SECURITIES AND EXCHANGE COMMISSION

WASHINGTON, D.C. 20549

FORM 10-K

(MARK ONE)

/X/ ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(D) OF THE
SECURITIES EXCHANGE ACT OF 1934

FOR THE FISCAL YEAR ENDED DECEMBER 31, 1999

OR

/ / TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(D) OF THE
SECURITIES EXCHANGE ACT OF 1934

FOR THE TRANSITION PERIOD FROM _____ TO _____

COMMISSION FILE NUMBER 000-19319

VERTEX PHARMACEUTICALS INCORPORATED

(Exact name of registrant as specified in its charter)

MASSACHUSETTS (State of incorporation)	04-3039129 (I.R.S. Employer Identification No.)
130 WAVERLY STREET CAMBRIDGE, MASSACHUSETTS (Address of principal executive offices)	02139-4242 (Zip Code)

(617) 577-6000

(Registrant's telephone number, including area code)

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

COMMON STOCK, $0.01 PAR VALUE

(Title of class)

Indicate by check mark whether the registrant: (1) has filed all reports required to be filed by Section 13 of 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. _____

As of February 28, 2000 there were outstanding 26,009,481 shares of Common Stock, $.01 par value per share. The aggregate market value of shares of Common Stock held by non-affiliates of the registrant, based upon the last sales price for such stock on that date as reported by The Nasdaq National Stock Market, was approximately $1,575,000,000.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the definitive Proxy Statement for the 2000 Annual Meeting of Stockholders to be held on May 23, 2000 are incorporated by reference into

Part III.

The "Company," "Vertex," "we" and "us," as used in this Annual Report on Form 10-K, refer to Vertex Pharmaceuticals Incorporated, a Massachusetts corporation.

This Annual Report on Form 10-K contains forward-looking statements based on current management expectations. When used in this Report, the words "expects," "anticipates," "estimates," "plans," "believes," and similar expressions are intended to identify forward-looking statements. Such statements are subject to risks and uncertainties. Factors that could cause actual results to differ from these expectations include, but are not limited to, those discussed in the section of Item 1 entitled "Risk Factors." These forward-looking statements speak only as of the date of this Report. Vertex expressly disclaims any obligation or undertaking to release publicly any updates or revisions to any forward-looking statements contained herein to reflect any change in Vertex's expectations with regard thereto or any change in the events, conditions or circumstances on which any such statement is based.

"Vertex" is a registered trademark of Vertex Pharmaceuticals Incorporated, and "Incel" is a trademark of Vertex Pharmaceuticals Incorporated. "Agenerase" is a trademark of the Glaxo Wellcome Group of companies. "Prozei" is a trademark of Kissei Pharmaceutical Co., Ltd.

PART I

ITEM 1. BUSINESS

BUSINESS

We design, develop and commercialize novel small molecule drugs that address significant markets with major medical needs, including the treatment of viral diseases, cancer, autoimmune and inflammatory diseases, and neurological disorders. Our drug discovery platform integrates advanced biology, chemistry, biophysics and information technologies in order to increase the speed and success rate of pharmaceutical research and development. We are distinguished by our research and development productivity. We have discovered and advanced nine drug candidates into clinical development, including one product--the HIV protease inhibitor Agenerase-TM- (amprenavir)--that has reached the market. We have a broad product pipeline, with seven drug candidates in Phase II clinical development.

We have significant collaborations with Glaxo Wellcome, Aventis, Schering AG (Germany), Eli Lilly, Kissei, and Taisho that provide us with financial support and other valuable resources for our research programs for the development of our clinical drug candidates, and for the marketing and sales of our marketed products. We believe that we are positioned to commercialize multiple products over the next two to five years, which we expect will generate increased product revenues and royalty payments. We have additional research programs underway, and we expect to advance novel drug candidates directed at hepatitis C and stroke into pre-clinical studies within the next 12 to 18 months.

