VERTEX PHARMACEUTICALS INC / MA

FORM 10-K
(Annual Report)

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Industry	Biotechnology & Drugs
Sector	Healthcare
Fiscal Year	12/31

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, 2003

or

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

For the transition period from to

Commission file number 000-19319

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

Massachusetts (State 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
(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 [X] No [ ]

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

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

The aggregate market value of the registrant's common stock held by non-affiliates of the registrant (without admitting that any person whose shares are not included in such calculation is an affiliate) based on the last reported sale price of the Common Stock on The Nasdaq Stock Market on June 30, 2003, was $826,746,640.

As of March 12, 2004, the registrant had 78,183,920 shares of common stock outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the definitive Proxy Statement for the 2004 Annual Meeting of Stockholders to be held on May 6, 2004 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.

trademark, and "Lexiva" and "Telzir" are trademarks, of GlaxoSmithKline. "Prozei" is a trademark of Kissei Pharmaceutical Co., Ltd. Other brands, names and trademarks contained in this Annual Report are the property of their respective owners.

Forward-Looking Statements

Our disclosure in this Annual Report on Form 10-K contains some forward-looking statements. Forward-looking statements give our current expectations or 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 terms 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 partnerships;
- 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 liabilities associated with our Kendall Square lease;
- 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 reference to 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 infection, inflammatory and autoimmune disorders and cancer, independently and with collaborators. Our principal focus is on the development and commercialization of new treatments for viral and inflammatory diseases. There are two Vertex-discovered products on the market now for the treatment of HIV and AIDS. Our pipeline of potential products includes several drug candidates targeting chronic hepatitis C virus infection, drug candidates targeting inflammatory diseases such as rheumatoid arthritis, osteoarthritis, acute coronary syndromes and psoriasis, and compounds directed at cancer therapy.

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 own product candidates to market. Our two marketed products to date were developed and commercialized in collaboration with GlaxoSmithKline, who provided us with development

capacity, financial support, commercial capabilities, and other valuable resources. We plan to continue to collaborate with existing and new partners to develop and market other Vertex-discovered products for selected major therapeutic areas. We also have begun developing certain potential products independently, for markets in which we believe we can commercialize products effectively and reach large patient populations, but expend comparatively fewer resources by using a sales force focused on specialists. We believe this dual approach will help us diversify risk and create the greatest number of product development and commercialization opportunities for Vertex.

Partnerships are a key component of our corporate strategy. We have collaborations with Aventis, GlaxoSmithKline, Novartis, Serono and other companies. These 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. We have had a long and fruitful collaboration with GlaxoSmithKline, resulting in our two marketed drugs, Agenerase and Lexiva, and the advancement of a third HIV protease inhibitor, VX-385, into clinical development. We expect that GlaxoSmithKline will commence a Phase II trial of VX-385 in 2004. We currently are collaborating with Aventis in the development of pralnacasan, an ICE inhibitor for the treatment of rheumatoid arthritis, osteoarthritis and other inflammatory diseases. Our collaboration with Eli Lilly, now ended, produced one of our HCV drug candidates, VX-950.

We plan to continue adding promising potential products to our development pipeline through the conduct of our state-of-the-art research programs. 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 a distinguishing feature of the Company. We currently are conducting a productive research program in the area of ion channel modulation, and have been engaged in a broad scale kinase inhibitor collaboration with Novartis since 2000. We expect that future development candidates from these programs will be focused on the treatment of wide variety of diseases and conditions including cancer and neuropathic 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.

In two independent transactions closed in March and December 2003, we sold the assets of our Discovery Tools and Services business for an aggregate of $101 million in cash and the assumption of certain liabilities. As a result of the disposition of these assets, we now operate in a single operating segment: Pharmaceuticals.

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, and cancer.

Therapeutic Area and Product Candidate	Clinical Indications	Development Phase	Company With Marketing Rights (Region)
Antivirals			
Agenerase™(amprenavir)	HIV infection	Mktd	GlaxoSmithKline (Worldwide)*
Lexiva™(fosamprenavir calcium)**	HIV infection	Mktd/MAA filed	GlaxoSmithKline (Worldwide)*
VX-385	HIV infection	Phase I	GlaxoSmithKline (Worldwide)*
Merimepodib (VX-497)	Chronic hepatitis C	Phase II	Vertex (Worldwide)
VX-950	Chronic hepatitis C	Preclin	Vertex (Worldwide)
Inflammation and Autoimmune Disease			
VX-765	Inflammatory/autoimmune diseases	Phase I	Vertex (Worldwide)
VX-702	Acute coronary syndromes; inflammatory diseases	Phase II	Kissei (Japan); Vertex (R.O.W.)

Pralnacasan (VX-740)	Rheumatoid arthritis (RA); osteoarthritis (OA); other inflammatory/autoimmune diseases	Phase II	Aventis (Worldwide)*
Cancer			
VX-680	Oncology	Preclin	Novartis (Worldwide)†
VX-944	Oncology	Phase I	Vertex (Worldwide)

* Vertex has co-promotion rights in the U.S. and the E.U. Kissei has marketing rights to amprenavir (Prozei™) in Japan.

** GlaxoSmithKline is seeking marketing approval in the E.U. under the name "Telzir™".

† Vertex may elect by June 30, 2004 to continue the development of VX-680 under the original terms of the Novartis agreement, in which event Novartis will hold an option on worldwide commercial rights.

Antiviral Programs

HIV/AIDS

Background: Treatment of HIV/AIDS

Infection with human immunosufficiency virus (HIV) leads to AIDS, a severe, life-threatening impairment of the immune system. The World Health Organization estimates that approximately 36.1 million individuals worldwide are infected with HIV. The U.S. Centers for Disease Control and Prevention (CDC) estimates that there are 980,000 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 Agenerase and Lexiva 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. We estimate that approximately 75% of Lexiva patients are treated concomitantly with ritonavir.

Currently, approximately 175,000 of the HIV patients receiving drug treatment in the U.S. take at least one PI. The market for HIV PIs is highly competitive, with seven different PIs vying for a share. Worldwide sales of HIV PIs were estimated at more than $1.8 billion in 2003, and U.S. sales alone during the same period were estimated at more than $1 billion.

Vertex HIV/AIDS Products

Agenerase

Our first marketed product is the HIV protease inhibitor Agenerase (amprenavir), an orally administered drug for the treatment of HIV infection and AIDS. Agenerase received regulatory approval in the U.S. in April 1999. We created and developed Agenerase in collaboration with GlaxoSmithKline. GlaxoSmithKline markets, and we co-promote, Agenerase in the U.S. and Europe. We collaborated with Kissei Pharmaceutical Co., Ltd. to develop amprenavir in Japan, where it is sold by Kissei under the trade name Prozei™.

Regulatory authorities have approved once-daily use of Agenerase on the basis of data demonstrating that ritonavir (a PI) significantly boosts levels of Agenerase in the bloodstream in both once-daily and twice-daily dosing regimens.

We receive royalties on sales of amprenavir by GlaxoSmithKline and Kissei. We also supply bulk amprenavir drug substance to Kissei.

Lexiva

Our second HIV protease inhibitor, Lexiva (fosamprenavir calcium), was co-discovered by Vertex and GlaxoSmithKline and has been developed by GlaxoSmithKline under our collaboration. GlaxoSmithKline has worldwide marketing rights for Lexiva, and we have the right to co-promote Lexiva 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.

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 reverse transcriptase inhibitors as part of the combination regimen.

Data from the Phase III clinical program was presented at various medical conferences in 2002 and 2003. In the NEAT trial, 66% of 166 HIV-positive patients achieved an undetectable viral load with Lexiva (<400 copies/ml vRNA), compared to 52% of 83 patients taking nelfinavir. In the SOLO study, 69% of 322 HIV-positive patients achieved undetectable viral load with Lexiva/ritonavir compared to 68% of 327 patients taking nelfinavir. Forty-eight-week data from the CONTEXT study has shown similar efficacy responses in BID regimens of both Lexiva/ritonavir and lopinavir/ritonavir. The incidence of adverse events was low in the Lexiva treatment groups.

In December 2002, GlaxoSmithKline filed a New Drug Application (NDA) with the U.S. Food and Drug Administration (FDA) and a Marketing Authorization Application (MAA) in the European Union (E.U.) for marketing approval of Lexiva in the U.S. and E.U. The submissions for registration 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. GlaxoSmithKline currently is seeking marketing approval for Lexiva (under the name Telzir) in the E.U. We anticipate that E.U. marketing approval will be granted in 2004.

Lexiva is a prodrug of amprenavir. A prodrug is an inactive compound that is metabolized by the body to become the active drug. Administration of a prodrug can result in a smaller pill burden for patients, due to the need to use fewer fillers, with a resulting higher ultimate drug load per pill. HIV-infected patients typically require a large number of pills daily as part of combination drug regimens. We believe that Lexiva will offer important new benefits to HIV patients, including a low pill count and the ability to be dosed once or twice a day. This dosing benefit could lead to a material increase in physician acceptance of Lexiva, and patient compliance with Lexiva dosing regimens, as compared to other Agenerase and certain other currently marketed PIs. We also believe that trends in HIV patient demographics and emerging themes in HIV treatment strategy in Western countries may result in increased use of protease inhibitors generally, including Lexiva.

We believe that Lexiva retains many of the favorable properties associated with amprenavir, including:

- 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;
- well tolerated;
- relatively low levels of cross-resistance to other protease inhibitors; and
- a favorable lipid profile.

VX-385

We have a third novel, orally available HIV protease inhibitor in clinical development, VX-385 (GW640385), which was co-discovered by Vertex and GlaxoSmithKline. VX-385 is chemically distinct from Agenerase, Lexiva, and other currently marketed protease inhibitors. Preclinical results presented at medical meetings in 2003 demonstrate that VX-385 is a highly potent inhibitor and demonstrates anti-HIV activity against HIV strains resistant to a number of currently marketed protease inhibitors. Clinical results to date 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 and plans to initiate a Phase II clinical trial of the compound in the second half of 2004.

HEPATITIS C VIRUS INFECTION

Background: Treatment of Hepatitis C

Hepatitis C virus (HCV) 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 CDC have estimated that approximately 2.7 million Americans, or approximately 1% of the population, 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 hepatitis C infection. The current standard treatment for hepatitis C viral infection is a combination of pegylated interferon and ribavirin. At present, however, approximately 50% of patients still fail to show long-term sustained response to pegylated interferon/ribavirin combination therapy. As a result, new safe and effective treatment options for HCV infection are needed.

Vertex HCV Drug Candidates

Vertex is developing two drug candidates targeting hepatitis C virus infection by different mechanisms. The most advanced compound is merimepodib, which targets HCV indirectly and is currently in Phase II development. Vertex's second HCV drug candidate, VX-950, targets the hepatitis C virus directly, by inhibiting hepatitis C NS3-4A protease, an enzyme necessary for HCV replication. We expect to begin Phase I clinical trials of VX-950 in 2004. Vertex holds all marketing rights to both merimepodib and VX-950.

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). Vertex has conducted *in vitro* experiments that demonstrate that merimepodib has an additive antiviral effect, *in vitro*, in combination with pegylated interferon and ribavirin.

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 six months of treatment, with an optional 6-month extension phase for patients who responded to therapy. In 2003, we reported six-month 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 HCV viral RNA after six months of treatment.

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 an attractive target for inhibition of rapid cell proliferation and/or viral replication. Some viruses, including HCV, may be more sensitive to disruptions in the pathway catalyzed by IMPDH. 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 proposed that merimepodib may increase the likelihood of ribavirin incorporation into viral RNA during replication,

resulting either in decreased replication or in the production of immature or non-infective viral particles.

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 have also 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 interferon, as compared to patients receiving interferon alone. Patients receiving a 100 mg dose of merimepodib three times daily showed a greater reduction in HCV-RNA after 28 days. 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.

We expect to initiate expanded clinical studies of merimepodib in 2004. If our clinical activities progress as planned, we believe we may be able to file a new drug application (NDA) for merimepodib as early as 2007.

VX-950

In 2001, we selected VX-950, a potent orally-administered HCV protease inhibitor, for preclinical development. We believe that VX-950 is among the most advanced drug development candidates in a new class of antiviral drugs being studied to inhibit hepatitis C NS3-4A protease, an enzyme thought to be necessary for HCV replication. We believe that therapeutics such as VX-950 which directly target viral replication may significantly increase the number of patients that achieve a complete viral response, clearing HCV from the body permanently. VX-950 has the potential to become one of the first compounds targeting HCV directly and could provide an important treatment advance for individuals with chronic HCV infection. Promising preclinical results for VX-950 were presented in multiple medical and research forums in 2003. Based on progress in preclinical development in 2003, we expect to begin Phase I clinical development of VX-950 in 2004, and we may initiate a first study in HCV patients in the second half of 2004. We hold worldwide marketing rights to VX-950 and all other second-generation HCV protease inhibitors discovered by Vertex in collaboration with Eli Lilly, and would pay Lilly royalties on certain future product sales.

Inflammatory and Autoimmune Disease

Background: ICE Inhibitors for Inflammatory Disease

Interleukin-1 b converting enzyme (ICE; caspase-1) is an enzyme that controls the release of active interleukin-1 b (IL-1 b , one of two forms of IL-1) and interleukin-18 (IL-18) from white blood cells into the bloodstream and within tissues. IL-1 b 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-1 b 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-1 b and IL-18 levels have been correlated with disease states in a number of acute and chronic inflammatory diseases.

Rheumatoid arthritis (RA) is a potential indication for small molecule ICE inhibitors. In patients with RA, increased activity of IL-1 b and IL-18 is observed in joint tissues during disease flare-ups, and

IL-1 b is known to activate osteoclasts, a cell type important in bone erosion characteristic of rheumatoid arthritis. IL-18 may have a similar effect.

There are more than 6 million patients with RA worldwide, including approximately 2.1 million in the United States. The main drugs currently used to treat RA are non-steroidal anti-inflammatory drugs (NSAIDs) such as Motrin (ibuprofen) and Celebrex (celecoxib). These drugs are palliative—they relieve pain and swelling but do not reverse or prevent the progression of the disease. Methotrexate is a disease-modifying drug that is widely used, but its use is associated with side effects that include liver toxicity. Even when they tolerate it well, many patients become unresponsive to methotrexate over the long term. Newer therapies including Enbrel® (etanercept) and Remicade® (infliximab) provide a strong rationale for a new kind of disease-modifying therapy that involves inhibition of the cytokine tumor necrosis factor (TNF) alpha. In 2001 Kineret® (anakinra) became the first therapy approved for RA targeting the cytokine IL-1. All of these newer agents are administered by injection, which can be inconvenient and painful for patients. We believe that a well tolerated oral ICE inhibitor may have significant commercial advantages over currently available treatments. In addition, we believe that anakinra's activity is different than that of Vertex's ICE inhibitors and is not predictive of the degree of efficacy our drug candidates could have.

Osteoarthritis (OA) is also a potential indication for treatment with small molecule ICE inhibitors. OA, a degenerative joint disease, is the most common form of arthritis, afflicting more than 240 million patients worldwide, including more than 21 million in the United States alone. Onset generally occurs after middle age, and as the disease progresses, it causes the loss of cartilage, damage to bone, formation of bone spurs, and inflammation of the soft tissues. OA may also occur in joints that have suffered previous injury, have been subjected to repetitive stress, or have been damaged by prior infection or inflammatory arthritis. Patients with OA experience pain, tenderness, swelling and progressive loss of mobility. Patients with OA currently are treated with over-the-counter drugs as well as palliative treatments such as NSAIDS and COX-2 inhibitors. These drugs do not address the underlying progressive joint destruction. Patients with more severe cases may become candidates for partial or total joint replacement surgery.

The inflammatory response plays a significant role in the joint damage characteristic of OA, and increased cytokine activity has been observed in patients with OA. IL-1 b is a key driver of pathology in OA, and results of tests conducted in animal models provide a strong rationale for pursuing IL-1 b modulation for the treatment of OA.

Vertex ICE Inhibitors for Inflammatory Disease

Vertex is developing ICE inhibitors for the treatment of acute and chronic inflammatory conditions. We have collaborated with Aventis

S.A. in the development of our most advanced ICE inhibitor, pralnacasan, and we are independently developing a second generation ICE inhibitor, VX-765. We hold worldwide rights to VX-765.

Pralnacasan

We are collaborating with Aventis S.A. in the clinical development of pralnacasan (VX-740). Aventis has invested in parallel clinical trials of pralnacasan in both RA and OA, in addition to ongoing nonclinical toxicology studies. In 2003, Aventis and Vertex voluntarily suspended the clinical development of pralnacasan, including an ongoing Phase II RA study, so that Aventis and Vertex could analyze findings that emerged from a 9-month nonclinical toxicology study. In the nonclinical study, high doses of pralnacasan were associated with the development of fibrosis in circumscribed areas of the liver of one species of animal. Aventis and Vertex are committed to exploring the toxicology issue with the goal of re-initiating clinical development as soon as prudently possible. The companies' best estimate is that, if the toxicology issue is satisfactorily addressed, development of pralnacasan will be delayed at least 12-24 months from the original timeline. If the toxicology findings cannot be satisfactorily addressed, development of pralnacasan may be discontinued.

In 2002, Aventis completed a 284 patient Phase IIa study 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-1 b , a cytokine that plays a role in inflammation and tissue damage.

In 2003, prior to the adverse nonclinical toxicology finding, 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 received one of three doses of pralnacasan or placebo for 12 weeks. Pralnacasan was well-tolerated across all three dosage groups. There was improvement (29-35%) in all four treatment groups in the primary endpoint, total WOMAC scores, during the 12 weeks of study. The WOMAC is the "Western Ontario and McMasters Universities" scale for measuring signs and symptoms in OA studies. However, 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 the progression of OA requires additional scientific understanding, which will require further clinical validation.

Under our 1999 agreement, Aventis holds an exclusive worldwide license to develop, manufacture and market pralnacasan in any indication, as well as an exclusive option for certain other compounds discovered under our previous research collaboration with Aventis. We will receive milestone payments for successful development of pralnacasan in RA, as well as for each additional indication, if any, for which it is developed. In addition, we will receive royalties on any sales of pralnacasan, and Aventis will partially fund a Vertex co-promotion effort in the U.S.

VX-765

VX-765 is the first clinical candidate to be selected for clinical development from our second generation ICE inhibitor research program. VX-765 is chemically distinct from pralnacasan. In 2003, we completed Phase I clinical studies of VX-765 in healthy volunteers. These studies demonstrated a dose-dependent decrease in levels of the cytokine interleukin-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. We plan to initiate additional clinical studies of VX-765 in an inflammatory or autoimmune disease in 2004. We hold worldwide development and commercial rights to VX-765.

Background: p38 MAP Kinase Inhibitors for Acute Coronary Syndromes and other 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 a human enzyme involved in the onset and progression of inflammation and apoptosis (cell death). When activated, the p38 MAP kinase triggers production of the cytokines IL-1, tumor necrosis factor-alpha (TNF-alpha), and interleukin-6 (IL-6). Excess levels of IL-1 and TNF-alpha are associated with a broad range of acute and chronic inflammatory diseases.

We have extensive pre-clinical and clinical experience with p38 MAP kinase inhibitors, which have the potential to be a powerful and broadly useful new class of oral anti-inflammatory drugs. The initial objective of our p38 program was to identify and extensively evaluate compounds that target p38 MAP kinase to develop novel, orally active drugs 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.

The central role of inflammation in many cardiovascular diseases has been well established. Specifically, inflammation is increasingly 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. P38 MAP kinase regulates the production of key proinflammatory cytokines implicated in the pathogenesis of ACS, including TNF-alpha, IL-l b and IL-6. As a potential once-daily therapy addressing a novel target for ACS, 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 U.S. each year.

VX-702—Vertex's p38 MAP kinase inhibitor for inflammatory diseases

We have collaborated with Kissei on the discovery and development of novel p38 MAP kinase inhibitors since 1997. The research portion of our collaboration with Kissei was completed in 2000. Kissei holds rights to our p38 MAP kinase inhibitor, VX-702, in Japan and certain other Asian countries, and we hold all development and commercial rights elsewhere.

We initiated a Phase I clinical study of VX-702 in June 2002. The 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.

We began Phase II development of VX-702 in 2003. We intend to explore the potential of VX-702 in a variety of disease settings in which inflammation plays an important role. We have decided to advance the clinical development of VX-702 initially in acute disease indications. The initial focus of the Phase II program is aimed at the use of VX-702 as an ACS therapy. We expect our pilot Phase II clinical trial of VX-702 in ACS to be completed in 2004. A third compound discovered by Vertex, VX-850, is in preclinical development and serves as a backup to VX-702.

Other Clinical Development Candidates

VX-680

VX-680 is the first kinase inhibitor to be advanced by Vertex with potential for the treatment of cancer. 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 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 the Aurora kinase (VX-680) profoundly inhibits tumor growth and induces tumor regression in *in vivo* cancer models.

Vertex has filed an IND for the clinical study of VX-680 in the United States, and we expect that Phase I clinical studies of VX-680 will be initiated in 2004. We discovered VX-680 in collaboration with Novartis. Under our amended agreement with Novartis, we may elect either to continue development of VX-680 under the terms of the original agreement with Novartis, using loan proceeds from the Novartis loan facility, or to develop VX-680 independently or with a third party. If we choose to

continue development under the original agreement, Novartis will have an option on worldwide commercial rights to VX-680.

VX-944

VX-944 is an oral IMPDH inhibitor with potential for the treatment of cancer. Results from certain preclinical studies of VX-944 have suggested that VX-944 has potent anti-tumor activity. Phase I clinical studies of VX-944 in healthy volunteers demonstrated that VX-944 is orally bioavailable and well-tolerated. Vertex is now evaluating the possibility of entering into a collaborative relationship for more advanced clinical development of VX-944.

RESEARCH and EARLY DEVELOPMENT 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 advanced 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 increase the speed and predictability of drug discovery and development.

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. Our patented GenomeScreen™ technology allows us to identify and validate targets by scanning the genome of living human cells and identifying those genes activated or repressed in various disease states. We have used GenomeScreen to assist us in mapping gene activation and cell signaling pathways and in characterizing poorly understood cellular processes. We also use antisense, siRNA, dominant negative cell lines, 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 are also 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 the ultra high-throughput screening (UHTSS) system, which integrates compound management, plate replication with miniaturized screening, hit (potential lead) identification and follow-up. The ultra high-throughput capability is achieved through the use of a 3,456 well assay microplate.

Instrumentation. Some of our ion channel research is conducted using E-VIPR, our proprietary screening technology which uses fluorescent probes and waves of electrical stimulation to study ion channels. E-VIPR provides an automated, high-throughput platform which 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 which 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 partners. 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 approximately 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 Iressa (AstraZeneca) 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 to collaborate on the discovery, development and commercialization of small molecule drugs directed at protein kinases. We expect the research effort under this agreement, which was amended in early 2004, 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 2003, we filed an Investigational New Drug Application (IND) with the FDA covering VX-680, a potent small molecule inhibitor of Aurora kinases and Flt-3 kinase. Aurora kinases are three closely-related proteins required in rapidly dividing cells. Inhibition of Aurora kinase activity with a small

molecule may provide a means of slowing or reversing the uncontrolled cell growth observed in cancer. In addition it is thought that more than 30% of patients with acute myelogenous leukemia (AML) have activating mutations of Flt-3. Thus VX-680 could provide therapeutic benefits for patients with solid tumors and hematological malignancies including AML. Under our restructured agreement with Novartis, we may either continue development of VX-680 under the terms of our original agreement with Novartis, or elect to develop and commercialize VX-680 independent of Novartis.

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 infrastructure created over the first three years of the Novartis/Vertex collaboration has enabled a parallel approach to drug discovery in the kinase gene family. Our researchers have determined the atomic structure of more than 20 kinase drug targets and more than 300 kinase/inhibitor co-complexes, providing information to help accelerate drug design and further our understanding of the role kinases play in disease. Most recently, Vertex researchers published structural interpretations of the process by which mutations in kinases like Flt-3 can lead to uncontrolled cellular proliferation and cancer. Using proprietary *in silico* and *in vitro* methodologies, Vertex has designed a diverse library of proprietary kinase inhibitors, leading to the filing of more than 90 patents covering many hundreds of distinct chemical scaffolds. Over the next several years, we expect to advance a number of kinase inhibitors as development candidates targeting multiple therapeutic areas.

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 500 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, neuropathic 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 neuropathic pain and cystic fibrosis. 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 the Cystic Fibrosis Foundation 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.

Caspase Program

The human caspase family is a subfamily of proteases which presently include 11 structurally related enzymes that play specific roles in inflammation and apoptosis (programmed cell death). We are conducting research focused on the design of small molecules which can potentially exert a protective effect on cells in specific tissues by inhibiting caspase-mediated apoptotic and inflammatory processes.

Through gene knockout studies, our scientists have gained important insight into the biological role of different caspases in the activation of apoptosis in specific cells and tissues. Vertex research teams have solved the three-dimensional atomic structures of four caspases, including one caspase from each of the three caspase subfamilies, and more than 50 enzyme/inhibitor complexes.

Potential indications for caspase inhibitor compounds include tissue damage related to acute conditions such as stroke, myocardial ischemia and sepsis, and neurodegenerative disorders such as Alzheimer's disease and Parkinson's disease. We are collaborating in a portion of our caspase program with Serono S.A. under an agreement signed in 2000, covering the development and commercialization of certain caspase inhibitors in the U.S. and the European Union.

Bacterial Gyrase

We are engaged in the discovery of novel antibiotics that target DNA gyrase B, an essential enzyme found in many bacteria. DNA gyrase is utilized during the bacterial replication process. DNA gyrase 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, we are targeting 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 par E subunit of topoisomerase IV, another essential bacterial enzyme. These dual gyrB/parE inhibitors not only appear to be potent in preclinical testing, but may also be less susceptible to the development of drug resistance, a major and growing problem with marketed antibiotics. We are currently optimizing this dual inhibitor class and may select a clinical candidate in 2004.

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 second generation HCV 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 Pharma AG to collaborate on the discovery, development and commercialization of small molecule drugs directed at protein kinases. We amended this collaboration agreement in February 2004. Under the original agreement, we were responsible for drug discovery and clinical proof-of-concept testing of all drug candidates. Novartis agreed, among other things, to pay us up to $200,000,000 in product research funding through April 2006, and to loan us up to $200,000,000 on a non-interest-bearing basis to support our clinical studies. We continue to be responsible for drug discovery under the amended agreement, and Novartis will continue to provide research funding through the end of the six-year research term. However, under the agreement as modified, Novartis will be responsible for all clinical and nonclinical development of drug candidates which it accepts for development, and consequently the loan facility has been eliminated. We may either continue development of VX-680 under the terms of the original agreement, using loan proceeds we have received under the Novartis loan facility, or elect to develop and commercialize VX-680 independent of Novartis. If we elect to develop and commercialize VX-680 independent of Novartis, loan amounts with respect to that drug candidate which are unspent and

uncommitted at the time of our election will be repayable immediately. At December 31, 2003, approximately $14 million in development loans previously advanced to us on account of VX-680 were unspent and uncommitted. The agreement also provides up to $35 million in license fees and milestones for each preclinical drug candidate nominated by us and accepted by Novartis. Novartis will have exclusive worldwide development, manufacturing and marketing rights to drug candidates that it accepts from us for development. We will receive royalties on any products that are marketed as part of the collaboration.

GlaxoSmithKline

In December 1993, we entered into a collaboration with GlaxoSmithKline covering the research, development and commercialization of HIV protease inhibitors, including Agenerase (amprenavir), Lexiva (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. 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. We began receiving royalties on sales of Agenerase in 1999 and on Lexiva in 2003. GlaxoSmithKline is also obligated to pay us additional development and commercialization milestone payments for subsequent drug candidates, including Lexiva and VX-385. In addition, GlaxoSmithKline is required to bear 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.

Aventis S.A.

In September 1999, we entered into an expanded agreement with Aventis S.A., formerly Hoechst Marion Roussel Deutschland GmbH (HMR), covering the development of pralnacasan. Aventis has an exclusive worldwide license to develop, manufacture and market pralnacasan, as well as an exclusive option for certain other compounds discovered as part of the research collaboration between HMR and us that ended in 1997. Aventis will fund the development of pralnacasan. We may co-promote the product in the United States and Europe and will receive royalties on global sales, if any. Under the agreement, Aventis has paid us a $20 million up-front payment for prior research costs, and has agreed to pay us up to $62 million in milestone payments for successful development by Aventis of pralnacasan for rheumatoid arthritis, the first targeted indication. Milestone payments are also due for each additional indication. The agreement also provides that Aventis will partially fund a Vertex co-promotion effort in the U.S. under certain conditions. Aventis has the right to terminate this agreement without cause upon six months' written notice. Termination by Aventis will end any license we have granted Aventis under the agreement.

Serono S.A.

In December 2000, we entered into a collaboration with Serono S.A. to discover, develop, and market certain types of caspase inhibitors. Under the terms of the agreement, we could receive up to $95 million of pre-commercial payments, based on the successful development and commercialization of more than one drug candidate, to support and expand our drug discovery activities in the caspase protein family. That amount would include milestone payments as drug candidates move through development. Of that total, we have received $5 million in up-front payments for prior research, and could also receive up to $20 million in research funding, some of which has been paid, over the five year agreement term. The two companies will share development costs. We have the option to establish a joint venture with Serono for the commercialization of products in North America, where we will share marketing rights and profits from the sale of drug products, if any. Serono will have exclusive rights to market caspase inhibitors in other territories, excluding Japan and certain other countries in the Far East, and will pay us for supplies of drug substance. Serono has the right to terminate the agreement without cause effective at the end of 2004 upon written notice delivered on or before the end of June 2004.

Other Collaborations

Schering AG (Germany). In August 1998, we entered into a collaboration with Schering AG 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. Vertex and Schering AG have an equal role in management of neurophilin ligand research and product development. Research funding under this agreement has concluded. We have amended the original agreement to extend Schering's option to designate a

compound or compounds for development under the agreement until September 2004. In North America, we will have manufacturing rights to, and we will share equally with Schering AG in the marketing expenses and profits from, any compounds which may be selected for development and commercialization. Schering AG 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. Schering AG has the right to terminate the agreement without cause upon six months' written notice.

Kissei Pharmaceutical Co., Ltd. Kissei launched our HIV protease inhibitor amprenavir (Agenerase) in Japan under the name Prozei in 1999 and 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. We are collaborating with Kissei in the development and commercialization of VX-702, a novel, orally active p38 MAP kinase inhibitor for the treatment of ACS and inflammatory diseases. Kissei has exclusive rights to develop and commercialize VX-702 in Japan and certain Southeast Asian countries, and semi-exclusive rights in China, Taiwan and South Korea. We retain exclusive marketing rights in the United States, Canada, Europe, and the rest of the world. In addition, we 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 any product sales. The research program ended on June 30, 2000, and we have received the full amount of research funding specified under the agreement. Kissei has the right to terminate the agreement without cause upon six months' notice.

Eli Lilly & Company. In June 1997, we entered into a collaboration with Eli Lilly covering the development of novel small molecule compounds to treat hepatitis C 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 pay Eli Lilly a royalty on any future sales of drug products developed from VX-950 and other certain other HCV protease inhibitor compounds.

Intellectual Property

We actively seek, when appropriate, protection for our products and proprietary information by means of United States and foreign patents, trademarks and contractual arrangements. 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 which 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, consultants and advisors to enter into confidentiality agreements that prohibit the disclosure of Vertex confidential information to anyone outside Vertex. These agreements typically require disclosure and assignment to Vertex of ideas, developments, discoveries and inventions made by employees, consultants and advisors.

Patents and Pending Applications

We have issued patents and pending 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 amprenavir and its pharmaceutical formulations, methods of manufacture and methods to treat HIV infection or AIDS-related central nervous system disorders. 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 fosamprenavir 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. These patents claim merimepodib, its combination with certain other therapeutic agents and the use thereof for treating HCV.

- 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 and VX-850, as well as compositions comprising those 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 filed applications worldwide claiming inhibitors of multiple kinase proteins.
- pending applications and an issued United States patent for methods of designing novel chemical inhibitors of protein kinases. The method involves using mutagenesis techniques to create hybrid kinases that act as surrogate targets for drug design and compound screening.
- pending applications claiming modulators of sodium ion channels, and uses thereof.

Manufacturing

We rely on third party manufacturers and collaborative partners 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 Agenerase and Lexiva is being done by GlaxoSmithKline. We retain the option to manufacture a portion of GlaxoSmithKline's requirements for bulk drug substance for Agenerase and Lexiva. 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 whether to develop internal manufacturing capabilities for certain of our potential products. However, if we are unable to obtain contract manufacturing, or 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. In the field of HIV protease inhibition, Abbott Laboratories, Inc., Bristol Myers Squibb, Gilead, Hoffmann-La 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 hepatitis C virus 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 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.

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 U.S. 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, are ordinarily 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 human clinical studies progress through the 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 into healthy human subjects prior to introduction into patients, the drug candidate is tested for safety, 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 and to provide an adequate basis for physician labeling. Each trial is conducted in accordance with certain standards under protocols that detail the objectives of the study, the parameters to be used to monitor safety and the efficacy criteria to be evaluated. 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 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 (the industry average is 12 years) 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
Pre-Clinical	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	2 to 4 years

	evaluation	
Phase III	Confirm efficacy, dosage regime and safety profile of the drug	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 are typically 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 was initially 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.

Under the Drug Price Competition and Patent Term Restoration Act of 1984, a sponsor may be granted marketing exclusivity for a period of time following FDA approval of certain drug applications, if FDA approval is received before the expiration of the patent's original term. This marketing exclusivity would prevent a third party from obtaining 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, 2003, we had more than 720 employees (approximately 714 full time, 10 part time), including approximately 486 in research and development and 238 in general and administrative functions. Approximately 80 of these employees were located at our U.K. research and development facility and 157 were located at our facility in San Diego. Our scientific staff members (278 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, 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.	52	Chairman and Chief Executive Officer
Vicki L. Sato, Ph.D.	55	President
John J. Alam, M.D.	42	Senior Vice President of Drug Evaluation and Approval

Lynne H. Brum	40	Vice President, Corporate Communications and Financial Planning
Iain P. M. Buchanan	50	Vice President, European Operations; Managing Director, Vertex Pharmaceuticals (Europe) Limited
Kenneth S. Boger	57	Senior Vice President and General Counsel
N. Anthony Coles, M.D.	43	Senior Vice President, Commercial Operations
Peter Mueller, Ph.D	47	Chief Scientific Officer and Senior Vice President, Drug Discovery and Innovation
Ian F. Smith, CPA	38	Senior Vice President and Chief Financial Officer
Eric K. Brandt	41	Director
Roger W. Brimblecombe, Ph.D., D.Sc.	74	Director
Stuart J. Collinson, Ph.D.	44	Director
Bruce I. Sachs	44	Director
Charles A. Sanders, M.D.	72	Director
Elaine S. Ullian	56	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.

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 A.M. and Ph.D. degrees 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. 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 1991-1997, including Director of Medical Research and Program Executive for Avonex (beta interferon). 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 a S.B. in Chemical Engineering from the Massachusetts Institute of Technology.

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. Buchanan joined Vertex in April 1994 from Cilag AG, a subsidiary of Johnson & Johnson based in Zug, Switzerland, where he served as its Regional Licensing Director beginning in 1987. He previously held the position of Marketing Director of Biogen S.A. in Switzerland. Prior to Biogen, Mr. Buchanan served in Product Management at Merck Sharp & Dohme (UK) Limited. Mr. Buchanan holds a B.Sc. from the University of St. Andrews, Scotland.

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, 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. degree 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 served as Senior Vice President, Research and Development, and was responsible for the development of all drug candidates in the company's worldwide portfolio in North America, beginning in 1997. 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 served as a partner in their Life

Science and Technology Practice since 1999. He had various responsibilities in the accounting, auditing and mergers and acquisitions groups. Mr. Smith initially joined Ernst & Young's U.K. firm in 1987, and then joined their 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.

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.

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 1997-1999, 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 also serves as a director of several companies located in Europe, Singapore and Australia. 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 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 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. 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 the Squibb Corporation, including that of Vice Chairman. Dr. Sanders has 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., Trimeris Inc., and Fisher Scientific International.

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.

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	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
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.	Tim Gill Professor of Medicine and Head of the Division of Infectious Diseases, University of Colorado Health Sciences Center
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.

RISK FACTORS

WE DO NOT KNOW WHETHER AGENERASE SALES WILL CONTINUE AT CURRENT LEVELS OR IF LEXIVA SALES WILL BE AT A LEVEL AT OR ABOVE SALES LEVELS FOR AGENERASE.

