VERTEX PHARMACEUTICALS INC / MA
Form 10-K
March 15, 2004

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UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

WASHINGTON, D.C. 20549

FORM 10-K

(Mark One)

ý **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

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

For the transition period from to
Commission file number 000-19319

Vertex Pharmaceuticals Incorporated

(Exact name of registrant as specified in its charter)

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

(617) 444-6100

(Registrant's telephone number, including area code)

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

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

Common Stock, $0.01 Par Value Per Share
(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.

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

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

IL-1b 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-1b is a key driver of pathology in OA, and results of tests conducted in animal models provide a strong rationale for pursuing IL-1b 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-1b, 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-lb 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 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.

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

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

	Year Ended December 31,				
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

	Year Ended December 31,	
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		

	December 31,	
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

	December 31,	

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)

	Years Ended December 31,		
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.

VERTEX PHARMACEUTICALS INCORPORATED

Consolidated Statements of Stockholders' Equity and Comprehensive Loss

	Common Stock		Additional Paid-In Capital	Deferred Compensation	Accumulated Other Comprehensive Income (Loss)	Accumulated Deficit	Total Stockholders' Equity	Comprehensive Income (Loss)
	Shares	Amount						
					(in thousands)			
Balance, December 31, 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)

	Common Stock				Accumulated Other Comprehensive Income (Loss)			
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

	Years Ended December 31,		
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

	Years Ended December 31,		
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

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				

December 31, 2002	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
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):

Year	Kendall Square Lease	Other Operating Leases	Total Operating 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	$ 25.97
Granted	3,465	14.59	2,952	17.49	4,451	28.98
Exercised	(914)	9.15	(944)	10.43	(1,401)	11.65
Canceled	(2,814)	31.00	(1,753)	36.44	(855)	38.58
Outstanding at end of year	16,802	$ 23.42	17,065	$ 25.73	16,810	$ 27.37
Options exercisable at year-end	10,205	$ 23.08	9,566	$ 22.85	7,476	$ 19.04
Weighted average fair value of options granted during the year		$ 9.46		$ 11.60		$ 14.97

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

	Three Months Ended			
Total costs and expenses	65,665	104,566	102,254	61,183
Loss from operations	(49,676)	(88,614)	(86,431)	(39,806)
Interest income	5,768	3,421	3,164	3,059
Interest expense	(4,363)	(4,342)	(4,334)	(4,259)
Loss from continuing operations	(48,271)	(89,535)	(87,601)	(41,006)
Income (loss) from discontinued operations:				
Gain on sales of assets	69,232		451	656
Income (loss) from discontinued operations	(350)	(393)	729	(679)
Total income (loss) from discontinued operations	68,882	(393)	1,180	(23)
Net income (loss)	$ 20,611	$ (89,928)	$ (86,421)	$ (41,029)
Basic and diluted net income (loss) per common share	$ 0.27	$ (1.17)	$ (1.12)	$ (0.53)
Basic weighted average number of common shares outstanding	76,411	76,764	77,067	77,758
Diluted weighted average number of common shares outstanding	77,362	76,764	77,067	77,758

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(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)

	Three Months Ended			
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