We have extended our technology platform to exploit the opportunities being generated by the wealth of information emerging from genomics research. By applying our structure based design techniques and other technologies to families of related proteins (as opposed to single proteins), we believe that we can obtain higher levels of drug discovery productivity and valuable intellectual property. We refer to this approach as "chemogenomics."

AGENERASE

Our first product, Agenerase, received accelerated approval from the FDA in April 1999 and was launched in May 1999. Agenerase, which was designed by Vertex, is marketed in the United States by Glaxo Wellcome. We co-promote Agenerase in the United States and, if approved, will also co-promote Agenerase in the European Union. Total sales of the drug for the last seven months of 1999

were $49.7 million, and we received $7.5 million in royalties in 1999 from Glaxo Wellcome. More than 10,000 patients

take Agenerase as part of combination therapy for the treatment of HIV. We believe that Agenerase is distinguished from other protease inhibitors by its:

- longer half-life, which allows for convenient twice-daily dosing;

- ability to be dosed effectively on a full or empty stomach; and

- lower levels of cross-resistance to other protease inhibitors.

Agenerase has also received regulatory approval in other countries, including Japan where the drug is sold under the trade name Prozei-TM- by Kissei. Approval of Agenerase is pending in other jurisdictions, including the European Union, where we anticipate approval in 2000 and the drug is being made available through early access programs.

PRODUCTS IN RESEARCH AND DEVELOPMENT

Agenerase is the first of many Vertex-discovered products that we intend to commercialize, by ourselves and with partners, in the coming years. The accompanying chart describes our drug candidates in Phase II clinical trials and our research programs.

DRUG	CLINICAL INDICATIONS	COMPANY WITH MARKETING RIGHTS (REGION)	ESTIMATED U.S. PATIENT POPULATION (MILLIONS)
PHASE II CLINICAL TRIALS			
ANTIVIRALS			
VX-175	HIV	Glaxo Wellcome (Worldwide) Vertex co-promote (U.S. & E.U.)	0.9
VX-497	Chronic hepatitis C	Vertex (Worldwide)	2.7
CANCER			
Incel-TM-	Multidrug resistant tumor cancers	Vertex (Worldwide)	0.5 (tumor incidence in target diseases)
VX-853	Multidrug resistant solid tumor cancers	Vertex (Worldwide)	0.5 (tumor incidence in target diseases)
AUTOIMMUNE AND INFLAMMATION			
VX-497	Psoriasis	Vertex (Worldwide)	0.9 (moderate-to-severe)
VX-740	Rheumatoid arthritis	Aventis (Worldwide) Vertex co-promote (U.S. & E.U.)	2.1
VX-745	Rheumatoid arthritis	Kissei (Japan); Vertex (Rest of world)	2.1
NEUROLOGICAL			
Timcodar	Diabetic neuropathy	Schering AG (Option) Vertex co-promote (U.S. & E.U.)	1.3 (symptomatic)
RESEARCH			
HCV protease	Hepatitis C	Eli Lilly (Worldwide) Vertex co-promote (U.S. & E.U.)	2.7
HCV helicase	Hepatitis C	Vertex (Worldwide)	2.7
Caspases	Stroke, Cardiovascular disease	Taisho (Japan); Vertex (Rest of world)	NA
Kinases	Cancer, Neurodegenerative diseases	Vertex (Worldwide)	NA

We are evaluating second generation compounds in the Company's IMPDH, ICE, p38, and neurophilin ligand programs, and expect to advance second generation candidates in each program in the next one to two years.

COMMERCIAL PRODUCT AND CLINICAL DEVELOPMENT PROGRAMS

We have one product on the market and seven drug candidates in clinical development to treat viral diseases, cancer, autoimmune and inflammatory diseases and neurological disorders, as well as a number of earlier stage research programs.