Agenerase's share of the worldwide protease inhibitor market may decrease due to competitive forces and market dynamics, including the launch of Lexiva, which took place in the fourth quarter of 2003. Similarly, Lexiva may face similar competitive pressures. Other HIV protease inhibitors and a number of other products, including Gilead'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 Agenerase or Lexiva. 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 less use of HIV protease inhibitors. In addition, the clinical benefit of strategies used by clinicians to boost drug levels of Agenerase (and possibly

Lexiva) 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, in the U.S. and Europe, may decline, decreasing the sales potential of Agenerase and Lexiva. Further, although we co-promote Agenerase and Lexiva in the U.S. and key markets in Europe (if Lexiva is approved in Europe), GlaxoSmithKline directs the majority of the marketing and sales efforts and we will have little control over the success of those efforts. GlaxoSmithKline has the right to terminate its agreement with us without cause upon 12 months' notice.

WE MAY NOT SUCCESSFULLY DEVELOP OUR DRUG PIPELINE.

All of the products that we are pursuing independently and with partners 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 or receive the required regulatory approvals. Moreover, our products, if introduced, may not be commercially successful. The results of preclinical 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 such products or result in a marketable product. Findings in nonclinical studies conducted concurrently with clinical studies could adversely impact 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 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 development delays. 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 partnered.

IF DELAYS IN PATIENT ENROLLMENT SLOW OUR DEVELOPMENT PROGRESS WE MAY LOSE OUR 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 partnered. 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 WE DO NOT OBTAIN REGULATORY APPROVAL FOR OUR PRODUCTS ON A TIMELY BASIS, OR AT ALL, OUR REVENUES WILL BE NEGATIVELY IMPACTED.

The 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, including merimepodib, VX-385, VX-950, VX-765 and VX-702. It may also delay or prevent the commercialization of our products, including Lexiva (which is not yet approved in the European Union), which are developed and submitted for approval, for a considerable period of time, impose costly procedures upon our activities and provide competitive advantages 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 COLLABORATIVE PARTNERS FOR RESEARCH SUPPORT AND THE DEVELOPMENT AND COMMERCIALIZATION OF OUR PRODUCTS, WE MAY NOT BE ABLE TO FUND OUR RESEARCH AND DEVELOPMENT ACTIVITIES.

Our collaborative partners have agreed to fund portions of our research and development programs and/or to conduct certain research and development relating to specified products. In exchange, we have given them technology, product and marketing rights relating to those products. Some of our corporate partners, including Novartis, GlaxoSmithKline and Aventis, have rights to control the planning and execution of product development and clinical programs. Our collaborative partners may exercise their control rights in ways that may negatively impact the timing and success of those programs. Our collaborations are subject to termination rights by the collaborators. If any of Aventis, Novartis,

GlaxoSmithKline or Serono 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 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 collaboration with Novartis in the kinase field. That collaboration will end by its terms in April 2006. If we are unable to enter into collaborative arrangements which would extend or replace the Novartis collaboration, or to find other means of financing the effort currently devoted to the Novartis collaboration, 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. Under certain of our collaborative agreements, our collaborators have agreed to provide funding for only a portion of our research and development activities and we are committed to investing our own capital to fund the remainder of the agreed upon programs. However, we may not have adequate financial resources to satisfy those requirements.

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 novel, systematic approach to discover drugs based on gene families using proprietary drug targets, compound libraries, compound approaches, structural protein analysis and information technologies. Such a company might identify broadly applicable compound classes faster and more effectively than we do, impeding our ability to develop and market drugs based on our approach. 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 which 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. For example, we know of at least 15 drugs in development for HIV, 15 drugs in development for the treatment of hepatitis C infection, and 25 drugs in development for the treatment of rheumatoid arthritis or psoriasis, by competitors in the pharmaceutical and biotechnology industries. 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 are currently marketed. Many of our competitors, including major pharmaceutical companies such as GlaxoSmithKline, Novartis, Abbott and Merck, have substantially greater financial, technical and human resources than we do. In addition, many of our competitors have significantly greater experience than we do in conducting preclinical testing and human clinical trials of new pharmaceutical products, and in obtaining FDA and other regulatory approvals of products. 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 will also 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 necessary skills to develop our products. Our future success will depend in large part on the continued services of our key scientific and management personnel, including Dr. Joshua Boger, our Chief Executive Officer, and Dr. Vicki L. Sato, our President. While we have entered into employment agreements with Dr. Boger and Dr. Sato, they provide for termination by the employee upon six months' notice.

We face intense competition for our scientific personnel from our competitors, our collaborative partners and other companies throughout our industry. Moreover, the growth of local biotechnology companies and the expansion of major pharmaceutical companies into the Cambridge, MA 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 collaboration, 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 FDA and other 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 partners have manufacturing rights with respect to our products under development. We are, therefore, dependent on third party manufacturers and our collaborative partners for the production of our drug candidates for preclinical 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. As a result, our collaborators or we may encounter difficulties developing commercial formulations and manufacturing processes for our drug candidates that 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 biopharmaceutical 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.

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 2004. We believe that operating losses will continue beyond 2004, 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 will incur significant selling, general, and administrative expenses for 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 the Company will become profitable, if at all.

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;
- Agenerase and Lexiva 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 18 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. Any equity financings could result in dilution to our then-existing securityholders. 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 impact 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 collaborative partners 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 which are approved by the FDA. 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 to GlaxoSmithKline worldwide (except for amprenavir in Japan), and for pralnacasan to Aventis worldwide. Kissei has exclusive marketing rights to Prozei (amprenavir) and VX-702 in Japan. Even though we retain some co-promotion rights, to the extent that our collaborative partners 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. 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 which might be beneficial to the company or its securityholders. 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, shareholders 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 12 months ended December 31, 2003, our common stock traded between $7.83 and $18.75. 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 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, 2003, we had approximately $333.5 in long-term debt, including $315 million of 5% Convertible Subordinated Notes due September 2007. In a transaction completed on February 13, 2004, we exchanged $153.1 million of these notes for $153.1 million of 5.75% Convertible Senior Subordinated Notes due September 2011. The high level of our indebtedness will impact 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.

IF WE ARE NOT ABLE TO RESTRUCTURE OUR KENDALL SQUARE LEASE 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 the Kendall Square facility, which we lease under a 15-year agreement expiring in 2018. We have estimated our liability to restructure the lease, using assumptions and estimates we consider appropriate, to be $69.5 million as of December 31, 2003. In estimating the liability, we considered several possible outcomes of the potential lease restructuring, including a sublease of the entire space, a buy-out of our obligation, partial subleases by multiple parties, and other variations of these same outcomes. If we are unable to find a tenant or tenants willing to sublease 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 secure a sublease of the space, or if any of our other assumptions and estimates are inaccurate or circumstances

bearing upon the potential restructuring should change before we are able to restructure the lease, or if we are unable to reach agreement with the landlord on the terms of any such restructuring, our estimated liability could increase to as much as the full amount due under the lease. Our future obligations under the lease could be as much as $312,500,000, as set forth in "Off-Balance Sheet Commitments and Obligations at December 31, 2003" on page 40 of this Annual Report on Form 10-K.

ITEM 2. PROPERTIES

We lease an aggregate of approximately 624,000 square feet of laboratory and office space in eight facilities in Cambridge, Massachusetts. The leases have expiration dates ranging from 2005 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 building, which is currently unoccupied, will expire in 2018, with the option to extend the lease for two consecutive terms of 10 years each. The building is currently under construction and we are obligated to build out finished space to specifications approved by our landlord. We have decided not to occupy the Kendall Square building and are actively trying to restructure the lease obligation. We are considering several possible outcomes for the potential restructuring, including a sublease of the entire space, a buy-out of our obligation, partial subleases by multiple parties and other variations of these same outcomes. See "Management's Discussion and Analysis of Financial Condition and Results of Operations—Contractual Commitments and Obligations" at page 39.

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 also sublease an additional 12,500 square feet of space for our administrative functions in a nearby facility. The sublease for this additional space will expire on March 31, 2004 and we are consolidating activities in our larger facility.

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 U.K. business and research and development activities.

We believe our facilities are adequate for our current needs. We believe we can obtain additional space on commercially reasonable terms.

ITEM 3. LEGAL PROCEEDINGS

We were involved in a lawsuit filed against us in December 2001 by Oregon Heath Sciences University in the District Court of Oregon. The complaint in the suit sought to name Dr. Bruce Gold, an employee of Oregon Health Sciences University, as an inventor and Oregon Health Sciences University as part owner of five of our neurophilin patents, and associated damages. The suit stemmed from assays run on Vertex compounds by Dr. Gold under a sponsored research agreement in 1996. That lawsuit was settled on December 12, 2003 in connection with the establishment of a collaboration between Vertex and OHSU, under which we will fund scientific research by OHSU scientists in areas of mutual interest. We do not expect that the settlement terms will have a material impact on the Company's financial position.

On September 23, 2003, two purported shareholder class actions, *Carlos Marcano v. Vertex Pharmaceuticals, et al.* and *City of Dearborn Heights General Governmental Employees' Retirement System v. Vertex Pharmaceuticals, et al.* , were filed in the United States District Court for the District of Massachusetts, naming the Company and certain current and former officers and employees of the Company as defendants. Those actions were followed by three additional lawsuits, *Stephen Anish v. Vertex Pharmaceuticals, et al.* , *William Johns v. Vertex Pharmaceuticals, et al.* , and *Ben Harrington v. Vertex Pharmaceuticals, et al.* , also filed in the District of Massachusetts. All five cases contain substantially identical allegations and have been consolidated by the District Court into one lawsuit. The plaintiffs claim 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 seek certification as a class action, compensatory damages in an unspecified amount, and

unspecified equitable or injunctive relief. We believe that the claims are without merit and intend to contest them vigorously.

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, 2003.

PART II

ITEM 5. MARKET FOR REGISTRANT'S COMMON EQUITY AND RELATED STOCKHOLDER MATTERS

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, 2002:	High	Low
First quarter	$ 29.92	$ 17.78
Second quarter	32.45	15.02
Third quarter	23.96	12.67
Fourth quarter	21.60	15.34
Year Ended December 31, 2003:		
First quarter	$ 16.50	$ 9.59
Second quarter	18.75	9.94
Third quarter	16.77	11.73
Fourth quarter	14.19	7.83

Stockholders

As of March 12, 2004, there were 1,116 holders of record of our common stock (approximately 18,500 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.

ITEM 6. SELECTED CONSOLIDATED FINANCIAL DATA (Unaudited)

The following unaudited selected financial data for each of the five years in the period ended December 31, 2003 are derived from our audited consolidated financial statements. This 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,				
	2003	2002	2001(1)	2000(2)	1999
	(In thousands, except per share amounts)				
Consolidated Statement of Operations Data:					
Revenues:					
Royalties	$ 9,002	$ 10,054	$ 10,783	$ 12,036	$ 8,053
Collaborative and other research and development revenues	60,139	84,716	74,514	70,459	43,617
Total revenue	69,141	94,770	85,297	82,495	51,670
Costs and expenses:					

Royalty payments	3,126	3,334	3,594	3,965	2,925
Research and development	199,636	198,338	141,988	96,308	79,251
Sales, general and administrative	39,082	41,056	31,856	30,006	28,266
Restructuring and other expense	91,824	—	—	—	—
Merger related costs	—	—	22,960	—	—
Total costs and expenses	333,668	242,728	200,398	130,279	110,442
Loss from operations	(264,527)	(147,958)	(115,101)	(47,784)	(58,772)
Other income/(expense), net	(1,886)	11,000	24,532	20,239	10,487
Debt conversion expense	—	—	—	(14,375)	—
Gain on retirement of convertible subordinated notes	—	—	10,340	—	—
Loss from continuing operations before cumulative effect of changes in accounting principles	(266,413)	(136,958)	(80,229)	(41,920)	(48,285)
Income from discontinued operations(4):					
Gain on sales of assets	70,339	—	—	—	—
Income (loss) from discontinued operations	(693)	28,337	22,148	10,341	7,131
Total income from discontinued operations	69,646	28,337	22,148	10,341	7,131
Loss before cumulative effect of changes in accounting principles	$ (196,767)	$ (108,621)	$ (58,081)	$ (31,579)	$ (41,154)
Cumulative effect of change in accounting principle—revenue recognition	—	—	(25,901)	(3,161)	—
Cumulative effect of change in accounting principle—derivatives(3)	—	—	17,749	—	—
Net loss	$ (196,767)	$ (108,621)	$ (66,233)	$ (34,740)	$ (41,154)
Basic and diluted net loss per common share	$ (2.56)	$ (1.43)	$ (0.89)	$ (0.51)	$ (0.66)
Basic and diluted weighted average number of common shares outstanding	77,004	75,749	74,464	67,682	62,602
Pro forma amounts assuming the 2001 accounting change relating to revenue recognition is applied retroactively (1)					
Net loss	$ (196,767)	$ (108,621)	$ (40,332)	$ (45,860)	$ (38,234)
Net loss per weighted common share—basic and diluted	$ (2.56)	$ (1.43)	$ (0.54)	$ (0.68)	$ (0.61)

	December 31,				
	2003	**2002**	**2001**	**2000**	**1999**
Consolidated Balance Sheet Data:					
Cash, cash equivalents and marketable securities	$ 583,164	$ 634,984	$ 743,202	$ 814,061	$ 224,955
Other current assets	10,642	21,588	32,890	43,370	18,055
Property, plant and equipment	80,083	95,991	80,377	43,961	37,226
Restricted cash	26,061	26,091	26,190	14,713	17,113
Other non-current assets	24,461	37,066	42,472	25,031	9,989
Total assets	724,411	815,720	925,131	941,136	307,338
Current liabilities, excluding restructuring and other expense	69,541	64,597	91,553	41,527	27,184
Accrued restructuring and other expense	69,526	—	—	—	—
Collaborator development loan, excluding current portion	18,460	5,000	—	—	—
Deferred revenue, excluding current portion	51,771	46,598	35,201	28,329	12,234
Convertible notes (due 2007)(5)	315,000	315,000	315,000	345,000	—
Other long-term obligations	7,268	5,944	8,026	12,269	16,003
Stockholder's equity	192,845	378,581	475,351	514,011	251,917
Total liabilities and stockholder's equity	$ 724,411	$ 815,720	$ 925,131	$ 941,136	$ 307,338

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, we elected to change our revenue recognition policy for collaborative 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 the Company's on-going business operations and is more consistent with the industry practices following the implementation of SAB 101 in 2000 throughout the biotechnology industry. For further information please refer to Note C: "Change in Accounting Principle—Revenue Recognition" in the notes to our consolidated financial statements and our Management's Discussion and Analysis of Financial Condition and Results of Operations included in this Annual Report on Form 10-K.

(2) In the fourth quarter of 2000, we changed our method of accounting for revenue recognition in conjunction with our adoption of the SEC's Staff Accounting Bulletin No. 101, "Revenue Recognition in Financial Statements" which was retroactive to January 1, 2000.

(3) During 2001, we recorded a cumulative effect of change in accounting principle related to the adoption of Derivative Implementation Group Issue No. A17 ("DIG A17") in connection with the valuation of derivative instruments. Please refer to Note I: "Investments" in the notes to our consolidated financial statements included in this Annual Report on Form 10-K for further information.

(4) 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. Please refer to Note D: "Sale of Assets" in the notes to our consolidated financial statements included in this Annual Report on Form 10-K for further information.

(5) In February 2004, we exchanged approximately $153.1 million in aggregate principal amount of our 5% Convertible Subordinated Notes due 2007 for approximately $153.1 million in aggregate principal amount of newly issued 5.75% Convertible Senior Subordinated Notes due 2011.

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 marketing small molecule drugs for serious diseases including HIV infection, chronic hepatitis C virus infection, inflammatory and autoimmune disorders and cancer, independently and with collaborators. To date, we have discovered and advanced two products that have reached the market, Agenerase (amprenavir) and Lexiva (fosamprenavir calcium). Agenerase was approved and launched in the United States in early 1999, and Lexiva was approved and launched in the United States in late 2003. We earn a royalty on the sales of Agenerase and Lexiva and co-promote these products in collaboration with GlaxoSmithKline. Our drug candidate pipeline is principally focused on the development and commercialization of new treatments for viral and inflammatory diseases. We have built a drug discovery capability that integrates advanced 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. During this process, potential drug candidates are subjected to rigorous evaluation, driven in part by stringent regulatory considerations, designed to generate information concerning toxicity profiles, efficacy, proper dosage levels and a variety of other characteristics which are important in determining whether a proposed drug candidate should be approved for marketing. Most chemical compounds which are investigated as potential drug candidates never progress into formal development, and most drug candidates which do advance into formal development never become commercial products.

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 new insights into ongoing 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 which we expect to control throughout the development and commercialization process, and programs which we expect will be conducted in the development and commercial phase principally by a collaborative partner. Since we have incurred losses from our inception and expect to incur losses for the forseeable future, our business strategy is dependent in large part on our continued ability to raise significant funding to finance our operations and 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, 2003 we had $583 million of cash, cash equivalents and available for sale securities and $315 million of 5% Convertible Subordinated Notes due 2007 (the "2007 Notes"). During 2003 and early 2004 we took a number of steps to address our cash position and investment requirements in support of our existing business strategy.

Debt Exchange. On February 13, 2004, we exchanged approximately $153.1 million in aggregate principal amount of our 2007 Notes for approximately $153.1 million in aggregate principal amount of newly issued 5.75% Convertible Senior Subordinated Notes due 2011 (the

"2011 Notes"). This transaction had an effect of significantly deferring the repayment date for almost half of our outstanding debt.

Sale of Business. In two independent transactions closed in March and December 2003, we sold the assets of our Discovery Tools and Services business for an aggregate of $101 million of cash and the assumption of certain liabilities, to Invitrogen Corporation ("Invitrogen") and to a company organized by Telegraph Hill Partners, respectively. As a result of the disposition of the Discovery Tools and Services business, we now operate in a single operating segment: Pharmaceuticals.

Novartis Restructuring. In January 2004, we amended our existing collaboration agreement with Novartis. We will continue to receive research funding through April 2006, consistent with the original agreement, and up to $35 million in pre-commercial payments for each preclinical drug candidate which we propose and Novartis accepts for preclinical development. We will no longer be responsible for the early development of drug candidates through proof-of-concept, as required under the original agreement, except that we may elect to develop VX-680 under the terms of the original agreement. We believe the restructured agreement remains financially attractive for us, and we are now free to devote our internal development resources to Vertex-controlled compounds in our areas of principal therapeutic interest.

Rebalancing of Research and Development

During 2003, we elected to focus our internal development and commercialization activity on two principal areas for the intermediate term: viral and inflammatory diseases. Our most advanced drug candidates in these areas are merimepodib (HCV), VX-950 (HCV) and VX-765 (inflammatory diseases). In preparation for advancing these and other Vertex-controlled drug candidates, we restructured our operations during the second half of the year to rebalance our relative investment in research, development and commercialization. This restructuring included a workforce reduction and a decision not to occupy our Kendall Square facility in Cambridge, Massachusetts. Of the terminated employees, 59% were from research, 30% were from sales, general and administrative functions primarily supporting research, and 11% were from 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%. Collaborator-sponsored research increased approximately 14% while our Collaborator-sponsored development declined in 2003 by 44%. Overall we expect our total research and development investment in 2004 to be comparable to 2003, with any increases, if any, resulting principally from activities funded in whole or in part by new collaborators.

Collaborative Revenue

Collaborations have been and will continue to be an important component of our business strategy going forward.

We currently have significant collaborations with Novartis, Aventis, GlaxoSmithKline, and Serono. In these collaborations, we have retained a share of downstream product revenue and may be entitled to significant pre-commercial milestone payments as drug candidates progress in development. We currently receive research funding from Novartis and Serono, and we currently have drug candidates in clinical development and commercialization under the collaborations with GlaxoSmithKline and Aventis and under a collaboration with Kissei. In 2003 we realized $69.1 million in royalties and collaborative revenue, all of which was earned under our pharmaceutical partnerships. This represented a significant decline from the 2002 level of $94.8 million and reflected the conclusion of funding from our collaborations with Lilly, Taisho and Schering AG and our lack of any new source of collaboration

revenue since 2000. Our collaborations with Novartis and GlaxoSmithKline accounted for 64% and 17%, respectively, of our total revenue in 2003.

A significant portion of our total research effort is being conducted under our collaboration with Novartis, which is scheduled to conclude, along with our research funding from Novartis, in April 2006. Under the terms of our agreement with Novartis, we will retain all rights to the intellectual property which we generate during that collaboration, except for rights licensed to Novartis in connection with the development and commercialization of specific preclinical drug candidates that Novartis accepts for development. Our access to these retained rights may help us initiate other collaborative opportunities in the kinase inhibitor field if our collaboration with Novartis is not extended beyond 2006. We will need to seek those opportunities or other financing alternatives in order to maintain our discovery 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 2004 which could be material to our business. Our business development priorities include new collaborations to support development and commercialization, in Europe and Japan, of our HCV clinical candidates and our oral cytokine inhibitor, VX-765. Our product development pipeline also includes drug candidates that are outside our core therapeutic areas of viral and inflammatory diseases, such as VX-702 (acute coronary syndromes), VX-944 (oncology) and VX-680 (oncology). In 2004 and future periods we expect to identify collaborative development and commercialization opportunities for these drug candidates in order to continue their clinical advancement, as we maintain focus on our Company-sponsored opportunities. We are also seeking collaborators for our ion channels and other discovery programs.

Lease Restructuring

For the twelve months ended December 31, 2003, we recorded restructuring and other related expenses of $91.8 million, of which $78.7 million relates to the potential restructuring of our Kendall Square lease. The restructuring accrual remaining at December 31, 2003 was $69.5 million. The liability at December 31, 2003 represents our best judgment of the assumptions and estimates most appropriate in measuring the outcome of the potential lease restructuring. Although it is possible that this liability will be paid in full over the next 24 months, the actual amount and timing of any payments will depend on the actual terms of any lease restructuring transaction(s). If we are successful in restructuring the lease, we could potentially be relieved of a future lease obligation of approximately $16 to $18 million per year and a contractual construction obligation which could be in excess of $30 million through 2006.

Financial Guidance

The key financial measures for which we have provided guidance in 2004 are as follows:

- Our full year loss is expected to be between $140 and $150 million, before any gains or charges, including additional charges relating to the potential lease restructuring and the convertible note debt exchange.
- Total revenue is expected to be in the range of $90 to $100 million in 2004. This is expected to be comprised of $60 to $65 million in committed funding and milestones from existing collaborative partners, and $15 to $18 million from HIV product royalties. In addition, we are currently in discussions with pharmaceutical companies regarding strategic research and product development agreements, and the successful conclusion of such discussions may result in additional revenue and cash flow in 2004.

- As we prioritize our investment toward proprietary drug candidates and realize the benefits from the operational restructuring in drug discovery during 2003, we anticipate that research and development expenses will be in the range of $190 to $205 million for the full year of 2004.
- We expect sales, general and administrative expenses to be between $38 and $43 million in 2004.
- We expect cash, cash equivalents and available for sale securities to be in excess of $350 million at the end of 2004.

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, as referenced in the section below entitled "Forward-Looking Statements."

Contractual Commitments and Obligations

The first part of the following table sets forth commitments and obligations that have been recorded on our consolidated balance sheet as of December 31, 2003. Certain other obligations and commitments, while not required under accounting principles generally accepted in the United States ("GAAP") to be included in the consolidated balance sheets, may have a material impact on liquidity. We have presented these items, all of which 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, 2003	Less than 1 year	1 to 3 years	3 to 5 years	5 years or more	Total
			(in thousands)		
Commitments and Obligations Recorded on the Balance Sheet at December 31, 2003:					
Capital leases	$ 113	$ —	$ —	$ —	$ 113
Collaborator development loans	14,000	—	18,460	—	32,460
Convertible subordinated notes*	—	—	315,000	—	315,000
Off-Balance Sheet Commitments and Obligations at December 31, 2003:					
Operating leases	44,962	108,180	59,740	182,847	395,729
Purchase obligations	3,000	6,000	—	—	9,000
Research and development and other commitments	2,769	2,365	—	—	5,134

Total contractual obligations and commitments	$ 64,844	$ 116,545	$ 393,200	$ 182,847	$ 757,436

* See description below of our Note exchange, which closed on February 13, 2004, pursuant to which we have deferred approximately $153.1 million of principal repayment obligations from 2007 to 2011.

Commitments and Obligations Recorded on the Balance Sheet at December 31, 2003:

Capital leases relate to equipment leases that expire at various dates though June 2004.

The collaborator development loans in the table above represent indebtedness to Novartis in the amount of $32,460,000 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 which it accepts for development, and consequently the loan facility providing funding for development activities by Vertex has been terminated. We may either continue development of VX-680 under the terms of the original agreement using loan proceeds we have received under the Novartis loan facility, or elect to develop and commercialize VX-680 independent of Novartis. If we elect to develop and commercialize VX-680 independent of Novartis, loan amounts with respect to that drug candidate which are unspent and uncommitted at the time of our election will be repayable immediately. Outstanding loans which 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 not, the related loan will be repayable without interest in May 2008. At December 31, 2003, approximately $14 million in development loans previously advanced to us were unspent and uncommitted. Please refer to Note P to our consolidated financial statements included in this Annual Report on Form 10-K.

At December 31, 2003 we had $315,000,000 in 2007 Notes. On February 13, 2004, we concluded an exchange of approximately $153.1 million in aggregate principal amount of 2007 Notes for approximately $153.1 million in aggregate principal amount of newly issued 2011 Notes. As a result of this transaction, the Company has outstanding $161.9 million in aggregate principal amount of 2007 Notes and $153.1 million in aggregate principal amount of 2011 Notes. Our annual interest payment obligation increased by $1.1 million to $16.9 million, reflecting the slightly higher coupon rate on the 2011 Notes.

Off-Balance Sheet Commitments and Obligations at December 31, 2003:

At December 31, 2003, 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, 2003.

Our Kendall Square lease term began January 1, 2003 and lease payments commenced in May 2003. We have an obligation, staged over a number of years, to build out the space into finished laboratory and office space. The lease will expire in 2018 with options to extend the lease for two consecutive terms of ten years each, ultimately expiring in 2038. In June 2003, we decided not to occupy the space under this lease and to attempt to restructure the lease. See Note E to our consolidated financial statements included in this Annual Report on Form 10-K. The Company's future minimum commitments under this lease including lease payments and a construction obligation are $29.2 million for less than 1 year, $68.4 million for 1 to 3 years, $38.7 million for 3 to 5 years and $176.2 million for 5 years or more and are included in the table above.

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 annually for three years after the completion of the sale of certain assets of the Discovery Tools and Services business on March 28, 2003.

Liquidity and Capital Resources

We have incurred operating losses since our inception and have historically financed our operations principally through public stock offerings, private placements of our equity and debt securities, strategic collaborative agreements, which include research and development funding, milestones and royalties on the sales of products, proceeds from 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, 2003 we had cash, cash equivalents and marketable securities of $583,164,000, which is a decrease of $51,820,000 from $634,984,000 at December 31, 2002. The decrease of $51,820,000 is primarily the result of cash used by operations of $167,623,000 offset by the net cash consideration received from the sale of the assets of the Discovery Tools and Services business of approximately $96,561,000. Additionally, expenditures for property and equipment were $17,351,000, cash receipts from the issuance of common stock under our employee benefit programs were approximately $11,959,000 and we drew down $27,460,000 under the Novartis loan facility in 2003, bringing the balance outstanding under the loan facility to $32,460,000 at December 31, 2003.

As part of our strategy to manage our long term operational cash needs, in early 2004 we exchanged approximately $153.1 million in aggregate principal amount of our 2007 Notes for approximately $153.1 million in aggregate principal amount of newly issued 2011 Notes. The 2011 Notes were issued through a private offering 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.

The restructuring accrual remaining at December 31, 2003 of $69.5 million, relating to the potential Kendall Square lease restructuring, could possibly be paid in full over the next 24 months. However, the actual amount and timing of such payments will be dependent upon the ultimate terms of any lease restructuring. We review our estimates underlying the restructuring accrual on at least a quarterly basis, and the accrual could change with any future change in our estimates.

We expect to continue to invest significantly in our pipeline, particularly in clinical trials of merimepodib, VX-950 and VX-765, and in our ion channel and kinase discovery efforts. 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. We expect our capital expenditures to remain at levels consistent with 2003, and we expect to complete 2004 with cash, cash equivalents and marketable securities in excess of $350 million.

Beyond 2004, 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 we may enter, in order to help fund our research and development efforts.

From time to time during 2004, we may repurchase our existing 2007 Notes in privately negotiated transactions, or market purchases or otherwise, depending on market conditions. Any such repurchases may be material.

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 securities or other methods of financing. We will continue to manage our capital structure and consider financing opportunities to strengthen our long term liquidity profile. There can be no assurance that such financing 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, research and development expenses, and revenue recognition, 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 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 rate applied in the initial period.

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, development and commercialization, to better support our long-term objective of becoming an integrated drug company. The restructuring included a workforce reduction, write-offs of certain assets and a decision not to occupy the Kendall Square facility. We are actively trying to restructure the lease obligation.

As a result of the Company's restructuring plan and 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 updated the liability as changes in circumstances have required. For the twelve months ended December 31, 2003, we recorded restructuring and other related expenses of $91.8 million. The $91.8 million includes $78.7 million of potential lease restructuring expense (of which $34.9 million, $42.4 million and $1.4 million was recorded in the second, third and fourth quarters of 2003, respectively). In addition to the $78.7 million, other costs included in the $91.8 million charge include $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 potential lease restructuring is the most significant component of the total restructuring charge and requires us to make significant judgments and assumptions. We use probability weighted discounted cash flows in order to calculate the amount of the liability associated with the potential lease restructuring. In accordance with SFAS 146, we used a credit-adjusted risk-free rate of approximately 10% in discounting our estimated cash flows. The probability weighted cash flows are based on management's assumptions and estimates regarding the possible outcomes of the potential lease restructuring. In estimating the liability we considered several possible outcomes of the potential lease restructuring, including a sublease of the entire space, a buy-out of our obligation, partial subleases by multiple parties, and other variations of these same outcomes. We also included in these potential outcomes the contractually required commitment for build-out of the leased space. We validate our estimates and assumptions through consultations with independent third parties having relevant expertise. We increased our estimated lease restructuring expense from the second quarter to the third quarter by $42.4 million, based on our judgment that a significant decline in the real estate

market in Cambridge, Massachusetts had occurred. We believe an increase in available laboratory and office space in Cambridge, Massachusetts and certain other factors led to a corresponding overall decline in real estate market fundamentals from the previous quarter. Accordingly, we revised our expectations of attainable sublease terms, assuming lower sublease rental rates and a delay in occupancy by potential subtenants.

It is possible that our estimates and assumptions will change in the future resulting in additional adjustments to the amount of the liability, and the effect of such 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 $8 million. If the time to finalize the restructuring is delayed by six months from our estimated completion date, the impact could be as high as approximately $10 million in additional 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 ("SAB 101"), "Revenue Recognition in Financial Statements," as amended by SEC Staff Accounting Bulletin No. 104, "Revenue Recognition," 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 partners. The terms of these agreements typically include non-refundable up-front license fees, funding of research and development efforts, payments based upon achievement of certain milestones and royalties 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 impact 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 collaborative contract, are recognized as earned when the corresponding payment is considered 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. We did not receive any license payments in 2003.

Royalty revenue is recognized based upon actual and estimated net sales of licensed products in licensed territories, as provided by our collaborative partner, and is recognized in the period the sales

occur. Differences between actual royalty revenues and estimated royalty revenues, which have not been historically 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 as 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.

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 the 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 all periods presented. The reclassification of the amounts to discontinued operations have been prepared using estimates and assumptions we have deemed appropriate based upon the information currently available. Prior to 2002, the Discovery Tools and Services business was not separately managed operationally or financially and therefore, we have estimated certain operating expenses, based on certain assumptions, including relative costs of the business being sold compared to historical site costs. 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, 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 to 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.

Royalties consist primarily of Agenerase royalty revenue. Agenerase royalty revenue is based on actual and estimated worldwide net sales of Agenerase. We began earning royalties on sales of Lexiva in the United States in November 2003. We expect to receive marketing approval for Lexiva in the European Union in 2004. We pay a royalty to a third party on sales of Agenerase and Lexiva.

Collaborative and other research and development revenue decreased $24,577,000 or 29% in 2003 as compared with 2002. The decrease in collaborative and other research and development revenue 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
Serono	5,280	5,280
GlaxoSmithKline	2,500	1,500
Eli Lilly	—	12,054
Schering	—	5,000
Kissei	267	4,574
Taisho	—	4,187
Other	7,590	10,227
Total collaborative and other research and development revenue	$ 60,139	$ 84,716

We have not entered into any significant collaborative research and development agreements since 2000. Additionally as shown in the table above, research funding under our partnerships with Eli Lilly, Schering and Taisho concluded in 2002.

We expect that collaborative and other research and development revenues will continue to be a significant source of our total revenues and we believe we could enter into additional collaborative agreements in 2004 which could be material to our business.

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 has decreased due to the operational restructuring in June 2003 while our investment in development has increased as a result of our proprietary drug candidates entering and advancing through clinical development. In 2003 our clinical trials focused on multiple drug candidates. The results of these trials enabled us to focus our clinical pipeline on two core therapeutic areas—viral and inflammatory diseases. Our lead drug candidates in these areas are merimepodib (HCV), VX-950 (HCV) and VX-765 (inflammatory diseases). In 2003 our development investment also focused on drug candidates with potential therapeutic indications outside our current core therapeutic areas, such as VX-702 (acute coronary syndromes), VX-148 (autoimmune diseases), VX-944 (oncology) and VX-680 (oncology). In 2004 and future periods we will seek to identify licensing opportunities for these drug candidates in order to continue their clinical development. We continue to focus our main drug discovery efforts on the protein kinase and ion channel gene families as well as other targeted areas.

Our collaborative partners have agreed to fund portions of our research and development programs related to specified drug candidates. Our research and development expenses for 2003, 2002 and 2001 were as follows:

	2003			2002			2001		
	Research	Development	Total	Research	Development	Total	Research	Development	Total
Collaborator-Sponsored	$ 62,162	$ 19,935	$ 82,097	$ 54,509	$ 35,675	$ 90,184	$ 49,490	$ 20,262	$ 69,752
Company-Sponsored	51,273	66,266	117,539	65,897	42,257	108,154	43,427	28,809	72,236
Total	$ 113,435	$ 86,201	$ 199,636	$ 120,406	$ 77,932	$ 198,338	$ 92,917	$ 49,071	$141,988

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

Therapeutic Area and Product Candidate	Clinical Indications	Development Phase	Company With Marketing Rights (Region)
Antivirals			
Agenerase™(amprenavir)	HIV infection	Mktd	GlaxoSmithKline (Worldwide)*
Lexiva™(fosamprenavir calcium)**	HIV infection	Mktd/MAA filed	GlaxoSmithKline (Worldwide)*
VX-385	HIV infection	Phase I	GlaxoSmithKline (Worldwide)*
Merimepodib (VX-497)	Chronic hepatitis C	Phase II	Vertex (Worldwide)
VX-950	Chronic hepatitis C	Preclin	Vertex (Worldwide)
Inflammation and Autoimmune Disease			
VX-765	Inflammatory/autoimmune diseases	Phase I	Vertex (Worldwide)
VX-702	Acute coronary syndromes; inflammatory diseases	Phase II	Kissei (Japan); Vertex (R.O.W.)
Pralnacasan (VX-740)	Rheumatoid arthritis (RA); osteoarthritis (OA); other inflammatory/autoimmune diseases	Phase II	Aventis (Worldwide)*
Cancer			
VX-680	Oncology	Preclin	Novartis (Worldwide)†
VX-944	Oncology	Phase I	Vertex (Worldwide)

* Vertex has co-promotion rights in the U.S. and the E.U. Kissei has marketing rights to amprenavir (Prozei™) in Japan.

** GlaxoSmithKline is seeking marketing approval in the E.U. under the name "Telzir™".

† Vertex may elect by June 30, 2004 to continue the development of VX-680 under the original terms of the Novartis agreement, in which event Novartis will hold an option on worldwide commercial rights.

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 2004 to remain comparable with 2003. However, our anticipated 2004 research and development expenses could vary materially, depending on the occurrence and timing of clinical trials. We anticipate that research and development expenses will increase in future periods as we add personnel and capabilities to support the advancement of our lead drug candidates. However, 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 (the industry average is 12 years) 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
Pre-Clinical	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	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 are typically 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 through 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 of development. Data obtained from these activities also are susceptible to varying interpretations, which could delay, limit or prevent regulatory approval. The duration and the cost related to 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 cash flows. We do not expect to receive net cash inflows from any major discovery and development products until a drug candidate becomes a profitable commercial product.

