan facility to $19,997,000. Expenditures for property and equipment were $12,495,000. Cash receipts from the issuance of common stock under our employee benefit programs during 2004 were $8,742,000.

As part of our strategy to manage our long-term operating cash needs, we exchanged approximately $232.4 million in aggregate principal amount of newly issued 2011 Notes for an equal principal amount of our 2007 Notes. The 2011 Notes were issued through private offerings to qualified institutional buyers. The 2011 Notes are convertible, at the option of the holder, into common stock at a price equal to $14.94, subject to adjustment under certain circumstances. The 2007 Notes are convertible, at the option of the holder, into common stock at a price equal to $92.26, subject to adjustment under certain circumstances. Issuance costs associated with the 2011 Notes were $4.8 million.

The restructuring accrual relating to our decision not to occupy our facility in Kendall Square was $55.8 million at December 31, 2004. 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.

In connection with new collaborations in 2004, we received approximately $21.0 million in up-front payments. Consistent with our revenue recognition policy, we have deferred recognition of the majority of these payments, which will be recognized over the related contract term.

In February 2004, we amended the terms of our collaboration agreement with Novartis. Under the amended agreement, Novartis is responsible 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 pipeline, particularly in clinical trials of our anti-HCV infection and anti-cytokine product candidates, in our ion channel and kinase discovery efforts and in our effort to prepare for potential registration, regulatory approval and commercial launch of our product candidates. Consequently, we expect to incur losses on a quarterly and annual basis for the foreseeable future as we continue to develop and commercialize existing and future drug candidates. 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 2005 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 and the costs and timing of obtaining regulatory approvals for any of our product candidates. 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 in prior periods through new issues, privately negotiated transactions and market purchases, depending on market conditions and our perceived needs at the time. During 2005 we expect to continue pursuit of a general financial strategy that may lead us to undertake one or more additional capital transactions, which 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 will also 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 generally accepted accounting principles in the United States of America. 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 expenses, revenue recognition, research and development expenses and investments, all of which are important to our financial position 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, "Accounting for Costs Associated with Exit or Disposal Activities" ("SFAS 146"). These 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, the impact of which is measured using the credit-adjusted risk-free discount rate of approximately 10% applied in the period when we first incurred the liability.

On June 10, 2003, we announced a plan to restructure our operations in preparation for increased investment in the clinical development and commercialization of our drug candidates. We designed the restructuring to rebalance our relative investment in research and development, to better support our long-term objective of becoming an integrated pharmaceutical company. The restructuring included a workforce reduction, write-offs of certain assets and a decision not to occupy the Kendall Square facility. We have subleased approximately 45,000 square feet of this facility and are actively seeking to sublease the unoccupied portion to offset our ongoing lease obligations.

In accordance with SFAS 146, we recorded an initial estimate of the fair value of the estimated liability in the second quarter of 2003. We have reviewed our assumptions and estimates quarterly and have updated the estimated amount of the liability as changes in circumstances have required. For the twelve months ended December 31, 2004, we recorded restructuring and other expenses of

$17.6 million relating to our estimated net ongoing obligations under the Kendall Square lease. The $17.6 million of restructuring and other expense recorded is primarily the result of revising certain key estimates and assumptions about when subtenants will be identified and secured and incurring an imputed interest charge for the related restructuring liability. For the twelve months ended December 31, 2003, we recorded restructuring and other related expenses of $91.8 million. The $91.8 million included $78.7 million of lease restructuring expense for the Kendall Square Lease. In addition to the $78.7 million, other costs included in the $91.8 million charge included $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 charge for the lease restructuring was the most significant component of the total restructuring charge recorded during 2003 and the only component of the restructuring and other expense accrual remaining to be settled at December 31, 2004. We are required to make significant judgments and assumptions when estimating the liability for our net ongoing obligations under the Kendall Square Lease. In accordance with SFAS 146, we use a probability-weighted discounted cash-flow analysis to calculate the amount of the liability associated with the lease restructuring. We applied a discount rate of approximately 10%. The probability-weighted discounted cash-flow analysis is based on management's assumptions and estimates of our ongoing lease obligations, including contractual rental and build-out commitments, and sublease rentals, including estimates of sublease timing and sublease rental terms. We validate our estimates and assumptions through consultations with independent third parties having relevant expertise.

It is possible that our estimates and assumptions will change in the future, resulting in additional adjustments to the amount of the estimated liability, and the effect of any adjustments could be material. For example, if sublease rental rates differ from our assumption by approximately 10% in either direction, our recorded liability will be negatively or positively adjusted by approximately $6.6 million. If our estimated subleasing timetable is delayed by six months, the impact could be as high as approximately $5.4 million in additional estimated liability, or more, if there is further delay. We will review our assumptions and judgments related to the potential lease restructuring on at least a quarterly basis, until the outcome is finalized, and make whatever modifications we believe are necessary, based on our best judgment, to reflect any changed circumstances.

Revenue Recognition

Our revenue recognition policies are 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 collaborative and other research and development revenue is generated primarily through collaborative research and development agreements with strategic collaborators. The terms of these agreements typically include payment to us of non-refundable up-front license fees, funding for research and development efforts, payments to us based upon achievement of certain milestones, and royalties payable on product sales.

We recognize revenue from non-refundable, up-front license fees and milestones, not specifically tied to a separate earnings process, ratably over the contracted or estimated period of performance. Changes in estimates could materially affect revenue in the period the estimate is changed. If our estimate of the period of performance shortens or lengthens, the amount of revenue we recognize from non-refundable, up-front license fees and milestones could increase or decrease in the period the change in estimate becomes known. Future related revenues would be adjusted accordingly. To date, changes to our estimates have not had a material impact on our financial position or results of operations. Research funding is recognized ratably over the period of effort, as earned. Milestones that

are based on designated achievement points and that are considered at-risk and substantive at the inception of the collaboration agreement are recognized as earned when management considers the corresponding payment to be reasonably assured. We evaluate whether milestones are at-risk and substantive based on the contingent nature of the milestone, specifically reviewing factors such as the technological and commercial risk that must be overcome and the level of investment required.

Under EITF 00-21, in multiple-element arrangements, license payments are recognized together with any up-front payment and the research and development funding as a single unit of accounting, unless the delivered technology has stand-alone value to the customer and we have objective and reliable evidence of fair value of the undelivered elements in the arrangement. License payments received during the course of a collaboration that do not meet the separation criteria above are recognized, when earned, in proportion to the period of time completed on the contract relative to the total contracted or estimated period of performance on the underlying research and development collaboration, with the remaining amount deferred and recognized ratably over the remaining period of performance. Payments received after performance obligations are complete are recognized when earned.

Royalty revenue 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, facilities costs, overhead costs, clinical trial costs, contract services and other outside costs. Clinical trial, contract services and other outside costs require that we 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., for which we account 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.

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 on the consolidated financial statements under the heading "discontinued operations" for the twelve months ended December 31, 2003 and December 31, 2002.

The reclassification of the amounts to discontinued operations has been prepared 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, 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 revenue, as compared with $9,002,000 in royalties and $60,139,000 in collaborative research and development revenue 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/Telzir in the United States in November 2003 and in the European Union in November 2004. Lexiva has largely replaced Agenerase in the United States market. We pay a royalty to a third party on sales of Agenerase and Lexiva/Telzir.

Collaborative and other research and development revenue increased $25,256,000, or 42%, in 2004 as compared with 2003. The increase in collaborative and other research and development revenue is due to the execution of three new collaboration agreements — with Cystic Fibrosis Foundation Therapeutics Incorporated ("CFFT") (cystic fibrosis drug discovery), Mitsubishi Pharma Corporation (Far East development of VX-950), and Merck & Co., Inc. (research and development of Aurora kinase inhibitors, including VX-680) — and recognized revenue of approximately $4.1 million from a $10 million milestone payment 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 VX-385. The table presented below is a summary of significant revenue 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 significant collaborative revenue 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 funding under our collaboration with Serono concluded on September 30, 2004.

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 2005 that could be material to our business.

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 Pharmaceuticals, Inc. and VX-680 (oncology), which is now licensed to Merck & Co., Inc. During 2004, we continued clinical studies of our compound for the treatment of HCV infection, initiating a Phase IIb study (called the "METRO" study) of merimepodib in combination with Pegasys® (peginterferon alfa-2a) and Copegus® (ribavirin). We completed a Phase Ia study 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		
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		
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		

Our collaborators have agreed to fund portions of our research and development programs related to specific drug candidates. The following table details our collaborator- and company-sponsored research and development expenses for 2004 and 2003 (in thousands):

	2004			2003		
	Research	Development	Total	Research	Development	Total
Collaborator-sponsored	$ 62,181	$ 28,294	$ 90,475	$ 62,162	$ 19,935	$ 82,097
Company-sponsored	51,095	50,592	101,687	51,273	66,266	117,539
Total	$ 113,276	$ 78,886	$ 192,162	$ 113,435	$ 86,201	$ 199,636

Commercial Products and Clinical Development Programs

Our product pipeline is principally focused on viral diseases, inflammatory and autoimmune diseases, cancer, pain and bacterial infection.

Therapeutic Area and Product Candidate	Clinical Indications	Development Phase	Company With Marketing Rights (Region)
Viral Diseases			
Lexiva/Telzir (fosamprenavir calcium)*	HIV infection	Marketed	GlaxoSmithKline (Worldwide)**
Merimepodib (VX-497)	Chronic hepatitis C virus infection	Phase II	Vertex (Worldwide)
VX-950	Chronic hepatitis C virus infection	Phase I	Mitsubishi (Far East); Vertex (Rest of World)
VX-385	HIV infection	Phase II	Vertex (Far East); GlaxoSmithKline (Rest of World)*

Inflammatory and Autoimmune Diseases			
VX-765	Psoriasis and other autoimmune diseases	Phase II	Vertex (Worldwide)
VX-702	Rheumatoid arthritis and other inflammatory diseases	Phase II	Kissei (Far East); Vertex (Rest of World; co-exclusive in certain Far East countries)
Pralnacasan (VX-740)	Rheumatoid arthritis and other inflammatory and autoimmune diseases	Phase II	Sanofi-Aventis (Worldwide)†
Cancer			
VX-680	Oncology	Phase I	Merck (Worldwide)
VX-944	Oncology	Phase I	Avalon Pharmaceuticals (Worldwide)
VX-322	Oncology	Preclinical	Novartis (Worldwide)
Other			
VX-409	Pain	Preclinical	Vertex (Worldwide)
VX-692	Bacterial infection	Preclinical	Vertex (Worldwide)

* Fosamprenavir calcium is marketed under the trade names Lexiva in North America and Telzir in the European Union. Lexiva/Telzir, a prodrug of our first marketed HIV drug, Agenerase (amprenavir), also marketed by GlaxoSmithKline, is replacing Agenerase in world markets.

** Vertex has co-promotion rights in the United States and the European Union.

† Sanofi-Aventis has notified us that it intends to terminate our collaboration for the development of pralnacasan. Upon the effectiveness of that termination, all commercial and other rights to pralnacasan will revert to Vertex.

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 2005 to be greater than in 2004 due to increased clinical development as we advance our core programs. However, our anticipated 2005 research and development expenses could vary materially, depending on the occurrence and timing of clinical trials. 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 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 under approved labeling	6 months to 2 years

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

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 $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

In accordance with SFAS 146, we review on a quarterly basis the estimates and assumptions underlying our determination of the anticipated liability associated with the Kendall Square Lease and adjust the liability as changes in circumstances require. It is possible that those estimates and assumptions could change in the future resulting in incremental expense or, alternatively, in reversal of expense, and the effect of any such adjustments could be material.

Interest income decreased approximately $5,089,000 to $10,323,000 in 2004 from $15,412,000 in 2003. The decrease is mainly 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 the income from discontinued operations in 2003 is a gain on the sale of those assets of $70,339,000.

Year Ended December 31, 2003 Compared with Year Ended December 31, 2002

Our net loss for 2003 was $196,767,000, or $2.56 per basic and diluted common share, compared with a net loss for 2002 of $108,621,000, or $1.43 per basic and diluted common share. 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. Included in our net loss for 2002 was income from discontinued operations of $28,337,000.

In addition to restructuring and other expense, offset by income from discontinued operations, our net loss for 2003 as compared with our net loss for 2002 increased primarily as a result of decreased revenue and interest income.

Total revenues decreased to $69,141,000 in 2003 compared to $94,770,000 in 2002. In 2003, revenue was comprised of $9,002,000 in royalties and $60,139,000 in collaborative and other research and development revenue, as compared with $10,054,000 in royalties and $84,716,000 in collaborative research and development revenue in 2002.

The decrease in collaborative and other research and development revenue from 2002 to 2003 is due to the conclusion of certain of our collaborative research and development arrangements, mainly in late 2002, partially offset by additional revenue recognized under our Novartis collaboration and a milestone payment received from GlaxoSmithKline in connection with FDA approval of Lexiva. The table presented below is a summary of significant revenue arrangements for the year ended 2003 as compared with the year ended 2002.

	Year Ended December 31,	
	2003	2002
	(In thousands)	
Collaborative and other research and development revenue:		
Summary of significant collaborative revenue arrangements:		
Novartis	$ 44,502	$ 41,894
Eli Lilly	—	12,054
Schering	—	5,000
Other	15,637	25,768
Total collaborative and other research and development revenue	$ 60,139	$ 84,716

Research and development expenses remained relatively consistent at $199,636,000 in 2003 compared to $198,338,000 in 2002. Research expenditures were $113,435,000 in 2003 compared with $120,406,000 in 2002. Development expenditures were $86,201,000 in 2003 compared with $77,932,000 in 2002. Our investment in research decreased due to the operational restructuring in June 2003, while our investment in development increased as a result of an increased level of clinical trials activity with respect to our proprietary drug candidates in clinical development. In 2003, our clinical trials focused on multiple drug candidates in a variety of therapeutic areas. The results of these trials enabled us to direct our principal clinical focus toward compounds in two therapeutic areas —viral diseases and inflammatory and autoimmune diseases. Our lead drug candidates in these areas are merimepodib (HCV infection), VX-950 (HCV infection), VX-765 (autoimmune diseases) and VX-702 (inflammatory diseases). In 2003, we engaged in development activities with drug candidates targeting potential therapeutic indications outside the therapeutic areas of viral diseases and inflammatory and autoimmune diseases, including VX-944 (oncology), which is now licensed to Avalon Pharmaceuticals, Inc. and VX-680 (oncology), which is now licensed to Merck & Co., Inc.