ANTIVIRAL PROGRAMS

HIV/AIDS

AGENERASE-TM---OVERVIEW

Our first marketed product is Agenerase (amprenavir), an orally deliverable drug for the treatment of HIV infection and AIDS. A second generation HIV protease inhibitor, Agenerase was developed by us in collaboration with Glaxo Wellcome plc. Glaxo Wellcome is marketing Agenerase worldwide except for the Far East, and we have U.S. and European co-promotion. Agenerase

received regulatory approval in the United States in April 1999, and has also been approved in Brazil, Mexico, Uruguay, Argentina, Israel, and Switzerland. Agenerase has been submitted for approval in other markets worldwide, including the European Union (EU). In Japan, we collaborated with Kissei Pharmaceutical Co., Ltd. in the development of amprenavir, which is sold by Kissei under the trade name Prozei-TM-. We receive royalties on sales of amprenavir by Glaxo Wellcome and Kissei. We also supply amprenavir bulk drug substance to Kissei.

We anticipate market approval in the EU in 2000. To support the use of Agenerase in the marketplace, we and Glaxo Wellcome have undertaken a broad Phase IV clinical program aimed at evaluating the drug's use as part of different combinations in a variety of patient populations.

Kissei received approval for amprenavir under a special fast-track initiative by the Ministry of Health and Welfare in Japan in September 1999. Amprenavir's market launch as Prozei followed shortly thereafter. As a condition of accelerated approval, Kissei is conducting a Phase II/III clinical trial of amprenavir.

VX-175--OVERVIEW

We first synthesized the compound VX-175 (also referred to as GW433908) as part of our HIV research and development collaboration with Glaxo Wellcome. VX-175 is a prodrug of amprenavir that is designed to provide more compact dosing for patients. A prodrug is an inactive compound that is changed metabolically by the body to become active against disease. Preclinical studies showed the prodrug to be highly water-soluble and bioavailable in animals. In a Phase I study of 16 healthy volunteers completed during 1999, the prodrug formulation was found to be bioequivalent to amprenavir and also showed dose-proportionality. A dose-ranging Phase II clinical study to assess preliminary safety and efficacy and to help determine pharmacokinetics in HIV patients is now underway to determine the optimal dose of VX-175. We anticipate that Glaxo Wellcome will begin Phase III trials of VX-175 in 2000. The FDA has given VX-175 fast track designation. Fast track designation is granted to products that may provide a significant improvement in the safety or effectiveness of the treatment for a serious or life-threatening disease. Glaxo Wellcome is developing the prodrug and has marketing rights in the United States, Europe and certain countries of the Far East. Kissei has an option to develop and commercialize the prodrug in Japan. We have an option to co-promote the prodrug in the United States and the EU, and we will receive royalties on sales of VX-175, if any. We also retain rights to supply bulk drug substance to Glaxo Wellcome.

BACKGROUND: HIV/AIDS

Infection with the HIV virus leads to AIDS, a severe, life-threatening impairment of the immune system. The World Health Organization (WHO) estimates that approximately 33.6 million persons worldwide, including approximately 920,000 patients in North America, are infected with HIV.

Protease inhibitors (PIs) are used as part of combination regimens for the treatment of HIV. Currently, about 66% of the HIV patients receiving drug treatment in the U.S. take at least one protease inhibitor. The market for HIV protease inhibitors is highly competitive, with five different PIs vying for a share of a $1 billion U.S. market. Worldwide sales of HIV protease inhibitors were an estimated $2.2 billion in 1999, compared to $1.8 billion in 1998. There are now three 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 nevarapine, and protease inhibitors, including Agenerase. In the United States, more than 10,000 patients take Agenerase as part of combination therapy for the treatment of HIV infection.

We used our expertise in structure-based drug design to create and develop Agenerase to address critical unmet needs in the treatment of HIV. We believe that Agenerase has several advantages over other PIs in the market including:

- The pharmacological half-life in the body of Agenerase is 7 to 9.5 hours, which is longer than any other currently available protease inhibitor.

- Agenerase absorption is not significantly affected by the presence or absence of food (although the drug should not be taken with a high fat meal), and there are no substantial hydration requirements. In practical clinical terms, this allows the drug to be dosed twice daily regardless of meal times, without compromising the antiviral activity of the drug.