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

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 potential lease restructuring 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 $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 $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.

Year Ended December 31, 2002 Compared with Year Ended December 31, 2001

Our net loss for 2002 was $108,621,000 or $1.43 per basic and diluted common share compared to a net loss of $66,233,000 or $0.89 per basic and diluted common share for 2001. The net loss for 2002 includes income from discontinued operations of $28,337,000. The net loss for 2001 includes income from discontinued operations of $22,148,000, a charge of $25,901,000 representing a cumulative change in accounting principle related to revenue recognition and a gain of $17,749,000 representing a cumulative change in accounting related to derivative instruments.

Total revenues increased to $94,770,000 in 2002 compared to $85,297,000 in 2001. In 2002, revenue was comprised of $10,054,000 in royalties and $84,716,000 in collaborative and other research and development revenue, as compared with $10,783,000 in royalties and $74,514,000 in collaborative and other research and development revenue in 2001.

Collaborative and other research and development revenue increased $10,202,000 or 14% in 2002 as compared with 2001. The table presented below is a summary of significant revenue arrangements for the year ended 2002 as compared with the year ended 2001. As illustrated in the table below the overall increase in collaborative and other research and development revenue in 2002 is due to an increase in revenue recorded in connection with certan collaborations, such as Novartis and Eli Lilly, offset by a decrease in revenue earned under our arrangements with Kissei and Taisho. In 2002 we recognized an increased amount of revenue under our Novartis collaboration as a result of increased effort allocated to our kinase research program. In the fourth quarter of 2002, our research and development agreement with Lilly was restructured; the original contractual research term was to conclude in June 2003. In connection with the restructuring of the agreement and termination of the research term, we recognized approximately $1,637,000 in revenue that had been previously deferred. This deferred revenue related to the development milestone paid in December 2001 and the up-front payment received in June 1997 at the commencement of the collaboration. Additionally, in the fourth quarter of 2002 we received and recognized a milestone payment of $1,500,000 from GlaxoSmithKline in connection with the submission of a new drug application for market approval of Lexiva in the U.S.

We have not entered into any significant collaborative research and development agreements since 2000. Funding under our partnerships with Lilly, Schering and Taisho concluded in 2002.

	Year Ended December 31,	
	2002	2001
	(In thousands)	
Collaborative and other research and development revenue:		
Summary of significant collaborative revenue arrangements:		
Novartis	$ 41,894	$ 36,723
Serono	5,280	4,802
GlaxoSmithKline	1,500	—
Eli Lilly	12,054	6,686
Schering	5,000	5,000
Kissei	4,574	7,405
Taisho	4,187	5,583
Other	10,227	8,315
Total collaborative and other research and development revenue	$ 84,716	$ 74,514

Research and development expenses increased to $198,338,000 in 2002 from $141,988,000 in 2001, primarily due to investment in advancing our clinical pipeline and broadening our research efforts. Our clinical investment was directed primarily toward advancing our second generation p38 MAP kinase inhibitor (VX-702), our IMPDH inhibitors (VX-148 and merimepodib), our HCV protease inhibitor (VX-950) and ICE inhibitor (VX-765). Development investment increased from $49,071,000 in 2001 to $77,932,000 in 2002. Investment in research increased from $92,917,000 in 2001 to $120,406,000 in 2002, resulting principally from the expansion of our multi-target gene family research programs, including our kinase program and ion channel program. As a result of our continued expansion, personnel and facilities expenses also increased.

Sales, general and administrative expenses increased $9,200,000, or 29%, to $41,056,000 in 2002 from $31,856,000 in 2001. The increase is primarily attributable to increased personnel and professional expenses. Included in the increase in personnel and professional expenses is an increase in expenses relating to the addition of certain key executives, certain process consulting costs and legal and patent expenses related to continued protection of our intellectual property, including expenses associated with contesting a suit filed by Oregon Health Sciences University.

Merger related costs of $22,960,000 in 2001 consisted of investment banking, legal and accounting fees associated with the acquisition of Aurora Biosciences Corporation completed on July 18, 2001.

Interest income decreased approximately $16,411,000 to $28,722,000 in 2002 from $45,133,000 in 2001. The decrease is a result of both a lower level of invested funds, and lower portfolio yields due to a reduced interest rate environment.

Interest expense decreased to approximately $17,684,000 in 2002 from $19,318,000 in 2001. The decrease is a result of the reduction in principal amount of the 2007 Notes. In October 2001, we repurchased $30,000,0000 in principal amount of our 2007 Notes and recorded a gain of $10,340,000 on the retirement of the notes in the fourth quarter of 2001.

In April 2002, the Financial Accounting Standards Board ("FASB") issued Statement of Financial Accounting Standard ("SFAS") 145, "Recission of FASB Statements No. 4, 44 and 64, Amendment of FASB Statement No. 13, and Technical Corrections." FAS 145 recinds FAS 4 and FAS 64, which addressed the accounting for gains and losses from extinguishment of debt. Under FAS 145 the gain on retirement of convertible subordinated notes is considered an ordinary item. The gain on retirement of convertible subordinated notes was originally classified in 2001 as an extraordinary item but has been reclassified as part of loss from continuing operations. At December 31, 2002 and 2001, $315,000,000 of the 2007 Notes was outstanding.

Using the equity method of accounting, we recorded $662,000 as our share of loss in Altus Biologics Inc. (Altus), for the year ended December 31, 2001. The loss is included in other expense on the Statement of Operations. Effective September 28, 2001, coincident with a financial restructuring of Altus, we changed our method of accounting for Altus from the equity method to the cost method. See Note I to our consolidated financial statements included in this Annual Report on Form 10-K.

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

Pursuant to the 2001 change, we recorded a one-time, non-cash charge of $25,901,000, representing a cumulative change in accounting principle for periods prior to 2001. The amount of revenue recognized in 2003, 2002 and 2001 which was included in the one-time, non-cash charge was $2,809,000, $6,979,000 and $7,748,000, respectively. Additionally, $3,684,000, $3,628,000 and $1,053,000 will be recognized as revenue in 2004, 2005 and thereafter, respectively, which amounts were included in the January 2001 charge to income.

Effective July 1, 2001, we adopted Derivative Implementation Group Issue No. A17, "Contracts that Provide for Net Share Settlement" (DIG A17). Pursuant to the adoption of DIG A17, we recorded a $17,749,000 cumulative effect of a change in accounting principle to reflect the value of warrants held in Altus. This amount is included in investments in the December 31, 2001 balance sheet. As of September 30, 2001, the warrants no longer qualified as derivatives under DIG A17 due to changes in the terms of the warrants coincident with a financial restructuring of Altus.

Forward-looking Statements

This reports 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 continue to increase, but research expenses will not increase without new funding from collaborations; (iv) we will enter into additional strategic collaborations for the development of our drug candidates which are outside our focus areas of viral and inflammatory diseases; (v) our financial results for 2004 will be as set forth in this Annual Report on Form 10-K; (vi) we will continue to collaborate with existing and new partners to develop and market Vertex-discovered products for selected major therapeutic areas; (vii) we and our partners will begin clinical trials on a number of our development stage drug candidates during 2004; (viii) Lexiva will be approved and launched in the E.U. in 2004; (ix) we will initiate expanded clinical trials of merimepodib in 2004, and believe we may be able to file an NDA for merimepodib as early as 2007; (x) development of pralnacasan will be delayed by at least 12-24 months, if the adverse toxicology finding is satisfactorily addressed; (xi) our Phase II clinical trial of VX-702 will be complete in 2004; (xii) our research programs will produce additional development candidates, including numerous kinase inhibitors, in the next several years; and (xiii) our liability to restructure the Kendall Square lease will be as we have estimated and we may pay the full amount in the next 24 months. 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 2004 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, including Lexiva, 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 restructure our obligation under the Kendall Square facility 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 May 2003, the Financial Accounting Standards Board ("FASB") issued Statement of Financial Accounting Standards No. 150 ("SFAS 150"), Accounting for Certain Financial Instruments with Characteristics of both Liabilities and Equity. SFAS 150 establishes standards for how an issuer classifies and measures certain financial instruments with characteristics of both liabilities and equity. The adoption of SFAS 150 in the third quarter of 2003 did not have a material impact on our results of operations or financial position.

In April 2003, the FASB issued Statement of Financial Accounting Standards No. 149 ("SFAS 149"), Amendment of Statement 133 on Derivative Instruments and Hedging Activities. SFAS 149 amends and clarifies financial accounting and reporting for derivative instruments and for hedging activities under Statement of Financial Accounting Standards No. 133, *Accounting for Derivative Instruments and Hedging Activities* (SFAS 133). The adoption of SFAS 149 in the third quarter of 2003 did not have a material impact on our results of operations or financial position.

In November 2002, the FASB issued Interpretation No. 45, "Guarantor's Accounting and Disclosure Requirements for Guarantees, Including Indirect Guarantees of Indebtedness of Others" ("FIN 45"). FIN 45 elaborates on the disclosures the Company must make about obligations under certain guarantees that the company has issued. It also requires the Company to recognize, at the inception of a guarantee, a liability for the fair value of the obligations undertaken in issuing the guarantee. The initial recognition and initial measurement provisions are to be applied only to guarantees issued or modified after December 31, 2002. The adoption of FIN 45 did not have a material impact on our results of operations or financial position. We have provided additional disclosure with respect to guarantees in Note U to the Consolidated Financial Statements.

In January 2003, the FASB issued FASB Interpretation No. 46 ("FIN 46"), "Consolidation of Variable Interest Entities, an Interpretation of ARB No. 51" and in December 2003 issued a revised FIN 46 ("FIN 46R") which addresses the period of adoption of FIN 46 for entities created before January 31, 2003. FIN 46 provides a new consolidation model which determines control and consolidation based on potential variability in gains and losses. The provisions of FIN 46 are effective for enterpises with variable interest entities created after January 31, 2003. We must adopt the provisions of FIN 46 in the first quarter of 2004 and do not expect the adoption to have a material impact on our financial position or results of operations.

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 U.S. government and its agencies, investment grade corporate bonds and notes and money market instruments. These investments are denominnated in U.S. dollars. All of its 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-37 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

(a) **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 adequate and effective to ensure that material information relating to the Company, including its consolidated subsidiaries, was made known to them by others within those entities, particularly during the period in which this Annual Report on Form 10-K was being prepared. 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.

(b) **Changes in Internal Controls Over Financial Reporting.** No change in the Company's internal controls over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) occurred during the fourth quarter of our last fiscal year, that has materially affected, or is reasonably likely to materially affect, the Company's internal control over financial reporting.

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 2004 Annual Meeting of Stockholders (the "2004 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 2004 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.

We have adopted a written Code of Conduct and Ethics that applies to our principal executive officer, principal financial officer, and principal accounting officer or controller, or persons performing similar functions. Our Code of Conduct and Ethics also applies to our directors and all of our officers and employees. Our Code of Conduct and Ethics is available upon request without charge. Requests

for our Code of Conduct and Ethics should be directed to us at 130 Waverly St., Cambridge, MA 02139, Attention: Investor Relations, or by submitting an email request through the "Contact Us" tab in the "Investors" portion of our website, located at www.vrtx.com. Disclosure regarding any amendments to, or waivers from, provisions of the Code of Conduct and Ethics that apply to our principal executive and financial officers will be included in a Current Report on Form 8-K within five business days following the date of the amendment or waiver, unless website posting of such amendments or waivers is then permitted by the rules of The Nasdaq Stock Market.

ITEM 11. EXECUTIVE COMPENSATION

The information required by this Item 11 is included in the 2004 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 2004 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 2004 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 2004 Proxy Statement under "Employment Contracts and Change-in-Control Arrangements" and is incorporated herein by reference.

ITEM 14. PRINCIPAL ACCOUNTANT FEES AND SERVICES

The information required by this Item 14 is included in the 2004 Proxy Statement under "Independent Accountants" and is incorporated herein by reference.

PART IV

ITEM 15. EXHIBITS, FINANCIAL STATEMENT SCHEDULES, AND REPORTS ON FORM 8-K

(a)(1) **Financial Statements.** The Financial Statements required to be filed by Item 8 of this Annual Report on Form 10-K, and filed herewith, are as follows:

(a)(2) **Financial Statement Schedules.** 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, Aurora 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 filed with 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 filed with 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, as filed with the Secretary 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 filed with 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).

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 10.1 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, Amended and Restated as of July 17, 2002 (filed as Exhibit 10.3 to Vertex's 2002 Annual Report on Form 10-K [file No. 000-19319] and incorporated herein by reference).*

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 Form of Executive Employment Agreement executed by Joshua S. Boger and Vicki L. Sato (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 Form of Amendment to Employment Agreement executed by Joshua S. Boger and Vicki L. Sato (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 Executive Employment Agreement between Vertex and Iain P.M. Buchanan (filed as Exhibit 10.9 to Vertex's 2001 Annual Report on Form 10-K [File No. 000-19319] and incorporated herein by reference).*

10.10 Agreement dated December 21, 2000 between Vertex and Richard H. Aldrich (filed as Exhibit 10.10 to Vertex's 2000 Annual Report on Form 10-K [File No. 000-19319] and incorporated herein by reference).*

10.11 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).

10.12 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).

10.13 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).

10.14 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).

10.15 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).

10.16 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).

10.17 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).

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

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

10.20 Research and Development Agreement between Vertex and Eli Lilly and Company effective June 11, 1997 (filed, with certain confidential information deleted, as Exhibit 10.1 to Vertex's Quarterly Report on Form 10-Q for the quarter ended June 30, 1997 [File No. 000-19319] and incorporated herein by reference).

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

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

10.23 License, Development and Commercialization Agreement between Vertex and Hoechst Marion Roussel Deutschland GmbH dated September 1, 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).

10.24 Collaboration and Option Agreement between Vertex and Taisho Pharmaceutical Co., Ltd. dated November 30, 1999 (filed, with certain confidential information deleted, as Exhibit 10.27 to Vertex's 1999 Form 10-K [File No. 000-19319] and incorporated herein by reference).

10.25 Research and Early Development Agreement between Vertex and Novartis Pharma AG dated May 8, 2000 (filed, with certain confidential information deleted, as Exhibit 10.1 to Vertex's Quarterly Report on Form 10-Q for the quarter ended March 31, 2000 [File No. 000-19319] and incorporated herein by reference).

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

10.27 Letter Agreement between Aurora 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).*

10.28 Executive Employment Agreement between Vertex and Kenneth S. Boger (filed as Exhibit 10.28 to Vertex's 2001 Annual Report on Form 10-K [File No. 000-19319] and incorporated herein by reference).*

10.29 Executive Employment Agreement between Vertex and Ian F. Smith (filed as Exhibit 10.29 to Vertex's 2001 Annual Report on Form 10-K [File No. 000-19319] and incorporated herein by reference).*

10.30 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).*

10.31 Form of 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).

10.32	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).*
10.33	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.
10.34	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).
10.35	First Revised and Restated Research and Early Development Agreement between Vertex and Novartis Pharma AG dated February 3, 2004 (filed, with certain confidential information deleted, 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 Accountants, 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.

(b) **Reports on Form 8-K.**

On November 10, 2003, we furnished a report on Form 8-K-Item 9-Regulation FD Disclosure Item 12-Disclosure of Results of Operations and Financial Condition, reporting that the Company had issued two press releases, one regarding the development status of certain of its drug candidates and the second reporting that the Company had issued a press release to report the Company's financial results for the quarter ended September 30, 2003.

On December 5, 2003, we filed a report on Form 8-K-Item 5-Other Events, reporting that Joshua S. Boger, the Company's Chairman and CEO, entered into a plan with Goldman, Sachs & Co., pursuant to which Goldman will undertake to sell, subject to a limit order, an aggregate of 370,000 shares of the Company's stock issuable upon exercise of options held by Dr. Boger.

On December 5, 2003, we furnished a report on Form 8-K-Item 9-Regulation FD Disclosure, reporting that the Company had issued a press release on December 4, 2003 to announce the sale of certain instrumentation assets of Vertex's subsidiary Aurora Instruments LLC to Aurora Discovery, Inc., and updating our 2003 full-year financial guidance.

On December 16, 2003, we filed a report on Form 8-K-Item 5-Other Events, reporting that on November 17, 2003, Iain P.M. Buchanan, the Company's Vice President of European Operations, entered into a plan with Lehman Brothers Inc., pursuant to which Lehman will undertake to sell, subject to a limit order, an aggregate of 50,000 shares of the Company's stock issuable upon exercise of options held by Mr. Buchanan.

On December 19, 2003, we filed a report on Form 8-K-Item 5-Other Events, reporting that Vicki L. Sato, the Company's President, entered into a plan with Goldman, Sachs & Co., pursuant to which Goldman will undertake to sell, subject to a limit order, an aggregate of 344,509 shares of the Company's stock issuable upon exercise of options held by Dr. Sato.

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 15, 2004 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 15, 2004
/s/ IAN F. SMITH Ian F. Smith	Chief Financial Officer (Principal Financial Officer)	March 15, 2004
/s/ JOHANNA MESSINA POWER Johanna Messina Power	Controller (Principal Accounting Officer)	March 15, 2004
/s/ ERIC K. BRANDT Eric K. Brandt	Director	March 15, 2004
/s/ ROGER W. BRIMBLECOMBE Roger W. Brimblecombe	Director	March 15, 2004
/s/ STUART J. COLLINSON Stuart J. Collinson	Director	March 15, 2004
/s/ BRUCE I. SACHS Bruce I. Sachs	Director	March 15, 2004
/s/ CHARLES A. SANDERS Charles A. Sanders	Director	March 15, 2004
/s/ ELAINE S. ULLIAN Elaine S. Ullian	Director	March 15, 2004

VERTEX PHARMACEUTICALS INCORPORATED

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Page Number

Report of Independent Auditors

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

In our opinion, the accompanying consolidated balance sheets and the related consolidated statements of operations, of stockholders' equity and comprehensive loss and of cash flows present fairly, in all material respects, the financial position of Vertex Pharmaceuticals Incorporated and its subsidiaries at December 31, 2003 and 2002, and the results of their operations and their cash flows for each of the three years in the period ended December 31, 2003 in conformity with accounting principles generally accepted in the United States of America. These financial statements are the responsibility of the Company's management; our responsibility is to express an opinion on these financial statements based on our audits. We conducted our audits of these statements in accordance with auditing standards generally accepted in the United States of America, which require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements, assessing the accounting principles used and significant estimates made by management, and evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

As discussed in Note C to the consolidated financial statements, during the year ended December 31, 2001 the Company changed its method of accounting for revenue recognition. As discussed in Note I to the consolidated financial statements, during the year ended December 31, 2001 the Company changed its method of accounting for certain derivatives.

/s/ PricewaterhouseCoopers LLP

Boston, Massachusetts
March 10, 2004

VERTEX PHARMACEUTICALS INCORPORATED

Consolidated Balance Sheets

	December 31,	
	2003	2002
	(In thousands, except share and per share amounts)	
Assets		
Current assets:		
Cash and cash equivalents	$ 98,159	$ 108,098

Marketable securities, available for sale	485,005	526,886
Accounts receivable	7,324	13,200
Prepaid expenses and other current assets	3,318	8,388
Total current assets	593,806	656,572
Restricted cash	26,061	26,091
Property and equipment, net	80,083	95,991
Investments	18,863	26,433
Other assets	5,598	10,633
Total assets	$ 724,411	$ 815,720
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	$ 12,306	$ 16,745
Accrued expenses and other current liabilities	26,374	29,306
Accrued interest	4,455	4,463
Obligations under capital leases	113	1,965
Collaborator development loan	14,000	—
Deferred revenue	7,746	11,888
Accrued restructuring and other expense	69,526	—
Other obligations	4,547	230
Total current liabilities	139,067	64,597
Obligations under capital leases, excluding current portion	—	99
Collaborator development loan, excluding current portion	18,460	5,000
Other obligations, excluding current portion	7,268	5,845
Deferred revenue, excluding current portion	51,771	46,598
Convertible subordinated notes (due September 2007)	315,000	315,000
Total liabilities	531,566	437,139
Commitments and contingencies		
Stockholders' equity:		
Preferred stock, $0.01 par value; 1,000,000 shares authorized; none issued and outstanding at December 31, 2003 and 2002, respectively	—	—
Common stock, $0.01 par value; 200,000,000 shares authorized; 78,025,002 and 76,357,412 shares issued and outstanding at December 31, 2003 and 2002, respectively	780	764
Additional paid-in capital	810,407	794,206
Deferred compensation, net	(1,112)	—
Accumulated other comprehensive income	2,690	6,764
Accumulated deficit	(619,920)	(423,153)
Total stockholders' equity	192,845	378,581
Total liabilities and stockholders' equity	$ 724,411	$ 815,720

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

VERTEX PHARMACEUTICALS INCORPORATED

Consolidated Statements of Operations

	Years Ended December 31,		
	2003	2002	2001
	(In thousands, except per share data)		
Revenues:			
Royalties	$ 9,002	$ 10,054	$ 10,783
Collaborative and other research and development revenues	60,139	84,716	74,514
Total revenues	69,141	94,770	85,297
Costs and expenses:			
Royalty payments	3,126	3,334	3,594
Research and development	199,636	198,338	141,988
Sales, general and administrative	39,082	41,056	31,856
Restructuring and other expense	91,824	—	—
Merger related costs	—	—	22,960
Total costs and expenses	333,668	242,728	200,398
Loss from operations	(264,527)	(147,958)	(115,101)
Interest income	15,412	28,722	45,133
Interest expense	(17,298)	(17,684)	(19,318)
Gain on retirement of convertible subordinated notes	—	—	10,340
Other expense	—	(38)	(1,283)
Loss from continuing operations before cumulative effect of changes in accounting principles	$ (266,413)	$ (136,958)	$ (80,229)
Income from discontinued operations:			
Gain on sales of assets	70,339	—	—
Income (loss) from discontinued operations	(693)	28,337	22,148
Total income from discontinued operations	69,646	28,337	22,148
Loss before cumulative effect of changes in accounting principles	$ (196,767)	$ (108,621)	$ (58,081)
Cumulative effect of change in accounting principle—revenue recognition	—	—	(25,901)
Cumulative effect of change in accounting principle—derivatives	—	—	17,749
Net loss	$ (196,767)	$ (108,621)	$ (66,233)
Basic and diluted net loss per common share from continuing operations before cumulative effect of changes in accounting principles	$ (3.46)	$ (1.81)	$ (1.08)
Discontinued operations	0.90	0.38	0.30
Cumulative effect of changes in accounting principle-revenue recognition	—	—	(0.35)
Cumulative effect of change in accounting principle-derivatives	—	—	0.24
Basic and diluted net loss per common share	$ (2.56)	$ (1.43)	$ (0.89)
Basic and diluted weighted average number of common shares outstanding	77,004	75,749	74,464
Unaudited pro forma amounts assuming the 2001 accounting change relating to revenue recognition is applied retroactively (Note C):			
Net loss	$ (196,767)	$ (108,621)	$ (40,332)
Basic and diluted net loss per common share	$ (2.56)	$ (1.43)	$ (0.54)

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

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, 2000	73,474	735	757,522	(174)	4,227	(248,299)	514,011	
Net change in unrealized holding gains/(losses) on marketable securities					7,218		7,218	$ 7,218
Translation adjustments					(311)		(311)	(311)
Net loss						(66,233)	(66,233)	(66,233)
Comprehensive loss								$ (59,326)
Issuances of common stock:								
Benefit plans	1,581	16	19,637				19,653	
Equity compensation for services rendered			320				320	
Tax benefit of disqualifying position			539				539	
Amortization of deferred compensation				154			154	
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	

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

VERTEX PHARMACEUTICALS INCORPORATED

Consolidated Statements of Cash Flows

	Years Ended December 31,

	2003	2002	2001
		(In thousands)	
Cash flows from operating activities:			
Net loss	$ (196,767)	$ (108,621)	$ (66,233)
Net income from discontinued operations	(69,646)	(28,337)	(22,148)
Loss from continuing operations	(266,413)	(136,658)	(88,381)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization	23,438	24,905	17,802
Non-cash based compensation expense	3,146	2,894	1,501
Non-cash restructuring and other expense	4,395	—	—
Write-down of marketable securities and investments	—	666	2,100
Other non-cash items, net	—	1,220	31
Loss on disposal of property and equipment	116	51	1,107
Realized (gains)/losses on marketable securities	(1,249)	(2,048)	(3,081)
Equity in losses of unconsolidated subsidiary	—	—	662
Gain on retirement of convertible subordinated notes	—	—	(10,340)
Cumulative effects of changes in accounting principles	—	—	8,152
Changes in operating assets and liabilities:			
Accounts receivable	1,574	3,064	5,515
Prepaid expenses	596	2,479	(3,213)
Other current assets	(2)	2,283	8,359
Accounts payable	(2,151)	4,770	3,732
Accrued expenses and other current liabilities	(4,050)	1,483	10,945
Accrued restructuring and other expense	69,526	—	—
Accrued interest		4	(424)
Deferred revenue	4,683	2,012	13,452
Effect of discontinued operations on operating activities	(1,232)	13,636	25,034
Net cash used in operating activities	(167,623)	(79,539)	(7,047)
Cash flows from investing activities:			
Purchases of marketable securities	(555,842)	(702,986)	(1,252,781)
Sales and maturities of marketable securities	593,998	727,582	1,176,143
Expenditures for property and equipment	(17,351)	(38,881)	(49,391)
Proceeds from the sale of equipment	—	6	—
Restricted cash	30	(4)	(15,966)
Investments and other assets	1,603	101	(3,116)
Effect of discontinued operations on investing activities	97,147	(1,780)	24
Net cash (used in) provided by investing activities	119,585	(15,962)	(145,087)
Cash flows from financing activities:			
Issuances of common stock, net	11,959	13,327	18,626
Repurchase of convertible debentures	—	—	(18,900)
Proceeds from notes payable, capital lease and loan obligations	27,460	5,000	—
Principal payments on capital leases and other obligations	(1,951)	(3,986)	(4,417)
Effect of discontinued operations on financing activities	—	(499)	(318)
Net cash (used in) provided by financing activities	37,468	13,842	(5,009)
Effect of changes in exchange rates on cash	631	552	(311)
Net increase (decrease) in cash and cash equivalents	(9,939)	(81,107)	(157,454)
Cash and cash equivalents—beginning of period	108,098	189,205	346,659

Cash and cash equivalents—end of period	$ 98,159	$ 108,098	$ 189,205
Supplemental disclosure of cash flow information:			
Cash paid for interest	$ 15,896	$ 16,078	$ 18,244
Cash paid for taxes	$ —	$ 118	$ 156

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

VERTEX PHARMACEUTICALS INCORPORATED

Notes to 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 infection, inflammatory and autoimmune disorders and cancer, independently and with collaborators. At December 31, 2003 the Company had three facilities worldwide with more than 720 employees. The Company's facilities are located in Cambridge, MA, San Diego, CA and Abingdon, UK.

The Company's principal focus is on the development and commercialization of new treatments for viral and inflammatory diseases. There are two Vertex discovered products, Agenerase (amprenavir) and Lexiva (fosamprenavir calcium), on the market now for the treatment of HIV and AIDs. Agenerase was approved and launched in the United States in April 1999. Lexiva was granted marketing approval by the FDA in October 2003, and was launched by Vertex and GlaxoSmithKline shortly thereafter. Vertex earns a royalty on the sales of Agenerase and Lexiva and co-promotes these products in partnership with GlaxoSmithKline. Vertex's pipeline of potential products includes drug candidates targeting chronic hepatitis C infection, drug candidates targeting inflammatory diseases such as rheumatoid arthritis, osteoarthritis, acute coronary syndromes and psoriasis, and drug candidates directed at cancer therapy. Additionally, Vertex has built a drug discovery capability that integrates biology, chemistry, biophysics, automation and information technologies, to make the drug discovery process more efficient and productive.

Partnerships are a key component of Vertex's corporate strategy. Currently, Vertex has significant collaborations with Aventis, GlaxoSmithKline, Novartis, and Serono. These collaborations provide Vertex with financial support and other valuable resources for its research programs, development of its clinical drug candidates, and marketing and sales of its products. Vertex currently has drug candidates in clinical development under collaborations with GlaxoSmithKline, Aventis and Kissei.

The Company has begun developing certain potential products independently, for markets where Vertex believes it can commercialize products effectively and reach large patient populations, but expend comparatively fewer resources by using a sales force focused on specialists. At the same time, Vertex is collaborating with partners to discover, develop and market other Vertex-discovered products for selected major therapeutic areas.

In July 2001, Vertex completed a merger with Aurora BioSciences Corporation ("Aurora"). Aurora specialized in industry-leading assay development, screening and cell biology capabilities. The Company acquired all of Aurora's outstanding common stock in a tax-free, stock for stock transaction, for approximately 14.1 million shares of Vertex common stock. Prior to its acquisition by Vertex, Aurora completed a merger with PanVera Corporation. PanVera Corporation was a biotechnology company engaged in the development, manufacture and worldwide supply of proteins for evaluation as targets and drug screening assays for high-throughput screening. Both mergers were accounted for under the pooling of interests method of accounting.

In July 2002, Vertex began to commercialize the Aurora instruments and services, along with PanVera Corporation's reagents and probes business, under the name PanVera LLC. PanVera LLC's core business included commercialization of fluorescence assay technologies, assay development services, the manufacture and sale of proteins, reagents and probes, and the development and sale of instrumentation systems. Upon completion of this reorganization, PanVera LLC comprised the Company's Discovery Tools and Services business and Aurora's remaining business continued to operate at the former Aurora's San Diego site, as Vertex Pharmaceuticals (San Diego) LLC, dedicated to the Company's pharmaceuticals business.

In March and December 2003, in two independent transactions, Vertex sold the assets of the Discovery Tools and Services business. 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 D "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, dependence on key personnel, uncertain protection of proprietary technology, clinical trial uncertainty, dependence on collaborative partners, 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 mergers with Aurora and PanVera have been accounted for as a pooling of interests under Accounting Principles Board Opinion No. 16, "Business Combinations" ("APB 16"), and accordingly, the results of operations, financial position and cash flows for Aurora and PanVera have been included in the consolidated financial statements of the Company for all periods presented.

The sale of the assets of the Company's Discovery Tools and Services business 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 all periods presented. The results of discontinued operations prior to 2002 have been prepared using estimates and assumptions the Company has deemed appropriate based upon the 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 and therefore, Vertex has estimated certain operating expenses based on certain assumptions, including relative costs of the business being sold compared to historical site costs. Please refer to Note D "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 U.S. 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 potential lease restructuring, 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 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 years ended December 31, 2002 and 2001, the Company recorded $666,000 and $600,000, respectively, in charges to write down certain marketable securities because the decline in value was considered other-than-temporary. There were no charges to write-down marketable securities in 2003. Realized gains and losses are determined on the specific identification method and are included in interest income.

Investments

Investments at December 31, 2003 and 2002 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. For the year ended December 31, 2001, the Company recorded $1,500,000 in charges related to the write-down of an investment because the decline in the value of the investment was considered other-than-temporary. There were no charges to write-down investments in 2002 or 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 2003 the Company had significant revenue transactions with Novartis and GlaxoSmithKline, which accounted for 64% and 17%, respectively, of the Company's total revenue. In 2002 and 2001, the Company had significant revenue transactions with Novartis, which accounted for 26% and 22%, respectively, of the Company's total revenue.

GlaxoSmithKline and Novartis represented approximately 41% and 29%, respectively, of the Company's accounts receivable balance at December 31, 2003. Kissei Pharmaceuticals and GlaxoSmithKline represented approximately 27% and 19%, respectively, of the Company's accounts receivable balance at December 31, 2002. Management believes that credit risks associated with these collaborative partners 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.

Assets Held for Sale

The Company classifies long-lived assets as held for sale so long as such assets are available for immediate sale in their present condition, the Company has the intent and ability to transfer the assets to a buyer within one year and the sale of such assets is considered probable at the balance sheet date. The Company considers a sale probable when a definitive purchase and sale agreement has been signed. Assets held for sale are measured at the lower of book value or fair value less cost to sell. No assets were classified as held for sale at December 31, 2003 or 2002.

Long-Lived Assets

The Company accounts for the impairment and disposition of long-lived assets in accordance with Statement of Financial Accounting Standards ("SFAS") No. 144, "Accounting for the Impairment or Disposal of Long-Lived Assets." 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.

Retirement of Convertible Subordinated Notes

In October 2001, the Company repurchased and retired $30,000,000 in principal amount of its 5% Convertible Subordinated Notes due September 2007 ("2007 Notes"), which resulted in a gain of $10,340,000. In April 2002, the FASB issued SFAS 145, "Recission of FASB Statements No. 4, 44 and 64, Amendment of FASB Statement No. 13, and Technical Corrections." SFAS 145 recinds SFAS 4 and SFAS 64, which addressed the accounting for gains and losses from extinguishment of debt. Under SFAS 145 the gain on retirement of convertible subordinated notes is considered an ordinary item. The gain on retirement of convertible subordinated notes originally was classified as an extraordinary item in 2001, but has since been reclassified to loss from continuing operations.

Stock-Based Compensation

In December 2002, the FASB issued SFAS No. 148, "Accounting for Stock-Based Compensation, Transition and Disclosure" ("SFAS 148"). SFAS 148 amends SFAS No. 123 "Accounting for Stock-Based Compensation" ("SFAS 123"), to provide alternative methods of transition for a voluntary change to the fair-value based method of accounting for stock-based employee compensation. In addition, SFAS 148 amends the disclosure requirements of SFAS 123 to require prominent disclosures in both annual and interim financial statements about the method of accounting for stock-based compensation and the effect of the method used on reported results. The Company has adopted the quarterly and annual disclosure requirements of SFAS 148 as required.

In accordance with SFAS 148, the Company has adopted the disclosure-only provisions of SFAS 123 and 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 other criteria are met, when the exercise price of options granted to employees under these plans equals the market price of the common stock on the date of grant, no compensation cost is required. When the exercise price of options granted to employees under these plans 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, 2003 the Company had three stock-based employee compensation plans, which are described more fully in Note O "Common and Preferred Stock." For the year ended December 31, 2003, the Company recorded $16,000 in compensation expense related to restricted shares issued to employees in 2003. No stock-based employee compensation cost related to stock options is reflected in the 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 nonemployees, the Company recognizes compensation costs in accordance with the requirements of SFAS 123. SFAS 123

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.

	Year Ended December 31,		
	2003	2002	2001
	(In thousands, except per share data)		
Net loss attributable to common shareholders, as reported	$ (196,767)	$ (108,621)	$ (66,233)
Add: Employee stock-based compensation expense included in net loss	16	—	—
Deduct: Total stock-based employee compensation expense determined under the fair value based method for all awards	(51,180)	(54,686)	(55,295)
Pro forma net loss	$ (247,931)	$ (163,307)	$ (121,528)
Basic and diluted net loss per common share, as reported	$ (2.56)	$ (1.43)	$ (0.89)

Basic and diluted net loss per common share, pro forma	$ (3.22)	$ (2.16)	$ (1.63)

Restructuring and Other Expense

In June 2002, the FASB issued SFAS 146 "Accounting for Costs Associated with Exit or Disposal Activities" ("SFAS 146"). SFAS 146 addresses financial accounting and reporting for costs associated with exit or disposal activities and nullifies EITF 94-3 "Liability Recognition for Certain Employee Termination Benefits and other Costs to Exit an Activity (including Certain Costs Incurred in a Restructuring)." The principal differences between SFAS 146 and EITF 94-3 relate to the timing of recording a liability and the value of the liability recorded; SFAS 146 requires that a liability for a cost associated with an exit or disposal activity be recognized when the liability is incurred and that the liability be recorded at fair value. SFAS 146 is effective for exit or disposal activities initiated after December 31, 2002.

The Company adopted SFAS 146 as required and accordingly records costs and liabilities associated with exit and disposal activities, as defined in SFAS 146, at fair value in the period the liability is incurred. In periods subsequent to initial measurement, changes to the liability are measured using the credit-adjusted risk-free rate applied in the initial period. In 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 E "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." In third quarter of 2003, the Company adopted Emerging Issues Task Force Issue No. 00-21, "Revenue Arrangements with Multiple Deliverables" ("EITF 00-21"). EITF 00-21 addresses certain aspects of the accounting for arrangements that involve the delivery or performance of multiple products, services and/or rights to use assets. The provisions of EITF 00-21 apply to revenue

arrangements entered into after June 30, 2003. The Company generates revenues through collaborative research and development agreements and royalties on commercialized products.