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, 2003 and 2002 (in thousands):

	2003	2002	$ Change	% Change
Research Expenses:				
Salary and benefits	$ 38,140	$ 35,724	$ 2,416	6.8%
Laboratory supplies and other direct expenses	20,025	20,046	(21)	(0.1)%
Contractual services	6,390	14,718	(8,328)	(56.6)%
Infrastructure Costs	48,880	49,918	(1,038)	(2.1)%
Total research expenses	$ 113,435	$ 120,406		
Development Expenses:				
Salary and benefits	$ 19,796	$ 16,300	$ 3,496	21.4%
Laboratory supplies and other direct expenses	5,307	6,976	(1,669)	(23.9)%
Contractual services	42,594	39,697	2,897	7.3%
Infrastructure Costs	18,504	14,959	3,545	23.7%
Total development expenses	$ 86,201	$ 77,932		
Total Research and Development Expenses:				
Salary and benefits	$ 57,936	$ 52,024	$ 5,912	11.4%
Laboratory supplies and other direct expenses	25,332	27,022	(1,690)	(6.3)%
Contractual services	48,984	54,415	(5,431)	(10.0)%
Infrastructure Costs	67,384	64,877	2,507	3.9%
Total research and development expenses	$ 199,636	$ 198,338		

The following table details our collaborator and company-sponsored research and development expenses for 2003 and 2002 (in thousands):

	2003			2002		
	Research	Development	Total	Research	Development	Total
Collaborator-Sponsored	$ 62,162	$ 19,935	$ 82,097	$ 54,509	$ 35,675	$ 90,184
Company-Sponsored	51,273	66,266	117,539	65,897	42,257	108,154
Total	$ 113,435	$ 86,201	$ 199,636	$ 120,406	$ 77,932	$ 198,338

Sales, general and administrative expenses decreased $1,974,000, or 5%, to $39,082,000 in 2003 from $41,056,000 in 2002, due primarily to a reduction in personnel resulting from our consolidation of

certain general and administration functions to our corporate office location in Cambridge, Massachusetts, and from our restructuring in the second quarter of 2003.

Restructuring and other expense for the twelve months ended December 31, 2003 was $91.8 million. 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

Interest income decreased approximately $13,310,000 to $15,412,000 in 2003 from $28,722,000 in 2002. The decrease is mainly the result of both a lower level of invested funds and lower portfolio yields due to a reduced interest rate environment.

Income from discontinued operations increased to $69,646,000 in 2003 from $28,337,000 in 2002, due to our sale of the assets of our Discovery Tools and Services business in 2003. Included in the income from discontinued operations in 2003 is a gain on the sale of those assets of $70,339,000.

Forward-looking Statements

This report contains forward-looking statements about our business, including our expectation that (i) we are positioned to commercialize multiple products in the coming years that we expect will generate increased revenues; (ii) our losses will continue; (iii) research and development expenses will increase, but research expenses will not increase without new funding from collaborations; (iv) we will continue to focus our development activities on product candidates in the areas of HCV infection and inflammatory and autoimmune diseases and cancer; (v) we will concentrate on identifying collaborative relationships for development of our HCV infection and inflammation product candidates outside North America; (vi) our financial results for 2005 will be as set forth in this Annual Report on Form 10-K; (vii) we and our collaborators will advance clinical trials on a number of our development stage drug candidates during 2005; (viii) our drug candidates will progress in development during 2005; and (ix) we will advance additional kinase inhibitors as development candidates targeting multiple therapeutic areas over the remaining period of our collaboration with Novartis; (x) we will be able to negotiate third party manufacturing agreements on commercially reasonable terms; (xi) our liability in connection with the Kendall Square Lease will be as we have estimated; (xii) future development candidates will be focused on a wide variety of diseases and conditions, including cancer, cystic fibrosis and pain; and (xiii) we will enter into new collaborations that will provide additional funding for our research and development efforts, including possibly our ion channels program. 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. These risks and uncertainties include, among other things, our inability to further identify, develop and achieve commercial success for new products and technologies; the possibility of delays in the research and development necessary to select drug development candidates; the possibility of delays in the commencement or completion of clinical trials; the risk that clinical activities planned for 2005 may not commence as scheduled; the risk that clinical trials may not result in marketable products; the risk that we may be unable to successfully finance and secure regulatory approval of and market our drug candidates; our dependence upon existing and new pharmaceutical and biotechnology collaborations; the levels and timing of payments under our collaborative agreements; uncertainties about our ability to

obtain new corporate collaborations on satisfactory terms, if at all; the development of competing systems; our ability to protect our proprietary technologies; patent-infringement claims; risks of new, changing and competitive technologies; the risk that there may be changing and new regulations in the U.S. and internationally; and uncertainty about our ability to sublease to third parties space covered by the Kendall Square Lease. Please see the "Risk Factors" appearing elsewhere in this report for more details regarding these and other risks. 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 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," supercedes APB Opinion No. 25, "Accounting for Stock Issued to Employees," 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 period. Compensation cost is measured at the fair value of the award at the grant date and 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. The statement is effective in the first interim or annual reporting period beginning after June 15, 2005. The impact of adopting SFAS No. 123(R) cannot be accurately estimated at this time, as it will depend on the market value and the amount of share-based awards granted in future periods. However, had the Company adopted SFAS No. 123(R) in prior periods, the impact of the standard would have approximated the impact of SFAS No. 123 as described in the disclosure of pro forma net loss and net loss per share in Note B, "Accounting Policies", to the consolidated financial statements included in this Annual Report on Form 10-K. The Company is currently evaluating the three prescribed transition methods for accounting for and reporting stock options, and will select one prior to the adoption date for FASB 123(R).

ITEM 7A. QUANTITATIVE AND QUALITIVE DISCLOSURES ABOUT MARKET RISK

As part of its investment portfolio, Vertex owns financial instruments that are sensitive to market risks. The investment portfolio is used to preserve Vertex's capital until it is required to fund operations, including Vertex's research and development activities. None of these market risk sensitive instruments are held for trading purposes. Vertex does not have derivative financial instruments in its investment portfolio.

Interest Rate Risk

Vertex invests its 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 U.S. dollars. All of Vertex's interest-bearing securities are subject to interest rate risk, and could decline in value if interest rates fluctuate. Substantially all of Vertex's 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, Vertex does not believe that it has 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-2 through F-35 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 Rules 13(a)—15(e) and 15d—15(e)) 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.

Vertex's management assessed the effectiveness of the Company's internal control over financial reporting as of December 31, 2004. 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 conclude that, as of December 31, 2004, 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, 2004, has been audited by PricewaterhouseCoopers LLP, an independent registered public accounting firm, as stated in their report which appears on page F-2 of this Annual Report on Form 10-K.

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 2005 Annual Meeting of Stockholders (the "2005 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 2005 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 2005 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 2005 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 2005 Proxy Statement under "Security Ownership of Certain Beneficial Owners and Management" and "Executive Compensation—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 2005 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 ACCOUNTANT FEES AND SERVICES

The information required by this Item 14 is included in the 2005 Proxy Statement under "Independent Registered Public Accounting Firm" and is incorporated herein by reference.

PART IV

ITEM 15. EXHIBITS AND FINANCIAL STATEMENT SCHEDULES

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

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

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

Exhibit Number	Exhibit Description
2.1	Agreement and Plan of Merger dated as of April 29, 2001, by and among Vertex Pharmaceuticals Incorporated, Aurora Biosciences Corporation and Ahab Acquisition Sub Inc. (filed as Exhibit 2 to Vertex's Current Report on Form 8-K dated April 29, 2001 [File No. 000-19319] and incorporated herein by reference).
2.2	Asset Purchase Agreement among Vertex, PanVera LLC and Invitrogen Corporation dated February 4, 2003 (filed as Exhibit 2.2 to Vertex's 2002 Annual Report on Form 10-K [file No. 000-19319] and incorporated herein by reference).
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 1997 Annual Report on Form 10-K [File No. 000-19319] and incorporated herein by reference).
3.2	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 1997 Annual Report on Form 10-K [File No. 000-19319] and incorporated herein by reference).
3.3	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 1997 Annual Report on Form 10-K [File No. 000-19319] 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 May 21, 2001 (filed as Exhibit 3.4 to Vertex's registration statement on Form S-4 [Registration Number 333-61480] and incorporated herein by reference.)
3.5	By-laws of Vertex, as amended and restated as of March 12, 2001 (filed as Exhibit 3.4 to Vertex's 2000 Annual Report on Form 10-K [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] or amendments thereto and incorporated herein by reference).

4.2	Stockholder Rights Plan (filed as Exhibit 4.2 to Vertex's Registration Statement on Form S-1 [Registration No. 33-40966] or amendments thereto 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 1996 Annual Report on Form 10-K [File No. 000-19319] and incorporated herein by reference).
4.4	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).
4.5	Supplemental Indenture, dated as of December 12, 2000, between Vertex and State Street Bank and Trust Company (filed as Exhibit 4.2 to Pre-Effective Amendment No. 1 to the Form S-3 filed by Vertex [Registration No. 333-49844] and incorporated herein by reference).
4.6	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).
4.7	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	1991 Stock Option Plan, as amended and restated as of September 14, 1999 (filed as Exhibit 10.1 to Vertex 1999 Annual Report on Form 10-K [File No. 000-19319] and incorporated herein by reference).*
10.2	1994 Stock and Option Plan, as amended and restated as of September 14, 1999 (filed as Exhibit 10.2 to Vertex 1999 Annual Report on Form 10-K [File No. 000-19319] and incorporated herein by reference).*
10.3	1996 Stock and Option Plan, as amended and restated as of March 14, 2005 (filed herewith).*
10.4	Non-Competition and Stock Repurchase Agreement between Vertex and Joshua Boger, dated April 20, 1989 (filed as Exhibit 10.2 to Vertex's Registration Statement on Form S-1 [Registration No. 33-40966] or amendments thereto and incorporated herein by reference).*
10.5	Form of Employee Stock Purchase Agreement (filed as Exhibit 10.3 to Vertex's Registration Statement on Form S-1 [Registration No. 33-40966] or amendments thereto and incorporated herein by reference).*
10.6	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] or amendments thereto and incorporated herein by reference).*
10.7	Executive Employment Agreement executed between Vertex and Joshua S. Boger (filed as Exhibit 10.6 to Vertex's 1994 Annual Report on Form 10-K [File No. 000-19319] and incorporated herein by reference).*
10.8	Amendment to Employment Agreement 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).*
10.9	Lease, dated March 3, 1995, between Fort Washington Realty Trust and Vertex, relating to the premises at 130 Waverly Street, Cambridge, MA (filed as Exhibit 10.15 to Vertex's 1994 Annual Report on Form 10-K [File No. 000-19319] and incorporated herein by reference).
10.10	First Amendment to Lease, dated December 29, 1995 between Fort Washington Realty Trust and Vertex (filed as Exhibit 10.15 to Vertex's 1995 Annual Report on Form 10-K [File No. 000-19319] and incorporated herein by reference).

10.11 Second Amendment to Lease and Option Agreement, dated June 12, 1997, between Fort Washington Realty Trust and Vertex (filed as Exhibit 10.17 to Vertex 1999 Annual Report on Form 10-K [File No. 000-19319] and incorporated herein by reference).

10.12 Third, Fourth and Fifth Amendments to Lease between Fort Washington Realty Trust and Vertex (with certain confidential information deleted) (filed as Exhibit 10.14 to Vertex's 2001 Annual Report on Form 10-K [File No. 000-19319] and incorporated herein by reference).†

10.13 Lease, by and between Trustees of Fort Washington Realty Trust, Landlord, and Vertex, executed September 17, 1999 (filed, with certain confidential information deleted, 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).†

10.14 Lease, by and between Kendall Square, LLC, Landlord, and Vertex, executed January 18, 2001 (filed, with certain confidential information deleted, as Exhibit 10.16 to Vertex's 2000 Annual Report on Form 10-K [File No. 000-19319] and incorporated herein by reference).†

10.15 Agreement for Lease of Premises at 88 Milton Park, Abingdon, Oxfordshire between Milton Park Limited and Vertex Pharmaceuticals (Europe) Limited and Vertex Pharmaceuticals Incorporated (filed as Exhibit 10.18 to Vertex 1999 Annual Report on Form 10-K [File No. 000-19319] and incorporated herein by reference).

10.16 Research and Development Agreement, dated April 13, 1993, between Vertex and Kissei Pharmaceutical Co., Ltd. (filed, with certain confidential information redacted, 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).†

10.17 Research Agreement and License Agreement, both dated December 16, 1993, between Vertex and Burroughs Wellcome Co. (filed, with certain confidential information redacted, as Exhibit 10.16 to Vertex's 1993 Annual Report on Form 10-K [File No. 000-19319] and incorporated herein by reference).†

10.18 Salary Amendments to Employment Arrangements with Named Executive Officers (filed herewith).*

10.19 Research and Development Agreement between Vertex and Kissei Pharmaceutical Co. Ltd., effective September 10, 1997 (filed, with certain confidential information redacted, 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).†

10.20 Research Agreement between Vertex and Schering AG, dated as of August 24, 1998 (filed, with certain confidential information redacted, 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).†

10.21 License, Development and Commercialization Agreement between Vertex and Hoechst Marion Roussel Deutschland GmbH dated September 1, 1999 (filed, with certain confidential information redacted, 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).†

10.22 Research Agreement between Vertex and Laboratoires Serono S.A., dated December 11, 2000 (filed, with certain confidential information redacted, as Exhibit 10.26 to Vertex's 2000 Annual Report on Form 10-K [File No. 000-19319] and incorporated herein by reference).†

10.23 Letter Agreement between Vertex and Stuart J. Collinson (filed as Exhibit 10.26 to Vertex's registration statement on Form S-4 [Registration No. 333-61480] and incorporated herein by reference).*

10.24 Letter Agreement between Vertex and N. Anthony Coles, M.D. (filed as Exhibit 10.30 to Vertex's 2001 Annual Report on Form 10-K [File No. 000-19319] and incorporated herein by reference).*

10.25 Non-Competition Agreement between Vertex and Invitrogen Corporation, dated March 28, 2003 (filed as Exhibit 10.31 to Vertex's 2002 Annual Report on Form 10-K [File No. 000-19319] and incorporated herein by reference).