- Agenerase appears to have less cross-resistance with other PIs, allowing the drug to be used as a first or a follow-on PI.

Preliminary data have also shown that Agenerase is less associated with high cholesterol and triglyceride levels, and less associated with syndromes of fat redistribution than have been reported for other protease inhibitors. Further study will be required to confirm these preliminary data and to understand more fully the clinical significance of Agenerase's resistance profile.

HEPATITIS C VIRUS (HCV) INFECTION

VX-497-- OVERVIEW

VX-497 is a novel, orally administered IMPDH inhibitor that we designed. VX-497 has demonstrated potent biological activity and oral bioavailability in preclinical and early clinical studies. We are conducting a Phase II clinical trial of VX-497 for the treatment of hepatitis C virus (HCV) infection. We retain all commercial rights to VX-497 and any second generation compounds resulting from our IMPDH research and development program.

In November 1999, we announced preliminary data from a Phase II clinical trial of VX-497, indicating that VX-497 was well tolerated and appears to reduce liver inflammation in patients with HCV infection. Preliminary Phase II data also indicate that the drug was well-tolerated and resulted in reduced levels of serum alanine aminotransferase, a marker of liver inflammation, in HCV patients treated for 28 days. We are now conducting a three-month extension study to further explore the safety and pharmacokinetics of VX-497 as a monotherapy in patients with HCV, treating a continuing group of patients who were unresponsive to prior treatment with interferon-alpha. In 2000, we plan to begin a Phase II study of VX-497 combined with interferon-alpha in treatment-naive patients. VX-497 is also in Phase II clinical trials for psoriasis.

BACKGROUND: HCV

IMPDH is a cellular enzyme that regulates the production of nucleotides which are the building blocks of RNA and DNA. Viruses that invade the body depend on these nucleotides for replication, and depletion of nucleotides may cripple a virus's ability to replicate and infect new cells. IMPDH catalyzes a

key step in nucleotide biosynthesis. Most cell types can use an alternative pathway if IMPDH is inhibited, but a few cell types, such as lymphocytes and virus-infected cells, are completely dependent on this enzyme. IMPDH inhibitors thus selectively block the proliferation of lymphocytes and the replication of certain viruses, and we believe that IMPDH inhibitors may be useful both in immunosuppression and as antiviral agents.

Data from a Phase I trial in healthy volunteers, completed in early 1998, show that VX-497 is well-tolerated in single escalating doses and achieves blood levels well above those necessary to achieve potent inhibition of IMPDH IN VITRO. As an immunosuppressive, VX-497 may block the activity of certain lymphocyte populations that result in inflammation of the liver in HCV patients. VX-497 may also have a direct antiviral effect on HCV and other viruses.

CANCER

MDR PROGRAM--OVERVIEW

We are developing novel compounds to treat and prevent the occurrence of drug resistance associated with the failure of cancer chemotherapy. We are developing Incel-TM- (also referred to as biricodar dicitrate or VX-710), a compound that blocks major multidrug resistance (MDR) mechanisms, including P-glycoprotein, or P-gp, and multidrug resistance associated protein, or MRP. Incel, an intravenous compound, is intended to be administered in combination with cancer chemotherapy agents, such as doxorubicin, paclitaxel, vincristine, etoposide and mitoxantrone. We are conducting Phase II clinical trials of Incel in five different types of cancer. In addition, we are conducting a Phase I/II clinical trial of the compound VX-853, an oral MDR inhibitor, in patients with solid tumors. We retain all commercial rights to Incel worldwide.

Our development strategy is to evaluate Incel in a broad range of tumor types in combination with widely used anti-cancer agents. Multiple Phase II clinical studies have been undertaken in ovarian, breast, small cell lung and prostate cancers, and in soft tissue sarcoma. Exploratory studies have also been conducted in liver cancer. The objective of these trials is to assess Incel's safety and pharmacokinetics and identify the tumor type, drug and dosage regimens to be studied further in Phase III clinical trials. Incel is being evaluated in combination with doxorubicin and paclitaxel, two of the most widely used anti-cancer agents, as well as with mitoxantrone, prednisone and vincristine. Historical response rates of patients who have failed first-line chemotherapy (refractory patients) who attempt chemotherapy a second time are extremely low. Preliminary analysis of response rates using Incel in conjunction with chemotherapy suggests a potential benefit to combination therapy for refractory patients.