Collaborative and Other Research and Development Revenue

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

In the third quarter of 2001, in connection with an overall review of accounting policies concurrent with the merger with Aurora, Vertex elected to change its 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 retroactively to January 1, 2001. Under the Substantive Milestone Method, 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. Because Vertex's adoption of the Substantive Milestone Method in the third quarter of 2001 was retroactive to January 1, 2001, the results of the first two quarters of 2001 have been restated in accordance with the new revenue policy. Pursuant to the 2001 change, Vertex recorded a one-time non-cash charge of $25,901,000, representing a cumulative change in accounting principle for periods prior to 2001.

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. The Company did not receive any license payments during 2003. 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

Royalty revenue is recognized based upon actual and estimated net sales of licensed products in licensed territories as provided by the

collaborative partner and is recognized in the period the sales occur. Differences between actual royalty revenues and estimated royalty revenues, which have not been historically 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.

Advertising

All advertising costs are expensed as incurred. During the years ended December 31, 2002 and 2001, advertising expenses totaled $431,000 and $444,000, respectively. There were no advertising costs in 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 sheet. 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 income (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 remeasured into U.S. dollars at rates of exchange in effect at the end of the year. Revenue and expense amounts are remeasured using the average exchange rates for the period. Net unrealized gains and losses resulting from foreign currency remeasurement are included in other comprehensive income (loss), which is a separate component of stockholders' equity.

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 unvested restricted shares of common stock. Common equivalent shares have not been included in the net loss per share calculations as their effect would be anti-dilutive. Total potential gross common equivalent shares, before applying the treasury stock method, at December 31, 2003, 2002 and 2001 consisted of 16,802,000, 17,065,000 and 16,810,000 stock options outstanding, respectively, with a weighted average exercise price of $23.42, $25.73 and $27.37, respectively. At December 31, 2003, 2002 and 2001 there were notes convertible into 3,414,264 shares of common stock at a conversion price of $92.26 per share. At December 31, 2003 there were 124,481 unvested restricted shares of common stock. Please refer to Note M "Convertible Subordinated Notes" for further information about Vertex's recent exchange of convertible notes.

New Accounting Pronouncements

In May 2003, the Financial Accounting Standards Board ("FASB") issued Statement of Financial Accounting Standards No. 150, "Accounting for Certain Financial Instruments with Characteristics of both Liabilities and Equity" ("SFAS 150"). SFAS 150 establishes standards for how an issuer classifies and measures certain financial instruments with characteristics of both liabilities and equity. The adoption of SFAS 150 in the third quarter of 2003 did not have a material impact on the Company's results of operation or financial position.

In April 2003, the FASB issued Statement of Financial Accounting Standards No. 149, "Amendment of Statement 133 on Derivative Instruments and Hedging Activities" ("SFAS 149"). SFAS 149 amends and clarifies financial accounting and reporting for derivative instruments and for hedging activities under Statement of Financial Accounting Standards No. 133, *Accounting for Derivative Instruments and Hedging Activities* . The adoption of SFAS 149 in the third quarter of 2003 did not have a material impact on the Company's results of operation or financial position.

In November 2002, the FASB issued Interpretation No. 45, "Guarantor's Accounting and Disclosure Requirements for Guarantees, Including Indirect Guarantees of Indebtedness of Others" ("FIN 45"). FIN 45 elaborates on the disclosures the Company must make about obligations under certain guarantees that the company has issued. It also requires the Company to recognize, at the inception of a guarantee, a liability for the fair value of the obligations undertaken in issuing the guarantee. The initial recognition and initial measurement provisions are to be applied only to guarantees issued or modified after December 31, 2002. The adoption of FIN 45 did not have a material impact on the Company's results of operations or financial position. The Company has provided additional disclosure with respect to guarantees in Note U "Guarantees."

In January 2003, the FASB issued FASB Interpretation No. 46 ("FIN 46"), "Consolidation of Variable Interest Entities, an Interpretation of ARB No. 51" and in December 2003 issued a revised FIN 46 ("FIN 46R") which addresses the period of adoption of FIN 46 for entities created before January 31, 2003. FIN 46 provides a new consolidation model which determines control and consolidation based on potential variability in gains and losses. The provisions of FIN 46 are effective for enterprises with variable interest entities created after January 31, 2003. The Company must adopt the provisions of FIN 46 in the first quarter of fiscal 2004 and does not expect the adoption to have a material impact on the consolidated financial statements.

C. Change in Accounting Principle—Revenue Recognition

In the third quarter of 2001, in connection with an overall review of accounting policies concurrent with the merger with Aurora, Vertex elected to change its revenue recognition policy for collaborative and other research and development revenues from the EITF 91-6 Method to the Substantive Milestone Method adopted retroactively to January 1, 2001. Vertex believes this method is preferable because it is more reflective of the Company's on-going business operations and is more consistent with industry practices following the implementation of SAB 101 throughout the biotechnology industry in 2000. Under the Substantive Milestone Method, 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 inception of the contract, are recognized as earned, and a separate earnings process is complete, when 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.

Pursuant to the 2001 change in accounting principle to the Substantive Milestone Method, Vertex recorded a one-time non-cash charge of $25,901,000, representing a cumulative effect of a change in accounting principle for periods prior to 2001. The impact of the adoption of this new accounting policy for revenue recognition for collaborative and other research and development revenues was to defer revenue recognition for certain portions of revenue previously recognized under Vertex's collaborative agreements into future accounting periods. Since Vertex's adoption of the Substantive Milestone Method in the third quarter of 2001 was retroactive to January 1, 2001, the results of the first two quarters of 2001 have been restated in accordance with this revenue recognition policy. Included in collaborative and other research and development revenue is $2,809,000 and $6,979,000 of revenue recognized in 2003 and 2002, respectively, that was included in the one-time non-cash charge of $25,901,000. The amount of revenue to be recognized in future years that was included in the one-time non-cash charge of $25,901,000 is $3,684,000, $3,628,000 and $1,053,000 in 2004, 2005 and thereafter, respectively.

D. Sale of Assets

In March and December 2003, in two independent transactions, Vertex 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. In connection with the sale, Mirus Corporation ("Mirus") exercised a right of first refusal with respect to shares of Mirus owned by PanVera. Additionally, on the same date, Mirus acquired certain of PanVera's assets. The aggregate gross consideration received by PanVera for the assets conveyed to Invitrogen and Mirus was approximately $97 million in cash and assumption of certain liabilities.

In connection with the sale, Vertex obtained a license from Invitrogen to make and use the reagents and probes sold to Invitrogen solely for its drug discovery activities, independently and with

partners, 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. It is anticipated that operating losses will be 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. It is anticipated that operating losses will be 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 all periods presented. The reclassification of the amounts to discontinued operations have 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. Prior to 2002, the Discovery Tools and Services business was not separately managed operationally or financially and therefore, certain operating expenses were estimated based on certain assumptions, including relative costs of the business sold compared to historical site costs.

Income from discontinued operations is comprised of the following revenue and expenses:

	Year Ended December 31,		
	2003	2002	2001
	(In thousands)		
Revenues from discontinued operations	$ 11,574	$ 66,315	$ 82,193
Expenses from discontinued operations	12,267	37,978	60,045
Gain from sale of discontinued operations	70,339	—	—
Income from discontinued operations	$ 69,646	$ 28,337	$ 22,148

E. Restructuring and Other Expense

On June 10, 2003, Vertex adopted a plan to restructure its operations in preparation for investments in advancing major products through clinical development to commercialization. The restructuring was designed to rebalance the Company's relative investment in research, development and commercialization, to better enable the Company to pursue its 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 the Kendall Square facility. The facility is approximately 290,000 square feet of specialized laboratory and office space in Cambridge, Massachusetts ("Kendall Square Lease"). The lease commenced in January 2003 and has a 15-year term. The Company is actively trying to restructure the lease obligation. The Company recorded restructuring and other related expenses of $91.8 million for the twelve months ended December 31, 2003. The $91.8 million includes $78.7 million of potential lease restructuring expense, $6.0 million of lease operating expense incurred prior to the decision not to occupy the Kendall Square facility, $2.6 million for severance and related employee transition benefits and $4.5 million for a write-off of leasehold improvements and other assets.

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

	Charge for the Twelve Months Ended December 31, 2003	Cash Payments in 2003	Non-cash Write-off in 2003	Accrual as of December 31, 2003
Lease restructuring expense and other operating lease expense	$ 84,726	$ 15,200	$ —	$ 69,526
Employee severance, benefits and related costs	2,616	2,616	—	—
Leasehold improvements and asset impairments	4,482	—	4,482	—
Total	$ 91,824	$ 17,816	$ 4,482	$ 69,526

As a result of the Company's restructuring plan and in accordance with SFAS 146, "Accounting for Costs Associated with Exit or Disposal Activities," the Company recorded an initial estimate, at fair value, in the second quarter of 2003. The Company reviews its assumptions and estimates quarterly and updates the liability as changes in circumstances require. Of the $78.7 million of the potential lease restructuring expense for the year ended December 31, 2003, $34.9 million, $42.4 million and $1.4 million was recorded in the second, third and fourth quarters of 2003, respectively. As prescribed

by SFAS 146, the liability recorded with respect to the potential lease restructuring was calculated using probability weighted discounted cash flows based on the Company's assumptions and estimates regarding the possible outcomes of the potential lease restructuring, including contractual rental and build-out commitments, lease buy-out, time to sublease the space and sublease rental rates. 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 incremental $42.4 million charge recorded in the third quarter of 2003 resulted from revised expectations of the Company's potential liability due to an increase in available laboratory and office space in Cambridge, Massachusetts and certain other factors which led to a corresponding overall decline in real estate market fundamentals. Accordingly, the Company revised its expectations of attainable sublease terms, assuming lower sublease rental rates and a delay in occupancy by a subtenant.

The expense and liability related to the potential lease restructuring requires the Company to make significant estimates and assumptions. The Company will review the estimates and assumptions on at least a quarterly basis, until the outcome is finalized, and make whatever modifications management believes to be necessary, based on the Company's best judgment, to reflect any changed circumstances. It is possible that such estimates could change in the future resulting in additional adjustments, and the effect of any such adjustments could be material. Because the Company's estimate of the liability related to the potential lease restructuring includes the application of a discount rate to reflect the time value of money, the estimate of the liability will change as a result of time passing. Any such 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. 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 payment of the remaining accrued liability of approximately $69.5 million related to the potential lease restructuring and other expense is dependent upon the ultimate terms of any restructuring of the lease.

F. Marketable Securities

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

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

December 31, 2002	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
Cash and cash equivalents				
Cash and money market funds	$ 102,598			$ 102,598
Corporate debt securities	5,500			5,500
Total cash and cash equivalents	$ 108,098			$ 108,098
Marketable securities				
Total equity securities	$ 265	$ 75		$ 340
US government securities				
Due within 1 year	44,770			45,056
Due within 1 to 5 years	75,969			77,720
Total US government securities	120,739	2,037		122,776
Corporate debt securities				
Due within 1 year	257,347			259,619
Due within 1 to 5 years	141,548			144,151

Total corporate debt securities	398,895	4,881	6	403,770
Total marketable securities	$ 519,899	$ 6,993	$ 6	$ 526,886
Total cash, cash equivalents and marketable securities	$ 627,997	$ 6,993	$ 6	$ 634,984

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. Gross realized gains and losses for 2001 were $3,134,000 and $53,000, respectively. Maturities stated are effective maturities.

G. Restricted Cash

At December 31, 2003 and 2002, the Company held $26,061,000 and $26,091,000 in restricted cash, respectively. At December 31, 2003 and 2002 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.

On January 5, 2004, the Company issued a stand-by letter of credit in the amount of $11,500,000 pursuant to certain operating lease requirements.

H. Property and Equipment

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

	2003	2002
Furniture and equipment	$ 92,497	$ 92,330
Leasehold improvements	62,412	56,177
Computers	16,289	14,271
Software	15,336	11,564
Building	—	6,133
Construction in process	—	1,519
Total property and equipment, gross	186,534	181,994
Less accumulated depreciation and amortization	106,451	86,003
Total property and equipment, net	$ 80,083	$ 95,991

Depreciation expense for the years ended December 31, 2003, 2002 and 2001 was $27,988,000, $24,003,000 and $16,385,000, respectively.

The sale of certain assets of the Discovery Tools and Services business in March 2003 included the laboratory, production and office facility owned by the Company in Madison, Wisconsin. This asset appears in the table above with a book value of $6,133,000 for the year ended December 31, 2002.

In 2003 and 2002, 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 $148,000.

I. Investments

In February 1999, Vertex restructured its investment in Altus Biologics Inc. ("Altus"), which was a majority owned subsidiary, so that Altus would operate independently from Vertex. As part of the transaction, Vertex provided Altus $3,000,000 of cash and surrendered its shares of Altus preferred stock in exchange for two new classes of preferred stock and warrants. Vertex accounted for its investment in Altus under the equity method of accounting.

In September and November of 2001, Altus underwent financial restructurings, which reduced Vertex's relative ownership in Altus to approximately 14% and 11% on the respective dates. Accordingly, effective September 28, 2001, Vertex began accounting for its investment in Altus using the cost method. For the period from January 1, 2001 through September 28, 2001, Vertex recorded $662,000 as its share of Altus' losses under the equity method of accounting. The loss is included in other expense on the statement of operations.

In the third quarter of 2001, Vertex adopted Derivative Implementation Group Issue No. A17, "Contracts that Provide for Net Share Settlement" ("DIG A17"). Subsequent to the issuance of SFAS No. 133, "Accounting for Certain Derivative Instruments and Certain Hedging Activities," the FASB established the Derivatives Implementation Group to address and interpret practice issues relating to that standard. On April 10, 2001, the FASB published DIG A17 relating to contracts that provide for net share settlement, including warrants of a privately held company. Pursuant to the adoption of DIG A17 on July 1, 2001, Vertex recorded a $17,749,000 cumulative effect of a change in accounting principle to reflect the value of warrants held in Altus as income with a corresponding increase to Investments. The valuation of the warrants was determined based on an independent appraisal that used the Black-Scholes option pricing model. Significant assumptions used in the Black-Scholes model included the fair value of Altus' common stock, which was based on a valuation of Altus using projected discounted cash flows and comparable market values using multiples of revenue, volatility of 70%, risk-free interest rates between 4.9% to 5.6% and warrant terms per the agreements ranging from 3.5 to 11.6 years. As of September 30, 2001, the warrants no longer qualified as derivatives under DIG A17 due to changes in the terms of the warrants coincident with the financial restructuring of Altus. The Company's cost basis carrying value in its outstanding equity and warrants of Altus was $18,813,000 at December 31, 2003 and 2002, respectively. At December 31, 2003 the Company did not have any additional investments in privately held companies. The Company held investments in other privately held companies at December 31, 2002, which investments were disposed of in the sale of certain assets of the Discovery Tools and Services business in March 2003.

In accordance with the Company's policy, as outlined in Note B, the Company has assessed its investment in Altus and determined that there had not been any adjustments to the respective fair values indicating a decrease in the fair value of the investment below the carrying value that would require the Company to write-down the investment basis of the investment at December 31, 2003.

J. Accrued Expenses and Other Current Liabilities

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

	2003	2002
Research and development contract costs	$ 11,098	$ 11,435
Payroll and benefits	8,399	11,100
Professional fees	5,940	3,324
Other	937	3,447
	$ 26,374	$ 29,306

K. Capital Leases

At December 31, 2003, the Company had obligations under capital leases for the short-term only; there are 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.

L. Commitments

The Company leases its facilities and certain equipment under non-cancelable operating leases. The Company's leases have terms through the year 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 over a number of years, to build out the space into finished laboratory and office space. The lease will expire in 2018 with options to extend the lease for two consecutive terms of ten years each, ultimately expiring in 2038. In June 2003, the Company decided not to occupy the space under this lease and is actively seeking to restructure the lease and to secure subtenancies acceptable to the landlord. See Note E for further information.

At December 31, 2003, future minimum commitments under facility operating leases with non-cancelable terms of more than one year (including the Kendall Square Lease) are as follows (in thousands):

	Kendall Square	Other Operating	Total Operating

Year	Lease	Leases	Leases
2004	$ 29,188	$ 15,774	$ 44,962
2005	27,415	15,685	43,100
2006	22,476	12,401	34,877
2007	18,541	11,663	30,204
2008	19,296	11,663	30,959
Thereafter	195,537	16,090	211,627
Total minimum lease payments	$ 312,453	$ 83,276	$ 395,729

Rental expense, primarily related to facilities, was $15,449,000, $15,847,000, and $15,447,000 for the years ended December 31, 2003, 2002 and 2001, respectively.

The Company has future contractual commitments in connection with its research and development programs. For 2004 and 2005 the amounts committed under these contracts are $2,769,000 and $2,365,000, respectively.

In connection with the PanVera Asset Sale (see Note D), 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.

M. Convertible Subordinated Notes

On September 19, 2000, the Company issued $345,000,000 of 5% Convertible Subordinated Notes due September 2007 ("2007 Notes"). In October 2001, the Company repurchased $30,000,000 in principal amount of the 2007 Notes for cash consideration of $18,900,000. As a result of this transaction, the Company recorded a gain on the early extinguishment of debt of $10,340,000, net of $760,000 of deferred debt costs, in the fourth quarter of 2001. At December 31, 2003, the 2007 Notes

had an outstanding balance of $315,000,000 and a fair value of $282,860,000 as obtained from a quoted market source.

The 2007 Notes are convertible, at the option of the holder, into common stock at a price equal to $92.26 per share, subject to adjustment under certain circumstances. The 2007 Notes bear interest at the rate of 5% per annum, and the Company is required to make semi-annual interest payments on the outstanding principal balance of the notes on March 19 and September 19 of each year. The 2007 Notes are redeemable by the Company at any time on or after September 19, 2003 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 financing costs associated with the sale of the convertible notes, which are classified as long-term other assets, were $9,297,000 of which $1,401,000, $1,401,000 and $1,498,000 and were amortized to interest expense in 2003, 2002 and 2001, respectively.

On February 13, 2004, Vertex exchanged approximately $153.1 million in aggregate principal amount of the 2007 Notes for approximately $153.1 million in aggregate principal amount of newly issued 5.75% Convertible Senior Subordinated Notes due 2011 ("2011 Notes"). The 2011 Notes were issued through a private offering 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 per share, subject to adjustment under certain circumstances. The 2011 Notes bear interest at the rate of 5.75% per annum, and the Company is required to make semi-annual interest payments on the outstanding principal balance on February 15 and August 15 of each year. On or after February 15, 2007, the Company may redeem the notes at a redemption price equal to the principal amount plus accrued and unpaid interest, if any. The 2011 Notes are senior in right of payment to the 2007 Notes. Upon completion of the exchange, the Company had approximately $161.9 million in aggregate principal amount of 2007 Notes and approximately $153.1 million in aggregate principal amount of 2011 Notes.

N. Income Taxes

For the year ended December 31, 2003, there is no provision for income taxes included in the Consolidated Statement of Operations. For the years ended December 31, 2002 and December 31, 2001, the Company provided approximately $276,000 and $630,000, respectively, 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 2003, 2002 and 2001 was 34%. The Company has incurred losses from operations but has not recorded an income tax benefit for 2003, 2002 and 2001 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):

	2003	2002
Deferred Tax Assets:		
Net operating loss	$ 210,928	$ 207,691
Tax credits carryforward	24,944	23,471
Property, plant and equipment	10,484	6,400
Deferred revenue	—	1,690
Capitalized research and development	53,154	43,193
Other	31,754	2,688
Gross deferred tax asset	331,264	285,133
Valuation allowance	(320,206)	(274,075)
Deferred Tax Liabilities:		
Gain on Investment	(11,058)	(11,058)
Net deferred tax asset	$ —	$ —

Of the $320,206,000 gross deferred tax asset at December 31, 2003, $102,919,000 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, 2003, the Company had net operating loss carryforwards of approximately $542,726,000 and tax credits of $15,686,000 which may be used to offset future income. The operating loss carryforwards will expire as follows: $1,329,000 in 2005, $4,462,000 in 2006 and $536,935,000 thereafter. The tax credit carryforwards begin to expire in 2004. A valuation allowance has been established for the full amount of the 2003 deferred tax asset since it is more likely than not that the deferred tax asset will not be realized. The Company also has foreign net operating loss carryforwards of $1,400,000, which have no expiration date.

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.

O. 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"). 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 and 1994 Plans, 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.

In July 2001, in connection with the acquisition of Aurora, the Company assumed the obligations under the Aurora 1996 Stock Plan (the "Aurora Stock Plan"), the 1993 Stock Plan of PanVera Corporation (the "PanVera Plan") and certain non-plan stock option agreements ("Non-Plan Stock Option Agreements") under which 1,039,596, 3,328 and 2,697 shares of Vertex's common stock, respectively, were reserved for issuance at December 31, 2003.

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, 2003, the Company had a total of 5,026,815 shares of common stock available for future grant under its 1991, 1994 and 1996 stock option plans. No shares remain available for grant under the Aurora Stock Plan, the PanVera Plan or Non-Plan Stock Option Agreements.

Consolidated stock option activity for the years ended December 31, 2003, 2002 and 2001 is as follows (shares in thousands):

	2003		2002		2001	
	Shares	Weighted Average Exercise Price	Shares	Weighted Average Exercise Price	Shares	Weighted Average Exercise Price
Outstanding at beginning of year	17,065	$ 25.73	16,810	$ 27.37	14,615	$ 25.9
Granted	3,465	14.59	2,952	17.49	4,451	28.9
Exercised	(914)	9.15	(944)	10.43	(1,401)	11.6
Canceled	(2,814)	31.00	(1,753)	36.44	(855)	38.5
Outstanding at end of year	16,802	$ 23.42	17,065	$ 25.73	16,810	$ 27.3
Options exercisable at year-end	10,205	$ 23.08	9,566	$ 22.85	7,476	$ 19.0
Weighted average fair value of options granted during the year		$ 9.46		$ 11.60		$ 14.9

The fair value of each option granted under the 1991, 1994 and 1996 plans during 2003, 2002 and 2001 was estimated on the date of grant using the Black-Scholes option pricing model with the following weighted average assumptions:

	2003	2002	2001
Expected life (years)	5.50	5.50	5.50
Expected volatility	75.00%	75.00%	58.00%
Risk-free interest rate	3.27%	4.18%	4.86%
Dividend yield	—	—	—

The fair value of each option granted under the Aurora Stock Plan, PanVera Plan and Non-plan Stock Option Agreements during 2001 was estimated on the date of grant using the Black-Scholes option pricing model with the following weighted average assumptions:

	2001
Expected life (years)	5.50
Expected volatility	93.00%
Risk-free interest rate	4.35%
Dividend yield	—

The following table summarizes information about stock options outstanding and exercisable at December 31, 2003 (shares in thousands):

	Options Outstanding			Options Exercisable	
Range of Exercise Prices	Number Outstanding	Weighted Average Remaining Contractual Life	Weighted Average Exercise Price	Number Exercisable	Weighted Average Exercise Price
$1.22-$10.19	2,396	3.16	$ 8.78	1,966	$ 8.72
10.28-13.11	1,846	6.03	$ 12.78	1,404	$ 12.79
13.15-13.67	1,740	4.50	$ 13.63	1,693	$ 13.64
13.69-15.56	1,192	4.11	$ 15.25	1,070	$ 15.30

15.60-15.60	1,938	9.05	$	15.60	307	$ 15.60
15.66-16.53	1,873	8.45	$	15.95	503	$ 15.95
16.59-20.91	799	6.89	$	18.78	501	$ 18.79
20.97-24.66	1,962	7.89	$	24.47	823	$ 24.47
24.69-58.88	1,146	7.24	$	38.62	751	$ 41.21
59.37-135.49	1,910	6.89	$	73.06	1,187	$ 73.81
$1.22-$135.49	16,802	6.38	$	23.42	10,205	$ 23.08

In December 2003, the Company issued 124,481 shares of restricted Common Stock to employees and all of the shares were outstanding and unvested at December 31, 2003. The restricted shares vest over four years in four equal annual installments. The fair value of the Company's Common Stock on the date of grant was $9.07 and the price per share was $0.01 per share, which is the par value of the Company's Common Stock. The Company recorded deferred compensation of approximately $1,128,000 related to the issuance of the restricted shares.

Stock Based Compensation

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 of $16,000, $20,000, and $154,000 was recognized during 2003, 2002 and 2001, respectively.

Compensation cost, calculated using a Black-Scholes option pricing model, recognized in connection with the issuance of stock options to nonemployees was $161,826, $292,000 and $320,000 in 2003, 2002 and 2001, respectively.

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 to 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 connection with the acquisition of Aurora in July 2001, the Company assumed the obligations under the Aurora 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 2003, 2002, and 2001 the following shares were issued to employees under the Vertex Purchase Plan (shares in thousands):

	2003	2002	2001
Number of shares	379	220	155
Average price paid	$ 9.49	$ 15.85	$ 20.54

Had the Company adopted SFAS 123, the weighted average fair value of each purchase right granted during 2003, 2002 and 2001 would have been $5.86, $6.04, and $7.45 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:

	2003	2002	2001
Expected life (years)	1.0	.50	.50
Expected volatility	75.00%	75.00%	58.00%
Risk-free interest rate	1.17%	1.53%	2.97%
Dividend yield	—	—	—

Rights

Each holder of a share of outstanding Common Stock also holds one share purchase right (a "Right") for each share of Common Stock. 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, 2003, 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	21,829
Common stock under the Vertex Purchase Plan	249
Common stock under the Vertex 401(k) Plan	125
Total	22,203

P. Significant Revenue Arrangements

The Company has formed strategic collaborations with major 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 research programs and development of clinical drug candidates, product development and 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 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 terms of each agreement vary. The Company has entered into significant research and development collaborations with large pharmaceutical companies.

P. Significant Revenue Arrangements

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. Under the 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 under the agreement. 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. At December 31, 2003 and 2002 $32,455,000 and $5,000,000, respectively, were outstanding under this loan facility. Novartis has exclusive worldwide development, manufacturing and marketing rights to clinically and commercially relevant drug candidates that it accepts from the Company for development. Vertex will receive royalties on any products that are marketed as part of the collaboration. Novartis had the right to terminate this agreement without cause upon one year's written notice effective no earlier than May 2004. In 2003, 2002 and 2001 the Company recognized approximately $44,502,000, $41,894,000 and $36,723,000, respectively, in revenue under this agreement.

In February 2004 the Company amended the Novartis collaboration. Vertex will continue to be responsible for drug discovery under the amended agreement, and Novartis will continue to provide research funding through the end of the research term in April 2006. However, under the agreement as modified, Novartis will be responsible for all clinical and nonclinical development of drug candidates which it accepts for development, and consequently the loan facility has been eliminated. The Company may either continue development of its drug candidate VX-680 under the terms of the original agreement, using loan proceeds from the Novartis loan facility, or elect to develop and commercialize VX-680 independent of Novartis. Upon selection of a pre-clinical drug candidate under the restructured agreement, Novartis will pay Vertex a $10 million selection milestone, and Vertex may receive up to $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. Outstanding loans which 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 not, the related loan will be repayable without interest in May 2008. If the Company elects to develop and commercialize VX-680 independent of Novartis, loan amounts with respect to that drug candidate which are unspent and uncommitted at the time of the Company's election will be repayable immediately. At December 31, 2003, approximately $14 million in development loans previously advanced to Vertex on account of VX-680 were unspent and uncommitted. Novartis no longer has the right to terminate this agreement without cause.

GlaxoSmithKline

In December 1993, the Company and GlaxoSmithKline ("GSK") entered into a collaborative agreement to research, develop and commercialize HIV protease inhibitors, including Agenerase (amprenavir), Lexiva (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 protease inhibitors by GSK. The Company began earning a royalty from GSK in 1999 on sales of Agenerase, and in the fourth quarter of 2003 on sales of Lexiva. GSK is also obligated to pay additional development and commercialization milestone payments for subsequent drug candidates, including Lexiva and VX-385. In the fourth quarter of 2003, GSK paid the Company a milestone payment of $2,500,000 for the 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 for the submission of a new drug application for market approval of Lexiva in the United States and the European Union. GSK is required to bear the costs of development in its territory of drug candidates 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. 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 $11,502,000, $11,554,000, and $10,783,000 in 2003, 2002 and 2001, 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.

Aventis S.A.

In September 1999, the Company and Aventis S.A. ("Aventis"), formerly Hoechst Marion Roussel Deutschland GmbH, entered into an expanded agreement covering the development of pralnacasan, an orally active inhibitor of interleukin-1 b converting enzyme. Under the agreement, Aventis agreed to make a $20,000,000 up-front payment to the Company for prior research costs, and up to $62,000,000 in milestone payments for successful development by Aventis of pralnacasan in the treatment of rheumatoid arthritis, the first targeted indication. Milestone payments are also due for each additional indication. The research collaboration under this agreement ended in 1997. Aventis has an exclusive worldwide license to develop, manufacture and market pralnacasan. Aventis will fund the development of pralnacasan. Vertex may co-promote pralnacasan in the U.S. and Europe. Vertex will receive royalties on global sales, if any. The agreement also provides that Aventis

will partially fund a Vertex co-promotion effort in the United States under certain conditions. Aventis may terminate this agreement without cause upon six months' written notice. Termination by Aventis will end any license granted to Aventis by Vertex under the agreement. The Company did not earn any revenue in connection with the Aventis collaboration in 2003, 2002 or 2001.

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. Under the agreement, the Company could receive up to $95,000,000 in pre-commercial payments, comprised of $5,000,000 in up-front payments for prior research, up to $20,000,000 in product research funding over five years and up to $70,000,000 in further license fees and milestone payments. These amounts are based on the development of more than one drug candidate. The two companies will

share development costs. Vertex has the option to establish a joint venture with Serono for the commercialization of products in North America, where the two companies will share marketing rights and profits from the sale of drug products, if any. Serono will have exclusive rights to market caspase inhibitors in other territories, excluding Japan and certain other countries in the Far East, and will pay Vertex for the supply of drug substance. Serono has the right to terminate the agreement without cause effective at the end of 2004, upon written notice delivered on or before the end of June 2004.

In 2003, 2002 and 2001, the Company recognized approximately $5,280,000, $5,280,000 and $4,802,000 as revenue, respectively, from Serono.

The Company in 2003, 2002 and 2001 recognized an aggregate of $267,000, $25,815,000 and $24,674,000, respectively, in revenue from collaborations with Kissei Pharmaceuticals Co. Ltd., Eli Lilly & Company, Taisho Pharmaceuticals Co., LTD and Schering AG.

Q. 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 Company shares. The match is paid in fully vested Company shares and employees have the ability to transfer funds from Company stock as they choose. The Company declared matching contributions to the Vertex 401(k) Plan as follows (in thousands, except share data):

	2003	2002	2001
Discretionary matching contributions for the year ended December 31,	$ 2,237	$ 2,558	$ 1,399
Shares issued for the year ended December 31,	185,040	104,344	15,215
Shares issuable as of the year ended December 31,	60,781	64,931	32,284

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") covering substantially all employees of Aurora and its wholly-owned subsidiaries who have 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 and $453,000 in 2002 and 2001 respectively.

R. Related Party Transactions

As of December 31, 2003, the Company had a loan outstanding to an officer in the amount of $170,000. The loan is interest free and will be forgiven prorated over a four-year term ending in the second quarter of 2006.

The brother of the Company's Chairman and Chief Executive Officer was a partner in a law firm representing the Company to which $200,000 in legal fees were paid in 2001. As of September 24, 2001,

he was no longer a partner with that firm and was hired as Senior Vice President and General Counsel of Vertex.

In January 2002, the Company forgave an interest free loan outstanding to a director in the amount of $132,000 in accordance with the terms of a retention and non-compete agreement executed by the Company in April 2001.

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 $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 sale of certain of assets of PanVera LLC on March 28, 2003. The Company believes that the amounts charged 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 and $3,348,000 in 2002 and 2001, respectively. No revenue was recognized in 2003 from this agreement. Revenue recognized from this agreement is included in discontinued operations on the consolidated financial statements for all periods presented.

S. 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 September 23, 2003, two purported shareholder class actions, *Carlos Marcano v. Vertex Pharmaceuticals, et al.* and *City of Dearborn Heights General Governmental Employees' Retirement System v. Vertex Pharmaceuticals, et al.* , were filed in the United States District Court for the District of Massachusetts, naming the Company and certain current and former officers and employees of the Company as defendants. Those actions were followed by three additional lawsuits, *Stephen Anish v. Vertex Pharmaceuticals, et al.* , *William Johns v. Vertex Pharmaceuticals, et al.* , and *Ben Harrington v. Vertex Pharmaceuticals, et al.* , also filed in the District of Massachusetts. All five cases contain substantially identical allegations and have been consolidated by the District Court into one lawsuit. The plaintiffs claim 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 seek certification as a class action, compensatory damages in an unspecified amount, and unspecified equitable or injunctive relief. The Company believes that the claims are without merit and intends to contest them vigorously.

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 due diligence 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 judgement 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.

T. 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 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 term of these indemnification provisions generally survives the termination of the agreement, although the provision 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. Vertex has purchased insurance policies covering personal injury, property damage and general liability that reduce our exposure for indemnification and would enable us 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. The Company believes the estimated fair value of these indemnification arrangements 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. The Company believes the estimated fair value of these indemnification arrangements 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 2007 Notes for approximately $153.1 million of 2011 Notes. The Dealer Manager Agreement requires the Company to indemnify UBS Securities LLC against any loss it may suffer by reason of the Company's breach of certain representations and warranties, its failure to perform certain covenants, 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 exchange of convertible notes. The representations, warranties and covenants in the Dealer Manager Agreement are of a type customary in agreements of this sort. The Company believes the estimated fair value of these indemnification obligations is minimal.

U. Quarterly Financial Data (unaudited)

(in thousands, except per share data)

	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

(in thousands, except per share data)

	Three Months Ended			
	March 31, 2002	June 30, 2002	Sept. 30, 2002	Dec. 31, 2002
Revenues:				
Royalties	$ 2,319	$ 2,384	$ 2,610	$ 2,741
Collaborative and other research and development revenues	19,502	21,158	20,662	23,394
Total revenues	21,821	23,542	23,272	26,135
Costs and expenses:				
Royalty payments	773	772	880	909
Research and development	45,999	45,816	49,345	57,178
Sales, general and administrative	8,544	11,437	11,227	9,848
Total costs and expenses	55,316	58,025	61,452	67,935
Loss from operations	(33,495)	(34,483)	(38,180)	(41,800)
Interest income	8,458	7,468	6,812	5,984
Interest expense	(4,450)	(4,433)	(4,411)	(4,390)
Other expense	(6)	(25)	(1)	(6)
Loss from continuing operations	(29,493)	(31,473)	(35,780)	(40,212)
Income from discontinued operations	7,426	10,454	2,328	8,129
Net loss	$ (22,067)	$ (21,019)	$ (33,452)	$ (32,083)
Basic and diluted net loss per common share	$ (0.29)	$ (0.28)	$ (0.44)	$ (0.42)
Basic and diluted weighted average number of common shares outstanding	75,161	75,660	75,979	76,287

QuickLinks

EXHIBIT 10.35

(WITH CERTAIN CONFIDENTIAL INFORMATION DELETED AND MARKED WITH BRACKETED
ASTERIKS]

FIRST REVISED AND RESTATED

RESEARCH AND EARLY DEVELOPMENT AGREEMENT

BETWEEN

VERTEX PHARMACEUTICALS INCORPORATED

AND

NOVARTIS PHARMA AG

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FIRST REVISED AND RESTATED

RESEARCH AND EARLY DEVELOPMENT AGREEMENT

First Revised and Restated Agreement made this 3rd day of February, 2004, (as so revised and restated, the "Research Agreement"), revising and restating that certain Research And Early Development Agreement dated May 8, 2000 (the "Original Agreement"), between VERTEX PHARMACEUTICALS INCORPORATED ("VERTEX"), a Massachusetts corporation with principal offices at 130 Waverly Street, Cambridge, MA 02139-4242, and NOVARTIS PHARMA AG ("NOVARTIS"), a Swiss corporation with principal offices at Lichtstrasse 35, CH-4056 Basel, Switzerland.

This Research Agreement is intended by the parties to replace and supercede the rights and obligations of the parties under the Original Agreement with respect to the subject matter thereof, except that the terms of the Original Agreement shall be deemed to govern the rights and obligations of the parties with respect to the Compounds known as VX-680 and VX-528, subject to the provisions of Section 4.8(b) of this Research Agreement.