10.26 Form of letter agreement with John J. Alam, Senior Vice President of Drug Evaluation and Approval; Lynne H. Brum, Vice President of Corporate Communications and Financial Planning; Pamela Fritz, Vice President, Human Resources; Peter Mueller, Chief Scientific Officer and Senior Vice President, Drug Discovery and Innovation; Mark Murcko, Vice President and Chief Technology Officer; Steven Schmidt, Vice President, Information Systems; John A. Thomson, Vice President, Research; and Jeffrey D. Wilson, Vice President, Pharmaceutical Operations, covering special rights upon a change of control transaction (filed as Exhibit 10.32 to Vertex's 2002 Annual Report on Form 10-K [File No. 000-19319] and incorporated herein by reference).*

10.27 Dealer Manager Agreement, dated February 10, 2004, between Vertex and UBS Securities LLC, (filed as Exhibit 10.1 to Vertex's Current Report on Form 8-K dated February 23, 2004 [File No. 000-19319] and incorporated herein by reference).

10.28 Resale Registration Rights Agreement, dated as of February 13, 2004, between Vertex and UBS Securities LLC (filed as Exhibit 10.2 to Vertex's Current Report on Form 8-K dated February 23, 2004 [File No. 000-19319] and incorporated herein by reference).

10.29 First Revised and Restated Research and Early Development Agreement between Vertex and Novartis Pharma AG, dated February 3, 2004 (filed, with certain confidential information redacted, as Exhibit 10.35 to Vertex's Amended 2003 Annual Report dated September 8, 2004 [File No. 000-19319] and incorporated herein by reference).†

10.30 License, Development and Commercialization Agreement, dated June 11, 2004, between Vertex and Mitsubishi Pharma Corporation (filed, with certain confidential information redacted, 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)†

10.32 Research, Development and Commercialization Agreement, dated May 24, 2004, between Vertex and Cystic Fibrosis Foundation Therapeutics Incorporated (filed with certain confidential information redacted, 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).†

10.32 Exclusive Research Collaboration, License and Commercialization Agreement, dated June 21, 2004, between Vertex Pharmaceuticals Incorporated and Merck & Co., Inc. (filed, with certain confidential information redacted, 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).†

10.33 Dealer Manager Agreement, dated September 13, 2004, between Vertex and UBS Securities LLC, (filed as Exhibit 10.1 to Vertex's Current Report on Form 8-K dated September 17, 2004 [File No. 000-19319] and incorporated herein by reference).

10.34 Resale Registration Rights Agreement, dated as of September 17, 2004, between Vertex and UBS Securities LLC (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).

10.35 Form of Amendment, dated November 8, 2004, to Letter Agreement covering special rights upon a change of control transaction with each of the individuals listed on Schedule 1 thereto (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).*

10.36 Form of Restricted Stock Agreement between the Company 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).*

10.37	Second Amendment, dated November 8, 2004, to Employment Agreement 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).*
10.38	Amended and Restated Employment Agreement, dated 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).*
10.39	Amendment, dated November 8, 2004, to Letter Agreement between Vertex and N. Anthony Coles (filed as Exhibit 10.12 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).*
10.40	Amended and Restated Employment Agreement, dated 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).*
10.41	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).*
10.42	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).*
10.43	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).*
10.44	Summary of Non-employee Director Compensation Policy (filed herewith).
18.1	Letter from PricewaterhouseCoopers LLP dated November 14, 2001 re: Change in Accounting Principle (filed as Exhibit 18.1 to Vertex's Quarterly Report on Form 10-Q for the quarter ended September 30, 2001 [File No. 000-19319] and incorporated herein by reference).
21	Subsidiaries of Vertex (filed herewith).
23.1	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).

* Compensatory plan or agreement applicable to management and employees.

† 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, 2005 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 and Chief Executive Officer (Principal Executive Officer)	March 16, 2005
/s/ IAN F. SMITH Ian F. Smith	Chief Financial Officer (Principal Financial Officer)	March 16, 2005
/s/ JOHANNA MESSINA POWER Johanna Messina Power	Controller (Principal Accounting Officer)	March 16, 2005
/s/ ERIC K. BRANDT Eric K. Brandt	Director	March 16, 2005
/s/ ROGER W. BRIMBLECOMBE Roger W. Brimblecombe	Director	March 16, 2005
/s/ STUART J. COLLINSON Stuart J. Collinson	Director	March 16, 2005
/s/ MATTHEW W. EMMENS Matthew W. Emmens	Director	March 16, 2005
/s/ BRUCE I. SACHS Bruce I. Sachs	Director	March 16, 2005
/s/ CHARLES A. SANDERS Charles A. Sanders	Director	March 16, 2005
/s/ EVE E. SLATER Eve E. Slater	Director	March 16, 2005
/s/ ELAINE S. ULLIAN Elaine S. Ullian	Director	March 16, 2005

VERTEX PHARMACEUTICALS INCORPORATED

Index to Consolidated Financial Statements

Report of Independent Registered Public Accounting Firm

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

We have completed an integrated audit of Vertex Pharmaceuticals Incorporated's 2004 consolidated financial statements and of its internal control over financial reporting as of December 31, 2004 and audits of its 2003 and 2002 consolidated financial statements in accordance with the standards of the Public Company Accounting Oversight Board (United States). Our opinions, based on our audits, are presented below.

Consolidated financial statements

In our opinion, the consolidated financial statements listed in the index appearing under Item 15(a)(1), present fairly, in all material respects, the financial position of Vertex Pharmaceuticals Incorporated and its subsidiaries at December 31, 2004 and 2003, and the results of their operations and their cash flows for each of the three years in the period ended December 31, 2004 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 of financial statements 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.

Internal control over financial reporting

Also, in our opinion, management's assessment, included in Management's Annual Report on Internal Control over Financial Reporting appearing under Item 9A, that the Company maintained effective internal control over financial reporting as of December 31, 2004 based on criteria established in *Internal Control—Integrated Framework* issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO), is fairly stated, in all material respects, based on those criteria. Furthermore, in our opinion, the Company maintained, in all material respects, effective internal control over financial reporting as of December 31, 2004, based on criteria established in *Internal Control—Integrated Framework* issued by the COSO. The Company's management is responsible for maintaining effective internal control over financial reporting and for its assessment of the effectiveness of internal control over financial reporting. Our responsibility is to express opinions on management's assessment and on the effectiveness of the Company's internal control over financial reporting based on our audit. We conducted our audit of internal control over financial reporting 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. An audit of internal control over financial reporting includes 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 consider necessary in the circumstances. We believe that our audit provides a reasonable basis for our opinions.

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 (i) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and

dispositions of the assets of the company; (ii) 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 (iii) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

/s/ PricewaterhouseCoopers LLP
Boston, Massachusetts
March 15, 2005

VERTEX PHARMACEUTICALS INCORPORATED

Consolidated Balance Sheets

	December 31,	
	2004	2003
	(In thousands, except share and per share amounts)	
Assets		
Current assets:		
Cash and cash equivalents	$ 55,006	$ 98,159
Marketable securities, available for sale	337,314	485,005
Accounts receivable	11,891	7,324
Prepaid expenses	2,501	3,318
Total current assets	406,712	593,806
Restricted cash	49,847	26,061
Property and equipment, net	64,225	80,083
Investments	18,863	18,863
Other assets	5,806	5,598
Total assets	$ 545,453	$ 724,411
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	$ 6,660	$ 12,306
Accrued expenses and other current liabilities	32,951	26,374
Accrued interest	5,862	4,455
Collaborator development loan	—	14,000
Deferred revenue	47,741	7,746
Accrued restructuring and other expense	55,843	69,526
Other obligations	4,688	4,660
Total current liabilities	153,745	139,067
Collaborator development loan	19,997	18,460
Other obligations	2,925	7,268
Deferred revenue	18,345	51,771
Convertible subordinated notes (due September 2007)	82,552	315,000
Convertible subordinated notes (due February 2011)	232,448	—
Total liabilities	510,012	531,566
Commitments and contingencies (Note K and Note R)		
Stockholders' equity:		
Preferred stock, $0.01 par value; 1,000,000 shares authorized; none issued and outstanding at December 31, 2004 and 2003, respectively	—	—
Common stock, $0.01 par value; 200,000,000 shares authorized; 80,764,904 and 78,025,002 shares issued and outstanding at December 31, 2004 and 2003, respectively	807	780
Additional paid-in capital	833,832	810,407
Deferred compensation, net	(11,657)	(1,112)
Accumulated other comprehensive income (loss)	(1,374)	2,690
Accumulated deficit	(786,167)	(619,920)
Total stockholders' equity	35,441	192,845
Total liabilities and stockholders' equity	$ 545,453	$ 724,411

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

VERTEX PHARMACEUTICALS INCORPORATED

Consolidated Statements of Operations

	Years Ended December 31,		
	2004	2003	2002
	(In thousands, except per share data)		
Revenues:			
Royalties	$ 17,322	$ 9,002	$ 10,054
Collaborative and other research and development revenues	85,395	60,139	84,716
Total revenues	102,717	69,141	94,770
Costs and expenses:			
Royalty payments	5,649	3,126	3,334
Research and development	192,162	199,636	198,338
Sales, general and administrative	42,139	39,082	41,056
Restructuring and other expense	17,574	91,824	—
Total costs and expenses	257,524	333,668	242,728
Loss from operations	(154,807)	(264,527)	(147,958)
Interest income	10,323	15,412	28,722
Interest expense	(18,317)	(17,298)	(17,684)
Charge for retirement of convertible subordinated notes	(3,446)	—	—
Other expense	—	—	(38)
Loss from continuing operations	$ (166,247)	$ (266,413)	$ (136,958)
Income from discontinued operations:			
Gain on sales of assets	—	70,339	—
Income (loss) from discontinued operations	—	(693)	28,337
Total income from discontinued operations	—	69,646	28,337
Net Loss	$ (166,247)	$ (196,767)	$ (108,621)
Basic and diluted loss per common share from continuing operations	$ (2.12)	$ (3.46)	$ (1.81)
Discontinued operations	—	0.90	0.38
Basic and diluted net loss per common share	$ (2.12)	$ (2.56)	$ (1.43)
Basic and diluted weighted average number of common shares outstanding	78,571	77,004	75,749

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, 2001	75,055	751	778,018	(20)	11,134	(314,532)	475,351	
Net change in unrealized holding gains/(losses) on marketable securities					(4,922)		(4,922)	$ (4,922)
Translation adjustments					552		552	552
Net loss						(108,621)	(108,621)	(108,621)
Comprehensive loss								$ (112,991)
Issuances of common stock:								
Benefit plans	1,302	13	15,896				15,909	
Equity compensation for services rendered			292				292	
Amortization of deferred compensation				20			20	
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	

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

VERTEX PHARMACEUTICALS INCORPORATED

Consolidated Statements of Cash Flows

	Years Ended December 31,		
	2004	2003	2002
		(In thousands)	
Cash flows from operating activities:			
Net loss	$ (166,247)	$ (196,767)	$ (108,621)
Net income from discontinued operations	—	(69,646)	(28,337)
Loss from continuing operations	$ (166,247)	(266,413)	(136,958)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization	29,640	23,438	24,905
Non-cash based compensation expense	4,165	3,146	2,894
Non-cash restructuring and other expense	—	4,395	—
Write-down of marketable securities and investments	—	—	666
Other non-cash items, net	—	—	1,220
Loss on disposal of property and equipment	—	116	51
Realized gains on marketable securities	(423)	(1,249)	(2,048)
Charge for retirement of convertible subordinated notes	3,446	—	—
Changes in operating assets and liabilities:			
Accounts receivable	(4,567)	1,574	3,064
Prepaid expenses	817	596	2,479
Other current assets	—	(2)	2,283
Accounts payable	(5,646)	(2,151)	4,770
Accrued expenses and other current liabilities	2,362	(4,050)	1,483
Accrued restructuring and other expense	(13,683)	69,526	—
Accrued interest	1,407	—	4
Deferred revenue	6,569	4,683	2,012
Net cash used in operating activities from continuing operations	(142,160)	(166,391)	(93,175)
Net cash (used in) provided by operating activities from discontinued operations	—	(1,232)	13,636
Net cash used in operating activities	(142,160)	(167,623)	(79,539)
Cash flows from investing activities:			
Purchases of marketable securities	(148,506)	(555,842)	(702,986)
Sales and maturities of marketable securities	292,351	593,998	727,582
Expenditures for property and equipment	(12,495)	(17,351)	(38,875)
Restricted cash	(23,786)	30	(4)
Investments and other assets	(136)	1,603	101
Net cash (used in) provided by investing activities from continuing operations	107,428	22,438	(14,182)
Net cash (used in) provided by investing activities from discontinued operations	—	97,147	(1,780)
Net cash (used in) provided by investing activities	107,428	119,585	(15,962)
Cash flows from financing activities:			
Issuances of common stock, net	8,742	11,959	13,327
Proceeds from notes payable, capital lease and loan obligations	—	27,460	5,000
Principal payments on capital leases and other obligations	(12,563)	(1,951)	(3,986)
Issuance costs related to 2011 notes	(4,805)	—	—
Net cash (used in) provided by financing activities from continuing operations	(8,626)	37,468	14,341
Net cash used in financing activities from discontinued operations	—	—	(499)
Net cash (used in) provided by financing activities	(8,626)	37,468	13,842
Effect of changes in exchange rates on cash	205	631	552
Net decrease in cash and cash equivalents	(43,153)	(9,939)	(81,107)
Cash and cash equivalents—beginning of period	98,159	108,098	189,205
Cash and cash equivalents—end of period	$ 55,006	$ 98,159	$ 108,098
Supplemental disclosure of cash flow information:			
Cash paid for interest	$ 15,597	$ 15,896	$ 16,078
Cash paid for taxes	$ —	$ —	$ 118

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 serious diseases, including HIV infection, chronic hepatitis C virus (HCV) infection, inflammatory and autoimmune disorders, cancer, pain and bacterial infection, independently and with collaborators. The Company's principal focus at this time is on the development and commercialization of new treatments for viral diseases, inflammatory and autoimmune diseases and cancer. Vertex earns a royalty on the sales of two Vertex-discovered products for the treatment of HIV infection, Lexiva/Telzir (fosamprenavir calcium) and Agenerase (amprenavir), and co-promotes these products in collaboration with GlaxoSmithKline plc. Lexiva has largely replaced Agenerase in the United States market and was launched in the European Union as Telzir in the third quarter of 2004. Vertex has 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.