There are currently five Phase II studies underway that we expect to complete in 2000, in ovarian cancer, breast cancer, soft tissue sarcoma, prostate cancer, and small cell lung cancer, the details of which are described in the following table:

INCEL-TM- PHASE II CLINICAL DEVELOPMENT SUMMARY

PATIENT POPULATION	REGIMEN	NUMBER OF PATIENTS	STATUS	CLINICAL RESPONSE RATE
Refractory ovarian cancer	Incel/paclitaxel	25	Ongoing	12% (1 CR, 2 PR)
Refractory breast cancer	Incel/paclitaxel	38	Final data analysis	17% (4 PR, 2 MR)
Refractory soft tissue sarcoma	Incel/doxorubicin	37	Final data analysis	10% (2 PR, 8 SD)
Hormone refractory prostate cancer	Incel/mitoxantrone & prednisone	40	Final data analysis	27%
Small cell lung cancer	Incel/doxorubicin/ vincristine	N/A	Ongoing	N/A

PR=partial response; MR=minor response; CR=complete response; SD=stable disease; N/A=not available

A second compound, VX-853, has been optimized by Vertex for oral administration. IN VITRO results show that VX-853 potently blocks MDR mediated by both P-gp and MRP. We are conducting a Phase I/II clinical trial with VX-853 to assess the safety and pharmacokinetics of the compound in combination with doxorubicin.

BACKGROUND: MDR

The American Cancer Society estimates that during 1999 more than 1.2 million people in the United States were diagnosed with invasive cancer and more than 560,000 people in the U.S. died from such cancers. A significant number of these patients failed to respond or relapsed following chemotherapy because of MDR.

A major contributing factor to MDR is the presence of molecular pumps, including P-gp and MRP, that expel chemotherapeutic agents from cancer cells, preventing the sustained delivery of the potent levels of the chemotherapeutic agents required for therapeutic benefit. As a consequence, these resistant tumor cells cannot be killed efficiently by anticancer drugs such as doxorubicin, vincristine, etoposide and paclitaxel. P-gp has been associated with MDR in a variety of cancers including liver cancer, breast cancer, soft tissue sarcoma, prostate cancer, colon cancer, pancreatic cancer, acute myelogenous leukemia, multiple myeloma and certain lung cancers. MRP has been identified as another drug efflux pump and is also associated with resistance.

No drug has been approved by the FDA specifically for the treatment of MDR, but several compounds are in advanced clinical studies. Certain agents, such as dex-verapamil and cyclosporin A, have been shown in preliminary human studies to have some promise for overcoming clinical resistance to certain commonly used chemotherapeutic agents. We believe that these drugs affect only a subset of the MDR pumps and may have side effects that could limit broad use. Second generation multidrug reversing agents, such as PSC 833 (valspodar), a cyclosporine derivative, are also currently being evaluated by other companies.

AUTOIMMUNE AND INFLAMMATORY DISEASES

AUTOIMMUNE DISEASE

VX-497--OVERVIEW

We are conducting a Phase II clinical trial of our IMPDH inhibitor VX-497 in psoriasis patients, to make a preliminary assessment of its clinical efficacy. There are approximately 900,000 patients in the U.S. with moderate to severe psoriasis.

We may expand clinical development of VX-497 into additional autoimmune, transplant and antiviral indications in the future. We are also continuing research and development activities to identify second generation IMPDH inhibitors.