INTRODUCTION

WHEREAS, VERTEX has undertaken a broad drug discovery program with the objective of designing novel, small-molecule compounds targeting the kinase protein super-family;

WHEREAS, NOVARTIS is also interested in developing and commercializing drugs targeting kinase proteins and has particular expertise in developing, registering, manufacturing, marketing and selling pharmaceuticals worldwide;

WHEREAS, both parties desire to revise and restate the Original Agreement to reflect agreed modifications to the original collaboration, which involve among other things a redirection of VERTEX's efforts from the delivery of compounds which have progressed through early clinical testing, to the delivery of Development Candidates, at an earlier stage in the development process, which target selected Kinases and meet certain pre-agreed Development Candidate Criteria; and

WHEREAS, NOVARTIS may elect to develop, market and sell any or all of those Compounds as drugs upon the terms set forth herein and in a License, Development and Commercialization Agreement identical in substance to EXHIBIT A hereto;

NOW THEREFORE, in consideration of the mutual covenants set forth in this Research Agreement, and other good and valuable consideration, the parties agree as follows:

ARTICLE I
DEFINITIONS

For purposes of this Agreement, the terms defined in this Article 1 shall have the following meanings whether used in their singular or plural forms. Use of the singular shall include the plural and vice versa, unless the context requires otherwise:

1.1. "AFFILIATE" shall mean, with respect to any Person, any other Person which directly or indirectly, by itself or through one or more intermediaries, controls, or is controlled by, or is under direct or indirect common control with, such Person. The term "control" means the possession, direct or indirect, of the power to direct or cause the direction of the management and policies of a Person, whether through the ownership of voting securities, by contract or otherwise. Control will be presumed if one Person owns, either of record or beneficially, more than 50% of the voting stock of any other Person. For the avoidance of any doubt, the Novartis Institute for Functional Genomics, Inc. and The Friedrich Miescher Institute, as currently operated, are not Affiliates of NOVARTIS for the purposes of this Research Agreement.

1.1.1. "BACK-UP COMPOUND" shall mean, [***].

1.2. "BULK DRUG SUBSTANCE" shall mean a Drug Product Candidate in bulk crystal, powder or other form suitable for incorporation in a Drug Product.

1.3. "COMPOUND" shall mean any chemical compound, including salts thereof, which affects a Kinase and which was or is synthesized and/or tested (including by screening) by or under the direction of VERTEX or its Affiliates during the term of the Research Program conducted under this Research Agreement, or was synthesized or tested by VERTEX or its Affiliates prior to the Effective Date in a program targeted toward Kinase modulation.

1.4. "CONTROLLED" shall mean the legal authority or right of a party hereto to grant a license or sublicense of intellectual property rights to another party hereto, or to otherwise disclose proprietary or trade secret information to such other party, without breaching the terms of any agreement with a Third Party, infringing upon the intellectual property rights of a Third Party, or misappropriating the proprietary or trade secret information of a Third Party.

1.5. (a) "DEVELOPMENT CANDIDATE" shall mean a Compound that meets the Development Candidate Criteria and which is either proposed by VERTEX, during the term of the Research Program [***], for formal pre-clinical development, or is selected by NOVARTIS on or before the Final Termination Date for formal pre-clinical development pursuant to the provisions of Section 4.1 hereof.

1.5. (b) "DEVELOPMENT CANDIDATE INFORMATION" will mean all material information known to VERTEX about a Development Candidate, including analytical results and raw data, which NOVARTIS reasonably needs in order to decide whether to exercise the Development Election with respect to the Development Candidate. The Development Candidate Information shall include any previously undisclosed information with respect to VERTEX Kinase Technology which is important to a scientific and commercial evaluation of the Development Candidate. Development Candidate Information will also include comparable information known to VERTEX concerning all Compounds which are Back-up Compounds, as defined herein, to the specific Development Candidate which is the subject of the Development Candidate Information. [***]

1.5.(c) "DEVELOPMENT CANDIDATE CRITERIA" shall mean (a) the criteria set forth on Schedule 2.4.3 hereof and (b) such further, more specific criteria to be determined by the JRC as soon as possible after the start of each research project with respect to each particular Kinase

target, each therapeutic application, special delivery forms, and the like, as set forth in Section 2.5.3 hereof.

1.6. "DEVELOPMENT ELECTION" shall have the meaning set forth in Section 4.1 hereof.

1.7. "DEVELOPMENT PROGRAM" shall mean activities associated with development of a Drug Product Candidate as specified in the License Agreement.

1.8. [This section has been intentionally left blank.]

1.9. "DRUG PRODUCT" shall mean a finished dosage form which is prepared from Bulk Drug Substance and is ready for administration to the ultimate consumer as a pharmaceutical.

1.10. (a) "DRUG PRODUCT CANDIDATE" shall mean a Development Candidate which has been selected by NOVARTIS for development and commercialization under the License Agreement, pursuant to exercise of its Development Election under Section 4.1 hereof.

1.10. (b) "DRUG PRODUCT CANDIDATE BACKUP CANDIDATE" shall mean any Back-up Compound for which NOVARTIS has exercised its Development Election under Section 4.5 hereof.

1.11. [This section has been intentionally left blank.]

1.12. "EFFECTIVE DATE" shall mean the effective date of the Original Agreement as set forth on the first page hereof.

1.13. "EXCLUDED COMPOUNDS" shall mean any chemical compounds the therapeutic effect of which in humans is thought to be principally derived from an effect on one or more Excluded Kinases. "Excluded Compounds" shall also include the Compound known as [***]. An "analog" shall mean any compounds (or salts thereof) which are claimed in [***] which NOVARTIS can demonstrate by written record were synthesized by NOVARTIS before the Effective Date. "Excluded Compounds" shall also include any Compounds directed toward modulation of a Kinase which has been added to the list of Excluded Kinases by the operation of Section 4.4 hereof; provided that in no event shall an Excluded Compound include a Drug Product Candidate.

1.14. "EXCLUDED KINASES" shall mean the human kinases specifically identified in Schedule 1.13 hereto. "Excluded Kinases" shall also include any Kinase hereafter added to the list of Excluded Kinases pursuant to the provisions of Section 4.4 hereof.

1.15. [This section has been intentionally left blank.]

1.16. "FIELD" shall mean the treatment or prevention of conditions or diseases in humans, principally by affecting a Kinase other than an Excluded Kinase.

1.17. "FINAL NOTICE PERIOD" shall have the meaning set forth in Section 4.1(d) hereof.

1.17.1. "FINAL REPORT" shall have the meaning set forth in Section 4.1(d) hereof.

1.17.2. "FINAL REPORT PERIOD" shall have the meaning set forth in Section 4.1(d) hereof.

1.17.3. "FINAL TERMINATION DATE" shall have the meaning set forth in Section 4.1(d) hereof.

1.18. "FTE" shall mean the equivalent of the work of one VERTEX scientist or other project managerial professional, full time for one year, which equates to a total of forty-seven (47) weeks or one thousand eight hundred eighty (1880) hours per year of work, on or directly related to the Research Program. Work in the Research Program can include, but is not limited to, experimental laboratory work, project and research management, activities directed toward evaluation of the commercial potential of a possible Drug Candidate, recording and writing up results, reviewing literature and references, holding scientific discussions, attending appropriate seminars and symposia, and carrying out Joint Research Committee duties. FTE's shall include equivalent scientific work in the Research Program delegated to and carried out by contractors, under the general direction of VERTEX scientists; provided, that the nature and quantity (as a percentage of total program FTE's) of the delegated work shall not be such that the most substantial parts of the overall Research Program, in terms of projected value creation, have been delegated to Third Parties. FTE's which result from work delegated to and carried out by contractors will be separately identified by VERTEX on its invoices provided to NOVARTIS under Section 12.19 hereof.

1.19. [This section has been intentionally left blank.]

1.20. [This section has been intentionally left blank.]

1.21. "JOINT RESEARCH COMMITTEE" OR "JRC" shall have the meaning ascribed to it in Section 2.5 of this Research Agreement.

1.22. "JOINT STEERING COMMITTEE" OR "JSC" shall have the meaning ascribed to it in Section 2.6 of this Research Agreement.

1.23. "KINASE" shall mean a human enzyme that catalyzes the transfer of a phosphate group from a nucleoside triphosphate to a protein.

1.24. "KINASE TECHNOLOGY" shall mean all data, technical information, know-how, experience, inventions (whether or not patented) trade secrets, processes and methods discovered, developed or applied (with the consent of its owner) and Controlled by either party or its Affiliates, in connection with performance by either party under the Research Program, or in connection with the conduct of a Development Program under the License Agreement prior to termination of the Research Program, that relate to the research, development, utilization, manufacture or use of Compounds, Development Candidates, Drug Product Candidates or Drug Products (other than any such technology which is exclusive to Excluded Kinases); provided, however, that the term Kinase Technology shall not apply to VERTEX's general drug design technology whether in hardware or software form, tangible or intangible.

1.25. "KNOW-HOW" means all Kinase Technology other than inventions which are the subject of Patents; and "LEAD PERIOD" shall have the meaning set forth in Section 4.5(a) hereof.

1.26. "LICENSE AGREEMENT" shall mean the License, Development and Commercialization Agreement, identical in substance to EXHIBIT A to this Research Agreement, to be executed by VERTEX and NOVARTIS with respect to each Drug Product Candidate; and "NOTICE PERIOD" shall have the meaning set forth in Section 4.1(b) hereof.

1.27. "NOVARTIS KNOW-HOW" shall mean all Know-How of NOVARTIS.

1.28. "NOVARTIS PATENTS" shall mean any Patents controlled by NOVARTIS or its Affiliates claiming Kinase Technology.

1.29. "NOVARTIS KINASE TECHNOLOGY" shall mean all NOVARTIS Patents and NOVARTIS Know-How.

1.30. "PATENTS" means all existing patents and patent applications and all patent applications hereafter filed, including any continuation, continuation-in-part, division, provisional or any substitute applications, any patent issued with respect to any such patent applications, any reissue, reexamination, renewal or extension (including any supplementary protection certificate) of any such patent, and any confirmation patent or registration patent or patent of addition based on any such patent, and all foreign counterparts of any of the foregoing.

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

1.32. [This section has been intentionally left blank.]

1.33. [This section has been intentionally left blank.]

1.34. "REFUSED CANDIDATE" shall have the meaning set forth in Section 4.4 hereof.

1.35. "REPLACEMENT CANDIDATE" shall have the meaning set forth in Section 4.5(b) hereof.

1.36. "RESEARCH PLAN" shall have the meaning set forth in Section 2.4.1 hereto.

1.37. (a) "RESEARCH PROGRAM" shall mean all research activities undertaken under this Research Agreement associated with the identification and design of Compounds and Development Candidates as provided herein; including but not limited to identification and initial testing of Compounds; the conduct of activities referenced in the Development Candidate Criteria with respect to Compounds; and selection of Development Candidates from Compounds.

1.37. (b) "RESEARCH TERMINATION DATE" shall mean the earlier of April 30, 2006 or the date upon which the Research Program is terminated under Sections 9.2, 9.3 or 9.5 hereof.

1.38. "RESEARCH YEAR" means a twelve-month period during the term of the Research Program commencing on May 1, and ending on April 30 of each year. The first Research Year hereunder shall be deemed to have commenced on May 1, 2000.

1.39. [This space has been intentionally left blank.]

1.40. "TECHNOLOGY" shall mean NOVARTIS Kinase Technology and VERTEX Kinase Technology.

1.41. "THIRD PARTY" shall mean any person or entity which is not a party or an Affiliate of any party to this Research Agreement.

1.42. "THIRD PARTY REFERRAL" shall mean the procedure for resolution of certain disputes hereunder which is set forth in Section 11.2(b) hereof.

1.43. "VERTEX KNOW-HOW" shall mean all Know-How of VERTEX.

1.44. "VERTEX PATENTS" shall mean any Patents Controlled by VERTEX or its Affiliates claiming Kinase Technology.

1.45. "VERTEX KINASE TECHNOLOGY" shall mean all VERTEX Patents and VERTEX Know-How.

Capitalized terms used but not otherwise defined herein which are defined in the License Agreement shall have the meaning ascribed to them therein.

ARTICLE II
RESEARCH PROGRAM

2.1. COMMENCEMENT. The Research Program originally commenced on May 1, 2000. VERTEX has principal responsibility for the conduct of the Research Program and NOVARTIS provides consultation, advice and such research effort as may be deemed appropriate by the JRC and accepted by NOVARTIS. The JRC shall review and coordinate all of the parties' efforts with respect to the Research Program.

2.2. TERM. The Research Program will conclude on May 1, 2006, unless earlier terminated in accordance with the provisions hereof. At the request of either party made during the fourth Research Year, the parties will discuss whether, and upon what basis, the Research Program might be extended on comparable terms beyond its initial 6 year term.

2.3. RESEARCH DILIGENCE. The common objective of the parties is to identify Development Candidates as soon as practicable for selection by NOVARTIS as Drug Product Candidates and for worldwide development and marketing under the terms of the License Agreement. VERTEX will work diligently and use all reasonable efforts, consistent with prudent business judgment, to identify Development Candidates for acceptance by NOVARTIS as Drug Product Candidates. VERTEX intends to dedicate to the Research Program at least that level of staffing referenced in
Section 3.2 hereof, and expects to employ an optimal combination of experience and training in the Field. As a matter of corporate strategy, VERTEX has chosen to dedicate a significant amount of its overall research efforts to work in the Field, and will not change that overall strategy during the term of the Research Program without prior notice to and approval by NOVARTIS.

2.4. RESEARCH PLAN; EARLY DEVELOPMENT PLAN.
2.4.1. General. VERTEX originally prepared an overall research plan for the Research Program which it submitted to the JRC for its review and comment at the first meeting of the JRC after the Effective Date. The research plan has been and will be revised, updated and submitted to the JRC at least annually for its review and comment (as so revised, updated and submitted, the "Research Plan").

2.4.2. [This section has been intentionally left blank.]

2.4.3. Plan Review. In developing the Research Plan, VERTEX will take into account the intention of the parties to produce Compounds which meet the Development

Candidate Criteria. VERTEX shall not perform any work under this Research Agreement with respect to Excluded Compounds or Excluded Kinases. The Research Plan will be reviewed as necessary at each meeting of the JRC, and at any other time upon the request of either party, and shall be modified as appropriate to reflect material scientific or commercial developments. Any disagreements among the parties with respect to these matters may be referred by either party to the Joint Steering Committee for resolution. Notwithstanding the foregoing, VERTEX shall have the final say with respect to the Research Plan.

2.5. JOINT RESEARCH COMMITTEE.

2.5.1. Composition and Purposes. VERTEX and NOVARTIS have established and will continue to participate in a Joint Research Committee ("JRC") consisting of at least eight (8) representatives (as may be increased or decreased by the JRC), half of whom shall be designated from time to time by each party. If the JRC chooses to designate a Committee Chair, the Chair will be appointed from among the members of the Committee designated by VERTEX. The JRC shall meet formally at least quarterly, or with such other frequency, and at such time and location, as may be established by the Committee, for the following purposes:

(i) To receive and review reports by VERTEX and its project teams, which shall be prepared and submitted to the JRC on a quarterly basis within fifteen (15) days after the end of each calendar quarter, such reports summarizing progress during the preceding quarter under the Research Plan; and to review information with respect to the Compounds under investigation (which VERTEX shall provide in form and content at least as extensive as customarily provided to the JRC under the Original Agreement);

(ii) To review a proposal by either party that specified Excluded Compounds or Excluded Kinases be included in the Research Program, or that a Kinase be added to the list of Excluded Kinases; provided that the JRC shall have no authority to include or exclude any Compound or Kinase from the Research Program, and that any such action must be the subject of a formally adopted amendment to this Research Agreement;

(iii) To define as soon as possible the further, more specific Development Criteria (x) for ongoing projects, after the signature of this Research Agreement, or (y) for new projects, after the start of such new research project;

(iv) To review Development Candidates proposed by VERTEX and to assess whether a given Development Candidate proposed by VERTEX meets the Development Criteria;

(v) To review the Research Plan and any proposed revisions thereto;

(vi) [This subsection has been intentionally left blank.]; and

(vii) To discuss matters relating to Patents, as may be presented to the JRC by VERTEX or NOVARTIS.

The party hosting a particular JRC meeting shall prepare and deliver to the members of the JRC, within thirty (30) days after the date of each meeting, minutes of such

meeting setting forth, INTER ALIA, all decisions of the JRC, and including a report on the progress of work performed. In case the JRC meets by means of telephone or video conferences, this responsibility shall lie with VERTEX.

2.5.2. Decision-Making.

(i) Each of VERTEX and NOVARTIS shall have one vote on the JRC. The objective of the JRC shall be to reach agreement by consensus on all matters within the scope of the Research Plan. However, in the event of a deadlock with respect to any action (which shall be deemed to have occurred if either party shall request a vote of the JRC on a matter and that vote shall either not be taken within thirty (30) days of the request or if taken shall result in a tie vote) and subject to the procedure set forth in subsection (ii) below as to certain matters, the vote of VERTEX, rendered after reasonable and open discussion among the members of the JRC, shall be final and controlling.

(ii) Notwithstanding the foregoing, with respect to JRC decisions (x) as to the nature and extent of any additional Development Candidate Criteria referenced in Section 2.5.3 hereof, any disagreement between the parties that cannot be resolved within forty-five (45) days by the JRC (as that period may be extended under (iii) below) shall be referred to the JSC for resolution and if not resolved within seven (7) business days after referral, shall be referred for final resolution in good faith by the Chief Executive Officer of VERTEX and the Chief Executive Officer of NOVARTIS, and failing final resolution, there will be no change to the Development Candidate Criteria; or
(y) as to whether or not Development Candidate Information provided by VERTEX, pursuant to subsection (iii) below, is complete or as to whether or not a given Compound proposed by VERTEX as a Development Candidate meets the Development Criteria, the matter shall be referred as provided in subsection (x) above to the JRC and the JSC and, failing agreement, the matter shall be referred for final resolution under the provisions of Section 11.2(b) of this Research Agreement.

(iii) In the event that NOVARTIS's representatives on the JRC reasonably believe that the Development Candidate Information with respect to a particular Development Candidate proposed by VERTEX to the JRC is incomplete, NOVARTIS shall provide written notice thereof to VERTEX within fifteen (15) business days after receipt of the Development Candidate Information, and VERTEX shall undertake reasonable efforts to furnish the requested additional Development Candidate Information within fifteen (15) business days after receipt of NOVARTIS's notice hereunder. The 45-day period provided for action by the JRC under subsection (ii) above shall be extended by the amount of time required for VERTEX to provide the requested information, but in any event not in excess of thirty (30) days.

(iv) Notwithstanding any of the foregoing, if VERTEX and NOVARTIS deadlock on any other matters being considered by the JRC which might have a significant impact on the time or likely success of the Research Program, the matter shall be referred to the JSC for resolution in accordance with
Section 2.6 hereof.

(v) Each party shall retain the rights, powers, and discretion granted to it under this Research Agreement, and the JRC shall not be delegated or vested with any such rights, powers or discretion except as expressly provided in this Research Agreement.

The JRC shall not have the power to amend or modify this Research Agreement, which may only be amended or modified as provided in Section 12.15.

2.5.3. ADDITIONAL DEVELOPMENT CANDIDATE CRITERIA. The parties acknowledge that it may be necessary or appropriate to adopt additional Development Candidate Criteria which more specifically define the pre-development characteristics of Compounds which the parties believe may be suitable for development and commercialization under the License Agreement, based upon the Kinase targeted by a specific project under the Research Program and the particular disease indication or indications thought to be addressed by Compounds modulating the Kinase which is the subject of that project. [***] Any disagreements with respect to the selection of additional Development Candidate Criteria hereunder will be addressed as provided in Section 2.5.2(ii).

2.6. JOINT STEERING COMMITTEE.
2.6.1. Composition and Purposes. VERTEX and NOVARTIS have established and will continue to participate in a Joint Steering Committee ("JSC") which shall consist of an equal number of senior executives as may be designated by each party from time to time. The JSC shall initially have four
(4) members. If the JSC chooses to designate a Committee Chair, the Chair will be appointed from among the members of the JSC designated by NOVARTIS. The JSC shall meet annually, or with such other frequency, and at such time and location, as may be established by the Committee, for the following purposes:

(i) General oversight of the entire collaboration between VERTEX and NOVARTIS, including the Research Program and any development and commercialization of a Drug Product Candidate under the License Agreement;

(ii) Periodically review the overall goals and strategy of the Research Program;

(iii) Discuss and attempt to resolve any deadlocked issues submitted to it by the JRC, although the vote of VERTEX's representatives shall prevail if the JSC is unable to reach a consensus on any matter other than matters submitted to the JSC under Section 2.5.2(ii).

2.7. EXCHANGE OF INFORMATION.
2.7.1. VERTEX, and at its sole discretion NOVARTIS, will share information with the JRC, as soon as it is available, necessary to facilitate mutual understanding of the status of the Research Program and decision-making in connection therewith.

2.7.2. Neither VERTEX nor NOVARTIS shall use Kinase Technology disclosed by the other party (excluding information which is no longer subject to confidentiality restrictions under Article V by reason of the exceptions set forth in Section 5.2) for any purpose, including the filing of patent applications containing such information, without the other party's consent, other than for carrying out the Research Program or discharging its responsibilities under the License Agreement, or as otherwise permitted under the Research Agreement or the License Agreement.

2.7.3. [This section has been intentionally left blank.]

2.7.4. [***]

2.8. [This section has been intentionally left blank.]

2.9. FREEDOM-OF-ACTION AND EXCLUSIVITY

2.9.1. [***]

2.9.2. [***]

2.9.3. [This section has been intentionally left blank.]

2.9.4. [This section has been intentionally left blank.]

2.9.5. [This section has been intentionally left blank.]

2.9.6. [This section has been intentionally left blank.]

ARTICLE III
PAYMENTS

3.1. SIGNATURE PAYMENT BY NOVARTIS. Upon the Effective Date of this Research Agreement NOVARTIS made an initial non-refundable payment of $15,000,000 to VERTEX.

3.2. STAFFING AND RESEARCH SUPPORT PAYMENTS. NOVARTIS has made or will make the payments specified below to VERTEX during each Research Year in support of the Research Program under this Research Agreement. The required payments are based upon the following assumptions: (a) the average number of FTE's which VERTEX will have employed in the Research Program during a Research Year will be approximately equal to the FTE Level listed in the third column below; and (b) the annual rate per FTE is approximately [***]. If the average FTE level for any Research Year is less than the level specified below for that year (the difference being referred to in this section as an "FTE Shortfall"), then the amount of funding specified below for that Research Year shall be reduced by an amount (the "FTE Shortfall Amount") which bears the same relation to the total funding specified below for that Research Year as the FTE Shortfall bears to the projected FTE Level for that Year. The FTE Shortfall Amount shall be carried over from year to year and applied to compensate VERTEX for FTE Levels in subsequent Research Years which exceed the level for those Years as specified below. In any such subsequent Research Year, VERTEX shall be entitled to receive out of any remaining FTE Shortfall Amount a payment equal to the value (computed with reference to the inflation-adjusted FTE rate specified above) of any FTE's actually employed during that Research Year in excess of the FTE Level specified for that year ("Excess FTE's"). Notwithstanding the foregoing, the FTE Shortfall Amount will not be applied to compensate VERTEX on account of more than 20 Excess FTE's in any one Research Year.

RESEARCH YEAR	FUNDING	FTE LEVEL
1	[***]	[***]
2	[***]	[***]
3	[***]	[***]

RESEARCH YEAR	FUNDING	FTE LEVEL
4	[***]	[***]
5	[***]	[***]
6	[***]	[***]

Research Year 1 will be deemed to have commenced on May 1, 2000. Payments due for each Research Year shall be made quarterly in advance on or before May 1, August 1, November 1 and February 1 of each Research Year except that the quarterly payment due May 1, 2000 was made within thirty business days after the Effective Date of this Research Agreement. All payments shall be made without deduction for withholding or other similar taxes, in United States dollars to the credit of such bank account as may be designated by VERTEX in writing to NOVARTIS. Any payments which fall due on a date which is a legal holiday in the Commonwealth of Massachusetts may be made on the next following day which is not a legal holiday in the Commonwealth.

3.3. DEVELOPMENT LOAN FACILITY. The existing development loan facility is hereby terminated. All currently outstanding loans made under the facility will be repaid by VERTEX on or before the earlier of: May 7, 2008, as specified in Section 3.3.3 of the Original Agreement; or the first anniversary of the effective date of any termination of this Research Agreement by NOVARTIS for cause under Section 9.2 hereof. Notwithstanding the foregoing, the provisions of Section 4.8 of this Research Agreement will apply as specified therein to repayment of development loans advanced on account of the Compounds known as VX-680 and VX-528.

3.4. RECORDS. VERTEX shall keep accurate records and books of accounts containing all data reasonably required for the calculation and verification of FTE's employed by VERTEX in the Research Program.

At NOVARTIS's request, VERTEX shall make those records available, no more than once a year, during reasonable working hours, for review by a recognized independent accounting firm acceptable to both parties, at NOVARTIS's expense, for the sole purpose of verifying the accuracy of those records in the calculation of Research Program FTE's. VERTEX shall not, however, be required to retain or make available to NOVARTIS or its accountants, any such records or books of account for any Research Year, beyond thirty-six (36) months from the conclusion of that Research Year. NOVARTIS shall cause the accounting firm to retain all such information in confidence.

In the event of a negative difference between the average number of FTE's stated to be involved in the Research Program and the number of FTE's actually employed, the amount previously advanced to VERTEX and attributable to any such negative difference shall be due and payable to NOVARTIS without delay. If the negative difference is more than [***] in any Research Year, then VERTEX shall also pay the reasonable costs of the independent accountant employed by NOVARTIS in the review. Interest at the rate of [***], assessed from the end of

the Research Year to which the negative difference relates, shall be due from VERTEX upon prior written notice.

ARTICLE IV
LICENSE, DEVELOPMENT AND COMMERCIALIZATION RIGHTS

4.1. DEVELOPMENT ELECTION.
(a) NOVARTIS shall have the exclusive right (the "Development Election") to develop and commercialize, under the terms and conditions set forth in the License Agreement and for any and all Indications, (i) each Drug Product Candidate proposed to it by VERTEX as set forth below, and related Back-up Compounds as provided in Section 4.5 hereof and selected by NOVARTIS, and (ii) any Compound or Compounds selected by NOVARTIS, as provided in Section 4.1(d) hereof, from Compounds which have met the Development Candidate Criteria, whether or not any such Compound or Compounds have been proposed as Development Candidates by VERTEX. While the Development Election is in effect, VERTEX will not grant to any Third Party rights to VERTEX Kinase Technology which are inconsistent with the grant of the Development Election to NOVARTIS hereunder. NOVARTIS's right to exercise Development Elections will expire and NOVARTIS shall no longer have the right to select Drug Candidates hereunder upon the first to occur of:

(1) The Final Termination Date as defined below;

(2) Termination of the Research Program by VERTEX under
Section 9.3 hereof;

(3) Termination of the Research Program by either party hereto for Scientific Cause under Section 9.5 hereof.

If NOVARTIS validly terminates the Research Program for cause under Section 9.2 hereof, the Development Election may nonetheless be exercised for the one-year period after the effective date of the termination for cause, but only with respect to Compounds which have met the Development Candidate Criteria prior to the effective termination date.

(b) VERTEX shall notify NOVARTIS and the JRC each time VERTEX has identified a Compound that, in the reasonable exercise of its scientific and business judgment, is a suitable Development Candidate and meets the Development Candidate Criteria. The corresponding notice shall be accompanied by the Development Candidate Information relating to the Development Candidate and its Back-up Compounds, provided that information concerning Compound structures shall be handled as specified in Section 5.1 hereof. NOVARTIS may, at its sole discretion, exercise its Development Election and accept the Development Candidate as a Drug Product Candidate by delivery of written notice to VERTEX
[***]. The total period of time from receipt of notice from VERTEX through [***] shall be referred to as the "Notice Period". Notwithstanding any other provisions of this Research Agreement, the Development Election with respect to any Development Candidate will not expire until the end of the Notice Period with respect to that Development Candidate.

(c) [This subsection has been intentionally left blank.]

(d) VERTEX will submit a final report (the "Final Report") to NOVARTIS covering the period beginning on the Research Termination Date [***] (the "Final Report Period"). The Final Report will contain Development Candidate Information for any Compound that VERTEX believes, in the reasonable exercise of its scientific and business judgment, meets the Development Candidate Criteria [***], along with information with respect to relevant Back-up Compounds. The procedure whereby NOVARTIS may exercise its Development Election and accept any Development Candidate identified in the Final Report, for further development as a Drug Product Candidate, will be the same as that described in subsection (b) above, and the time period from receipt of the Final Report from VERTEX through the end of the 90-day period referenced in that subsection (b) shall be called the "Final Notice Period".

In addition, [***] If NOVARTIS, based on this information, concludes that a given Compound does meet the Development Candidate Criteria, a formal Development Election procedure pursuant to Section 4.1(b) will be initiated for such Compound. If VERTEX disagrees with NOVARTIS's judgment that a given Compound meets the Development Candidate Criteria, the dispute resolution provisions in Section 2.5.2 (ii) shall apply.

The date upon which the Final Report Period, as and if extended by the parties as provided for in Section 4.3 hereof, expires shall be called the "Final Termination Date."

(e) [***]

(f) Promptly following exercise by NOVARTIS of its Development Election, the parties will execute a License Agreement substantially identical to the license agreement attached hereto as Exhibit A. NOVARTIS will develop and commercialize the Drug Product Candidate under the provisions of the License Agreement. If the Development Election has previously been exercised with respect to another Drug Product Candidate and a License Agreement is in effect, then the License Agreement will be amended to reflect the addition of another Drug Product Candidate. Development of each Drug Product Candidate shall proceed immediately after the Development Election is exercised, in accordance with the terms of the License Agreement.

4.2. [This section has been intentionally left blank.]

4.3. EXTENSION OF NOTICE PERIOD AND FINAL NOTICE PERIOD.

NOVARTIS may propose to VERTEX by written notice delivered during [***] the Notice Period with respect to a particular Development Candidate, or the Final Notice Period, with specific reference to one or more Compounds included in the Final Report and meeting the Development Candidate Criteria, that the Notice Period or the Final Notice Period, as the case may be, for a specific Development Candidate or Compound be extended for good reason for a specified time to permit NOVARTIS, at its expense and under its direction, to conduct such additional studies of that Development Candidate or Compound as may be specified in the notice. VERTEX shall discuss this request with NOVARTIS and the parties shall attempt in

good faith to reach mutual agreement with respect to the requested extension period and the conduct of additional studies, but failing agreement the applicable Notice Period or Final Notice Period shall expire as specified herein.

4.4. REFUSED CANDIDATE.

4.4.1. If NOVARTIS does not exercise its Development Election within the Notice Period or the Final Notice Period, as applicable, specified in

Section 4.1, with respect to a particular Development Candidate proposed by VERTEX, then the Development Election will expire with respect to that Development Candidate (a "Refused Candidate"), and (a) NOVARTIS will relinquish all rights under this Research Agreement and the License Agreement [***] (b) VERTEX may thereafter develop and commercialize the Refused Candidate and any such Excluded Compounds at its expense free of any further obligation to NOVARTIS with respect thereto; and [***], shall be considered Excluded Compounds under the provisions of this Section 4.4.1.

4.4.2. [This section has been intentionally left blank.]

4.5. BACK-UP COMPOUNDS. The following provisions will apply with respect to Back-up Compounds to any Drug Product Candidate.

(a) VERTEX RESTRICTIONS ON NOMINATION AND DEVELOPMENT. So long as NOVARTIS is using commercially reasonable efforts with respect to the development of a particular Drug Product Candidate or the commercialization of a particular Drug Product, VERTEX will not (i) propose a Compound for development under the License Agreement which is a Back-up Compound with respect to that Drug Product Candidate or Drug Product, or (ii) until after the period starting on the date on which NOVARTIS has exercised its Development Election for a particular Drug Product Candidate and ending [***] (the "Lead Period"), commence development of that Back-up Compound either directly or together with or through an Affiliate or a Third Party.

(b) TERMINATION OF DEVELOPMENT OR COMMERCIALIZATION. If, prior to the end of the Lead Period with respect to a particular Drug Product or Drug Product Candidate, NOVARTIS ceases to use commercially reasonable efforts to develop or commercialize that Drug Product Candidate or Drug Product, then the restrictions on nomination and development referenced in subsection (a) above will no longer apply with respect to Back-up Compounds for that Drug Product Candidate or Drug Product unless NOVARTIS, without delay, commences another Development Program under the License Agreement with another Compound (a "Replacement Candidate") targeting the same Kinase, which Replacement Candidate is a Back-up Compound associated with the discontinued Drug Product Candidate or Drug Product, and NOVARTIS shall have the right to select for this purpose any such Back-up Compound by providing VERTEX with notice of its Development Election in this regard. Any such Back-up Compound for which NOVARTIS has exercised its Development Election under this subsection (b) shall hereafter be a Drug Product Candidate subject to the terms and conditions of the License Agreement.

(c) TERMINATION OF RIGHTS TO BACK-UP COMPOUNDS. A Back-up Compound will no longer be subject to NOVARTIS's Development Election under the Research Agreement after the end of the Lead Period applicable to that Back-up Compound, except for Back-up Compounds which (i) subject to subsection (a) above, VERTEX has proposed for development on or before the Final Termination Date, and as to which NOVARTIS has exercised its Development Election hereunder; or (ii) have been or will be selected by NOVARTIS for development before the end of the applicable Lead Period under the provisions of subsection (b) above, or
(iii) for which NOVARTIS has exercised or will exercise its Development Election before the end of the applicable Lead Period under the provisions of subsection
(d) below.

(d) NOVARTIS RIGHTS TO LICENSE BACK-UP COMPOUNDS. Anytime prior to the expiry of the Lead Period with respect a particular Drug Product Candidate, NOVARTIS may also, by paying in each case the Back-up Election Fee provided under Section 6.1 of the License Agreement, exercise its Development Election with respect to any one or more Back-up Compounds associated with that Drug Product Candidate, provided that Drug Product Candidate, or a Back-up Compound selected pursuant to the provisions of subsection (b) above, is still in active development. Any such Back-up Compound for which NOVARTIS has exercised its Development Election under this subsection (d) shall become a "Drug Product Candidate Back-up Candidate" subject to the terms and conditions of the License Agreement.

(e) NOVARTIS OBLIGATIONS WITH RESPECT TO DRUG PRODUCT CANDIDATE BACK-UP CANDIDATES. So long as NOVARTIS is using commercially reasonable efforts, pursuant to the provisions of Sections 3.6 and 5.6 of the License Agreement, with respect to the development of a particular Drug Product Candidate or the commercialization of a particular Drug Product, NOVARTIS shall have no obligation to develop any of the Drug Product Candidate Back-up Candidates associated with that Drug Product Candidate or Drug Product. As soon as NOVARTIS ceases the development of a particular Drug Product Candidate, NOVARTIS's obligations to use diligent, commercially reasonable efforts will immediately shift from the discontinued Drug Product Candidate to an associated Drug Product Candidate Back-up Compound. If NOVARTIS ceases the development of a particular Drug Product Candidate and does not commence development of a Drug Product Candidate Back-up Compound pursuant to the foregoing, the license to the Drug Product Candidate and its Back-up Compounds under the License Agreement will expire and the license rights will revert to VERTEX.

4.6. [This section has been intentionally left blank.]

4.7. DRUG SUBSTANCE.

As soon as practicable after the exercise of its Development Election with respect to a Drug Product Candidate, VERTEX will deliver to NOVARTIS, if so requested by NOVARTIS, all drug substance for that Candidate in VERTEX's possession, if any, to the extent it is usable in connection with development of that Candidate. NOVARTIS will reimburse VERTEX for the Manufacturing Cost (as such term is defined in the License Agreement) of that material within thirty (30) days of receipt of VERTEX's invoice therefor.

4.8. SPECIAL PROVISIONS REGARDING VX-680, VX-528 AND VX-608.

The parties acknowledge that VERTEX is currently pursuing three Development Candidates which have been designated as VX-608, VX-680 and VX-528.

(a) VX-608. VX-608 will be governed by this Research Agreement and will be subject to the Development Election. The Notice Period with respect to VX-608 shall be deemed to have commenced on the later of (i) the date on which this Research Agreement is entered into, or (ii) the date by which NOVARTIS is in possession of the Development Candidate Information. If NOVARTIS exercises its Development Election with respect to VX-608 during the Notice Period, that Compound will become a Drug Product Candidate hereunder, and NOVARTIS will undertake all future development of VX-608 under the terms of the License Agreement. The Development Election Payment will be made to VERTEX and
[***]. If NOVARTIS fails to exercise its Development Election with respect to VX-608 during the Notice Period, then VX-608 will become a Refused Candidate hereunder and the provisions of Section 4.4 will be applicable thereafter. Any outstanding development loan will be repaid in accordance with Section 3.3 hereof.