Vertex focuses its efforts both on programs that it expects to control throughout the development and commercialization process, and programs that it expects will be conducted principally through the efforts of a collaborator. The Company expects to concentrate its Vertex-controlled development and commercialization efforts in North America, addressing therapeutic areas that the Company believes can be adequately served by a specialist-focused sales force. The most advanced products for which Vertex retains control over North American development are merimepodib (chronic HCV infection), VX-950 (chronic HCV infection), VX-702 (rheumatoid arthritis), and VX-765 (psoriasis).

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 clinical development under collaborations with Novartis Pharma AG, GlaxoSmithKline plc, Merck & Co., Inc., Mitsubishi Pharma Corp., Kissei Pharmaceutical Co., Ltd., and Cystic Fibrosis Foundation Therapeutics Incorporated.

In March and December 2003, in two independent transactions, Vertex sold the assets of its Discovery Tools and Services business, which had been acquired as a result of the merger with Aurora Biosciences Corporation ("Aurora") in 2001. In connection with those sales the buyers paid approximately $101 million in cash and assumed certain liabilities. As a result of the sales, the Company now operates in one operating segment: Pharmaceuticals. Please refer to Note C, "Sale of Assets", for further information.

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 and 2002. 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. 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 costs associated with a decision not to occupy a leased facility, the carrying value of the Company's investments in privately held companies and whether any decline in fair value is considered other than temporary, and useful lives for depreciation and amortization. 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

Cash equivalents, which are money market funds and debt securities, are valued at cost plus accrued interest. The Company considers all highly liquid investments with original maturities of three months or less at the date of purchase to be cash equivalents. Changes in cash and cash equivalents may be affected 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. Since these securities are available to fund current operations, they are classified as current assets on the balance sheet. Marketable securities are stated at fair value with their unrealized gains and losses included as a component of accumulated other comprehensive income (loss), which is a separate component of 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 income (loss) to the consolidated statement of operations. For the year ended December 31, 2002, the Company recorded $666,000 in charges to write down certain marketable securities because the decline in value was considered other-than-temporary. There were no write-downs of marketable securities in 2004 and 2003. Realized gains and losses are determined on the specific identification method and are included in interest income.

Investments

Investments at December 31, 2004 and 2003 include long term investments recorded under 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 statement of operations. There were no write-downs of investment in 2004 and 2003.

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 2004 the Company had significant revenue transactions with Novartis and GlaxoSmithKline, which 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. In 2002, the Company's only revenue transaction that accounted for more than 10% of the Company's total revenue was with Novartis, which accounted for 44%.

Receivables from GlaxoSmithKline and Mitsubishi represented approximately 46% and 15%, respectively, of the Company's accounts receivable balance at December 31, 2004. Receivables from GlaxoSmithKline and Novartis represented approximately 41% and 29%, respectively, of the Company's accounts receivable balance at December 31, 2003. 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 statement 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"), the Company has 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. When the exercise price of options or the issue price of restricted shares granted to employees is less than the market price of the common stock on the date of grant, compensation costs are expensed over the vesting period. Subsequent changes to option terms can also give rise to compensation costs.

At December 31, 2004, 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, 2004 and 2003, the Company recorded $1,661,000 and $16,000, respectively, in compensation expense related to restricted shares issued to employees in 2004 and 2003. No restricted shares were issued to employees in 2002. No 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.

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,		
	2004	2003	2002
	(In thousands, except per share data)		
Net loss attributable to common shareholders, as reported	$ (166,247)	$ (196,767)	$ (108,621)
Add: Employee stock-based compensation expense included in net loss	1,661	16	—
Deduct: Total stock-based employee compensation expense determined under the fair value based method for all awards	(39,504)	(51,180)	(54,686)
Pro forma net loss	$ (204,090)	$ (247,931)	$ (163,307)
Basic and diluted net loss per common share, as reported	$ (2.12)	$ (2.56)	$ (1.43)
Basic and diluted net loss per common share, pro forma	$ (2.60)	$ (3.22)	$ (2.16)

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 rate applied in the initial period. In 2004 and 2003, the Company recorded costs and liabilities for exit and disposal activities related to a restructuring plan, including a decision not to occupy a leased facility, 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's revenue recognition policies are 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").

Collaborative and Other Research and Development Revenue

The Company's collaborative and other research and development revenue is generated primarily through collaborative research, development and commercialization agreements with strategic collaborators for the discovery, development and commercialization of major pharmaceutical products. The terms of the agreements typically include payment to Vertex of non-refundable up-front license fees, funding of research and development efforts, payments to Vertex based upon achievement of certain milestones and royalties payable to Vertex on product sales.

The Company recognizes revenue from non-refundable, up-front license fees and milestones, not specifically tied to a separate earnings process, ratably over the contracted or estimated period of performance. Research funding is recognized as earned, ratably over the period of effort. Milestones based on designated achievement points that are considered at-risk and substantive at the inception of

the collaborative agreement are recognized as earned, when the earnings process is complete and the corresponding payment is reasonably assured. The Company evaluates whether milestones are at risk and substantive based on the contingent nature of the milestone, specifically reviewing factors such as the technological and commercial risk that needs to be overcome and the level of investment required.

Under EITF 00-21, in multiple-element arrangements, license payments are recognized together with any up-front payment and the research and development funding as a single unit of accounting, unless the delivered technology has stand alone value to the customer and there is objective and reliable evidence of fair value of the undelivered elements in the arrangement. License payments received during the course of a collaboration that do not meet the foregoing separation criteria are recognized, when earned, in proportion to the period of time completed on the contract relative to the total contracted or estimated period of performance on the underlying research and development collaboration, with the remaining amount deferred and recognized ratably over the remaining period of performance. Payments received after performance obligations are complete are recognized when earned.

Royalty Revenue

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

All research and development costs, including amounts funded in research collaborations, are expensed as incurred. Research and development expenses are comprised of costs incurred in performing research and development activities including salaries and benefits, facilities costs, overhead costs, clinical trial costs, contract services and other outside costs. Collaborator and Company-sponsored research and development expenses for 2004, 2003 and 2002 were as follows:

	2004			2003			2002		
	Research	Development	Total	Research	Development	Total	Research	Development	Total
Collaborator-sponsored	$ 62,181	$ 28,294	$ 90,475	$ 62,162	$ 19,935	$ 82,097	$ 54,509	$ 35,675	$ 90,184
Company-sponsored	51,095	50,592	101,687	51,273	66,266	117,539	65,897	42,257	108,154
Total	$ 113,276	$ 78,886	$ 192,162	$ 113,435	$ 86,201	$ 199,636	$ 120,406	$ 77,932	$ 198,338

Advertising

All advertising costs are expensed as incurred. During the year ended December 31, 2002 advertising expenses totaled $431,000. There were no advertising costs in 2004 or 2003.

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 related to expenses 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.

Comprehensive Income (loss)

Comprehensive income (loss) consists of net loss and other comprehensive income (loss), which includes foreign currency translation adjustments and unrealized gains and losses on certain marketable securities. For purposes of comprehensive income (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 subsidiaries.

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 re-measurement are included in other comprehensive loss, which is a separate component of stockholders' equity. Included in other comprehensive income (loss) is net unrealized gains related to foreign currency re-measurement with balances of $613,000 and $408,000 at December 31, 2004 and 2003, respectively.

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,		
	2004	2003	2002
Stock Options	15,820	16,802	17,065
Weighted-average exercise price (per share)	$ 22.67	$ 23.42	$ 25.73
Convertible Notes	16,454	3,414	3,414
Weighted-average conversion price (per share)	$ 19.15	$ 92.26	$ 92.26
Unvested restricted shares	1,399	125	—

Please refer to Note L, "Convertible Subordinated Notes," for further information about Vertex's recent exchanges of convertible notes.

New Accounting Pronouncements

In December 2004, the 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," supercedes APB Opinion No. 25, "Accounting for Stock Issued to Employees," 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 period. Compensation cost is measured at the fair value of the award at the grant date and 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. The statement is effective in the first interim or annual reporting period beginning after June 15, 2005. The impact of adopting SFAS No. 123(R) cannot be accurately estimated at this time, as it will depend on the market value and the amount of share based awards granted in future periods. However, had the Company adopted SFAS No. 123(R) in prior periods, the impact of the standard would have approximated the impact of SFAS No. 123 as described in the disclosure of pro forma net loss and net loss per share in this Note B. The Company is currently evaluating the three prescribed transition methods for accounting for and reporting stock options, and will select one prior to the adoption date for FASB 123(R).

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 Pan Vera 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 and non-current, on the condensed 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 and 2002. 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 and 2002 is comprised of the following revenue and expenses:

	Year Ended December 31,	
	2003	2002
Revenues from discontinued operations	$ 11,574	$ 66,315
Expenses from discontinued operations	12,267	37,978
Gain from sale of discontinued operations	70,339	—
Income from discontinued operations	$ 69,646	$ 28,337

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 investment in research and development, to better support the Company's long-term objective of becoming a profitable pharmaceutical company with industry-leading capabilities in research, development and commercialization of products. 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 ("Kendall Square Lease"). The Kendall Square Lease commenced in January 2003 and has a 15-year term. The Company is actively seeking to sublease the Kendall Square facility to third parties, to minimize its ongoing lease obligations. To date, the Company has subleased 45,000 square feet.

The Company recorded restructuring and other related expenses of $17.6 million and $91.8 million for the twelve months ended December 31, 2004 and 2003, respectively. The $17.6 million of restructuring and other expense recorded is primarily the result of revising certain key estimates and assumptions about when subtenants will be identified and secured and imputing an interest charge for the related restructuring liability. 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, 2004 and 2003, 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

	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 net ongoing costs associated with the Kendall Square Lease obligation was recorded at fair value in the second quarter of 2003. The Company reviews its assumptions and estimates quarterly and updates its estimate of this liability as changes in circumstances require. As prescribed by SFAS 146, the expense and liability recorded was calculated using probability-weighted discounted cash-flows associated with the ongoing lease obligations estimated by the Company, 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 build-out commitments under the lease, the time necessary to sublease the space, the projected sublease rental rates and the terms of any 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 outcome is finalized, and 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 as a result of the passage of time. Any changes to the Company's estimate of the liability are recorded as additional restructuring and other expense.

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 actual amount and timing of the payment of the remaining accrued liability of approximately $55.8 million is dependent upon the terms of any sublease(s) that the Company may ultimately enter.

E. Marketable Securities

A summary of cash equivalents and available-for-sale securities is shown below (in thousands):

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			15,781
Due within 1 to 5 years	47,899			47,461
Total US government securities	63,753	34	545	63,242
Corporate debt securities				
Due within 1 year	169,757			169,289
Due within 1 to 5 years	103,775			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

December 31, 2003	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
Cash and cash equivalents				
Cash and money market funds	$ 87,132			$ 87,132
Municipal bonds	6,406			6,406
Corporate debt securities	4,621			4,621
Total cash and cash equivalents	$ 98,159			$ 98,159
Marketable securities				
Municipal bond securities				
Due within 1 year	$ 2,016	$ —	$ 17	$ 1,999
US government securities				
Due within 1 year	11,250			11,427
Due within 1 to 5 years	70,706			71,199
Total US government securities	81,956	728	58	82,626
Corporate debt securities				
Due within 1 year	176,034			176,593
Due within 1 to 5 years	222,717			223,787
Total corporate debt securities	398,751	1,900	271	400,380
Total marketable securities	$ 482,723	$ 2,628	$ 346	$ 485,005
Total cash, cash equivalents and marketable securities	$ 580,882	$ 2,628	$ 346	$ 583,164

The aggregate fair value of investments in an unrealized loss position for less than a year was approximately $299.5 million at December 31, 2004. The aggregate fair value of investments in an unrealized loss position for greater than a year was approximately $8.1 million at December 31, 2004. The aggregated fair value of investments in an unrealized loss position for less than a year was approximately $119.9 million at December 31, 2003. The Company did not hold any investments with unrealized loss positions greater than a year at December 31, 2003.

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. Investments in an unrealized loss position for greater than a year were comprised of municipal bond securities and corporate debt securities. The unrealized losses were due to fluctuations in interest rates. 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 Company has reviewed those securities with unrealized losses as of December 31, 2004 and 2003 and has concluded that no other-than-temporary impairment existed as of December 31, 2004 and 2003.

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. Gross realized gains and losses for 2002 were $2,281,000 and $233,000, respectively. Maturities stated are effective maturities.

F. Restricted Cash

At December 31, 2004 and 2003, the Company held $49,847,000 and $26,061,000 in restricted cash, respectively. At December 31, 2004 and 2003 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):

	2004	2003
Furniture and equipment	$ 90,893	$ 92,497
Leasehold improvements	65,294	62,412
Computers	18,421	16,289
Software	16,411	15,336
Total property and equipment, gross	191,019	186,534
Less accumulated depreciation and amortization	126,794	106,451
Total property and equipment, net	$ 64,225	$ 80,083

Depreciation expense for the years ended December 31, 2004, 2003 and 2002 was $28,353,000 $27,988,000, and $24,003,000, respectively.

In 2004 and 2003, 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 certain assets that were not fully depreciated. The total expense for those assets was $43,000 for 2004 and $148,000 for 2003.

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, 2004 and December 31, 2003. The Company's cost basis carrying value in its outstanding equity and warrants of Altus was $18,863,000 at December 31, 2004 and 2003, respectively.

I. Accrued Expenses and Other Current Liabilities

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

	2004	2003
Research and development contract costs	$ 14,883	$ 11,098
Payroll and benefits	11,114	8,399
Professional fees	5,658	5,940
Other	1,296	937
	$ 32,951	$ 26,374

J. Capital Leases

There are no capital lease obligations at December 31, 2004. At December 31, 2003, the Company had obligations under capital leases for the short-term only; there were no obligations under long-term capital leases. At December 31, 2003, the Company had capital lease obligations due of $113,000, of which $2,000 represents interest payments, which are included in Other obligations on the consolidated balance sheets.

K. 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. In June 2003, the Company decided not to occupy the space under the Kendall Square Lease and is actively seeking to sublease the space to third parties to minimize its ongoing lease obligations. See Note D, "Restructuring and Other Expense" for further information.

At December 31, 2004, 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	Other Operating Leases	Total Operating Leases
2005	29,941	15,682	45,623
2006	23,999	15,455	39,454
2007	19,061	14,713	33,774
2008	21,422	13,961	35,383
2009	21,490	10,698	32,188
Thereafter	196,168	9,483	205,651
Total minimum lease payments	$ 312,081	$ 79,992	$ 392,073

Rental expense excluding the Kendall Square Lease, primarily related to facilities, was $16,303,000, $15,449,000, and $15,847,000 for the years ended December 31, 2004, 2003, and 2002, respectively.