INFLAMMATORY DISEASE

VX-740--OVERVIEW

We are conducting research and development on inhibitors of interleukin-1 beta converting enzyme (ICE) for the treatment of acute and chronic inflammatory conditions, including rheumatoid arthritis. We are collaborating with Aventis S.A. in the development of the ICE inhibitor compound VX-740 (which Aventis calls HMR 3480). Aventis is conducting a Phase II clinical trial of VX-740 in patients with rheumatoid arthritis. Inhibitors of ICE may have application to a wide range of chronic and acute inflammatory diseases, such as rheumatoid arthritis, osteoarthritis, inflammatory bowel disease, atherosclerosis, sepsis, and pancreatitis. We are also independently conducting research into second generation ICE inhibitors.

In September 1999, we announced an agreement under which Aventis holds an exclusive worldwide license to develop, manufacture and market VX-740 in any indication, as well as an exclusive option for all other compounds discovered under a previous research collaboration between Vertex and Hoechst Marion Roussel (HMR). HMR and Rhone-Poulenc Rorer merged to form Aventis in December 1999. As part of the agreement, Aventis may pay us up to $62 million for the development of VX-740 in rheumatoid arthritis, the first targeted indication, and Aventis will pay for all development costs. Aventis is conducting a Phase II clinical trial of VX-740 in patients with rheumatoid arthritis which began in September 1999. The primary goal of the study is to evaluate the safety and pharmacokinetics of multiple doses of VX-740 in rheumatoid arthritis patients. We anticipate that a larger Phase II study of VX-740 will be initiated by Aventis in 2000. A Phase I clinical trial of the compound, completed by Aventis earlier in 1999, showed that the compound was well-tolerated in humans in a range of single doses. We are continuing research into second generation ICE inhibitors, as well as other caspase inhibitors.

BACKGROUND: ICE INHIBITORS FOR INFLAMMATORY DISEASE

ICE is an enzyme that controls the release of active Interleukin-1 (IL-1) beta (one of two forms of Interleukin-1) from white blood cells into the bloodstream and within tissues. IL-1 beta is a cytokine that mediates a wide range of immune and inflammatory responses in many cell types. Early in the inflammatory process, IL-1 beta is released from white blood cells, initiating a complex cascade of events that results in inflammation and tissue damage. Elevation of IL-1 beta levels has been correlated to disease state in a number of acute and chronic inflammatory diseases.

Rheumatoid arthritis is the lead indication of the VX-740 development program. In patients with rheumatoid arthritis, increased activity of IL-1 beta is seen in joint tissues during disease flare-ups, and IL-1 beta is known to activate osteoclasts, a cell type important in bone erosion characteristic of rheumatoid arthritis. In mice genetically modified to lack the ICE gene, systemic IL-1 beta levels are sharply reduced, and the mice are resistant to experimentally induced arthritis. In normal mice in which

arthritis has been successfully induced, treatment with VX-740 significantly reduces severity of arthritis compared to control.

There are more than six million patients with rheumatoid arthritis worldwide, including approximately 2.1 million in the United States. The main drugs used to treat rheumatoid arthritis 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 limited by side effects that include bone marrow suppression and liver toxicity. Even when tolerated well, over the long term many patients become unresponsive to methotrexate. 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. However, both Enbrel and Remicade are injectable, and therefore, we believe that an oral cytokine inhibitor such as VX-740 has significant dosing advantages.

Vertex and Aventis scientists began collaborating in 1993 to discover and develop orally available inhibitors of ICE. Their design efforts were based on the three-dimensional atomic structure of ICE, which was solved by Vertex researchers in 1994. As the result of an extensive, jointly conducted synthesis and research program, HMV 3480/VX-740 was selected as a development candidate in 1996. HMR 3480/VX-740 is the first caspase inhibitor to be advanced to Phase II clinical trials.

VX-745--OVERVIEW

We are collaborating with Kissei on the design, development and commercialization of inhibitors of p38 MAP kinase. During 1999, we started a Phase II clinical trial with VX-745 in patients with rheumatoid arthritis. VX-745 is a novel orally administered investigational drug targeting p38 MAP kinase. The p38 MAP kinase is a human enzyme involved with the onset and progression of inflammation and apoptosis, or programmed cell death. The enzyme plays a central role in regulating the cytokines TNF alpha and IL-1 beta. The objective of our research collaboration with Kissei is 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, and Crohn's disease, and neurological diseases such as stroke.