(b) VX-680 AND VX-528. The Compounds designated by VERTEX as VX-680 and VX-528 are in early development under the provisions of the Original Agreement, and the terms of the Original Agreement shall continue to govern the rights and obligations of VERTEX and NOVARTIS with respect to VX-680 and VX-528 only, with the following modifications: [***]

At its sole discretion exercisable by notice in writing from VERTEX to NOVARTIS delivered on or before [***], VERTEX may elect to consider VX-680 and VX-528 as Development Candidates which have become Refused Candidates under the Research Agreement, and the terms and conditions of the Research Agreement as they apply to any Refused Candidate shall thereafter apply in the case of VX-680 and VX-528. Contemporaneously with the aforementioned notice, VERTEX shall repay to NOVARTIS that portion of the total amount of any development loan previously advanced by NOVARTIS to VERTEX on account of either Compound, which is unspent and uncommitted as of the notice date. The balance of any development loan shall be repaid as provided in Section 3.3 hereof.

ARTICLE V
CONFIDENTIALITY

5.1. UNDERTAKING. During the term of this Research Agreement, each party shall keep confidential, and other than as provided herein shall not use or disclose, directly or indirectly, any trade secrets, confidential or proprietary information, or any other knowledge, information, documents or materials, owned, developed or possessed by the other party, whether in tangible or intangible form, the confidentiality of which such other party takes reasonable measures to protect, including but not limited to VERTEX Kinase Technology and NOVARTIS Kinase Technology.

(a) Each party shall take any and all lawful measures to prevent the unauthorized use and disclosure of such information, and to prevent unauthorized persons or entities from obtaining or using such information.

(b) Each party further agrees to refrain from directly or indirectly taking any action which would constitute or facilitate the unauthorized use or disclosure of such information. Each party may disclose such information to its officers, employees and agents, to authorized licensees and sublicensees, and to subcontractors in connection with the development or manufacture of Drug Candidates, Drug Product Candidates or Drug Products, to the extent necessary to enable such parties to perform their obligations hereunder or under the applicable license, sublicense or subcontract, as the case may be; provided, that such officers, employees, agents, licensees, sublicensees and subcontractors have entered into appropriate confidentiality agreements for secrecy and non-use of such information which by their terms shall be enforceable by injunctive relief at the instance of the disclosing party.

(c) Each party shall be liable for any unauthorized use and disclosure of such information by its officers, employees and agents and any such sublicensees and subcontractors.

(d) NOVARTIS will ensure that information with respect to the chemical structure of any Development Candidate which is delivered to NOVARTIS under Section 4.1(b) hereof as part of the Development Candidate Information with respect to that Development Candidate and its associated Back-up Compounds will be distributed or otherwise made known only to [***] The foregoing limitation on distribution of information will cease being applicable at such time as NOVARTIS exercises its Development Election with respect to that Development Candidate.

5.2. EXCEPTIONS. Notwithstanding the foregoing, the provisions of Section 5.1 hereof shall not apply to knowledge, information, documents or materials which the receiving party can conclusively establish:

(a) have entered the public domain without such party's breach of any obligation owed to the disclosing party;

(b) are permitted to be disclosed by the prior written consent of the disclosing party;

(c) have become known to the receiving party from a source other than the disclosing party, other than by breach of an obligation of confidentiality owed to the disclosing party;

(d) are disclosed by the disclosing party to a Third Party without restrictions on its disclosure;

(e) are independently developed by the receiving party without breach of this Research Agreement; or

(f) are required to be disclosed by the receiving party to comply with applicable laws or regulations, to defend or prosecute litigation or to comply with governmental regulations, provided that the receiving party provides prior written notice of such disclosure to the disclosing party and takes reasonable and lawful actions to avoid or minimize the degree of such disclosure.

Either VERTEX or NOVARTIS may at any time, by notice in writing to the other party, waive any or all of the confidentiality obligations to which the other party is subject hereunder, for any length of time or with respect to any specific information.

5.3. PUBLICITY. The parties will agree upon the timing and content of any initial press release or other public communications relating to this First Revised and Restated Agreement and the transactions contemplated herein.

(a) Except to the extent already disclosed in that initial press release or other public communication, no public announcement concerning the existence or the terms of this Research Agreement or concerning the transactions described herein shall be made, either directly or indirectly, by VERTEX or NOVARTIS, except as may be legally required by applicable laws, regulations, or judicial order, without first obtaining the approval of the other party and agreement upon the nature, text, and timing of such announcement, which approval and agreement shall not be unreasonably withheld.

(b) The party desiring to make any such public announcement shall provide the other party with a written copy of the proposed announcement in sufficient time prior to public release to allow such other party to comment upon such announcement, prior to public release.

5.4. SURVIVAL. The provisions of this Article V shall survive the termination of this Research Agreement and shall extend for a period of five (5) years thereafter.

ARTICLE VI
PUBLICATION

Each of NOVARTIS and VERTEX reserves the right to publish or publicly present the results (the "Results") of the Research Program, subject to the following terms and conditions. The party proposing to publish or publicly present the Results (the "publishing party") will submit a draft of any proposed manuscript or speech to the other party (the "non-publishing party") for comments at least thirty (30) days prior to submission for publication or oral presentation. The non-publishing party shall notify the publishing party in writing within fifteen (15) days of receipt of such draft whether such draft contains (i) information of the non-publishing party which it considers to be confidential under the provisions of Article V hereof, (ii) information that if published would have an adverse effect on a patent application covering the subject matter of this Research Agreement which the non-publishing party intends to file, or (iii) information which the non-publishing party reasonably believes would be likely to have a material adverse impact on the development or commercialization of a Drug Product Candidate. In any such notification, the non-publishing party shall indicate with specificity its suggestions

regarding the manner and degree to which the publishing party may disclose such information. In the case of item (ii) above, the non-publishing party may request a delay and the publishing party shall delay such publication, for a period not exceeding ninety (90) days, to permit the timely preparation and filing of a patent application or an application for a certificate of invention on the information involved. In the case of item (i) above, no party may publish confidential information of the other party without its consent in violation of Article V of this Research Agreement. In the case of item (iii) above, if the publishing party shall disagree with the non-publishing party's assessment of the impact of the publication, then the issue shall be referred to the JSC for resolution. If the JSC is unable to reach agreement on the matter within thirty
(30) days after such referral, the matter shall be referred by the JSC to the Chief Executive Officer of NOVARTIS and the Chief Executive Officer of VERTEX who shall attempt in good faith to reach a fair and equitable resolution of this disagreement. If the disagreement is not resolved in this manner within two (2) weeks of referral by the JSC as aforesaid, then the decision of the publishing party as to publication of any information generated by it, subject always to the confidentiality provisions of Article V hereof, shall be final, provided that such decision shall be exercised with reasonable regard for the interests of the non-publishing party. The parties agree that authorship of any publication will be determined based on the customary standards then being applied in the relevant scientific journal. The parties will use their best efforts to gain the right to review proposed publications relating to the subject matter of the Research Program by consultants or contractors.

This Article VI shall terminate with the termination of this Research Agreement, but the provisions of Article V hereof shall continue to govern the disclosure by one party, whether by publication or otherwise, of Confidential Information of the other, during the period set forth in Section 5.4.

ARTICLE VII
INDEMNIFICATION

7.1. INDEMNIFICATION BY VERTEX. VERTEX will indemnify and hold NOVARTIS and its Affiliates, and their employees, officers and directors harmless against any loss, damages, action, suit, claim, demand, liability, expense, bodily injury, death or property damage (a "Loss"), that may be brought, instituted or arise against or be incurred by such persons to the extent such Loss is based on or arises out of:

(a) the development, manufacture, use, sale, storage or handling of a Compound, a Development Candidate, a Drug Product Candidate or a Drug Product by VERTEX or its Affiliates or their representatives, agents, authorized sublicensees or subcontractors under this Research Agreement, or any actual or alleged violation of law resulting therefrom (with the exception of Losses based on infringement or misappropriation of intellectual property rights); or

(b) the breach by VERTEX of any of its covenants, representations or warranties set forth in this Research Agreement; and

(c) provided however, that the foregoing indemnification shall not apply to any Loss to the extent such Loss is caused by the negligent or willful misconduct of NOVARTIS or its Affiliates.

7.2. INDEMNIFICATION BY NOVARTIS. NOVARTIS will indemnify and hold VERTEX, and its Affiliates, and their employees, officers and directors harmless against any Loss that may be brought, instituted or arise against or be incurred by such persons to the extent such Loss is based on or arises out of:

(a) the development, manufacture, use, sale, storage or handling of a Compound, a Development Candidate, a Drug Product Candidate or a Drug Product by NOVARTIS or its Affiliates or their representatives, agents, authorized sublicensees or subcontractors under this Research Agreement, or any actual or alleged violation of law resulting therefrom (with the exception of Losses based on infringement or misappropriation of intellectual property rights); or

(b) the breach by NOVARTIS of any of its covenants, representations or warranties set forth in this Research Agreement; and

(c) provided that the foregoing indemnification shall not apply to any Loss to the extent such Loss is caused by the negligent or willful misconduct of VERTEX or its Affiliates.

7.3. CLAIMS PROCEDURES. Each Party entitled to be indemnified by the other Party (an "Indemnified Party") pursuant to Section 7.1 or 7.2 hereof shall give notice to the other Party (an "Indemnifying Party") promptly after such Indemnified Party has actual knowledge of any threatened or asserted claim as to which indemnity may be sought, and shall permit the Indemnifying Party to assume the defense of any such claim or any litigation resulting therefrom; provided:

(a) That counsel for the Indemnifying Party, who shall conduct the defense of such claim or any litigation resulting therefrom, shall be approved by the Indemnified Party (whose approval shall not unreasonably be withheld) and the Indemnified Party may participate in such defense at such party's expense (unless (i) the employment of counsel by such Indemnified Party has been authorized by the Indemnifying Party; or (ii) the Indemnified Party shall have reasonably concluded that there may be a conflict of interest between the Indemnifying Party and the Indemnified Party in the defense of such action, in each of which cases the Indemnifying Party shall pay the reasonable fees and expenses of one law firm serving as counsel for the Indemnified Party, which law firm shall be subject to approval, not to be unreasonably withheld, by the Indemnifying Party); and

(b) The failure of any Indemnified Party to give notice as provided herein shall not relieve the Indemnifying Party of its obligations under this Research Agreement to the extent that the failure to give notice did not result in harm to the Indemnifying Party.

(c) No Indemnifying Party, in the defense of any such claim or litigation, shall, except with the approval of each Indemnified Party which approval shall not be unreasonably withheld, consent to entry of any judgment or enter into any settlement which (i)

would result in injunctive or other relief being imposed against the Indemnified Party; or (ii) does not include as an unconditional term thereof the giving by the claimant or plaintiff to such Indemnified Party of a release from all liability in respect to such claim or litigation.

(d) Each Indemnified Party shall furnish such information regarding itself or the claim in question as an Indemnifying Party may reasonably request in writing and shall be reasonably required in connection with the defense of such claim and litigation resulting therefrom.

7.4. COMPLIANCE. The parties shall comply fully with all applicable laws and regulations in connection with their respective activities under this Research Agreement.

ARTICLE VIII
PATENTABLE INVENTIONS

8.1. OWNERSHIP. All inventions made and all Know-How generated exclusively by either party or its Affiliates (directly or through others acting on its behalf) prior to and during the term of this Research Agreement shall be owned by the party making the invention or generating the Know-How claimed, or if such invention is made jointly (a "Joint Invention"), shall be owned jointly, all as determined in accordance with United States laws of inventorship.

8.2. PREPARATION. VERTEX shall take responsibility for the preparation, filing, prosecution and maintenance of all VERTEX Patents, and any patents and patent applications claiming Joint Inventions, and NOVARTIS shall take responsibility for the preparation, filing, prosecution and maintenance of all NOVARTIS Patents. VERTEX shall provide the JRC with periodic reports listing, by name, Patents filed by VERTEX in the United States and other jurisdictions, along with a general summary of the claims made and the jurisdictions of filing. In good time, before the deadline for foreign filing of any patent application filed in the United States, VERTEX will notify NOVARTIS whether it intends to foreign file such patent application, and if it intends to do so, in what countries it proposes to foreign file. Upon timely written notice from NOVARTIS, VERTEX will file in such additional countries -- all being countries in which NOVARTIS would customarily file its own cases dealing with similar subject matter -- as NOVARTIS shall request.

8.3. COSTS.
(a) During the Research Program. NOVARTIS shall reimburse VERTEX for
[***]. If the full amount of any reimbursement commitment is not applied in any Research Year, the unused balance may be carried over from year to year during the Research Program.

(b) After the Research Program. Upon expiration of the Research Program, the parties shall determine which Patents covering Drug Product Candidates and Drug Products, and Development Candidates and Back-up Compounds as to which the Development Election is still applicable (until it expires), are included in the Kinase Technology, and thereafter [***]. Either party may at any time thereafter elect, by written notice to the other party, to discontinue support for one or more such Patents (a "Discontinued Patent") and shall not be responsible for any costs

relating to a Discontinued Patent which are incurred more than sixty (60) days after receipt of that notice by the other party. In such case, the other party may elect at its sole discretion to continue preparation, filing, prosecution or maintenance of the Discontinued Patent at its sole expense. The party so continuing shall own any such Patent, and if the party electing to discontinue support is the owner of the Discontinued Patent, it shall execute such documents of transfer or assignment and perform such acts as may be reasonably necessary to transfer ownership of the Discontinued Patent to the other party and enable that party to file or to continue prosecution or maintenance, if the other party elects to do so. Discontinuance may be on a country-by-country basis or for a Patent series in total.

ARTICLE IX
TERM AND TERMINATION

9.1. TERM.
9.1.1. This Research Agreement shall have retroactive effect to the Effective Date, replacing and superceding the rights and obligations of the parties under the Original Agreement, except that the terms of the Original Agreement shall be deemed to govern the rights and obligations of the parties with respect to the Compounds known as VX-680 and VX-528, pursuant to the provisions of Section 4.8 of this Research Agreement. This Research Agreement will extend until the Final Termination Date as defined herein, unless earlier terminated by either party hereto in accordance with this Research Agreement, or unless extended by mutual agreement of the parties; provided that the Agreement will be deemed to continue in effect with respect to any Drug Product Candidate during the Lead Period with respect to that Candidate, but only insofar as necessary to enable NOVARTIS to exercise its Development Election under Section 4.5 hereof with respect to any Back-up Compounds for that Drug Product Candidate.

9.2. TERMINATION OF THE RESEARCH PROGRAM BY NOVARTIS FOR CAUSE. Upon written notice to VERTEX, NOVARTIS may at its sole discretion unilaterally terminate the Research Program and this Research Agreement upon the occurrence of any of the following events:

(a) VERTEX shall materially breach any of its material obligations, such as its obligations under Section 3.2 hereof, under this Research Agreement or the License Agreement, and such material breach shall not have been remedied or steps initiated to remedy the same to NOVARTIS's reasonable satisfaction, within sixty (60) days after NOVARTIS sends written notice of breach to VERTEX; or

(b) VERTEX shall cease to function as a going concern by suspending or discontinuing its business for any reason except for interruptions caused by Force Majeure, strike, labor dispute or any other events over which it has no control.

In the event of any valid termination under this Section 9.2, NOVARTIS shall not be required to make any payments under Section 3.2 hereof which are not due and payable prior to receipt by VERTEX of the notice of breach referenced under Section 9.2(a) or receipt by VERTEX of the notice of termination pursuant to Section 9.2(b), as the case may be. Notwithstanding the foregoing, any License Agreement then in effect shall continue in effect unless it is expressly terminated in accordance with its terms.

9.3. TERMINATION OF THE RESEARCH PROGRAM BY VERTEX FOR CAUSE. VERTEX may at its sole discretion terminate this Research Agreement upon written notice to NOVARTIS upon the occurrence of any of the following events:

(a) NOVARTIS shall materially breach any of its material obligations under this Research Agreement or the License Agreement and such material breach shall not have been remedied or steps initiated to remedy the same to VERTEX's reasonable satisfaction, within sixty (60) days after VERTEX sends written notice of breach to NOVARTIS; or

(b) NOVARTIS shall cease to function as a going concern by suspending or discontinuing its business for any reason except for interruptions caused by Force Majeure, strike, labor dispute or any other events over which it has no control.

Notwithstanding the foregoing, any License Agreement then in effect shall continue in effect unless it is expressly terminated in accordance with its terms.

9.4. [This section has been intentionally left blank.]

9.5. TERMINATION FOR SCIENTIFIC CAUSE.

Either party may terminate this Research Agreement upon six months' prior written notice to the other party, if the terminating party can demonstrate to the reasonable satisfaction of the other party that, by reason of scientific developments unknown on the Effective Date, the Research Program is unlikely to produce any Compounds that can achieve a commercially viable therapeutic effect through an effect on a Kinase target.

9.6. EFFECT OF TERMINATION.
(a) Except where explicitly provided elsewhere herein, termination of this Research Agreement for any reason, or expiration of this Research Agreement, will not affect: (i) obligations which have accrued as of the date of termination or expiration, and (ii) obligations and rights which, expressly or from the context thereof, are intended to survive termination or expiration of this Research Agreement, including obligations of confidentiality under Article V hereof, the indemnification provisions of Article VII hereof and the rights and obligations of the parties during the Lead Period under Sections 4.1 and 4.5 with respect to a particular Drug Product Candidate and related Back-up Compounds.

(b) Upon termination or expiration of this Research Agreement, NOVARTIS and VERTEX will retain exclusive rights to their respective Kinase Technology (including intellectual property), except NOVARTIS shall hold those rights to VERTEX Technology provided in any License Agreement in effect on the Final Termination Date covering Drug Product Candidates selected by NOVARTIS, and shall hold those rights to Back-up Compounds and Drug Product Candidate Back-up Compounds provided in Sections 4.1(e) and 4.5.

ARTICLE X
REPRESENTATIONS AND WARRANTIES

10.1. REPRESENTATIONS AND WARRANTIES OF VERTEX. VERTEX represents and warrants to NOVARTIS as follows:

(a) Authorization. This Research Agreement has been duly executed and delivered by VERTEX and constitutes the valid and binding obligation of VERTEX, enforceable against VERTEX in accordance with its terms except as enforceability may be limited by bankruptcy, fraudulent conveyance, insolvency, bankruptcy, reorganization, moratorium and other laws relating to or affecting creditors' rights generally and by general equitable principles. The execution, delivery and performance of this Research Agreement have been duly authorized by all necessary action on the part of VERTEX, its officers and directors.

(b) No Third Party Rights. VERTEX owns or possesses adequate licenses or other rights to use all VERTEX Kinase Technology relating to the Field and to grant the licenses herein. The granting of the Development Election to NOVARTIS hereunder does not violate any right known to VERTEX of any Third Party.

(c) Third Party Patents. Except as disclosed in writing between the parties to this Research Agreement or their respective agents, VERTEX is not aware of any issued patents or pending patent applications that, if issued, would be infringed by the development, manufacture, use or sale of any Compound, Development Candidate or Drug Product Candidate pursuant to this Research Agreement.

10.2. REPRESENTATIONS AND WARRANTIES OF NOVARTIS. NOVARTIS represents and warrants to VERTEX as follows:
(a) Authorization. This Research Agreement has been duly executed and delivered by NOVARTIS and constitutes the valid and binding obligation of NOVARTIS, enforceable against NOVARTIS in accordance with its terms except as enforceability may be limited by bankruptcy, fraudulent conveyance, insolvency, bankruptcy, reorganization, moratorium and other laws relating to or affecting creditors' rights generally and by general equitable principles. The execution, delivery and performance of this Research Agreement have been duly authorized by all necessary action on the part of NOVARTIS, its officers and directors.

(b) Third Party Rights. NOVARTIS owns or possesses adequate licenses or other rights to use all NOVARTIS Kinase Technology relating to the Field in accordance with the provisions of this Research Agreement.

(c) Third Party Patents. Except as disclosed in writing between the parties to this Research Agreement or their respective agents, NOVARTIS is not aware of any issued patents or pending patent applications that, if issued, would be infringed by the development, manufacture, use or sale of any Compound, Development Candidate or Drug Product Candidate pursuant to this Research Agreement.

ARTICLE XI
DISPUTE RESOLUTION

11.1. GOVERNING LAW, AND JURISDICTION. This Research Agreement shall be governed and construed in accordance with the internal laws of the State of New York.

11.2. DISPUTE RESOLUTION PROCESS.

(a) General. Except as set forth in (b) below or as otherwise explicitly provided herein, in the event of any controversy or claim arising out of or relating to any provision of this Research Agreement, or the collaborative effort contemplated hereby, the parties shall, and either party may, initially refer such dispute to the JSC, and failing resolution of the controversy or claim within thirty (30) days after such referral, the matter shall be referred to the Chief Executive Officer of VERTEX and the Chief Executive Officer of NOVARTIS who shall, as soon as practicable, attempt in good faith to resolve the controversy or claim. If such controversy or claim is not resolved within sixty (60) days of the date of initial referral of the matter to the JSC, either party shall be free to initiate proceedings in any court having requisite jurisdiction.

(b) Third Party Referral. Any dispute or claim relating to the "Referral Matters" as defined below which the parties are unable to resolve pursuant to the other dispute resolution mechanisms provided in this Research Agreement (other than litigation) shall, upon the written request of one party delivered to the other party, be submitted to and settled by a panel of Third Parties (a "Third Party Panel") appointed by VERTEX and NOVARTIS as provided below. The "Referral Matter" shall consist solely of disagreements concerning whether a particular Compound has satisfied all of the applicable Development Candidate Criteria. Within thirty (30) days after delivery of the above-referenced written request, each party will appoint one person who is not an Affiliate of the party appointing that person, and who is knowledgeable in the areas of pharmaceutical science, business and commercial aspects of drug development and sale, or the clinical development of pharmaceuticals, to hear and determine the dispute. The two persons so chosen will select another impartial Third Party and their majority decision will be final and conclusive upon the parties hereto. If either party fails to designate its appointee within the thirty (30) day period referenced above, then the appointee who has been designated by the other party will serve as the sole member of the Third Party Panel and will be deemed to be the single, mutually approved party to resolve the dispute. Each party will bear its own costs in the Third Party Referral process, and the parties will split equally the costs of the Third Party Panel members. The Third Party Panel will, upon the request of either party, issue its final determination in writing.

ARTICLE XII
MISCELLANEOUS PROVISIONS

12.1. OFFICIAL LANGUAGE. English shall be the official language of this Research Agreement and the License Agreement, and all communications between the parties hereto shall be conducted in that language.

12.2. WAIVER. No provision of this Research Agreement may be waived except in writing by both parties hereto. No failure or delay by either party hereto in exercising any right or remedy hereunder or under applicable law will operate as a waiver thereof, or a waiver of any right or remedy on any subsequent occasion.

12.3. FORCE MAJEURE.

Neither party will be in breach hereof by reason of its delay in the performance of or failure to perform any of its obligations hereunder, if that delay or failure is caused by strikes, acts of God or the public enemy, riots, incendiaries, interference by civil or military authorities, compliance with governmental priorities for materials, or any fault beyond its control or without its fault or negligence.

12.4. SEVERABILITY. Should one or more provisions of this Research Agreement be or become invalid, then the parties hereto shall attempt to agree upon valid provisions in substitution for the invalid provisions, which in their economic effect come so close to the invalid provisions that it can be reasonably assumed that the parties would have accepted this Research Agreement with those new provisions. If the parties are unable to agree on such valid provisions, the invalidity of such one or more provisions of this Research Agreement shall nevertheless not affect the validity of the Agreement as a whole, unless the invalid provisions are of such essential importance for this Research Agreement that it may be reasonably presumed that the parties would not have entered into this Research Agreement without the invalid provisions.

12.5. GOVERNMENT ACTS. In the event that any act, regulation, directive, or law of a country or its government, including its departments, agencies or courts, should make impossible or prohibit, restrain, modify or limit any material act or obligation of NOVARTIS or VERTEX under this Research Agreement, the party, if any, not so affected, shall have the right, at its option, to suspend or terminate this Research Agreement as to such country, if good faith negotiations between the parties to make such modifications therein as may be necessary to fairly address the impact thereof, are not successful after a reasonable period of time in producing mutually acceptable modifications to this Research Agreement.

12.6. GOVERNMENT APPROVALS. Each party will obtain any government approval required in its country of domicile to enable this Research Agreement to become effective, or to enable any payment hereunder to be made, or any other obligation hereunder to be observed or performed. Each party will keep the other informed of progress in obtaining any such government approval, and will cooperate with the other party in any such efforts.

12.7. EXPORT CONTROLS. This Research Agreement is made subject to any restrictions concerning the export of materials and Technology from the United States which may be imposed upon or related to either party to this Research Agreement from time to time by the Government of the United States. Furthermore, NOVARTIS will not export, directly or indirectly, any VERTEX Kinase Technology or any Bulk Drug Substance, Drug Product Candidates or Drug Products utilizing such Technology to any countries for which the United States Government or any agency thereof at the time of export requires an export license or other governmental approval, without first obtaining the written consent to do so from the Department of Commerce or other agency of the United States Government when required by applicable statute or regulation.

12.8. ASSIGNMENT.

This Research Agreement may not be assigned or otherwise transferred by either party without the prior written consent of the other party; provided, however, that either party may assign this Research Agreement, without the consent of the other party, (i) to any of its Affiliates, if the assigning party guarantees the full performance of its Affiliates' obligations hereunder, or
(ii) in connection with the transfer or sale of all or substantially all of its assets or business or in the event of its merger or consolidation with another company. Any purported assignment in contravention of this Section 12.8 shall, at the option of the non-assigning party, be null and void and of no effect. No assignment shall release either party from responsibility for the performance of any accrued obligation of such party hereunder. This Research Agreement shall be binding upon and enforceable against the successor to or any permitted assignees from either of the parties hereto.

12.9. AFFILIATES. Each party may perform its obligations hereunder personally or through one or more Affiliates, although each party shall nonetheless be solely responsible for the performance of its Affiliates. Neither party shall permit any of its Affiliates to commit any act (including any act or omission) which such party is prohibited hereunder from committing directly. The use of subcontractors by either party shall not increase the financial obligations of the other party hereunder in any respect.

12.10. COUNTERPARTS. This Research Agreement may be executed in duplicate, each of which shall be deemed to be original and both of which shall constitute one and the same Agreement.

12.11. NO AGENCY. Nothing herein contained shall be deemed to create an agency, joint venture, amalgamation, partnership or similar relationship between NOVARTIS and VERTEX. Notwithstanding any of the provisions of this Research Agreement, neither party to this Research Agreement shall at any time enter into, incur, or hold itself out to third parties as having authority to enter into or incur, on behalf of the other party, any commitment, expense, or liability whatsoever, and all contracts, expenses and liabilities in connection with or relating to the obligations of each party under this Research Agreement shall be made, paid, and undertaken exclusively by such party on its own behalf and not as an agent or representative of the other.

12.12. NOTICE. All communications between the parties with respect to any of the provisions of this Research Agreement will be sent to the addresses set out below, or to such other addresses as may be designated by one party to the other by notice pursuant hereto, by prepaid, certified air mail (which shall be deemed received by the other party on the seventh business day following deposit in the mails), or by facsimile transmission, or other electronic means of communication (which shall be deemed received when transmitted), with confirmation by first class letter, postage pre-paid, given by the close of business on or before the next following business day:

if to NOVARTIS, at:

NOVARTIS PHARMA AG
Business Development and Licensing

P.O. Box
CH-4002
Basel, Switzerland
Attention: Victor A. Hartmann, Vice President

with a copy to: Legal Services, at the address referenced above

if to VERTEX, at:

Vertex Pharmaceuticals Incorporated
130 Waverly Street
Cambridge, MA U.S.A. 02139-4211

Attention: President

with a copy to: Legal Department Attention: General Counsel

12.13. HEADINGS. The paragraph headings are for convenience only and will not be deemed to affect in any way the language of the provisions to which they refer.

12.14. AUTHORITY. The undersigned represent that they are authorized to sign this Research Agreement on behalf of the parties hereto. The parties each represent that no provision of this Research Agreement will violate any other agreement that such party may have with any other person or company. Each party has relied on that representation in entering into this Research Agreement.

12.15. ENTIRE AGREEMENT. This Research Agreement, together with the Original Agreement insofar as it remains applicable, as set forth in the Recitals, in Section 4.8 and elsewhere herein, with respect to VX-680 and VX-528 only, and the respective License Agreements thereto, contains the entire understanding of the parties relating to the matters referred to herein, and may only be amended by a written document, duly executed on behalf of the respective parties.

12.16. STANDSTILL.
[***]

12.17. NOTICE OF PHARMACEUTICAL SIDE-EFFECTS. During the term of this Research Agreement, the parties shall keep each other promptly and fully informed and will promptly notify appropriate authorities in accordance with applicable law, after receipt of information with respect to any serious adverse event (as defined by the ICH Harmonized Tripartite Guideline on Clinical Safety Data Management), directly or indirectly attributable to the use or application of Compounds, a Development Candidate, Bulk Drug Substance, a Drug Product Candidate or a Drug Product.

12.18. INFLATION ADJUSTMENT. All payments required to be made to VERTEX hereunder (except any royalty payments required to be made under the provisions of Section 6.3 of the License Agreement) shall be adjusted at the beginning of each Research Year (commencing at the beginning of Research Year 2) to reflect the impact of inflation since the Effective Date of the Agreement, as measured by the biotech worker inflation rate defined and reported in the Radford Survey (Radford/AON Consulting Inc., San Francisco, CA), or other mutually acceptable index. Notwithstanding the foregoing, no adjustment shall be required in any Research Year in which the appropriate inflation adjustment, if applied, would result in a change of less than [***] in the relevant payment amount.

12.19. INVOICE REQUIREMENT. Any amounts payable to VERTEX hereunder (except any royalty payments required to be made under the provisions of Section 6.3 of the License Agreement) shall be made within thirty days after receipt by NOVARTIS, or its nominee designated for that purpose in advance by NOVARTIS in writing to VERTEX, of an invoice covering such payment, which invoice shall conform to the extent reasonably practicable to the form of invoice contained in Exhibit B to this Research Agreement.

12.20. HARDSHIP. If as a result of unforeseen events or developments relating to the subject matter of this Research Agreement, the performance of this Research Agreement shall cause inequitable economic hardship for one party which runs counter to the objectives of this Research Agreement and which the other party cannot reasonably and in good faith expect the first party to bear unrelieved, the parties will meet and seek in good faith to find equitable means of amending this Research Agreement to reestablish a fair and reasonable economic balance under this Research Agreement between the parties hereto.

VERTEX PHARMACEUTICALS INCORPORATED

By: /s/ Kenneth S. Boger
Kenneth S. Boger
Title: Senior Vice President and General Counsel

NOVARTIS PHARMA AG

By: /s/ Stephanie Lassarat
Title: Senior Legal Counsel

By: /s/ W. Steiger
Title: Head of Administration, NIBR Basil

SCHEDULE 1.13

EXCLUDED COMPOUNDS AND EXCLUDED KINASES

Excluded Kinases	SWISSPROT Designation
[***]	[***]
[***]	[***]
[***]	[***]
[***]	[***]
[***]	[***]
[***]	[***]
[***]	[***]
[***]	[***]
[***]	[***]
[***]	[***]
[***]	[***]
[***]	[***]
[***]	[***]
[***]	[***]

Excluded Compounds

[***]

SCHEDULE 2.4.3

DEVELOPMENT CANDIDATE CRITERIA

[***]

EXHIBIT A

FORM OF LICENSE, DEVELOPMENT AND COMMERCIALIZATION AGREEMENT

First Revised and Restated

Research and Early Develoment Agreement - Confidential Exhibit A

EXHIBIT B

FORM OF INVOICE

[COMPANY Letterhead]

[Date]

Novartis Pharma AG
Zentraler Faktureneingang
Attn: Ms. R. Aschwanden
Lichtstrasse 35
CH - 4002 Basel
Switzerland

Dear Ms. Aschwanden

Re: [COMPANY] License Agreement for [PRODUCT]

This is an invoice requesting payment in connection the above-captioned Agreement between [COMPANY] and Novartis Pharma AG.

Novartis Contract Code N DEG.:	[will be assigned within Novartis following execution]
Novartis Cost Centre:	630926 / 393120
SPECIFICATION:	[PLEASE SPECIFY THE EVENT FOR WHICH THE INVOICE IS DUE, AND ADD ANY COPIES OF INVOICES FROM THIRD PARTIES IN CASE REIMBURSEMENT FOR THIRD PARTY WORK IS AGREED TO]
Amount and Currency:	[self-explanatory]
Bank address and Account N DEG.:	[insert the name and address of the bank to which the payment should be sent and the account number to which it should be credited]

Sincerely yours,
[COMPANY]

EXHIBIT A

LICENSE, DEVELOPMENT AND COMMERCIALIZATION AGREEMENT

BETWEEN

VERTEX PHARMACEUTICALS INCORPORATED

AND

NOVARTIS PHARMA AG

LICENSE, DEVELOPMENT AND COMMERCIALIZATION AGREEMENT

This Agreement is made and entered into as of _____, _____ (the "Effective Date") between Vertex Pharmaceuticals Incorporated (hereinafter "VERTEX"), a Massachusetts corporation with principal offices at 130 Waverly Street, Cambridge, MA 02139-4242, and NOVARTIS PHARMA AG (hereinafter "NOVARTIS"), a Swiss corporation with principal offices at Lichtstrasse 35, CH-4056 Basel, Switzerland.

INTRODUCTION

WHEREAS, VERTEX and NOVARTIS are parties to a certain First Revised and Restated Research Agreement dated January __, 2004 (the "Research Agreement") which revised and restated a certain Research and Early Development Agreement dated May 8, 2000 (the "Original Agreement"), under which VERTEX is attempting to design novel, small-molecule compounds targeting the Kinase protein superfamily; and

WHEREAS, NOVARTIS may elect to develop and commercialize compounds proposed by VERTEX under the Research Agreement; and

WHEREAS, in accordance with the Research Agreement NOVARTIS has elected to develop and commercialize the Drug Product Candidates designated on SCHEDULE 1.12 hereto, and the parties therefore wish to execute this License, Development and Commercialization Agreement, which is identical in substance to the agreement attached as Exhibit A to the Research Agreement, to memorialize the provisions specific to development and commercialization of Drug Product Candidates;

WHEREAS, the parties have special rights and obligations with respect to Back-up Compounds to the Drug Product Candidates (as defined in the Research Agreement); and

NOW THEREFORE, in consideration of the foregoing premises, the parties agree as follows:

ARTICLE I
DEFINITIONS

For purposes of this Agreement, the terms defined in this Article 1 shall have the following meanings whether used in their singular or plural forms. Use of the singular shall include the plural and vice versa, unless the context requires otherwise:

1.1. "AFFILIATE" shall mean, with respect to any Person, any other Person which directly or indirectly, by itself or through one or more intermediaries, controls, or is controlled

by, or is under direct or indirect common control with, such Person. The term "control" means the possession, direct or indirect, of the power to direct or cause the direction of the management and policies of a Person, whether through the ownership of voting securities, by contract or otherwise. Control will be presumed if one Person owns, either of record or beneficially, more than 50% of the voting stock of any other Person. For the avoidance of any doubt, the Novartis Institute for Functional Genomics, Inc. and The Friedrich Miescher Institute, as currently operated, are not Affiliates of NOVARTIS for the purposes of this Agreement.

1.1.1. "CHANGE OF CONTROL" shall mean (a) a transaction which results in the voting securities of VERTEX immediately prior to such transaction ceasing to represent more than fifty percent (50%) of the combined voting power of the surviving entity immediately after such transaction; (b) any Third Party (other than any trustee or other fiduciary holding securities under an employee benefit plan, or any corporation or other entity owned directly or indirectly by the stockholders of such party in substantially the same portion as their ownership of stock of such party) becoming the beneficial owner of more than fifty percent (50%) of the combined voting power of the outstanding securities of VERTEX; or (c) a sale to a Third Party of all or substantially all of the business of VERTEX necessary for VERTEX's performance under this Agreement.

1.2. "GLOBAL BRAND TEAM" OR "GBT" shall have the meaning set forth in Section 5.2 hereof; and "Back-up Compound" shall have the meaning set forth in Section 1.1.1 of the Research Agreement.

1.3. [This section has been intentionally left blank.]

1.4. "BULK DRUG SUBSTANCE" shall mean a Drug Product Candidate in bulk crystal, powder or other form suitable for incorporation in a Drug Product.