The Company has future contractual commitments in connection with its research and development programs. For 2005 and 2006 the amount committed under these contracts is $2,115,000 and $750,000, 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. 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.

L. 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 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 2004 Notes") in exchange for an equal principal amount of its 2007 Notes. The terms of the September 2004 Notes are identical to those of the February 2011 Notes (the February 2011 Notes and the September 2004 Notes are referred to together as the "2011 Notes"). The 2011 Notes were issued through private offerings to qualified institutional buyers.

The 2011 Notes are convertible, at the option of the holder, into common stock at a price equal to $14.94, subject to adjustment under certain circumstances. The 2011 Notes bear an interest rate of 5.75% per annum, and the Company is required to make semi-annual interest payments on the outstanding principal balance of the 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 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 balances of the 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 then in effect 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 was $9,297,000. At December 31, 2004, the amount remaining in Other Assets relating to the 2007 Notes was $932,000.

At December 31, 2004, the Company had approximately $82.6 million of the 2007 Notes and approximately $232.4 million of the 2011 Notes outstanding. At December 31, 2004, the 2007 Notes and the 2011 Notes had a fair value of $79.3 million and $231.9 million, respectively, as obtained from a quoted market source. As a result of the exchange transactions, the Company recorded a charge on the retirement of $153.1 million of the 2007 Notes in February 2004 in the amount of $2,453,000, and a charge on the retirement of $79.3 million of the 2007 Notes in September 2004 in the amount of $993,000. These charges represent that portion of the unamortized deferred issuance costs applicable to the amount of 2007 Notes that were retired. The deferred issuance costs associated with the issuance of the 2011 Notes, which are classified as long-term other assets, were $2,970,000 for the February 2011 Notes and $1,879,000 for the September 2011 Notes. For the year ended December 31, 2004, $1,287,000 was amortized to interest expense for the issuance costs of the 2007 Notes and the 2011 Notes. For the years ended December 31, 2003 and 2002, $1,401,000 and $1,401,000, respectively, were amortized to interest expense for the issuance costs associated with the 2007 Notes.

M. Income Taxes

For the years ended December 31, 2004 and 2003, there is no provision for income taxes included in the Consolidated Statement of Operations. For the year ended December 31, 2002, the Company provided approximately $276,000 for income taxes, which was recorded in other expense on the Consolidated Statement of Operations. The provision principally relates to certain foreign obligations. The Company's federal statutory income tax rate for 2004, 2003 and 2002 was 34%. The Company has incurred losses from operations but has not recorded an income tax benefit for 2004, 2003 and 2002 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.

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 deferred taxes at December 31 were as follows (in thousands):

	2004	2003
Deferred Tax Assets:		
Net operating loss	$ 303,332	$ 210,928
Tax credits carryforward	25,987	24,944
Property, plant and equipment	12,135	10,484
Deferred revenue	19,577	—
Capitalized research and development	27,351	53,154
Other	19,348	31,754
Gross deferred tax asset	407,730	331,264
Valuation allowance	(396,672)	(320,206)
Deferred Tax Liabilities:		
Gain on Investment	(11,058)	(11,058)
Net deferred tax asset	$ —	$ —

Of the $396,672,000 net deferred tax asset at December 31, 2004, $103,928,000 relates to deductions for nonqualified stock options, which will be credited to additional paid-in capital, if realized.

For federal income tax purposes, as of December 31, 2004, the Company had net operating loss carryforwards of approximately $804,579,000 and tax credits of $19,160,000 which may be used to offset future income tax liability, respectively. These operating loss carryforwards will expire as follows: $1,329,000 in 2005, $4,462,000 in 2006 and $798,788,000 thereafter. The tax credit carryforwards began expiring in 2004. A valuation allowance has been established for the full amount of the 2004 deferred tax asset since it is more likely than not that the deferred tax asset will not be realized.

Ownership changes, as defined by Internal Revenue Code, may have limited 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, 2004, the Company had approximately 4,554,000 shares of common stock available for future grants under the 1996 Plan.

Consolidated stock option activity for the years ended December 31, 2004, 2003 and 2002 is as follows (shares in thousands):

	2004		2003		2002	
	Shares	Weighted Average Exercise Price	Shares	Weighted Average Exercise Price	Shares	Weighted Average Exercise Price
Outstanding at beginning of year	16,802	$ 23.42	17,065	$ 25.73	16,810	$ 27.37
Granted	1,554	10.35	3,465	14.59	2,952	17.49
Exercised	(732)	7.09	(914)	9.15	(944)	10.43
Canceled	(1,804)	25.37	(2,814)	31.00	(1,753)	36.44
Outstanding at end of year	15,820	$ 22.67	16,802	$ 23.42	17,065	$ 25.73
Options exercisable at year-end	10,695	$ 24.34	10,205	$ 23.08	9,566	$ 22.85
Weighted average fair value of options granted during the year		$ 5.00		$ 9.46		$ 11.60

The fair value of each option granted under the Plans during 2004, 2003 and 2002 was estimated on the date of grant using the Black-Scholes option pricing model with the following weighted average assumptions:

	2004	2003	2002
Expected life (years)	4.00	5.50	5.50
Expected volatility	60.00%	75.00%	75.00%
Risk-free interest rate	2.95%	3.27%	4.18%
Dividend yield	—	—	—

The following table summarizes information about stock options outstanding and exercisable at December 31, 2004 (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–$9.69	1,789	6.29	$ 9.37	986	$ 9.36
9.74–13.11	2,953	6.10	$ 11.86	2,073	$ 12.17
13.15–14.46	1,761	3.65	$ 13.68	1,721	$ 13.69
14.50–15.56	907	2.70	$ 15.47	841	$ 15.51
15.60–15.60	1,713	8.05	$ 15.60	609	$ 15.60
15.66–17.80	1,719	7.34	$ 16.04	809	$ 16.09
17.91–23.06	683	6.03	$ 19.45	500	$ 19.44
23.22–24.66	1,613	6.90	$ 24.65	984	$ 24.65
24.69–70.75	2,492	6.06	$ 57.63	2,000	$ 58.26
71.62–135.49	190	5.67	$ 93.24	172	$ 94.18
$1.22–$135.49	15,820	6.07	$ 22.67	10,695	$ 24.34

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 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. None of those shares were vested at December 31, 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.

In December 2003, the Company issued 124,481 shares of restricted stock with a fair value on the date of grant of $9.07.

The Company has recorded deferred compensation net of cancellations of approximately $12,206,000 and $1,128,000 related to the issuance of restricted shares during the twelve months ended December 31, 2004 and 2003, respectively. The Company recorded compensation expense of approximately $1,661,000 and $16,000 for the twelve months ended December 31, 2004 and 2003, respectively, related to all restricted shares outstanding during those periods. There was no deferred compensation expense in 2002 related to restricted shares.

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. Amortization of deferred compensation expense related to stock options of $20,000 was recognized during 2002. There was no deferred compensation expense related to stock options in 2004 and 2003.

Compensation cost, calculated using a Black-Scholes option pricing model, recognized in connection with the issuance of stock options to nonemployees was $161,826, and $292,000 in 2003 and 2002, respectively. There was no compensation cost recognized in 2004 related to the issuance of stock options to nonemployees.

Employee Stock Purchase Plans

On July 1, 1992, Vertex adopted the Vertex Pharmaceuticals Incorporated Employee Stock Purchase Plan (the "Vertex Purchase Plan"). On May 17, 2002, at the Company's annual meeting, the shareholders approved certain amendments to the Vertex Purchase Plan. One of the amendments reserved an additional 600,000 shares for issuance under the Vertex Purchase Plan. 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. In September 2002, the Vertex Purchase Plan was further amended by the Company's Board of Directors to make certain changes to the administration of the Vertex Purchase Plan. In May 2004, an additional 1,500,000 shares were reserved for issuance under the Vertex Purchase Plan.

In connection with the acquisition of Aurora in July 2001, the Company assumed Aurora's obligations under its Employee Stock Purchase Plan (the "Aurora Purchase Plan"). The Aurora Purchase Plan provided for all eligible employees to purchase the Company's common stock, through payroll withholdings, at a price of 85% of the lesser of fair market value on the start date of each overlapping two-year offering period or on the date on which each semi-annual purchase period ends. The Aurora Purchase Plan was terminated in the second quarter of 2002 following a semi-annual purchase.

During 2004, 2003, and 2002 the following shares were issued to employees under the Vertex Purchase Plan (shares in thousands):

	2004	2003	2002
Number of shares	468	379	220
Average price paid	$ 7.60	$ 9.49	$ 15.85

Had the Company adopted SFAS 123, the weighted average fair value of each purchase right granted during 2004, 2003 and 2002 would have been $5.34, $5.86, and $6.04, 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:

	2004	2003	2002
Expected life (years)	.80	.80	.50
Expected volatility	65.00%	75.00%	75.00%
Risk-free interest rate	1.35%	1.17%	1.53%
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 (the "Purchase Price"). The Rights are not exercisable until the earlier of acquisition by a person or group of 15% or more of the outstanding Common Stock (an "Acquiring Person"), or 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. In the event that any person or group becomes an Acquiring Person, each holder of a Right other than the Acquiring Person will thereafter have the right to receive upon exercise that number of shares of Common Stock having a market value of two times the Purchase Price and, in the event that 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 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. Under certain specified circumstances, 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 in whole at a price of $0.01 per Right.

Common Stock Reserved for Future Issuance

At December 31, 2004, 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	20,374
Common stock under the Vertex Purchase Plan	1,281
Common stock under the Vertex 401(k) Plan	485
Total	22,140

O. Significant Revenue Arrangements

The Company has formed strategic collaborations with pharmaceutical companies in the areas of drug discovery, development, and commercialization. Research and development 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 and Development Agreements

In the Company's collaborative research, development and commercialization programs the Company seeks to discover, develop and commercialize major pharmaceutical products in conjunction with and supported by the Company's collaborators. Collaborative research and development arrangements provide research funding over an initial contract period with renewal and termination options that vary by agreement. The agreements 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 and Novartis Pharma AG ("Novartis") entered into an agreement to collaborate on the discovery, development and commercialization of small molecule drugs directed at targets in the kinase protein family. The agreement was amended in February 2004. Under the original agreement, Novartis agreed to pay the Company an up-front payment of $15,000,000 made upon signing of the agreement, up to $200,000,000 in product research funding over six years and further license fees, milestone payments and cost reimbursements based in part on the progress of drug candidates through development. The Company was responsible for drug discovery and clinical proof-of-concept testing of all drug candidates. Under the agreement, Novartis created a $200,000,000 loan facility to support the Company's early clinical development activities. The agreement provided that the loans would be interest-free and Novartis would forgive the full amount of any advances with respect to a particular drug candidate accepted by Novartis for development under the agreement. In February 2004, the Company amended the terms of the Novartis collaboration agreement. Pursuant to the amended agreement, the Company continues to be responsible for drug discovery and Novartis continues to provide research funding through the balance of the research term ending in April 2006. However, pursuant to the amended agreement, Novartis will now be responsible for all nonclinical and clinical development of drug candidates that it accepts for development, and, consequently, the loan facility providing funding for development activities by Vertex has been terminated. Novartis will pay Vertex a $10 million selection milestone for each drug candidate it selects for development meeting certain pre-agreed criteria, and Vertex may receive up to an additional $25 million per drug candidate in pre-commercial milestones. Vertex will continue to receive royalties on sales of products that are commercialized as part of the collaboration. In November 2004, Novartis selected VX-322, a dual inhibitor of Flt-3 and c-kit kinases, for the treatment of leukemia and potentially other cancers, for preclinical development. In connection with the selection of VX-322, Novartis paid the Company a $10 million milestone of which $4.1 million was recognized as revenue in 2004 and the remainder will be recognized as revenue over the term of the contract. In 2004, 2003, and 2002, the Company recognized approximately $50,497,000, $44,502,000, and $41,894,000, 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, 2004, there was approximately $20.0 million in loans outstanding under the loan facility.

GlaxoSmithKline

In December 1993, the Company and GlaxoSmithKline plc ("GSK") entered into a collaborative agreement to research, develop and commercialize HIV protease inhibitors, including Agenerase (amprenavir), Lexiva/Telzir (fosamprenavir calcium) and VX-385. Under the collaborative agreement, GSK agreed to pay the Company up to $42,000,000, comprised of an up-front $15,000,000 license payment made in 1993, $14,000,000 of product research funding over five years and $13,000,000 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. Vertex is also entitled to royalties on sales of its HIV protease inhibitors by GSK. The Company began earning a royalty from GSK in 1999 on sales of Agenerase, in the fourth quarter of 2003 on sales of Lexiva, and in the fourth quarter of 2004 on sales of Telzir. GSK is also obligated to pay additional development and commercialization milestone payments for subsequent drug candidates, including VX-385.

In the third quarter of 2004, GSK paid the Company a milestone payment of $1,500,000 in connection with the regulatory approval of Telzir in the European Union. In the fourth quarter of 2004, GSK paid the Company a milestone payment of $1,000,000 based on the initiation of Phase II clinical trials for VX-385. In the fourth quarter of 2003, GSK paid the Company a milestone payment of $2,500,000 upon FDA approval of Lexiva in the United States. In the fourth quarter of 2002, GSK paid the Company a milestone payment of $1,500,000 in connection with the submission of a new drug application for marketing approval of Lexiva in the United States and the European Union.

GSK is required to bear the costs of development of drug candidates in its territory under the collaboration. Under the original agreement, GSK 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 GSK's territory for development and commercialization of Lexiva/Telzir. The Company has retained certain bulk drug manufacturing rights and certain co-promotion rights in territories licensed to GSK. GSK has the right to terminate its arrangement with the Company without cause upon twelve months' notice. Termination of the agreement by GSK will relieve it of its obligation to make further commercialization and development milestone and royalty payments and will end any license granted to GSK by Vertex under the agreement. Revenues and royalties earned from GSK were $19,822,000, $11,502,000, and $11,554,000 in 2004, 2003 and 2002, respectively.