1.5. "CONTROLLED" shall mean the legal authority or right of a party hereto to grant a license or sublicense of intellectual property rights to another party hereto, or to otherwise disclose proprietary or trade secret information to such other party, without breaching the terms of any agreement with a Third Party, infringing upon the intellectual property rights of a Third Party, or misappropriating the proprietary or trade secret information of a Third Party.

1.6. [This section has been intentionally left blank.]

1.7. (a) "DEVELOPMENT CANDIDATE" shall have the meaning ascribed to it in the Research Agreement.

(b) "DEVELOPMENT ELECTION FEE" and "BACK-UP ELECTION FEE" shall each have the meaning ascribed to it in Section 6.1 hereof.

1.8. "DEVELOPMENT PLAN" shall have the meaning ascribed to it in Section 3.2.2 hereof.

1.9. "DEVELOPMENT PROGRAM" shall mean activities associated with development of a Drug Product Candidate which are conducted by or at the direction of NOVARTIS after the Development Election has been exercised with respect to that Drug Product Candidate, including but not limited to (a) manufacture and formulation of Drug Product Candidates for use in pre-clinical, non-clinical and clinical studies; (b) pre-clinical and non-clinical animal studies

performed in accordance with GLP (or the applicable equivalent); (c)planning, implementation, evaluation and administration of human clinical trials; (d) manufacturing process development, scale-up and commercial manufacture of Drug Product; (e) preparation and submission of applications for Regulatory Approval; and (f) post-market surveillance of approved drug indications, as required or agreed as part of a marketing approval by any governmental regulatory authority.

1.10. [This Section has been intentionally left blank.]

1.11. "Drug Product" shall mean a finished dosage form which is prepared from Bulk Drug Substance and is ready for administration to the ultimate consumer as a pharmaceutical.

1.12. "DRUG PRODUCT CANDIDATE" shall mean any Development Candidate or Drug Product Candidate Back-up Candidate listed from time to time on Schedule 1.12 hereof, as to which NOVARTIS has exercised the Development Election under the Research Agreement and which has become a subject of this License Agreement in accordance with the provisions thereof; and "Drug Product Candidate Back-up Candidate" shall have the meaning set forth in Section 7.4 of this Agreement.

1.13. "EFFECTIVE DATE" shall mean the effective date of this Agreement as set forth on the first page hereof.

1.14. [This section has been intentionally left blank.]

1.15. "FIELD" shall mean the treatment or prevention of conditions or diseases in humans, principally by affecting a Kinase other than an Excluded Kinase.

1.16. "FIRST COMMERCIAL SALE" shall mean the first sale of a Drug Product by NOVARTIS or an Affiliate or sublicensee of NOVARTIS in a country in the Territory following Regulatory Approval of the Drug Product in that country or, if no such Regulatory Approval or similar marketing approval is required, the date upon which the Drug Product is first commercially launched in such country.

1.17. "FILING OUTSIDE THE U.S." shall mean any application or regulatory filing to be made hereunder with a regulatory authority outside the United States, for approval to manufacture and sell Drug Product(s) outside the U.S., and any correspondence, approvals or governmental licenses relating thereto.

1.18. [This section has been intentionally left blank.]

1.19. "GMP" shall mean the current Good Manufacturing Practice regulations promulgated by the FDA, published at 21 CFR Part 210 et seq., as such regulations may from time to time be amended, and such equivalent regulations or standards of countries outside the United States as may be applicable to activities conducted hereunder; and "GLP" shall mean the current Good Laboratory Practices regulations promulgated by the FDA, published at 21 CFR Part 58, as such regulations may be from time to time amended, and such equivalent regulations or standards of countries outside the United States as may be applicable to activities conducted hereunder.

1.20. "INDICATION" shall mean a recognized disease or condition, an important manifestation of a disease or condition, or symptom associated with a disease or syndrome for which use of a Drug Product is indicated, as would be identified in the Drug Product's label under applicable FDA regulations or the foreign equivalent thereof.

1.21. "IND" shall mean the investigational new drug application relating to a Drug Product Candidate filed with the FDA pursuant to 21 CFR Part 312, including any amendments thereto. References herein to IND shall include, to the extent applicable, any comparable Filing(s) Outside the U.S. (such as a CTX in the European Union).

1.22. "INTERNATIONAL PROJECT TEAM" or "IPT" shall have the meaning set forth in Section 3.2.1 hereof.

1.23. "JOINT STEERING COMMITTEE" or "JSC" shall have the meaning set forth in Section 2.6 of the Research Agreement.

1.24. "KNOW-HOW" means all proprietary material and information including data, technical information, know-how, experience, inventions, discoveries, trade secrets, compositions of matter and methods, whether currently existing or developed or obtained during the course of this Agreement and whether or not patentable or confidential, that are now Controlled by a Party or its Affiliates and that relate to the development, utilization, manufacture or use of any Drug Product Candidate or Drug Product, including but not limited to processes, techniques, methods, products, materials and compositions; provided however, that for the purposes of the definition of VERTEX Know-How only, the term "Know-How" shall not include VERTEX's general drug design technology, whether in software or hardware, tangible or intangible, form; and "Lead Period" shall mean the period starting on date this Agreement is effective with respect to a particular Drug Product Candidate and ending on the second anniversary thereafter.

1.25. "MAJOR MARKETS" shall mean those countries listed on Schedule 1.25 hereto.

1.26. "MANUFACTURING COST" shall mean [***].

1.27. "NET SALES" with respect to any Drug Product shall mean the gross amount invoiced by NOVARTIS and any NOVARTIS Affiliate, licensee or sublicensee for that Drug Product sold to Third Parties in bona fide, arms-length transactions, less [***]; all as determined in accordance with NOVARTIS' usual and customary accounting methods, which are in accordance with generally accepted accounting principles (GAAP).

1.27.1. In the case of any sale or other disposal of a Drug Product between or among NOVARTIS and its Affiliates, licensees and sublicensees, for resale, Net Sales shall be calculated as above only on the value charged or invoiced on the first arm's-length sale thereafter to a Third Party;

1.27.2. In the case of any sale which is not invoiced or is delivered before invoice, Net Sales shall be calculated at the time of shipment or when the Drug Product is paid for, if paid for before shipment or invoice;

1.27.3. In the case of any sale or other disposal for value, such as barter or counter-trade, of any Drug Product, or part thereof, other than in an arm's length transaction

exclusively for money, Net Sales shall be calculated as above on the value of the consideration received or the fair market price (if higher) of the Drug Product in the country of sale or disposal;

1.27.4. In the event the Drug Product is sold in a finished dosage form containing the Drug Product in combination with one or more other active ingredients (a "Combination Product"), the Net Sales of the Drug Product, for the purposes of determining royalty payments, shall be determined by [***].

1.28. "NOVARTIS KNOW-HOW" shall mean all Know-How of NOVARTIS.

1.29. "NOVARTIS PATENTS" shall mean any Patents Controlled by NOVARTIS or any of its Affiliates claiming Bulk Drug Substance, a Drug Product Candidate or a Drug Product, or a formulation or prodrug thereof, discovered or identified by NOVARTIS or its Affiliates during the course of the Research Program or a Development Program, or a method of making or using Bulk Drug Substance, a Drug Product Candidate or a Drug Product, or a prodrug thereof, or an improvement to the subject matter of a Patent covering any of the foregoing. A list of NOVARTIS Patents is appended hereto as Schedule 1.29 and will be updated periodically to reflect additions thereto during the term of this Agreement. NOVARTIS shall keep VERTEX periodically informed in writing of all NOVARTIS Patents.

1.30. "NOVARTIS TECHNOLOGY" shall mean all NOVARTIS Patents and all NOVARTIS Know-How which is applied by NOVARTIS to the development, manufacture or use of Bulk Drug Substance, a Drug Product Candidate or a Drug Product.

1.31. "PATENTS" means all existing patents and patent applications and all patent applications hereafter filed, including any continuation, continuation-in-part, division, provisional or any substitute applications, any patent issued with respect to any such patent applications, any reissue, reexamination, renewal or extension (including any supplementary protection certificate) of any such patent, and any confirmation patent or registration patent or patent of addition based on any such patent, and all foreign counterparts of any of the foregoing.

1.32. "PERSON" shall mean any individual, corporation, partnership, association. joint-stock company, trust, unincorporated organization or government or political subdivision thereof.

1.33. "PIVOTAL REGISTRATION STUDY" shall mean a human clinical trial conducted for inclusion in (i) that portion of the FDA submission and approval process which provides for the continued trials of a Drug Candidate on sufficient numbers of patients to generate safety and efficacy data to support Regulatory Approval in the proposed therapeutic indication, as more fully defined in 21 CFR. Section 312.21(c), and (ii) equivalent submissions with similar requirements in other countries.

1.34. "REGULATORY APPROVAL" shall mean, with respect to any country, all authorizations by the appropriate governmental entity or entities necessary for commercial sale of a Drug Product in that country including, without limitation and where applicable, approval of labeling, price, reimbursement and manufacturing. "Regulatory Approval" in the United States shall mean final approval of a new drug application pursuant to 21 CFR Section 314, permitting marketing of the applicable Drug Product in interstate commerce in the United States. "Regulatory Approval" in the European Union shall mean final approval of a Marketing

Authorization Application pursuant to Council Directive 75/319/EEC, as amended, or Council Regulation 2309/93/EEC, as amended.

1.35. "RESEARCH AGREEMENT" shall mean that certain First Revised and Restated Research and Early Development Agreement between VERTEX and NOVARTIS dated February 3, 2004.

1.36. [This section has been intentionally left blank.]

1.37. [This section has been intentionally left blank.] =

1.38. "Technology" shall mean VERTEX Technology and NOVARTIS Technology.

1.39. "Territory" shall mean all the countries in the world.

1.40. "Third Party" shall mean any person or entity which is not a party or an Affiliate of any party to this Agreement.

1.41. [This section has been intentionally left blank.]

1.42. "VALID PATENT CLAIM" shall mean either (a) a claim of an issued and unexpired Patent which has not been revoked or held permanently unenforceable or invalid by a decision of a court or other governmental agency of competent jurisdiction, unappealable or unappealed within the time allowed for appeal, and which has not been admitted to be invalid or unenforceable through reissue or disclaimer or otherwise, or (b) a claim of a pending patent application which claim was filed in good faith and has not been abandoned or finally disallowed without the possibility of appeal or refiling of said application.

1.43. "VERTEX KNOW-HOW" shall mean all Know-How of VERTEX.

1.44. "VERTEX PATENTS" shall mean any Patents Controlled by VERTEX or any of its Affiliates claiming Bulk Drug Substance, a Drug Product Candidate or a Drug Product, or a formulation or prodrug thereof, discovered or identified by VERTEX or its Affiliates during the course of the Research Program and the Development Program, or a method of making or using Bulk Drug Substance, a Drug Product Candidate or a Drug Product, or a prodrug thereof, or an improvement to the subject matter of a Patent covering any of the foregoing. A list of VERTEX Patents is appended hereto as Schedule 1.44 and will be updated periodically to reflect additions thereto during the term of this Agreement.

1.45. "VERTEX TECHNOLOGY" shall mean all VERTEX Patents and all VERTEX Know-How.

1.46. The term "European Union" shall mean those countries which are now or later become members of the European Union.

Capitalized terms used but not otherwise defined herein which are defined in the Research Agreement shall have the meaning ascribed to them therein.

ARTICLE II
LICENSE

2.1. GRANT TO NOVARTIS.

(a) Subject to the other provisions of this Agreement, VERTEX hereby grants to NOVARTIS an exclusive worldwide license under VERTEX Technology to the extent useful to permit NOVARTIS to carry out its rights and obligations set forth in this Agreement and to develop, manufacture, have manufactured, market, use, sell and import for sale, as provided herein, Bulk Drug Substance, Drug Product Candidates and Drug Products worldwide. NOVARTIS shall have the right to sublicense under this Agreement. Subject to the provisions of this Agreement, VERTEX shall have the right to use VERTEX Technology to discharge its obligations and exercise its rights under this Agreement. VERTEX retains all rights to VERTEX Technology except to the extent explicitly granted to NOVARTIS hereunder.

(b) NOVARTIS may subcontract its rights to manufacture Bulk Drug Substance, Drug Product Candidates, and Drug Product and may contract with reputable organizations to conduct or assist in the conduct of human clinical trials and the evaluation of trials data, after prior notice to, but without the consent of, VERTEX. NOVARTIS shall be responsible to VERTEX for the performance of any of its sublicensees or subcontractors under any provisions of this Agreement for which NOVARTIS is responsible. NOVARTIS shall not permit any subcontractors or sublicensees to use VERTEX Technology without provisions safeguarding confidentiality at least equivalent to those provided in this Agreement. Any such provisions will allow VERTEX the right to directly enforce the obligations of confidentiality with respect to VERTEX Technology in possession of the Third Party.

(c) [***]

2.2. GRANT TO VERTEX. Subject to the other provisions of this Agreement, NOVARTIS hereby grants to VERTEX a non-exclusive, worldwide license or (as appropriate) sublicense under NOVARTIS Technology, only to the extent necessary to permit VERTEX to carry out the activities which it is permitted to undertake in this Agreement. VERTEX shall not sublicense such license to the NOVARTIS Technology without the consent of NOVARTIS (which shall not be unreasonably withheld). Any permitted sublicense will contain provisions safeguarding confidentiality at least equivalent to those provided in this Agreement, which will allow NOVARTIS the right to directly enforce the obligations of confidentiality with respect to NOVARTIS Technology in possession of the Third Party. NOVARTIS retains all rights to NOVARTIS Technology except to the extent explicitly granted to VERTEX hereunder.

2.3. Information Transfer.
(a) [***]

(b) [***]

(c) [***]

ARTICLE III
DEVELOPMENT

3.1. COMMENCEMENT OF DEVELOPMENT PROGRAM. NOVARTIS shall promptly and diligently commence and pursue a Development Program with respect to each Drug Product Candidate as soon as practicable after exercise by NOVARTIS of its Development Election with respect to that Drug Product Candidate.

3.2. INTERNATIONAL PROJECT TEAM.

3.2.1. FORMATION AND RESPONSIBILITIES. As soon as practicable after the exercise by NOVARTIS of its Development Election with respect to a Drug Product Candidate, NOVARTIS will establish an International Project Team ("IPT") which shall include one representative designated by VERTEX from time to time; provided, however, an IPT shall no longer include a representative designated by VERTEX in case of a Change of Control of VERTEX. Additional IPT's, which shall also include one VERTEX representative, may be established from time to time in connection with the development of additional Drug Product Candidates. The IPT (or its successor organization, as designated by NOVARTIS) will be the principal organization through which the development of a Drug Product Candidate is planned, administered, evaluated and completed, subject to appropriate review and approval at senior management levels as required by NOVARTIS from time to time. In addition to the VERTEX member, the IPT will typically have members from the various functional groups (e.g., research, preclinical safety, clinical, regulatory, marketing) which are or will be expected to be involved in development and launch of the Drug Product Candidate and Drug Product. NOVARTIS will appoint the IPT Chair. The IPT will typically meet every four to six weeks, depending on the level of current development activity, and will be responsible for preparation and implementation of the Development Plan described in Section 3.2.2 below with respect to each Drug Product Candidate.

3.2.2. DEVELOPMENT PLAN. The IPT shall prepare and oversee the implementation of the overall Development Plan for each Drug Product Candidate. The Development Plan shall, among other things, detail, schedule and fully describe the proposed toxicology studies, clinical trials, regulatory plans, clinical trial and commercial material requirements, and process development and manufacturing plans for each Drug Product Candidate, along with relevant budget information for the described items, and will outline the key elements involved in obtaining Regulatory Approval in each country where the Drug Product is to be marketed. The parties expect that development tasks will be advanced in parallel rather than serially where practicable and appropriate, if doing so would be likely to advance the ultimate date of Regulatory Approval and launch and is otherwise commercially reasonable.

3.2.3. MEETING MATERIALS. The IPT will consider all information that is material to an assessment of the status, direction and progress of the Development Program, including all clinical trials protocols, data and reports. The IPT Leader will ensure that full and complete minutes are prepared and distributed to each member of the IPT promptly after each meeting. Those minutes shall contain a full report on the activities of the IPT during its meeting. VERTEX's representative on the IPT will receive all documents and information distributed or communicated to members of the IPT generally, and may review copies of all other information relative to the development of a Drug Product Candidate unless the IPT Leader denies access to that information for good reason.

3.2.4. [This section has been intentionally left blank.]

3.3. DEVELOPMENT RESPONSIBILITY AND COSTS. Except as provided in Section 3.5 below, NOVARTIS will have sole responsibility for, and bear the cost of conducting, the Development Program with respect to each Drug Product Candidate.

3.4. REGULATORY APPROVALS. NOVARTIS shall be solely responsible for preparing and submitting registration dossiers for Regulatory Approval of Drug Product Candidates in the Territory.

3.4.1. NOVARTIS OWNERSHIP. All Regulatory Approvals shall be held by and in the name of NOVARTIS, and NOVARTIS shall own all submissions in connection therewith, provided that VERTEX shall have a right of reference to all or any part of the submissions if the "Assistance Rights" become effective under Section 3.5 hereof.

3.4.2. PRINCIPAL INTERFACE. All formulary or marketing approvals shall also be obtained by and in the name of NOVARTIS, and NOVARTIS will be the principal interface with and will otherwise handle all interactions with regulatory agencies concerning any Drug Product including, to the extent legally possible, being the sole contact with such agencies, subject to the rights of VERTEX under Section 3.4.3.

3.4.3. REGULATORY MEETINGS. To the extent not prohibited by law or regulation, VERTEX shall have the right, after consultation with NOVARTIS and unless VERTEX's presence would impede the regulatory approval process, to have one representative participate in all material meetings between representatives of NOVARTIS and any of the FDA, the EMEA and Koseisho (MHW Japan).

(a) NOVARTIS will undertake to provide VERTEX with information reasonably in advance of the meeting sufficient to ensure that the VERTEX representative is adequately informed about the issues to be presented at any such meeting.

(b) VERTEX may request NOVARTIS to provide VERTEX with a copy of any correspondence between the FDA, the EMEA and Koseisho that relates to any material issues involving Regulatory Approval of a Drug Product Candidate, and NOVARTIS shall provide that information upon request, unless NOVARTIS has good reason to withhold any such correspondence, in which case it will notify VERTEX of that reason promptly.

(c) Notwithstanding the foregoing, NOVARTIS will have sole discretion as to the regulatory strategy and decision-making for any Drug Product Candidate or Drug Product.

3.5. Assistance Rights. [***]

3.5.1. [***]

3.5.2. If VERTEX pursues its Assistance Rights:

(a) REGULATORY ACTIONS. NOVARTIS will continue to make any necessary and appropriate regulatory filings with respect to the Development Work and will, if required for VERTEX to exercise its Assistance Rights effectively, transfer to VERTEX at VERTEX's expense any IND material (or equivalents thereof) relevant to such Development Work.

(b) MANUFACTURE OF CLINICAL SUPPLY OF DRUG PRODUCT CANDIDATE. NOVARTIS will supply VERTEX (for up to two years) with the necessary clinical supply of Drug Product Candidate required to perform such Development Work in accordance with NOVARTIS' then current scale of manufacturing at NOVARTIS' Manufacturing Cost and upon such other reasonable and customary terms as to shipment, delivery and similar matters as may be agreed.

(c) MILESTONES. If NOVARTIS elects to resume the Development Program for a Drug Product Candidate, it will provide VERTEX with ninety (90) days prior notice thereof, and will reimburse VERTEX for the actual direct cost of the Development Work of good quality, if such work conforms with the requirements of the relevant Development Plan. NOVARTIS will pay VERTEX interest on the reimbursable costs incurred by VERTEX in the conduct of the Development Work, at a rate compounded quarterly equal to the thirty-day London InterBank Offered Rate ("LIBOR") for the local currency in which payment is made, as quoted in THE FINANCIAL TIMES as determined on the date the Development Work is first undertaken by VERTEX and on the last Business Day of each calendar quarter thereafter.

3.6. REASONABLE EFFORTS IN DEVELOPMENT. NOVARTIS will use diligent, commercially reasonable efforts consistent with those used by NOVARTIS for its own compounds of similar commercial potential to develop Drug Product Candidates into Drug Products. NOVARTIS will promptly notify VERTEX in writing if it should determine that development of any Drug Product Candidate or Drug Product is not technically feasible or commercially justifiable, specifying in reasonable detail the reasons for that determination.

ARTICLE IV
MANUFACTURING AND SUPPLY

4.1. Supply of Bulk Drug Substance and Drug Product. NOVARTIS will be responsible for manufacturing and supply of all Bulk Drug Substance, Drug Product Candidates and Drug Product as necessary for the conduct of the Development Plan and for all commercial purposes in the Territory. Pursuant to the provisions of Section 4.7 of the Research Agreement, the parties will agree on reasonable and appropriate measures by which manufacturing previously being undertaken by VERTEX shall be transitioned to NOVARTIS following the exercise of its Development Election with respect to a particular Drug Product Candidate. The objective of both parties will be to accomplish a smooth and timely transition. Any Bulk Drug

Substance provided to NOVARTIS during the transition period will be supplied at VERTEX's reasonable Manufacturing Cost.

4.2. [This section has been intentionally left blank.]

4.3. FORMULATION AND PACKAGING. In all events, NOVARTIS will be responsible for formulation and packaging of Drug Products.

ARTICLE V
COMMERCIALIZATION

5.1. MARKETING AND PROMOTION. NOVARTIS shall have exclusive rights to market, sell and distribute all Drug Products in the Territory. NOVARTIS will book all sales of Drug Products and will report those sales to VERTEX as specified in Section 6.5 of this Agreement.

5.2. GLOBAL BRAND TEAM. Not later than six months prior to the commencement of Phase III Clinical Trials for any Drug Product Candidate, NOVARTIS will form a Global Brand Team ("GBT"), which will include one representative designated by VERTEX; provided, however, [***]. Additional GBT's, which shall also include one VERTEX representative, may be established from time to time in connection with the marketing of additional Drug Product Candidates. The GBT (or its successor organization, as designated by NOVARTIS) will be the principal organization through which the marketing of a Drug Product is planned, administered, evaluated and effected, subject to appropriate review at senior management levels as required by NOVARTIS. NOVARTIS will appoint the chair of the GBT, who will normally be the Brand Director. The GBT will periodically meet as necessary, depending on the level of marketing activity at the time.

5.2.1. MARKETING PLANS. The Global Brand Team will prepare and oversee the implementation of a detailed marketing plan (a "Marketing Plan") for the launch of each Drug Product, addressing the overall branding and branding elements as well as the key promotional product claims. The GBT will select an external agency or agencies which will be charged with the execution of some components of the Marketing Plan. The Marketing Plan will contain among other things budgets, schedules, product positioning, pricing, market research plans and results and other customary planning and marketing material with respect to marketing and launch of the Drug Product. The Marketing Plan will be periodically updated to reflect changes in market information, sales performance and forecasts, sales force deployment, communication plans and information concerning competition and competitors.

5.2.2. LOCAL PRODUCT TEAMS. Local Product Teams will be established in each country to prepare and execute the product launch for a Drug Product within the framework of the Marketing Plan. .

5.2.3. CAMPAIGNS AND PROMOTIONAL MATERIALS. The GBT will review all general product campaigns (including target audience and principal messages) and may from time to time review the principal promotional material to be used in connection with the marketing and sale of a Drug Product.

5.2.4. [This section has been intentionally left blank.]

5.3. [This section has been intentionally left blank.]

5.4. [This section has been intentionally left blank.]

5.5. CO-LABELING. To the extent not prohibited by law or regulation and subject to any required Regulatory Approval, Drug Products (including labels, packaging and inserts) and all promotional materials for the same, sold in North America, the countries of the European Union and Japan will bear both NOVARTIS' and VERTEX's company names and logos with equal prominence (including equal sized type face), or if equal prominence is prohibited by law, with such prominence as may otherwise be permitted by law. To the extent not prohibited by law or regulation and subject to any required Regulatory Approval, Drug Products (including labels, packaging and inserts) and all promotional materials for the same, sold in the rest of the world will include VERTEX's company name (in the English alphabet) and logo with the designation: "under license from"; provided, however, that this provision shall no longer apply in case of a Change of Control of VERTEX. Any trademark for a Drug Product will be selected by, and will be the property of, NOVARTIS.

5.5.1. REVIEW OF REGULATORY FILINGS. NOVARTIS will permit VERTEX to review all material regulatory filings which relate to product labeling, and all proposed labels, packaging, package inserts, and promotional materials required under the Agreement to bear VERTEX's name, if permitted by law, prior to the filing of any such materials with any regulatory authority; provided, however, that this provision shall no longer apply in case of a Change of Control of VERTEX.

5.5.2. REGULATORY COMMUNICATIONS.

(a) NOVARTIS will permit VERTEX to participate with NOVARTIS in material communications with regulatory officials which concern the matters referenced in this Section 5.5; provided, however, [***].

(b) NOVARTIS will immediately inform VERTEX of any material regulatory communications received by NOVARTIS which might operate to restrict VERTEX's rights under this Section 5.5.2, and will cooperate with any reasonable request of VERTEX aimed at facilitating approval by a regulatory authority for co-labeling consistent with this provision.

5.6. DUE DILIGENCE. NOVARTIS shall use diligent and commercially reasonable efforts consistent with the requirements of the Development Program and sound and reasonable business practices and judgment to effect introduction of Drug Products into Major Markets as soon as reasonably practicable, devoting the same degree of attention and diligence to such efforts that it devotes to such activities for other of its products of comparable market potential. Following the First Commercial Sale of a Drug Product and until the expiration of this Agreement, NOVARTIS shall endeavor to keep Drug Products reasonably available to the public in each of the Major Markets. NOVARTIS shall promptly notify VERTEX if it shall determine that the marketing and sale of a Drug Product in any country is not commercially reasonable or economically profitable or if for other unforeseen reasons further commercial support of the Drug Product in certain territories is no longer prudent or practical. In determining whether NOVARTIS is in compliance with the foregoing provisions, there shall be taken into account the

normal course of assertive drug development programs in the pharmaceutical industry conducted with sound and reasonable business practices and judgment.

ARTICLE VI
PAYMENTS

6.1. DEVELOPMENT ELECTION PAYMENT. NOVARTIS will pay to VERTEX a milestone payment in the amount of [***] (a "Development Election Fee") each time NOVARTIS exercises its Development Election with respect to a Development Candidate. Each time NOVARTIS exercises its Development Election under Section 4.1 of the Research Agreement with respect to a Compound which is a Back-up Compound to a Drug Product Candidate, NOVARTIS will pay to VERTEX a milestone payment in the amount of [***] (the "Back-up Election Fee"); [***]

6.2. Development Milestone Payments by NOVARTIS.

6.2.1. NOVARTIS will make the following payments to VERTEX upon the achievement of any of the following milestones with respect to a Drug Product Candidate:

[***]	[***]
[***]	[***]
[***]	[***]
[***]	[***]
[***]	[***]
[***]	[***]
[***]	[***]

6.2.2. [This section has been intentionally left blank.]

6.2.3. All payments shall be made by wire transfer in United States dollars ("Dollars") to the credit of such bank account as may be designated by VERTEX in writing to NOVARTIS. Any payment which falls due on a date which is a Saturday, Sunday or a legal holiday in the Commonwealth of Massachusetts may be made on the next succeeding day which is not a Saturday, Sunday or a legal holiday in the Commonwealth.

6.2.4. If a Drug Product Candidate is abandoned during the term of this Agreement for any scientific or medical reasons after any one or more of the foregoing milestone payments are made, and if a Back-up Compound to that Drug Product Candidate is developed to replace the abandoned Drug Product Candidate for the same Indications, then no milestone

payment shall be required with respect to the Back-up Compound to the extent that that milestone payment has already been made with respect to the abandoned Drug Product Candidate.

6.3. ROYALTIES. NOVARTIS shall pay to VERTEX the following annual royalties on Net Sales of each Drug Product in the Territory. [***]

6.3.1. Third Party Royalties: If NOVARTIS is required to pay royalties to any Third Party in order to exercise its rights to sell a Drug Product in a country, then
[***]payable to such Third Party in any calendar quarter for such Drug Product in such country shall be deductible from the royalties payable to VERTEX under this Agreement in respect of sales of that Drug Product in such country for the same calendar quarter, provided that in no event shall the net royalty rate payable fall below [***], as a result of the application of this Sections 6.3.1 and 6.3.2.

6.3.2. Unlicensed Competition: If in any country a Third Party sells a pharmaceutical product which is a "generic version" of a Drug Product being sold in that country (a "Third Party Product") -- where "generic version" means a pharmaceutical product (other than a product originally sold as a Drug Product) that includes the same active ingredient as that used in a Drug Product -- then for the period in which the sales of such Third Party Product in such country are at least [***], the royalties payable to VERTEX by NOVARTIS on sales of such Product in such country for such period shall be [***] in Section 6.3 , but in no event shall the royalties owed for such Drug Product in such country, when combined with any royalty reduction provided under Section 6.3.1 hereof, reduce the royalties payable on Net Sales of such Drug Product in that country by more than [***]

6.4. [This section has been intentionally left blank.]

6.5. SALES REPORTS.
(a) During the term of this Agreement and after the First Commercial Sale of a Drug Product, NOVARTIS shall furnish or cause to be furnished to VERTEX on a quarterly basis a written report or reports covering each calendar quarter (each such calendar quarter being sometimes referred to herein as a "reporting period") showing (i) the Net Sales of each Drug Product in each country in the world during the reporting period by NOVARTIS and each Affiliate and sublicensee; (ii) the royalties, payable in Dollars, which shall have accrued under Section 6.3 hereof in respect of such sales and the basis of calculating those royalties; (iii) withholding taxes, if any, required by law to be deducted in respect of any such sales; (iv) the exchange rates used in converting into Dollars, from the currencies in which sales were made, any payments due which are based on Net Sales; and (v) dispositions of Drug Products other than pursuant to sale for cash. With respect to sales of Drug Products invoiced in Dollars, the Net Sales amounts and the amounts due to VERTEX hereunder shall be expressed in Dollars. With respect to sales of Drug Products invoiced in a currency other than Dollars, the Net Sales

and amounts due to VERTEX hereunder shall be expressed in the domestic currency of the party making the sale, together with the Dollar equivalent of the amount payable to VERTEX, calculated using NOVARTIS' then-current standard exchange rate methodology for the translation of foreign currency sales into U.S. dollars. In each report the methodology will be disclosed, will be identical to that employed by NOVARTIS, generally, in its external financial reporting, as reviewed and approved by its independent auditors and will be in conformity with NOVARTIS' usual and customary general accounting principles consistently applied. If any sublicensee makes any sales invoiced in a currency other than its domestic currency, the Net Sales shall be converted to its domestic currency in accordance with the sublicensee's normal accounting principles. NOVARTIS shall furnish to VERTEX appropriate evidence of payment of any tax or other amount required by applicable laws or regulations to be deducted from any royalty payment, including any tax or withholding levied by a foreign taxing authority in respect of the payment or accrual of any royalty. Reports shall be due on the thirtieth (30th) day following the close of each reporting period, although NOVARTIS shall also provide VERTEX with a "flash" report of Net Sales, only, within ten (10) business days after the end of each month. NOVARTIS shall keep accurate records in sufficient detail to enable the amounts due hereunder to be determined and to be verified by VERTEX.

(b) Amounts shown to have accrued by each sales report provided for under subsection 6.5(a), above, shall be due and payable on the date such sales report is due.

(c) All payments shall be made in Dollars. If at any time legal restrictions prevent the prompt remittance of any payments with respect to any country of the Territory where Drug Products are sold, NOVARTIS or its sublicensees shall have the right and option to make such payments by depositing the amount thereof in local currency to VERTEX's account in a bank or depository in such country.

(d) Upon the written request of VERTEX, at VERTEX's expense and not more than once in or in respect of any calendar year, NOVARTIS shall permit an independent accountant of national prominence selected by VERTEX, to have access during normal business hours to those records of NOVARTIS as may be reasonably necessary to verify the accuracy of the sales reports furnished by NOVARTIS pursuant to this Section 6.5, in respect of any calendar year ending not more than thirty-six (36) months prior to the date of such notice. NOVARTIS shall include in each sublicense entered into by it pursuant to this Agreement a provision requiring the sublicensee to keep and maintain adequate records of sales made pursuant to such sublicense and to grant access to such records by the aforementioned independent accountant for the reasons specified in this
Section 6.5. Upon the expiration of thirty-six (36) months following the end of any calendar year, the calculation of amounts payable with respect to such fiscal year shall be binding and conclusive upon VERTEX, and NOVARTIS and its sublicensees shall be released from any liability or accountability with respect to payments for such year. The report prepared by such independent accountant, a copy of which shall be sent or otherwise provided to NOVARTIS by such independent accountant at the same time it is sent or otherwise provided to VERTEX, shall contain the conclusions of such independent accountant regarding the audit and will specify that the amounts paid to VERTEX pursuant thereto were correct or, if incorrect, the amount of any underpayment or overpayment. If such independent accountant's report shows any underpayment, NOVARTIS shall remit or shall cause its sublicensees to remit to VERTEX within thirty (30) days after NOVARTIS' receipt of such report, (i) the amount of such underpayment and (ii) if such underpayment exceeds [***] owed for the calendar year then being

audited, the reasonable and necessary fees and expenses of such independent accountant performing the audit, subject to reasonable substantiation thereof. Any overpayments shall be fully creditable against amounts payable in subsequent payment periods. VERTEX agrees that all information subject to review under this
Section 6.5 or under any sublicense agreement is confidential and that VERTEX shall retain and cause its accountant to retain all such information in confidence.

(e) In case of any delay in payment by NOVARTIS to VERTEX not occasioned by Force Majeure, interest at the rate of [***], assessed from the thirty-first day after the due date of the payment, shall be due from NOVARTIS upon prior written notice.

6.6. WITHHOLDING TAX. If during the term of this Agreement, withholding tax should be required by law to be deducted from any payments required to be made by NOVARTIS to VERTEX hereunder, the parties will agree upon an equitable division of liability for any sum which is withheld and for which VERTEX is not compensated or reimbursed by way of usable tax credits or otherwise. In that connection VERTEX at NOVARTIS' request shall sign a usual and customary exemption application and in addition shall apply for a tax refund at the request of NOVARTIS from any tax authority to which NOVARTIS has paid withholding tax on account of any payments made by NOVARTIS to VERTEX hereunder.

ARTICLE VII
BACK-UP COMPOUNDS

Notwithstanding the provisions under the Research Agreement with respect to Back-up Compounds and for the sake of clarity, it is reminded that the parties agreed the following with respect to Back-up Compounds in
Section 4.5 of the Research Agreement.

7.1 VERTEX RESTRICTIONS ON NOMINATION AND DEVELOPMENT. So long as NOVARTIS is using commercially reasonable efforts with respect to the development of a particular Drug Product Candidate or the commercialization of a particular Drug Product, pursuant to Sections 3.6 and 5.6 hereof, VERTEX will not (i) propose a Compound for development under the License Agreement which is a Back-up Compound with respect to that Drug Product Candidate or Drug Product, or (ii) until after the period starting on the date on which NOVARTIS has exercised its Development Election for a particular Drug Product Candidate and ending [***] (the "Lead Period"), commence development of that Back-up Compound either directly or together with or through an Affiliate or a Third Party.

7.2 TERMINATION OF DEVELOPMENT OR COMMERCIALIZATION. If, prior to the end of the Lead Period with respect to a particular Drug Product or Drug Product Candidate, pursuant to Sections 3.6 and 5.6 hereof, NOVARTIS ceases to use commercially reasonable efforts to develop or commercialize that Drug Product Candidate or Drug Product, then the restrictions on nomination and development referenced in Section 7.1 above will no longer apply with respect to Back-up Compounds for that Drug Product Candidate or Drug Product unless NOVARTIS, without delay, commences another Development Program under the License Agreement with another Compound (a "Replacement Candidate") targeting the same Kinase, which Replacement Candidate is a Back-up Compound

associated with the discontinued Drug Product Candidate or Drug Product, and NOVARTIS shall have the right to select for this purpose any such Back-up Compound by providing VERTEX with notice of its Development Election in this regard. Any such Back-up Compound for which NOVARTIS has exercised its Development Election under this Section 7.2 shall hereafter be a Drug Product Candidate subject to the terms and conditions of this Agreement.

7.3. TERMINATION OF RIGHTS TO BACK-UP COMPOUNDS. A Back-up Compound will no longer be subject to NOVARTIS' Development Election under the Research Agreement after the end of the Lead Period applicable to that Back-up Compound, except for Back-up Compounds which (i) subject to Section 7.1 above, VERTEX has proposed for development on or before the Final Termination Date, and as to which NOVARTIS has exercised its Development Election hereunder; or (ii) have been or will be selected by NOVARTIS for development before the end of the applicable Lead Period under the provisions of Section 7.2 above, or (iii) for which NOVARTIS has exercised or will exercise its Development Election before the end of the applicable Lead Period under the provisions of Section 7.4 below.

7.4 NOVARTIS RIGHTS TO LICENSE BACK-UP COMPOUNDS. Anytime prior to the expiry of the Lead Period with respect a particular Drug Product Candidate, NOVARTIS may also, by paying in each case the Back-up Election Fee provided under Section 6.1 of the this Agreement, exercise its Development Election with respect to any one or more Back-up Compounds associated with that Drug Product Candidate, provided that Drug Product Candidate, or a Back-up Compound selected pursuant to the provisions of Section 7.2 above, is still in active development. Any such Back-up Compound for which NOVARTIS has exercised its Development Election under Section 7.4 shall become a "Drug Product Candidate Back-up Candidate" subject to the terms and conditions of this Agreement.

7.5 NOVARTIS OBLIGATIONS WITH RESPECT TO DRUG PRODUCT CANDIDATE BACK-UP CANDIDATES. So long as NOVARTIS is using commercially reasonable efforts, pursuant to the provisions of Sections 3.6 and 5.6 of this Agreement, with respect to the development of a particular Drug Product Candidate or the commercialization of a particular Drug Product, NOVARTIS shall have no obligation to develop any of the Drug Product Candidate Back-up Candidates associated with that Drug Product Candidate or Drug Product. As soon as NOVARTIS ceases the development of a particular Drug Product Candidate, NOVARTIS' obligations to use diligent, commercially reasonable efforts will immediately shift from the discontinued Drug Product Candidate to an associated Drug Product Candidate Back-up Compound. If NOVARTIS ceases the development of a particular Drug Product Candidate and does not commence development of a Drug Product Candidate Back-up Compound pursuant to the foregoing, the license to the Drug Product Candidate and its Back-up Compounds under this Agreement will expire and the license rights will revert to VERTEX.

ARTICLE VIII
INTELLECTUAL PROPERTY

8.1. PATENTABLE INVENTIONS AND KNOW-HOW.

8.1.1. Ownership. Any inventions made and all Know-How generated by either party or its Affiliates during the term of this Agreement, and Controlled by such party, relating to the manufacture or use of Bulk Drug Substance, a Drug Product Candidate or a Drug Product, or a prodrug thereof, will be disclosed to the other party promptly after the disclosing party recognizes the significance thereof. All patents and technology shall be owned by the party making the invention claimed or contained therein or, if such invention is made jointly, shall be owned jointly, all as determined in accordance with U.S. laws of inventorship.

8.1.2. Patent Prosecution. VERTEX shall be responsible for the preparation, filing, prosecution and maintenance of all patents and patent applications included in VERTEX Patents and all patents and patent applications included in Patents claiming inventions jointly owned with NOVARTIS. NOVARTIS shall be responsible for the preparation, filing, prosecution and maintenance of all patents and patent applications included in NOVARTIS Patents. In each case the responsible party shall consult from time to time with the other party with respect thereto. VERTEX shall provide NOVARTIS with periodic reports listing the jurisdictions in which the VERTEX Patents licensed hereunder have been filed. Subject to the next succeeding sentences, VERTEX will file patent applications with respect to those VERTEX Patents in such other countries as NOVARTIS shall request in writing, all such other countries being countries in which NOVARTIS would customarily file its own cases dealing with similar subject matters. The party initially responsible for preparation, filing, prosecution and maintenance of a particular Patent (the "Initial Responsible Party") shall give thirty (30) days advance notice (the "Discontinuance Election") to the other party of any decision to cease preparation, filing, prosecution and maintenance of that Patent in any jurisdiction (a "Discontinued Patent"). In such case, the other party may elect at its sole discretion to continue preparation, filing and prosecution or maintenance of the Discontinued Patent at its sole expense. The party so continuing shall own any such Patent; and the Initial Responsible Party shall execute such documents and perform such acts as may be reasonably necessary for the other party to file or to continue prosecution or maintenance, including assigning ownership of such Patent to such electing party. Discontinuance may be on a country-by-country basis or for a patent application or patent series in total.

Each party will consult the other party with respect to its choice of patent counsel and will keep that party continuously informed of all matters relating to the preparation, filing, prosecution and maintenance of Patents covered by this Agreement. Each party shall endeavor

in good faith to coordinate its efforts with those of the other party to minimize or avoid interference with the prosecution of the other party's patent applications.

8.1.3. Costs. Costs incurred in the preparation, prosecution and maintenance of Patents shall be borne by each party as set forth in Section 8.3 of the Research Agreement.

8.2. Infringement Claims by Third Parties.

8.2.1. Notice. If the manufacture, use or sale of Bulk Drug Substance and/or Drug Product results in a claim against a party hereto for patent infringement or for inducing or contributing to patent infringement ("Infringement Claim"), the party first having notice of an Infringement Claim shall promptly notify the other in writing. The notice shall set forth the facts of the Infringement Claim in reasonable detail.

8.2.2. Third Party Licenses. In the event that practicing the Technology in connection with the manufacture, use or sale of a Drug Product in any country would infringe a Third Party's patent, then VERTEX will use reasonable efforts to obtain a license under the Third Party's patents with a right to sublicense to NOVARTIS, under terms reasonably acceptable to both VERTEX and NOVARTIS,
[***]

8.2.3. Discontinued Sales, License or Defense of Suit. If the required license is either unavailable or its terms are unacceptable both to VERTEX and to NOVARTIS, then NOVARTIS may elect in its sole discretion to discontinue sales of the Drug Product in such country or to undertake the defense of a patent infringement action or the prosecution of a declaratory judgment action with respect to the Third Party patents. [***] Provided that NOVARTIS is conducting the defense of the Infringement Claim or the prosecution of such declaratory judgment actions, [***]. The costs and expenses of all suits brought by a party under this Section 8.2.3 shall be reimbursed to such party and then to the other party, if it participates in such suit, PRO RATA, out of any damages or other monetary awards recovered therein in favor of VERTEX or NOVARTIS. [***] No settlement or consent judgment or other voluntary final disposition of a suit under this Section 8.2 may be entered into without the joint consent of VERTEX and NOVARTIS (which consent shall not be unreasonably withheld).

8.3. Infringement Claims Against Third Parties.

8.3.1. VERTEX and NOVARTIS each agree to take reasonable actions to protect their respective patents and technology from infringement and from unauthorized possession or use.

8.3.2. If any VERTEX Patents or NOVARTIS Patents are infringed or VERTEX Know-How or NOVARTIS Know-How is misappropriated, as the case may be, by a Third Party, the party to this Agreement first having knowledge of such infringement or misappropriation, or knowledge of a reasonable probability of such infringement or misappropriation, shall promptly notify the other in writing. The notice shall set forth the facts of such infringement or misappropriation in reasonable detail. The owner of the patent or technology, or VERTEX, in the case of joint ownership between the parties hereto, shall have the primary right, but not the obligation, to institute, prosecute, and control with its own counsel any action or proceeding with respect to infringement or misappropriation of such patent or technology and the other party shall have the right, at its own expense, to be represented in such action by its own counsel. If the

party having the primary right or responsibility to institute, prosecute, and control such action or prosecution fails to do so within a period of one hundred twenty (120) days after receiving notice of the infringement, the other party shall have the right to bring and control any such action by counsel of its own choice, and the other shall have the right, at its own expense, to be represented in any such action by counsel of its own choice. If one party brings any such action or proceeding, the second party may be joined as a party plaintiff and, in case of joining, the second party agrees to give the first party reasonable assistance and authority to file and to prosecute such suit. The costs and expenses of all suits brought by a party under this Section 8.3.2 shall be reimbursed to such party and to the other party, if it participates in such suit, PRO RATA, out of any damages or other monetary awards recovered therein in favor of VERTEX or NOVARTIS. [***] No settlement or consent judgment or other voluntary final disposition of a suit under this Section 8.3 may be entered into without the joint consent of VERTEX and NOVARTIS (which consent shall not be unreasonably withheld).

8.4. NOTICE OF CERTIFICATION. VERTEX and NOVARTIS each shall immediately give notice to the other of any certification filed under the U.S. "Drug Price Competition and Patent Term Restoration Act of 1984" claiming that a VERTEX Patent or a NOVARTIS Patent is invalid or that any infringement will not arise from the manufacture, use or sale of any product by a third party. If VERTEX decides not to bring infringement proceedings against the entity making such a certification, VERTEX shall give notice to NOVARTIS of its decision not to bring suit within twenty-one (21) days after receipt of notice of such certification. NOVARTIS may then, but is not required to, bring suit against the party that filed the certification. Any suit by NOVARTIS or VERTEX shall either be in the name of NOVARTIS or in the name of VERTEX, or jointly by NOVARTIS and VERTEX, as may be required by law. For this purpose, the party not bringing suit shall execute such legal papers necessary for the prosecution of such suit as may be reasonably requested by the party bringing suit.

8.5. PATENT TERM EXTENSIONS. The parties shall cooperate in good faith with each other in gaining patent term extension wherever applicable to VERTEX Patents and NOVARTIS Patents covering Drug Product Candidates or Drug Products. NOVARTIS and VERTEX shall mutually determine which patents shall be extended. All filings for such extension shall be made by the party who owns the patent, provided, however, that in the event that the party who owns the patent elects not to file for an extension, such party shall (i) inform the other party of its intention not to file and (ii) grant the other party the right to file for such extension.

ARTICLE IX
REPRESENTATIONS AND WARRANTIES

9.1. REPRESENTATIONS AND WARRANTIES OF VERTEX. VERTEX represents and warrants to NOVARTIS as follows:

9.1.1. AUTHORIZATION. This Agreement has been duly executed and delivered by VERTEX and constitutes the valid and binding obligation of VERTEX, enforceable against VERTEX in accordance with its terms except as enforceability may be limited by bankruptcy, fraudulent conveyance, insolvency, reorganization, moratorium and other laws relating to or affecting creditors' rights generally and by general equitable principles.

The execution, delivery and performance of this Agreement have been duly authorized by all necessary action on the part of VERTEX, its officers and directors.

9.1.2. NO THIRD PARTY RIGHTS. Except as previously disclosed in writing to NOVARTIS on or before the date set forth on the first page hereof, (a) VERTEX owns or possesses adequate licenses or other rights to use all VERTEX Technology, and to grant the licenses herein; and (b) the granting of the licenses to NOVARTIS hereunder does not violate any right known to VERTEX of any Third Party.

9.1.3. NO THIRD PARTY PATENTS. Except as disclosed in writing by VERTEX to NOVARTIS or its agents, to VERTEX's knowledge and based on its current understanding of the Drug Product Candidate(s) and its use, the development, manufacture, use or sale of any Bulk Drug Substance, Drug Product Candidates or Drug Products pursuant to this Agreement will not infringe or conflict with any Third Party right or patent, and VERTEX is not aware of any issued patent or pending patent application that, if issued, would be infringed by the development, manufacture, use or sale of any Bulk Drug Substance, Drug Product Candidates or Drug Products pursuant to this Agreement.

9.1.4. MAINTENANCE OF PATENTS AND LICENSES. Subject to the provisions of Section 8.1.2 with respect to Discontinued Patents, VERTEX will take all reasonable steps to obtain any consent required for and to maintain in effect, including by means of extension, any license, sublicense, patent or patent application applicable to the Field for which it has granted rights to NOVARTIS hereunder.

9.2. REPRESENTATIONS AND WARRANTIES OF NOVARTIS. NOVARTIS represents and warrants to VERTEX as follows:

9.2.1. AUTHORIZATION. This Agreement has been duly executed and delivered by NOVARTIS and constitutes the valid and binding obligation of NOVARTIS, enforceable against NOVARTIS in accordance with its terms, except as enforceability may be limited by bankruptcy, fraudulent conveyance, insolvency, reorganization, moratorium and other laws relating to creditors' rights generally and by general equitable principles. The execution, delivery and performance of this Agreement have been duly authorized by all necessary action on the part of NOVARTIS, its officers and directors.

9.2.2. NO THIRD PARTY RIGHTS. Except as previously disclosed in writing to VERTEX on or before the date set forth on the first page hereof, (a) NOVARTIS owns or possesses adequate licenses or other rights to use all NOVARTIS Technology, and to grant the licenses herein; and (b) the granting of the licenses to VERTEX hereunder does not violate any right known to NOVARTIS of any Third Party.

9.2.3. NO THIRD PARTY PATENTS. Except as disclosed in writing by NOVARTIS to VERTEX or its agents, to NOVARTIS' knowledge and based on its current understanding of the Drug Product Candidate(s) and its use, the manufacture, use or sale of any Bulk Drug Substance, Drug Product Candidates or Drug Products pursuant to this Agreement will not infringe or conflict with any Third Party right or patent, and NOVARTIS is not aware of any issued patent or pending patent application that, if issued, would be infringed by the development, manufacture, use or sale of any Bulk Drug Substance, Drug Product Candidates or Drug Products pursuant to this Agreement.

9.2.4. MAINTENANCE OF PATENTS AND LICENSES. Subject to the provisions of Section 8.1.2 with respect to Discontinued Patents, NOVARTIS will take all reasonable steps to obtain any consent required for and to maintain in effect, including by means of extension, any license, sublicense, patent or patent application applicable to the Field for which it has granted rights to VERTEX hereunder.

ARTICLE X
CONFIDENTIALITY

10.1. UNDERTAKING. During the term of this Agreement, each party shall keep confidential, and other than as provided herein shall not use or disclose, directly or indirectly, any trade secrets, confidential or proprietary information, or any other knowledge, information, documents or materials, owned, developed or possessed by the other party, whether in tangible or intangible form, the confidentiality of which such other party takes reasonable measures to protect, including but not limited to VERTEX Technology and NOVARTIS Technology.

10.1.1. Each party shall take any and all lawful measures to prevent the unauthorized use and disclosure of such information, and to prevent unauthorized persons or entities from obtaining or using such information.

10.1.2. Each party further agrees to refrain from directly or indirectly taking any action which would constitute or facilitate the unauthorized use or disclosure of such information. Each party may disclose such information to its officers, employees and agents, to authorized licensees and sublicensees, and to subcontractors in connection with the development or manufacture of Bulk Drug Substance, Drug Product Candidates or Drug Products, to the extent necessary to enable such parties to perform their obligations hereunder or under the applicable license, sublicense or subcontract, as the case may be; provided, that such officers, employees, agents, licensees, sublicensees and subcontractors have entered into appropriate confidentiality agreements for secrecy and non-use of such information which by their terms shall be enforceable by injunctive relief at the instance of the disclosing party.

10.1.3. Each party shall be liable for any unauthorized use and disclosure of such information by its officers, employees and agents and any such sublicensees and subcontractors.

10.2. EXCEPTIONS. Notwithstanding the foregoing, the provisions of Section 10.1 hereof shall not apply to knowledge, information, documents or materials which the receiving party can conclusively establish:

10.2.1. have entered the public domain without such party's breach of any obligation owed to the disclosing party;

10.2.2. are permitted to be disclosed by the prior written consent of the disclosing party;

10.2.3. have become known to the receiving party from a source other than the disclosing party, other than by breach of an obligation of confidentiality owed to the disclosing party;

10.2.4. are disclosed by the disclosing party to a Third Party without restrictions on its disclosure;

10.2.5. are independently developed by the receiving party without breach of this Agreement; or

10.2.6. are required to be disclosed by the receiving party to comply with applicable laws or regulations, to defend or prosecute litigation or to comply with governmental regulations, provided that the receiving party provides prior written notice of such disclosure to the disclosing party and takes reasonable and lawful actions to avoid or minimize the degree of such disclosure.

10.3. PUBLICITY. The parties will agree upon the timing and content of any initial press release or other public communications relating to this Agreement and the transactions contemplated herein.

10.3.1. Except to the extent already disclosed in that initial press release or other public communication, no public announcement concerning the existence or the terms of this Agreement or concerning the transactions described herein shall be made, either directly or indirectly, by VERTEX or NOVARTIS, except as may be legally required by applicable laws, regulations, or judicial order, without first obtaining the approval of the other party and agreement upon the nature, text, and timing of such announcement, which approval and agreement shall not be unreasonably withheld.

10.3.2. The party desiring to make any such public announcement shall provide the other party with a written copy of the proposed announcement in sufficient time prior to public release to allow such other party to comment upon such announcement, prior to public release.

10.4. SURVIVAL. The provisions of this Article X shall survive the termination of this Agreement and shall extend for a period of five (5) years thereafter.

ARTICLE XI
PUBLICATION

NOVARTIS reserves the sole right to publish or publicly present the results of the Development Program and information concerning Drug Product Candidates and Back-up Compounds (collectively, the "Results"), subject to the following terms and conditions. NOVARTIS will submit a draft of any proposed manuscript or speech to VERTEX for comments at least thirty (30) days prior to submission for publication or oral presentation. VERTEX shall notify NOVARTIS in writing within fifteen (15) days of receipt of such draft whether such draft contains (i) information of VERTEX which it considers to be confidential under the provisions of Article IX hereof, or (ii) information that if published would have an adverse effect on a patent application covering the subject matter of this Agreement which VERTEX intends to file,. In any such notification, VERTEX shall indicate with specificity its suggestions regarding the manner and degree to which NOVARTIS may disclose such information. In the case of item (ii) above, VERTEX may request a delay and NOVARTIS shall delay such publication, for a period not exceeding ninety (90) days, to permit the timely preparation and filing of a patent application or an application for a certificate of invention on the information involved. In the case of item (i) above, NOVARTIS may not publish confidential information of VERTEX without its consent in violation of Article IX of this Agreement. The parties agree that authorship of any publication will be determined based on the customary standards then being applied in the relevant scientific journal.

This Article XI shall terminate with the termination of this Agreement, but the provisions of Article X hereof shall continue to govern the disclosure by one party, whether by publication or otherwise, of Confidential Information of the other, during the period set forth in Section 10.4.

ARTICLE XII
DISPUTE RESOLUTION

12.1. GOVERNING LAW, AND JURISDICTION. This Agreement shall be governed and construed in accordance with the internal laws of the State of New York.

12.2. DISPUTE RESOLUTION PROCESS. Except as otherwise explicitly provided herein, in the event of any controversy or claim arising out of or relating to any provision of this Agreement, or the collaborative effort contemplated hereby, the parties shall, and either party may, initially refer such dispute to the Joint Steering Committee, and failing resolution of the controversy or claim within thirty (30) days after such referral, the matter shall be referred to the Chief Executive Officer of VERTEX and the Chief Executive Officer of NOVARTIS who shall, as soon as practicable, attempt in good faith to resolve the controversy or claim. If such controversy or claim is not resolved within sixty (60) days of the date of initial referral of the matter to the JSC, either party shall be free to initiate proceedings in any court having requisite jurisdiction.

ARTICLE XIII

TERM AND TERMINATION

13.1. TERM. The term of this Agreement shall extend with respect to a Drug Product in a particular country until the later of: (a) the last to expire of any VERTEX Patents containing a Valid Patent Claim covering the Drug Product or its use or manufacture in that country; or (b) if there is no such Valid Patent Claim under a VERTEX Patent in a particular country, ten (10) years from the earlier of the date Regulatory Approval is received in that country for sale of the Drug Product, or the date of First Commercial Sale of the Drug Product in that country.

13.2. TERMINATION FOR CAUSE. In addition to rights of termination which may be granted to either party under other provisions of this Agreement, either party may terminate this Agreement upon sixty (60) days prior written notice to the other party upon the material breach by such other party of any of its obligations under this Agreement, provided that such termination shall become effective only if the breaching party shall fail to remedy or cure the breach within such sixty (60) day period.

13.3. TERMINATION FOR BANKRUPTCY. If at any time during the term of this Agreement, an Event of Bankruptcy (as defined below) relating to either party (the "Bankrupt Party") occurs, the other party (the "Other Party") shall have, in addition to all other legal and equitable rights and remedies available hereunder, the option to terminate this Agreement upon 30 days' written notice to the Bankrupt Party. It is agreed and understood that if the Other Party does not elect to terminate this Agreement upon the occurrence of an Event of Bankruptcy, except as may otherwise be agreed with the trustee or receiver appointed to manage the affairs of the Bankrupt Party, the Other Party shall continue to make all payments required of it under this Agreement as if the Event of Bankruptcy had not occurred, and the Bankrupt Party shall not have the right to terminate any license granted herein. As used above, the term "Event of Bankruptcy" shall mean (a) dissolution, termination of existence, liquidation or business failure of either party; (b) the appointment of a custodian or receiver for either party who has not been terminated or dismissed within 90 days; (c) the institution by either party of any proceeding under national, federal or state bankruptcy, reorganization, receivership or other similar laws affecting the rights of creditors generally or the making by either party of a composition or any assignment or trust mortgage for the benefit of creditors or under any national, federal or state bankruptcy, reorganization, receivership or other similar law affecting the rights of creditors generally, which proceeding is not dismissed within 90 days of filing.

13.4. TERMINATION BY NOVARTIS. [***]

13.5. EFFECT OF TERMINATION.

(a) Termination of this Agreement for any reason, or expiration of this Agreement, will not affect: (i) obligations, including the payment of any royalties and any supply price payments, which have accrued as of the date of termination or expiration, and (ii) rights and obligations which, from the context thereof, are intended to survive termination or expiration of this Agreement.

(b) For each country, at the end of the Agreement term as provided in Section 13.1 hereof in respect of a Drug Product, NOVARTIS shall have a perpetual, nonexclusive, transferable, paid-up, royalty-free license under VERTEX Technology, in each case which is in

existence at the end of such Agreement term, to use, make, have made and sell that Drug Product in that country and to make or have made Drug Product for use and sale in that country.

ARTICLE XIV
INDEMNIFICATION

14.1. INDEMNIFICATION BY VERTEX. VERTEX will indemnify and hold NOVARTIS and its Affiliates, and their employees, officers and directors harmless against any loss, damages, action, suit, claim, demand, liability, expense, bodily injury, death or property damage (a "Loss"), that may be brought, instituted or arise against or be incurred by such persons to the extent such Loss is based on or arises out of:

14.1.1. the development, manufacture, use, storage or handling of a Drug Product Candidate or a Drug Product by VERTEX or its Affiliates or their representatives, agents or subcontractors under this Agreement, or any actual or alleged violation of law resulting therefrom (with the exception of Losses based on infringement or misappropriation of intellectual property rights); or

14.1.2. the breach by VERTEX of any of its covenants, representations or warranties set forth in this Agreement; and

14.1.3. provided however, that the foregoing indemnification shall not apply to any Loss to the extent such Loss is caused by the negligent or willful misconduct of NOVARTIS or its Affiliates.

14.2. INDEMNIFICATION BY NOVARTIS. NOVARTIS will indemnify and hold VERTEX, and its Affiliates, and their employees, officers and directors harmless against any Loss that may be brought, instituted or arise against or be incurred by such persons to the extent such Loss is based on or arises out of:

14.2.1. the development, manufacture, use, sale, storage or handling of a Drug Product Candidate or a Drug Product by NOVARTIS or its Affiliates or their representatives, agents or subcontractors under this Agreement, or any actual or alleged violation of law resulting therefrom (with the exception of Losses based on infringement or misappropriation of intellectual property rights); or

14.2.2. the breach by NOVARTIS of any of its covenants, representations or warranties set forth in this Agreement; and

14.2.3. provided that the foregoing indemnification shall not apply to any Loss to the extent such Loss is caused by the negligent or willful misconduct of VERTEX or its Affiliates.

14.3. CLAIMS PROCEDURES. Each Party entitled to be indemnified by the other Party (an "Indemnified Party") pursuant to Section 14.1 or 14.2 hereof shall give notice to the other Party (an "Indemnifying Party") promptly after such Indemnified Party has actual knowledge of any threatened or asserted claim as to which indemnity may be sought, and shall permit the Indemnifying Party to assume the defense of any such claim or any litigation resulting therefrom;

provided: That counsel for the Indemnifying Party, who shall conduct the defense of such claim or any litigation resulting therefrom, shall be approved by the Indemnified Party (whose approval shall not unreasonably be withheld) and the Indemnified Party may participate in such defense at such party's expense (unless (i) the employment of counsel by such Indemnified Party has been authorized by the Indemnifying Party; or (ii) the Indemnified Party shall have reasonably concluded that there may be a conflict of interest between the Indemnifying Party and the Indemnified Party in the defense of such action, in each of which cases the Indemnifying Party shall pay the reasonable fees and expenses of one law firm serving as counsel for the Indemnified Party, which law firm shall be subject to approval, not to be unreasonably withheld, by the Indemnifying Party); and

14.3.1. The failure of any Indemnified Party to give notice as provided herein shall not relieve the Indemnifying Party of its obligations under this Agreement to the extent that the failure to give notice did not result in harm to the Indemnifying Party.

14.3.2. No Indemnifying Party, in the defense of any such claim or litigation, shall, except with the approval of each Indemnified Party which approval shall not be unreasonably withheld, consent to entry of any judgment or enter into any settlement which (i) would result in injunctive or other relief being imposed against the Indemnified Party; or (ii) does not include as an unconditional term thereof the giving by the claimant or plaintiff to such Indemnified Party of a release from all liability in respect to such claim or litigation.

14.3.3. Each Indemnified Party shall furnish such information regarding itself or the claim in question as an Indemnifying Party may reasonably request in writing and shall be reasonably required in connection with the defense of such claim and litigation resulting therefrom.

14.4. COMPLIANCE. The parties shall comply fully with all applicable laws and regulations in connection with their respective activities under this Agreement.

14.5. INSURANCE. Each party shall use all commercially reasonable efforts to maintain insurance, including product liability insurance, with respect to its activities hereunder.

14.5.1. Such insurance shall be in such amounts and subject to such deductibles as the parties may agree based upon standards prevailing in the industry at the time.

14.5.2. Either party may satisfy its obligations under this
Section through self-insurance to the same extent.

14.5.3. At such time as a Drug Product is being manufactured by a party for commercial sale, that party shall name the other party as an additional insured on any such policies.

ARTICLE XV
MISCELLANEOUS PROVISIONS

15.1. NOTICE OF PHARMACEUTICAL SIDE-EFFECTS. During the term of this Agreement, each of the parties will notify appropriate authorities in accordance with applicable law, and the other party, promptly after receipt of information with respect to any serious adverse event (as defined by the ICH Harmonized Tripartite Guideline on Clinical Safety Data Management), directly or indirectly attributable to the use or application of a Development Candidate, Bulk Drug Substance, a Drug Product Candidate or a Drug Product.

15.2. WAIVER. No provision of the Agreement may be waived except in writing by both parties hereto. No failure or delay by either party hereto in exercising any right or remedy hereunder or under applicable law will operate as a waiver thereof, or a waiver of a particular right or waiver of any right or remedy on any subsequent occasion.

15.3. FORCE MAJEURE. Neither party shall be held liable or responsible to the other party nor be deemed to have defaulted under or breached this Agreement for failure or delay in fulfilling or performing any term of this Agreement, other than an obligation to make a payment, when such failure or delay is caused by or results from fire, floods, embargoes, government regulations, prohibitions or interventions, war, acts of war (whether war be declared or not), insurrections, riots, civil commotions, strikes, lockouts, acts of God, or any other cause beyond the reasonable control of the affected party.

15.4. REGISTRATION OF LICENSE. NOVARTIS may, at its expense, register the license granted under this Agreement in any country where the use, sale or manufacture of a Drug Product in such country would be covered by a Valid Patent Claim. Upon request by NOVARTIS, VERTEX agrees promptly to execute any "short form" licenses submitted to it by NOVARTIS in order to effect the foregoing registration in such country, but such licenses shall in no way alter or affect the obligations of the parties hereunder.

15.5. SEVERABILITY. It is the intention of the parties to comply with all applicable laws domestic or foreign in connection with the performance of its obligations hereunder. In the event that any provision of this Agreement, or any part hereof, is found invalid or unenforceable, the remainder of this Agreement will be binding on the parties hereto, and will be construed as if the invalid or unenforceable provision or part thereof had been deleted, and the Agreement shall be deemed modified to the extent necessary to render the surviving provisions enforceable to the fullest extent permitted by law.

15.6. GOVERNMENT ACTS. In the event that any act, regulation, directive, or law of a government, including its departments, agencies or courts, should make impossible or prohibit, restrain, modify or limit any material act or obligation of NOVARTIS or VERTEX under this Agreement, the party, if any, not so affected shall have the right, at its option, to suspend or terminate this Agreement as to such country, if good faith negotiations between the parties to make such modifications to this Agreement as may be necessary to fairly address the impact thereof, are not successful after a reasonable period of time in producing mutually acceptable modifications to this Agreement.

15.7. GOVERNMENT APPROVALS. NOVARTIS will use reasonable efforts to obtain any government approval required to enable this Agreement to become effective, or to enable any payment hereunder to be made, or any other obligation hereunder to be observed or performed. Each party will keep the other informed of progress in obtaining any such approvals.

15.8. ASSIGNMENT. This Agreement may not be assigned or otherwise transferred by either party without the prior written consent of the other party; provided, however, that either party may assign this Agreement, without the consent of the other party, (i) to any of its Affiliates, if the assigning party guarantees the full performance of its Affiliates' obligations hereunder, or (ii) in connection with the transfer or sale of all or substantially all of its assets or business or in the event of its merger or consolidation with another company. Any purported assignment in contravention of this Section 15.8 shall, at the option of the non-assigning party, be null and void and of no effect. No assignment shall release either party from responsibility for the performance of any accrued obligation of such party hereunder. This Agreement shall be binding upon and enforceable against the successor to or any permitted assignee from either of the parties hereto.

15.9. AFFILIATES. Each party may perform its obligations hereunder personally or through one or more Affiliates, although each party shall nonetheless be solely responsible for the performance of its Affiliates. Neither party shall permit any of its Affiliates to commit any act (including any act of omission) which such party is prohibited hereunder from committing directly. The use of subcontractors by either party shall not increase the financial obligations of the other party hereunder in any respect.

15.10. COUNTERPARTS. This Agreement may be executed in duplicate both of which shall be deemed to be originals, and both of which shall constitute one and the same Agreement.

15.11. NO AGENCY. Nothing herein contained shall be deemed to create an agency, joint venture, amalgamation, partnership or similar relationship between NOVARTIS and VERTEX. Notwithstanding any of the provisions of this Agreement, neither party shall at any time enter into, incur, or hold itself out to third parties as having authority to enter into or incur, on behalf of the other party, any commitment, expense, or liability whatsoever, and all contracts, expenses and liabilities undertaken or incurred by one party in connection with or relating to the development, manufacture or sale of Bulk Drug Substance, Drug Product Candidates or Drug Products shall be undertaken, incurred or paid exclusively by that party, and not as an agent or representative of the other party.

15.12. NOTICE. All communications between the parties with respect to any of the provisions of this Agreement will be sent to the addresses set out below, or to other addresses as designated by one party to the other by notice pursuant hereto, by prepaid certified, air mail (which shall be deemed received by the other party on the seventh business day following deposit in the mails), or by cable, telex, facsimile transmission, or other electronic means of communication (which shall be deemed received when transmitted), with confirmation by letter given by the close of business on or before the next following business day:

If to NOVARTIS, at:

NOVARTIS PHARMA AG
Business Development and Licensing
P.O. Box
CH-4002
Basel, Switzerland
Attention: Victor A. Hartmann, Vice President

with a copy to: Legal Services, at the address referenced above and

if to VERTEX, at:

Vertex Pharmaceutical Incorporated
130 Waverly Street
Cambridge, MA U.S.A. 02139-4211
Attention: President

with a copy to:

Legal Department
Attention: General Counsel

15.13. HEADINGS. The paragraph headings are for convenience only and will not be deemed to affect in any way the language of the provisions to which they refer.

15.14. AUTHORITY. The undersigned represent that they are authorized to sign this Agreement on behalf of the parties hereto. The parties each represent that no provision of this Agreement will violate any other agreement that such party may have with any other person or company. Each party has relied on that representation in entering into this Agreement.

15.15. ENTIRE AGREEMENT. This Agreement, including the Schedules appended hereto, contains the entire understanding of the parties relating to the matters referred to herein, except as matters referenced herein are also addressed in the Research Agreement, and may only be amended by a written document, duly executed on behalf of the respective parties.

15.16. INFLATION ADJUSTMENT. All payments required to be made to VERTEX hereunder (except any royalty payments required to be made under the provisions of Section 6.3 hereof) shall be adjusted at the beginning of each calendar year to reflect the impact of inflation since the date of execution of the Revised and Restated Research Agreement, as measured by the biotech worker inflation rate defined and reported in the Radford Survey (Radford/AON Consulting Inc., San Francisco, CA), or other mutually acceptable index. Notwithstanding the foregoing, no adjustment shall be required in any calendar year in which the appropriate inflation adjustment, if applied, would result in a change of less than [***].

15.17. INVOICE REQUIREMENT. Any amounts payable to VERTEX hereunder (except any royalty payments required to be made under the provisions of Section 6.3 hereof) shall be made within thirty days after receipt by NOVARTIS, or its nominee designated for that purpose in advance by NOVARTIS in writing to VERTEX, of an invoice covering such payment, which

invoice shall conform to the extent reasonably practicable to the form of invoice contained in Exhibit B to the Research Agreement.

15.18. HARDSHIP. If as a result of unforeseen events or developments relating to the subject matter of this Agreement, the performance of this Agreement shall cause inequitable economic hardship for one party which runs counter to the objectives of this Agreement and which the other party cannot reasonably and in good faith expect the first party to bear unrelieved, the parties will meet and seek in good faith to find equitable means of amending this Agreement to reestablish a fair and reasonable economic balance under this Agreement between the parties hereto.

IN WITNESS WHEREOF, the parties hereto have caused this Agreement to be executed by their duly authorized representatives as of the day and year first above written.

VERTEX PHARMACEUTICALS INCORPORATED

By:

Kenneth S. Boger Title: Senior Vice President and General Counsel

NOVARTIS PHARMA AG

By:

Title:

By:

Title:

SCHEDULE 1.12

LIST OF DRUG PRODUCT CANDIDATES

To be supplied

SCHEDULE 1.25

LIST OF MAJOR MARKETS

[***]

SCHEDULE 1.29

NOVARTIS PATENTS

License, Development and Commercialization Agreement -- Confidential

SCHEDULE 1.44

VERTEX PATENTS

License, Development and Commercialization Agreement -- Confidential

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

EXHIBIT 23.1

CONSENT OF INDEPENDENT ACCOUNTANTS

We hereby consent to the incorporation by reference in the Registration Statements on Form S-8 (File Nos. 33-48030, 33-48348, 33-65472, 33-93224, 333-12325, 333-27011, 333-56179, 333-79549, 333-65664, 333-65666 and 333-104362) and on Form S-3 (File Nos. 333-37794 and 333-49844) of Vertex Pharmaceuticals Incorporated of our report dated March 10, 2004, relating to the consolidated financial statements, which appears in this Annual Report on Form 10-K.

PricewaterhouseCoopers LLP
Boston, Massachusetts
March 15, 2004

Exhibit 31.1

SECTION 302 CEO CERTIFICATION

I, Joshua S. Boger, certify that:

1. I have reviewed this annual report 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(s) 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)) 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) 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

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

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

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

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

Date: March 15, 2004

/s/ JOSHUA S. BOGER

Joshua S. Boger
Chairman and Chief Executive Officer

Exhibit 31.2

SECTION 302 CFO CERTIFICATION

I, Ian F. Smith, certify that:

1. I have reviewed this annual report 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(s) 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)) 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) 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

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

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

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

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

Date: March 15, 2004

/s/ IAN F. SMITH

Ian F. Smith
Senior Vice President and
Chief Financial Officer

Exhibit 32.1

SECTION 906 CEO/CFO CERTIFICATION

Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002 (Subsections (a) and (b) of Section 1350, Chapter 63 of Title 18, United States Code) each of the undersigned officers of Vertex Pharmaceuticals Incorporated, a Massachusetts corporation (the "Company"), does hereby certify, to such officer's knowledge, that:

The Annual Report on Form 10-K for the year ended December 31, 2003 (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.

DATED: MARCH 15, 2004 */s/ JOSHUA S. BOGER*

Joshua S. Boger
Chairman and Chief Executive Officer

DATED: MARCH 15, 2004 */s/ IAN F. SMITH*

Ian F. Smith
Senior Vice President and
Chief Financial Officer

A signed original of this written statement required by Section 906 has been provided to the Company and will be retained by the Company and furnished to the Securities and Exchange Commission or its staff upon request.