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

Cystic Fibrosis Foundation Therapeutics Incorporated (CFFT)

In May 2004, Vertex entered into an agreement with Cystic Fibrosis Foundation Therapeutics Incorporated ("CFFT") that allowed for an expanded collaboration with CFFT to provide 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. Under the expanded collaboration, CFFT agreed to pay up to $21.0 million of contracted research payments through December 31, 2005 and, potentially, a milestone payment upon advancement of the first compound into clinical development. CFFT has the right to terminate the agreement without cause effective June 30, 2005 upon 60 days' prior written notice. For the twelve months ended December 31, 2004, Vertex recognized $6,792,000 in revenue related to this agreement. During the first quarter of 2004, under an earlier agreement, Vertex earned revenue of $1,919,000.

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 currently in Phase I clinical trials. 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 $33.0 million in pre-commercial payments by Mitsubishi to Vertex, including an up-front license fee, development stage milestone payments and contributions to certain drug development costs for VX-950 through Phase II clinical development. The agreement also provides Vertex with royalties on any sales of VX-950 in the Mitsubishi territory. 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. Mitsubishi may terminate the agreement at any time without cause upon 60 days' prior written notice. In the fourth quarter of 2004, Mitsubishi Pharma paid the Company a milestone payment of $4,000,000 for first dosing of VX-950 in a patient in the Phase Ib clinical trial in the United States. Vertex recognized $1,840,000 of additional revenue in 2004 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 payment of $20.0 million, which was made in June 2004, and for research funding of $14.0 million over two years. In addition, Vertex could receive as much as $350.0 million in milestone payments, including up to $130.0 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 after June 30, 2005 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 or at any time when a product has marketing approval in a major market and the termination is not for a valid safety reason. Vertex recognized $8,367,000 of revenue related to this collaboration in 2004.

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 $22,000,000 comprised of a $4,000,000 license payment, $11,000,000 of product research funding over three years and $7,000,000 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 certain compounds 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 and drug supply payments on future product sales, if any. In 2004, 2003 and 2002, approximately $3,451,000, $267,000, and $4,565,000, respectively, was recognized as revenue under the p38 MAP kinase research and development program.

Serono S.A.

In December 2000, the Company and Serono S.A. ("Serono") entered into an agreement to collaborate on the discovery, development, and commercialization of certain types of caspase inhibitors. Serono terminated the agreement in accordance with its terms effective September 30, 2004. The Company has received the full amount of research funding and up-front payments specified under the agreement. In 2004, 2003, and 2002, the Company recognized approximately $5,241,000, $5,280,000, and $5,280,000 as revenue, respectively, from Serono.

The Company in 2002 recognized an aggregate of $21,250,000 in revenue from collaborations with Eli Lilly & Company, Taisho Pharmaceuticals Co., Limited and Schering AG.

In early 2005, Sanofi-Aventis gave notice that it intends to terminate its collaborative agreement with the Company covering the development of pralnacasan, an orally active inhibitor of interleukin-lb converting enzyme. Upon termination of the agreement, all rights to pralnacasan will revert to Vertex.

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 plan, subject to statutory limitations. The Company may declare discretionary matching contributions to the Vertex 401(k) Plan which 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):

	2004	2003	2002
Discretionary matching contributions for the year ended December 31,	$ 2,492	$ 2,237	$ 2,558
Shares issued for the year ended December 31,	239	185	104
Shares issuable as of the year ended December 31,	57	61	65

In connection with the acquisition of Aurora in July 2001, the Company assumed the Aurora 401(k) Retirement Savings Plan and 401(k) Profit Sharing Plan Trust (collectively, the "Aurora Plan") which covered substantially all employees of Aurora and its wholly-owned subsidiaries who had completed certain service requirements. Effective April 1, 2002, the Aurora Plan was merged into the Vertex 401(k) Plan, and all employees eligible to participate in the Aurora Plan were offered eligibility to participate in the Vertex 401(k) Plan. Participants in the Aurora Plan contributed a portion of their compensation to the Aurora Plan through payroll deductions. Company-paid Aurora Plan matching contributions, if any, were determined by the Company at its sole discretion and payable in the form of cash. The Company's cash contributions under the Aurora Plan totaled $77,000 in 2002.

Q. Related Party Transactions

As of December 31, 2004 and 2003, the Company had a loan outstanding to an officer in the amount of $97,000 and $170,000, respectively, which was initially advanced in April 2002. The loan is interest-free and is being forgiven on a pro rata basis over a four-year term ending in the second quarter of 2006.

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.

In April 2001, Aurora entered into an agreement with a customer, which included assay development services, product sales and licenses combined with the purchase of stock in the customer. At the time of the transaction, the Chief Executive Officer of the customer was a director of Aurora. As of July 18, 2001, upon the acquisition of Aurora by Vertex, the Chief Executive Officer of the customer was no longer a director of Aurora. The total investment in the customer was approximately $4,120,000 at December 31, 2002 and represented approximately 10% of the outstanding equity interest in the customer. The stock in the customer was transferred to Invitrogen Corporation in connection with the PanVera Asset Sale on March 28, 2003. The Company believes that the amounts charged to the customer by the Company for services, products and licenses are comparable to what the Company would have charged had it not purchased the stock in the customer and had the former director of Aurora not been affiliated with the customer. The investment was accounted for using the cost method and was included in Investments on the balance sheet at December 31, 2002. Total revenue recognized from this agreement was $3,035,000 in 2002. No revenue was recognized in 2004 or 2003 from this agreement. Revenue recognized from this agreement is included in discontinued operations on the consolidated financial statements.

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 February 23, 2005, the United States District Court for the District of Massachusetts entered judgment in favor of Vertex, pursuant to an order of the trial judge granting Vertex's motion to dismiss a purported class action lawsuit against the Company and certain of its officers and a former employee. In the lawsuit, the plaintiffs had claimed that the defendants made material misrepresentations and/or omissions of material fact regarding VX-745, an investigational agent with potential in the treatment of inflammatory and neurological diseases. The plaintiffs have the right to appeal the court's decision by filing a notice of appeal on or before March 25, 2005.

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. Goldman, Sachs & Co. LLP, a financial advisor to Aurora in the merger transaction, was initially named as a defendant but the lawsuit has now been dismissed as to Goldman, Sachs. 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. The plaintiff seeks certification as a class action, compensatory damages in an unspecified amount and unspecified equitable or injunctive relief. Vertex has certain indemnity obligations to Aurora's directors under the terms of the merger agreement between Vertex and Aurora, which could result in liability to Vertex for attorney's fees and costs in connection with this action, as well as for any ultimate judgment which 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.

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, 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, 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.

T. Quarterly Financial Data (unaudited)

(in thousands, except per share data)

	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 and other 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)
Charge for 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

	Three Months Ended			
	March 31, 2003	June 30, 2003	Sept. 30, 2003	Dec. 31, 2003
Revenues:				
Royalties	$ 1,921	$ 2,020	$ 2,003	$ 3,058
Collaborative and other research and development revenues	14,068	13,932	13,820	18,319
Total revenues	15,989	15,952	15,823	21,377
Costs and expenses:				
Royalty payments	652	668	797	1,009
Research and development	51,629	50,080	49,627	48,300
Sales, general and administrative	9,485	9,687	9,436	10,474
Restructuring and other expense	3,899	44,131	42,394	1,400
Total costs and expenses	65,665	104,566	102,254	61,183
Loss from operations	(49,676)	(88,614)	(86,431)	(39,806)
Interest income	5,768	3,421	3,164	3,059
Interest expense	(4,363)	(4,342)	(4,334)	(4,259)
Loss from continuing operations	(48,271)	(89,535)	(87,601)	(41,006)
Income (loss) from discontinued operations:				
Gain on sales of assets	69,232	—	451	656
Income (loss) from discontinued operations	(350)	(393)	729	(679)
Total income (loss) from discontinued operations	68,882	(393)	1,180	(23)
Net income (loss)	$ 20,611	$ (89,928)	$ (86,421)	$ (41,029)
Basic and diluted net income (loss) per common share	$ 0.27	$ (1.17)	$ (1.12)	$ (0.53)
Basic weighted average number of common shares outstanding	76,411	76,764	77,067	77,758
Diluted weighted average number of common shares outstanding	77,362	76,764	77,067	77,758

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Exhibit 10.3

VERTEX PHARMACEUTICALS INCORPORATED

1996 STOCK and OPTION PLAN

(as amended on March 14, 2005, and restated)

1. DEFINITIONS

Unless otherwise specified or unless the context otherwise requires, the following terms, as used in this Vertex Pharmaceuticals Incorporated 1996 Stock and Option Plan, have the following meanings:

Affiliate means a corporation which, for purposes of Section 424 of the Code, is a parent or subsidiary of the Company, direct or indirect.

Board of Directors means the Board of Directors of the Company.

Code means the United States Internal Revenue Code of 1986, as amended.

Committee means the Compensation Committee of the Board of Directors or any successor thereto appointed by the Board of Directors pursuant to Section 4 hereof to administer this Plan.

Common Stock means shares of the Company's common stock, $.01 par value.

Company means Vertex Pharmaceuticals Incorporated, a Massachusetts corporation.

Disability or **Disabled** means permanent and total disability as defined in Section 22(e)(3) of the Code.

Exchange Act means the Securities Exchange Act of 1934, as amended.

Fair Market Value of a Share of Common Stock on a particular date shall be the mean between the highest and lowest quoted selling prices on such date (the "valuation date") on the securities market where the Common Stock of the Company is traded, or if there were no sales on the valuation date, on the next preceding date within a reasonable period (as determined in the sole discretion of the Committee) on which there were sales. In the event that there were no sales in such a market within a reasonable period, the fair market value shall be as determined in good faith by the Committee in its sole discretion. The Fair Market Value as determined in this paragraph rounded down to the next lower whole cent if the foregoing calculation results in fractional cents.

ISO means an option intended to qualify as an incentive stock option under Code Section 422(b).

Key Employee means an employee of the Company or of an Affiliate (including, without limitation, an employee who is also serving as an officer or director of the Company or of an Affiliate), designated by the Committee to be eligible to be granted one or more Stock Rights under the Plan.

NQSO means an option which is not intended to qualify as an ISO.

Non-Employee Director means a member of the Board of Directors who is not an employee of the Company or any Affiliate.

Option means an ISO or NQSO granted under the Plan.

Participant means a Key Employee, Non-Employee Director, consultant or advisor of the Company to whom one or more Stock Rights are granted under the Plan. As used herein, "Participant" shall include "Participant's Survivors" and a Participant' s permitted transferees where the context requires.

Participant's Survivors means a deceased Participant's legal representatives and/or any person or persons who acquires the Participant's rights to a Stock Right by will or by the laws of descent or distribution.

Plan means this Vertex Pharmaceuticals Incorporated 1996 Stock and Option Plan, as amended from time to time.

Shares means shares of the Common Stock as to which Stock Rights have been or may be granted under the Plan or any shares of capital stock into which the Shares are changed or for which they are exchanged within the provisions of Section 3 of the Plan. The Shares issued upon exercise of Stock Rights granted under the Plan may be authorized and unissued shares or shares held by the Company in its treasury, or both.

Stock Agreement means an agreement between the Company and a Participant executed and delivered pursuant to the Plan, in such form as the Committee shall approve.

Stock Award means an award of Shares or the opportunity to make a direct purchase of Shares of the Company granted under the Plan.

Stock Right means a right to Shares of the Company granted pursuant to the Plan as an ISO, an NQSO or a Stock Award.

2. PURPOSES OF THE PLAN

The Plan is intended to encourage ownership of Shares by Key Employees, Non-Employee Directors and certain consultants and advisors to the Company in order to attract such persons, to induce them to work for the benefit of the Company or of an Affiliate and to provide additional incentive for them to promote the success of the Company or of an Affiliate. The Plan provides for the granting of Stock Rights to Key Employees, Non-Employee Directors, consultants and advisors of the Company.

3. SHARES SUBJECT TO THE PLAN

The number of Shares subject to this Plan as to which Stock Rights may be granted from time to time shall be 22,000,000 plus the number of shares of Common Stock previously reserved for the granting of options under the Vertex Pharmaceuticals Incorporated 1991 Stock Option Plan and 1994 Stock and Option Plan but not granted thereunder, or the equivalent of such number of Shares after the Committee, in its sole discretion, has interpreted the effect of any stock split, stock dividend, combination, recapitalization or similar transaction in accordance with Section 17 of this Plan.

If an Option granted hereunder or any option granted under the 1991 Stock Option Plan or 1994 Stock and Option Plan ceases to be "outstanding", in whole or in part, or if the Company shall reacquire any Shares issued pursuant to Stock Awards, the Shares which were subject to such Option and any Shares so reacquired by the Company shall also be available for the granting of other Stock Rights under the Plan. Any Stock Right shall be treated as "outstanding" until such Stock Right is exercised in full, or terminates or expires under the provisions of the Plan, or by agreement of the parties to the pertinent Stock Agreement, without having been exercised in full.

4. ADMINISTRATION OF THE PLAN

The Plan shall be administered by the Committee. Subject to the provisions of the Plan, the Committee is authorized to:

a. Interpret the provisions of the Plan or of any Option, Stock Award or Stock Agreement and to make all rules and determinations which it deems necessary or advisable for the administration of the Plan;

b. Determine which employees of the Company or of an Affiliate shall be designated as Key Employees and which of the Key Employees, Non-Employee Directors, consultants and advisors of the Company and its Affiliates shall be granted Stock Rights;

c. Determine the number of Shares and exercise price for which a Stock Right or Stock Rights shall be granted;

d. Specify the terms and conditions upon which a Stock Right or Stock Rights may be granted; and

e. In its discretion, accelerate the date of exercise of any installment of any Option; provided that the Committee shall not, without the consent of the Option holder accelerate the exercise date of any installment of any Option granted to any Key Employee as an ISO (and not previously converted into an NQSO pursuant to Section 20) if such acceleration would violate the annual vesting limitation contained in Section 422(d) of the Code, as described in Section 6.2.3.

provided, however, that all such interpretations, rules, determinations, terms and conditions shall be made and prescribed in the context of preserving the tax status under Code Section 422 of those Options which are designated as ISOs and shall be in compliance with any applicable provisions of Rule 16b-3 under the Exchange Act. Subject to the foregoing, the interpretation and construction by the Committee of any provisions of the Plan or of any Stock Right granted under it shall be final, unless otherwise determined by the Board of Directors, if the Committee is other than the Board of Directors.

The Committee may employ attorneys, consultants, accountants or other persons, and the Committee, the Company and its officers and directors shall be entitled to rely upon the advice, opinions or valuations of such persons. All actions taken and all interpretations and determinations made by the Committee in good faith shall be final and binding upon the Company, all Participants, and all other interested persons. No member or agent of the Committee shall be personally liable for any action, determination, or interpretation made in good faith with respect to this Plan or grants hereunder. Each member of the Committee shall be indemnified and held harmless by the Company against any cost or expense (including counsel fees) reasonably incurred by him or liability (including any sum paid in settlement of a claim with the approval of the Company) arising out of any act or omission to act in connection with this Plan unless arising out of such member's own fraud or bad faith. Such indemnification shall be in addition to any rights of indemnification the members of the Committee may have as directors or otherwise under the by-laws of the Company, or any agreement, vote of stockholders or disinterested directors, or otherwise.

5. ELIGIBILITY FOR PARTICIPATION

The Committee shall, in its sole discretion, name the Participants in the Plan, provided, however, that each Participant must be a Key Employee, Non-Employee Director, consultant or advisor of the Company or of an Affiliate at the time a Stock Right is granted. Notwithstanding the foregoing, the Committee may

authorize the grant of a Stock Right to a person not then an employee, Non-Employee Director, consultant or advisor of the Company or of an Affiliate; *provided*, *however*, that the actual grant of such Stock Right shall be conditioned upon such person becoming eligible to become a Participant at or prior to the time of execution of the Stock Agreement evidencing such Stock Right. The granting of any Stock Right to any individual shall neither entitle that individual to, nor disqualify him or her from, participation in other grants of Stock Rights. Nothwithstanding anything to the contrary contained in this Plan, no Stock Rights shall be granted to any director or officer of the Company except in accordance with the applicable rules of the Nasdaq Stock Market or other securities market where the Common Stock is traded.

6. TERMS AND CONDITIONS OF OPTIONS

6.1 *General.* Each Option shall be set forth in writing in a Stock Agreement, duly executed by the Company and, to the extent required by law or requested by the Company, by the Participant. The Committee may provide that Options be granted subject to such conditions as the Committee may deem appropriate including, without limitation, subsequent approval by the shareholders of the Company of this Plan or any amendments thereto, *provided*, *however*, that the option price per share of the Shares covered by each Option shall not be less than the Fair Market Value per share of the Common Stock on the date of grant (or par value if greater). Each Stock Agreement shall state the number of Shares to which it pertains, the date or dates on which it first is exercisable and the date after which it may no longer be exercised. Option rights may accrue or become exercisable in installments over a period of time, or upon the achievement of certain conditions or the attainment of stated goals or events. Exercise of any Option may be conditioned upon the Participant's execution of a Share purchase agreement in form satisfactory to the Committee providing for certain protections for the Company and its other shareholders, including requirements that the Participant's or the Participant's Survivors' right to sell or transfer the Shares may be restricted, and the Participant or the Participant's Survivors may be required to execute letters of investment intent and to acknowledge that the Shares will bear legends noting any applicable restrictions.

6.2 *ISOs.* ISOs shall be issued only to Key Employees. In addition to the minimum standards set forth in Section 6.1, ISOs shall be subject to the following terms and conditions, with such additional restrictions or changes as the Committee determines are appropriate but not in conflict with Code Section 422 and relevant regulations and rulings of the Internal Revenue Service:

6.2.1 *ISO Option Price:* The Option price per Share of the Shares subject to an ISO shall not be less than one hundred percent (100%) of the Fair Market Value per share of the Common Stock on the date of grant of the ISO; provided, however that the Option price per share of the Shares subject to an ISO granted to a Participant who owns, directly or by reason of the applicable attribution rules in Code Section 424(d), more than ten percent (10%) of the total combined voting power of all classes of share capital of the Company or an Affiliate, shall not be less than one hundred ten percent (110%) of the said Fair Market Value on the date of grant.

6.2.2 *Term of ISO:* Each ISO shall expire not more than ten (10) years from the date of grant; provided, however, that an ISO granted to a Participant who owns, directly or by reason of the applicable attribution rules in Code Section 424(d), more than ten percent (10%) of the total combined voting power of all classes of share capital of the Company or an Affiliate, shall expire not more than five (5) years from the date of grant.

6.2.3 *Limitation on Grant of ISOs:* No ISOs shall be granted after December 12, 2006, the date which is ten (10) years from the earlier of the date of the adoption of this Plan and the date of the approval of the Plan by the shareholders of the Company.

6.3 *Non-Employee Directors' Options.* Each Non-Employee Director, upon first being elected or appointed to the Board of Directors, shall be granted an NQSO to purchase 20,000 Shares. Each such Option shall (i) have an exercise price equal to the Fair Market Value (per share) on the date of grant of the Option, (ii) have a term of ten (10) years, and (ii) shall become cumulatively exercisable in sixteen (16) equal quarterly installments, upon completion of each full quarter of service on the Board of Directors after the date of grant. In addition, on June 1 of each year, each Non-Employee Director shall be granted a NQSO to purchase 10,000 shares. Each such Option shall (i) have an exercise price equal to the Fair Market Value (per share) on the date of grant of such Option, (ii) have a term of ten (10) years, and (iii) be exercisable in full immediately on the date of grant. Any director entitled to receive an Option grant under this Section may elect to decline the Option. Notwithstanding the provisions of Section 24 concerning amendment of the Plan, the provisions of this Subsection shall not be amended more than once every six months, other than to comport with changes in the Code, the Employee Retirement Income Security Act, or the rules thereunder. Notwithstanding anything to the contrary contained in any other provisions of this Plan, the Committee shall have no discretion to vary the terms of Options granted under this Section 6.3 from those set forth herein. The provisions of Sections 11, 13 and 14 below shall not apply to Options granted pursuant to this Subsection.

6.4 *Limitation on Number of Options Granted.* Notwithstanding anything in this Plan to the contrary, no Participant shall be granted Options in any calendar year for the purchase of more than 400,000 Shares (subject to adjustment pursuant to Section 17 to the extent consistent with Section 162(m) of the Code).

7. TERMS AND CONDITIONS OF STOCK AWARDS

Each Stock Award shall be set forth in a Stock Agreement, duly executed by the Company and, to the extent required by law or requested by the Company, by the Participant. The Stock Agreement shall be in the form approved by the Committee, with such changes and modifications to such form as the Committee, in its discretion, shall approve with respect to any particular Participant or Participants. The Stock Agreement shall contain terms and conditions which the Committee determines to be appropriate and in the best interest of the Company; provided, however, that the purchase price per share of the Shares covered by each Stock Award shall not be less than the par value per Share. Each Stock Agreement shall state the number of Shares to which the Stock Award pertains, the date prior to which the Stock Award must be exercised by the Participant, and the terms of any right of the Company to reacquire the Shares subject to the Stock Award, including the time and events upon which such rights shall accrue and the purchase price therefor, and any restrictions on the transferability of such Shares. All Stock Awards shall be subject to restrictions on transfer and a right of repurchase by the Company and shall vest over a period of not less than three years from the date of grant, or upon the later of one year after the date of grant or the achievement of such performance objectives as shall be approved by the Committee when granting the Stock Award. The Committee, in its discretion, may accelerate the vesting of Stock Awards in the event of (a) death or disability of the Participant, or (b) in connection with an Acquisition as defined in Section 17.2.

8. EXERCISE OF STOCK RIGHTS AND ISSUANCE OF SHARES

A Stock Right (or any part or installment thereof) shall be exercised by giving written notice to the Company, together with provision for payment of the full purchase price in accordance with this Section for the Shares as to which such Stock Right is being exercised, and upon compliance with any other condition(s) set forth in the Stock Agreement. Such written notice shall be signed by the person exercising the Stock Right, shall state the number of Shares with respect to which the Stock Right is being exercised and shall contain any representation required by the Plan or the Stock Agreement.

Payment of the purchase price for the Shares as to which such Stock Right is being exercised shall be made (a) in United States dollars in cash or by check acceptable to the Committee, or (b) at the discretion of the Committee, (i) through delivery of shares of Common Stock (which, in the case of shares acquired from the Company, have been held by the Participant for at least six (6) months) not subject to any restriction under any plan and having a fair market value equal as of the date of exercise to the cash exercise price of the Stock Right, determined in good faith by the Committee, or (ii) in accordance with a cashless exercise program established with a securities brokerage firm, and approved by the Company, or (iii) by any other means (excluding, however, delivery of a promissory note of the Participant) which the Committee determines to be consistent with the purpose of this Plan and applicable law, or (iv) by any combination of the foregoing. Notwithstanding the foregoing, the Committee shall accept only such payment on exercise of an ISO as is permitted by Section 422 of the Code.

The Company shall then as soon as is reasonably practicable deliver the Shares as to which such Stock Right was exercised to the Participant (or to the Participant's Survivors, as the case may be). It is expressly understood that the delivery of the Shares may be delayed by the Company in order to comply with any law or regulation which requires the Company to take any action with respect to the Shares prior to their issuance. The Shares shall, upon delivery, be fully paid, non-assessable Shares.

9. RIGHTS AS A SHAREHOLDER

No Participant to whom a Stock Right has been granted shall have rights as a shareholder with respect to any Shares covered by such Stock Right, except after due exercise thereof and tender of the full purchase price for the Shares being purchased pursuant to such exercise and registration of the Shares in the Company's share register in the name of the Participant.

10. ASSIGNABILITY AND TRANSFERABILITY OF STOCK RIGHTS

ISOs and, except as otherwise provided by the Committee, NQSOs and Stock Awards shall not be transferable by the Participant other than by will or by the laws of descent and distribution or pursuant to a qualified domestic relations order as defined by the Code or Title I of the Employee Retirement Income Security Act or the rules thereunder, provided, however, that the designation of a beneficiary of a Stock Right by a Participant shall not be deemed a transfer prohibited by this Section. Except as provided in the preceding sentence or as otherwise permitted under an NQSO or Stock Award Stock Agreement, a Stock Right shall be exercisable, during the Participant's lifetime, only by such Participant (or by his or her legal representative) and shall not be assigned, pledged or hypothecated in any way (whether by operation of law or otherwise) and shall not be subject to execution, attachment or similar process. Any attempted transfer, assignment, pledge, hypothecation or other disposition of any Stock Right or of any rights granted

thereunder contrary to the provisions of this Plan, or the levy of any attachment or similar process upon a Stock Right, shall be null and void.

11. EFFECT OF TERMINATION OF SERVICE

11.1 Except as otherwise provided in the pertinent Stock Agreement or as otherwise provided in Sections 12, 13 or 14, if a Participant ceases to be an employee, director, consultant or advisor with the Company and its Affiliates (for any reason other than termination "for cause", Disability, or death) (a "Termination of Service") before the Participant has exercised all Stock Rights, the Participant may exercise any Stock Right granted to him or her to the extent that the Stock Right is exercisable on the date of such Termination of Service, but only within the originally prescribed term of the Stock Right.

11.2 The provisions of this Section, and not the provisions of Section 13 or 14, shall apply to a Participant who subsequently becomes disabled or dies after the Termination of Service; provided, however, that in the case of a Participant's death within three (3) months after the Termination of Service, the Participant's Survivors may exercise the Stock Right within one (1) year after the date of the Participant's death, but in no event after the date of expiration of the term of the Stock Right.

11.3 Notwithstanding anything herein to the contrary, if subsequent to a Participant's Termination of Service, but prior to the exercise of a Stock Right, the Committee determines that, either prior or subsequent to the Participant's Termination of Service, the Participant engaged in conduct which would constitute "cause" (as defined in Section 12), then such Participant shall forthwith cease to have any right to exercise any Stock Right.

11.4 Absence from work with the Company or an Affiliate because of temporary disability or a leave of absence for any purpose, shall not, during the period of any such absence in accordance with Company policies, be deemed, by virtue of such absence alone, a Termination of Service, except as the Committee may otherwise expressly provide.

11.5 A change of employment or other service within or among the Company and its Affiliates shall not be deemed a Termination of Service, so long as the Participant continues to be an employee, director, consultant or advisor of the Company or any Affiliate.

12. EFFECT OF TERMINATION OF SERVICE FOR "CAUSE"

Except as otherwise provided in the pertinent Stock Agreement, in the event of a Termination of Service of a Participant "for cause" all outstanding and unexercised Stock Rights as of the date the Participant is notified his or her service is terminated "for cause" will immediately be forfeited. For purposes of this Section 12, "cause" shall include (and is not limited to) dishonesty with respect to the Company and its Affiliates, insubordination, substantial malfeasance or non-feasance of duty, unauthorized disclosure of confidential information, conduct substantially prejudicial to the business of the Company or any Affiliate, and termination by the Participant in violation of an agreement by the Participant to remain in the employ of the Company of an Affiliate. The determination of the Committee as to the existence of cause will be conclusive on the Participant and the Company. "Cause" is not limited to events which have occurred prior to a Participant's Termination of Service, nor is it necessary that the Committee's finding of "cause" occur prior to termination. If the Committee determines, subsequent to a Participant's Termination of Service but prior to the exercise of a Stock Right, that either prior or

subsequent to the Participant's termination the Participant engaged in conduct which would constitute "cause," then the right to exercise any Stock Right shall be forfeited. Any definition in an agreement between a Participant and the Company or an Affiliate which contains a conflicting definition of "cause" for termination and which is in effect at the time of such termination shall supersede the definition in this Plan with respect to that Participant.

13. EFFECT OF TERMINATION OF SERVICE FOR DISABILITY

Except as otherwise provided in the pertinent Stock Agreement, in the event of a termination of service with the Company and its Affiliates by reason of Disability, the Disabled Participant may exercise any Stock Right granted to him or her to the extent exercisable but not exercised on the date of Disability. A Disabled Participant may exercise such rights only within a period of not more than one (1) year after the date that the Participant became Disabled or, if earlier, within the originally prescribed term of the Stock Right.

The Committee shall make the determination both of whether Disability has occurred and of the date of its occurrence (unless a procedure for such determination is set forth in another agreement between the Company and such Participant, in which case such procedure shall be used for such determination). If requested, the Participant shall be examined by a physician selected or approved by the Committee, the cost of which examination shall be paid for by the Company.

14. EFFECT OF DEATH WHILE AN EMPLOYEE, DIRECTOR OR CONSULTANT

Except as otherwise provided in the pertinent Stock Agreement, in the event of death of a Participant while the Participant is an employee, director, consultant or advisor of the Company or of an Affiliate, any Stock Rights granted to such Participant may be exercised by the Participant's Survivors to the extent exercisable but not exercised on the date of death. Any such Stock Right must be exercised within one (1) year after the date of death of the Participant but in no event after the date of expiration of the term of the Stock Right.

15. PURCHASE FOR INVESTMENT

Unless the offering and sale of the Shares to be issued upon the particular exercise of an Stock Right shall have been effectively registered under the Securities Act of 1933, as now in force or hereafter amended (the "1933 Act"), the Company shall be under no obligation to issue the Shares covered by such exercise unless and until the following conditions have been fulfilled:

a. The person(s) who exercise such Stock Right shall warrant to the Company, at the time of such exercise or receipt, as the case may be, that such person(s) are acquiring such Shares for their own respective accounts, for investment, and not with a view to, or for sale in connection with, the distribution of any such Shares, in which event the person(s) acquiring such Shares shall be bound by the provisions of the following legend which shall be endorsed upon the certificate(s) evidencing their Shares issued pursuant to such exercise or such grant:

> "The shares represented by this certificate have been taken for investment and they may not be sold or otherwise transferred by any person, including a pledgee, unless (1) either (a) a Registration Statement with respect to such shares shall be effective under the Securities Act of 1933, as amended, or (b) the Company shall have received an opinion of counsel

satisfactory to it that an exemption from registration under such Act is then available, and (2) there shall have been compliance with all applicable state securities laws.

b. The Company shall have received an opinion of its counsel that the Shares may be issued upon such particular exercise in compliance with the 1933 Act without registration thereunder.

The Company may delay issuance of the Shares until completion of any action or obtaining of any consent which the Company deems necessary under any applicable law (including, without limitation, state securities or "blue sky" laws).

16. DISSOLUTION OR LIQUIDATION OF THE COMPANY

Upon the dissolution or liquidation of the Company (other than in connection with a transaction subject to the provisions of Section 17.2), all Stock Rights granted under this Plan which as of such date shall not have been exercised will terminate and become null and void; provided, however, that if the rights of a Participant have not otherwise terminated and expired, the Participant will have the right immediately prior to such dissolution or liquidation to exercise any Stock Right to the extent that such Stock Right is exercisable as of the date immediately prior to such dissolution or liquidation.

17. ADJUSTMENTS

Upon the occurrence of any of the following events, a Participant's rights with respect to any Stock Right granted to him or her hereunder which have not previously been exercised in full shall be adjusted as hereinafter provided, unless otherwise specifically provided in the written agreement between the Participant and the Company relating to such Stock Right or in any employment agreement between a Participant and the Company or an Affiliate:

17.1 *Stock Dividends and Stock Splits.* If the shares of Common Stock shall be subdivided or combined into a greater or smaller number of shares or if the Company shall issue any shares of Common Stock as a stock dividend on its outstanding Common Stock, the number of shares of Common Stock deliverable upon the exercise of such Stock Right shall be appropriately increased or decreased, and appropriate adjustments shall be made in the purchase price per share to reflect such subdivision, combination or stock dividend.

17.2 *Consolidations or Mergers.* In the event of a consolidation or merger in which the Company is not the surviving corporation or which results in the acquisition of substantially all the Company's outstanding stock by a single person or entity or by a group of persons and/or entities acting in concert, or in the event of the sale or transfer of substantially all the Company's assets (any of the foregoing, an "Acquisition"), all then outstanding Options shall terminate unless assumed pursuant to clause (i) below; provided, that either (i) the Committee shall provide for the surviving or acquiring entity or an affiliate thereof to assume the outstanding Options or grant replacement options in lieu thereof, any such replacement to be upon an equitable basis as determined by the Committee, or (ii) if there is no such assumption or substitution, all outstanding Options shall become immediately and fully exercisable immediately prior to the Acquisition, notwithstanding any restrictions or vesting conditions set forth therein.

17.3 *Recapitalization or Reorganization.* In the event of a recapitalization or reorganization of the Company (other than a transaction described in Section 17.2 above) pursuant to which securities

of the Company or of another corporation are issued with respect to the outstanding shares of Common Stock, a Participant upon exercising a Stock Right shall be entitled to receive for the purchase price paid upon such exercise the securities he or she would have received if he or she had exercised such Stock Right prior to such recapitalization or reorganization.

17.4 *Modification of ISOs.* Notwithstanding the foregoing, any adjustments made pursuant to Section 17.1, 17.2 or 17.3 with respect to ISOs shall be made only after the Committee determines whether such adjustments would constitute a "modification" of such ISOs (as that term is defined in Section 424(h) of the Code) or would cause any adverse tax consequences for the holders of such ISOs. If the Committee determines that such adjustments made with respect to ISOs would constitute a modification of such ISOs, it may refrain from making such adjustments, unless the holder of an ISO specifically requests in writing that such adjustment be made and such writing indicates that the holder has full knowledge of the consequences of such "modification" on his or her income tax treatment with respect to the ISO.

18. ISSUANCES OF SECURITIES

Except as expressly provided herein, no issuance (including for this purpose the delivery of shares held in treasury) by the Company of shares of stock of any class, or securities convertible into shares of stock of any class, shall affect, and no adjustment by reason thereof shall be made with respect to, the number or price of Shares subject to Options. Except as expressly provided herein, no adjustments shall be made for dividends paid in cash or in property (including without limitation, securities) of the Company.

19. FRACTIONAL SHARES

No fractional share shall be issued under the Plan and the person exercising any Stock Right shall receive from the Company cash in lieu of any such fractional share equal to the Fair Market Value thereof determined in good faith by the Board of Directors.

20. CONVERSION OF ISOs INTO NON-QUALIFIED OPTIONS: TERMINATION OF ISOs

Any Options granted under this Plan which do not meet the requirements of the Code for ISOs shall automatically be deemed to be NQSOs without further action on the part of the Committee. The Committee, at the written request of any Participant, may in its discretion take such actions as may be necessary to convert such Participant's ISOs (or any portion thereof) that have not been exercised on the date of conversion into NQSOs at any time prior to the expiration of such ISOs, regardless of whether the Participant is an employee of the Company or an Affiliate at the time of such conversion. Such actions may include, but not be limited to, extending the exercise period or reducing the exercise price of the appropriate installments of such Options. At the time of such conversion, the Committee (with the consent of the Participant) may impose such conditions on the exercise of the resulting NQSOs as the Committee in its discretion may determine, provided that such conditions shall not be inconsistent with this Plan. Nothing in the Plan shall be deemed to give any Participant the right to have such Participant's ISOs converted into NQSOs, and no such conversion shall occur until and unless the Committee takes appropriate action. The Committee, with the consent of the Participant, may also terminate any portion of any ISO that has not been exercised at the time of such termination.

21. WITHHOLDING

In the event that any federal, state, or local income taxes, employment taxes, Federal Insurance Contributions Act ("FICA") withholdings or other amounts are required by applicable law or governmental regulation to be withheld from the Participant's salary, wages or other remuneration in connection with the exercise of a Stock Right or a Disqualifying Disposition (as defined in Section 22), the Participant shall advance in cash to the Company, or to any Affiliate of the Company which employs or employed the Participant, the amount of such withholdings unless a different withholding arrangement, including the use of shares of the Company's Common Stock, is authorized by the Committee (and permitted by law), provided, however, that with respect to persons subject to Section 16 of the Exchange Act, any such withholding arrangement shall be in compliance with any applicable provisions of Rule 16b-3 promulgated under Section 16 of the Exchange Act. For purposes hereof, the Fair Market Value of any shares withheld for purposes of payroll withholding shall be determined in the manner provided in Section 1 above, as of the most recent practicable date prior to the date of exercise. If the Fair Market Value of the shares withheld is less than the amount of payroll withholdings required, the Participant my be required to advance the difference in cash to the Company or the Affiliate employer. The Committee in its discretion may condition the exercise of an Option for less than the then Fair Market Value on the Participant's payment of such additional withholding. In no event shall shares be withheld from any award in satisfaction of tax withholding requirements in an amount that exceeds the minimum tax withholding requirements of law.

22. NOTICE TO COMPANY OF DISQUALIFYING DISPOSITION

Each Key Employee who receives an ISO must agree to notify the Company in writing immediately after the Key Employee makes a "Disqualifying Disposition" of any Shares acquired pursuant to the exercise of an ISO. A Disqualifying Disposition is any disposition (as defined in Section 424(c) of the Code) of such shares before the later of (a) two years from the date the Key Employee was granted the ISO, or (b) one year after the date the Key Employee acquired Shares by exercising the ISO. If the Key Employee has died before such Shares are sold, the notice provisions of this Section 22 shall not apply.

23. EFFECTIVE DATE; TERMINATION OF THE PLAN

The Plan shall be effective on December 12, 1996, the date of its approval by the Board of Directors. The Plan will terminate on December 12, 2006. The Plan may be terminated at an earlier date by vote of the Board of Directors; provided, however, that any such earlier termination will not affect any Stock Rights granted or Stock Agreements executed prior to the effective date of such termination.

24. AMENDMENT OF THE PLAN; AMENDMENT OF STOCK RIGHTS

The Plan may be amended by the stockholders of the Company. The Plan may also be amended by the Board of Directors or the Committee, including, without limitation, to the extent necessary to qualify any or all outstanding Stock Rights granted under the Plan or Stock Rights to be granted under the Plan for favorable federal income tax treatment (including deferral of taxation upon exercise) as may be afforded incentive stock options under Section 422 of the Code, to the extent necessary to ensure that Stock Rights granted or to be granted under the Plan are in accordance with Rule 16b-3 under the Exchange Act, and to the extent necessary to qualify the shares issuable upon exercise of any outstanding Stock Rights granted, or Stock Rights to be granted, under the Plan for listing on any national securities exchange or quotation in

any national automated quotation system of securities dealers. No modification or amendment of the Plan shall adversely affect a Participant's rights under a Stock Right previously granted to the Participant without such Participant's consent.

In its discretion, the Committee may amend any term or condition of any outstanding Stock Right, *provided*, (i) such term or condition as amended is permitted by the Plan, (ii) if the amendment is adverse to the Participant, such amendment shall be made only with the consent of the Participant, (iii) any such amendment of any ISO shall be made only after the Committee determines whether such amendment would constitute a "modification" of any Stock Right which is an ISO (as that term is defined in Section 424(h) of the Code) or would cause any adverse tax consequences for the holder of such ISO, and (iv) with respect to any Stock Right held by any Participant who is subject to the provisions of Section 16(a) of the Exchange Act, any such amendment shall be made only after the Committee determines whether such amendment would constitute the grant of a new Stock Right. Notwithstanding the foregoing, the Committee may not reprice any Options, either directly through a reduction of the exercise price or indirectly by cancellation of outstanding Options in return for an immediate grant of Options with a lower exercise price.

25. EMPLOYMENT OR OTHER RELATIONSHIP

Nothing in this Plan or any Stock Agreement shall be deemed to prevent the Company or an Affiliate from terminating the employment, consultancy or director status of a Participant, nor to prevent a Participant from terminating his or her own employment, consultancy or director status or to give any Participant a right to be retained in employment or other service by the Company or any Affiliate for any period of time.

26. GOVERNING LAW

This Plan shall be construed and enforced in accordance with the law of The Commonwealth of Massachusetts.

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Exhibit 10.18

Salary Amendments to Employment Arrangements with Named Executive Officers

Named Executive Officer	2005 Annual Base Salary Rate Effective February 7, 2005
Dr. Joshua Boger	$547,319
Dr. Vicki Sato	$459,747
Dr. N. Anthony Coles	$383,352
Dr. Peter Mueller	$406,952
Mr. Ian Smith	$360,003

QuickLinks

Salary Amendments to Employment Arrangements with Named Executive Officers

QuickLinks -- Click here to rapidly navigate through this document

Exhibit 10.44

VERTEX PHARMACEUTICALS INCORPORATED
SUMMARY OF NON-EMPLOYEE DIRECTOR COMPENSATION POLICY

Effective as of March 14, 2005, the annual cash compensation for non-employee directors serving on the Board of Directors includes an annual retainer of $25,000, payable in quarterly installments, plus $2,500 for each Board meeting attended and $500 for each committee meeting attended on a regular Board meeting day. If a committeee meeting is held on a day other than a regular Board meeting day, the meeting fee is $1,000. Meetings held by conference call are compensated at the rate of $375 per meeting. The Chair of the Corporate Governance and Nominating Committee receives a $20,000 annual retainer. The Chair of the Audit Committee receives a $15,000 annual retainer. The Chair of the Management Development and Compensation Committee receives a $10,000 annual retainer.

Under the 1996 Stock and Option Plan, each non-employee director, upon initial election or appointment to the Board, receives a non-qualified option to purchase 20,000 shares of Common Stock at an exercise price equal to the Common Stock's then fair market value. Those options vest quarterly over a four-year period from the date of grant, based on continued service on the Board. Each non-employee director in office on June 1 of any year also receives a non-qualified option to purchase 10,000 shares of Common Stock under the 1996 Stock and Option Plan, exercisable immediately at a price equal to the fair market value per share of the Company's Common Stock on the date of grant.

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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

*** VSD Sub II LLC, a Delaware limited liability company

Vertex Holdings, Inc., a Delaware corporation

** Vertex Pharmaceuticals (Europe) Ltd., a U.K. limited liability company

** Vertex Securities Trust, a Massachusetts Business Trust

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* a subsidiary of Vertex Pharmaceuticals (San Diego) LLC

** indirect subsidiaries of Vertex Pharmaceuticals Incorporated

*** a subsidiary of VSD Sub I LLC

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Exhibit 23.1

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 on Form S-3 (Nos. 333-37794, 333-49844, 333-116376 and 333-120055) of Vertex Pharmaceuticals Incorporated of our report dated March 15, 2005 relating to the consolidated financial statements, management's assessment of the effectiveness of internal control over financial reporting and the effectiveness of internal control over financial reporting, which appears in this Form 10-K.

PricewaterhouseCoopers LLP
Boston, Massachusetts
March 15, 2005

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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, 2005

/s/ Joshua S. Boger

Joshua S. Boger
Chairman and Chief Executive Officer

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CERTIFICATION

Exhibit 31.2

CERTIFICATION

I, Ian F. Smith, certify that:

1. I have reviewed this annual report on Form 10-K of Vertex Pharmaceuticals Incorporated;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f) for the registrant and have:

   (a) designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   (c) evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (d) disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 16, 2005

/s/ Ian F. Smith

Ian F. Smith
Chief Financial Officer

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CERTIFICATION

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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, 2004 (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, 2005

/s/ JOSHUA S. BOGER

Joshua S. Boger
Chairman and Chief Executive Officer

Date: March 16, 2005

/s/ IAN F. SMITH

Ian F. Smith
Chief Financial Officer

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