During 1998, Vertex and Kissei selected VX-745 as a lead drug development candidate targeting p38 MAP kinase. We conducted a Phase I clinical trial of the compound in healthy volunteers in early 1999. Based on the results of that study, we began an exploratory Phase II trial in rheumatoid arthritis patients in Europe in October 1999. This trial is a 28-day study designed to test the tolerability and pharmacokinetics of VX-745 in ten patients with rheumatoid arthritis. The trial will also assess the pharmacodynamic activity of VX-745, and clinical disease activity markers will be monitored.

BACKGROUND: P38 INHIBITORS FOR INFLAMMATORY DISEASE

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. When activated, the p38 MAP kinase triggers production of the cytokines IL-1, IL-6 and tumor necrosis factor TNF-alpha. Excess levels of IL-1 and TNF-alpha are associated with a broad range of acute and chronic inflammatory diseases. They also play an important role in programmed cell death associated with ischemia and stroke, and in neurodegenerative diseases such as Alzheimer's and Parkinson's Disease. We are aware of several other companies that are developing p38 MAP kinase inhibitors. In addition, there are other drugs, in development or approved, that have different mechanisms of action for treating rheumatoid arthritis and other inflammatory diseases.

NEUROLOGICAL DISEASES

TIMCODAR--OVERVIEW

Timcodar dimesylate (also referred to as VX-853) is a novel, orally administered drug that may be useful in the treatment of neurological disorders such as peripheral neuropathies (including diabetic neuropathy), Parkinson's Disease, trauma, and amyotrophic lateral sclerosis, or ALS. In addition to timcodar, we are conducting research to discover and develop drugs through our Neurophilin Ligand Program. We have used an integrated drug design technique to synthesize a library of orally available small molecule compounds that have the potential to promote recovery of nerve function and nerve growth. We are engaged in a worldwide strategic partnership with Schering AG (Germany) for research, development and commercialization of neurophilin ligands for the treatment of a variety of neurological disorders. In 1999, we completed a Phase II clinical trial of timcodar in diabetic neuropathy patients. Schering AG has an option to co-develop timcodar with us under the collaboration agreement.

During 1999, we announced that orally administered neurophilin compounds discovered at Vertex, including compounds that do not interact with FKBP-12, significantly improve outcome in two different preclinical models of Parkinson's Disease. We also reported for the first time that compounds that do not interact with FKBP-12 can improve outcomes in animal models of peripheral neuropathies. In 1999, we completed a Phase II clinical trial with timcodar demonstrating that the drug was well-tolerated and was orally bioavailable in the range of doses tested. A single-dose Phase I study of four different doses of timcodar in healthy volunteers was completed in 1998, providing support for Phase II clinical development in the indication of diabetic neuropathy. IN VITRO results have shown timcodar's ability to promote neurite outgrowth, and IN VIVO results have shown that timcodar can prevent neural dysfunction in a model of diabetic polyneuropathy.

BACKGROUND: NEUROLOGICAL DISEASES

Neurodegenerative disorders are among the diseases with the fewest available effective treatments. Central nervous system disorders such as Alzheimer's Disease, Parkinson's Disease and multiple sclerosis affect millions of patients worldwide, and for some of these there are no approved therapies that alter the course of disease progression. Peripheral neuropathies encompass a wide spectrum of clinical syndromes for which treatments of only limited efficacy are available. Diabetic neuropathy is the most common identifiable cause of neuropathy. There are approximately 1.3 million patients with moderate to severe diabetic neuropathy in the United States.

Effective treatment of both central and peripheral neurological disorders has long been hampered by the inability to slow, arrest, or reverse nerve damage or progression. Other companies are developing various neurotrophic factors (proteins) for these indications, but we believe that their clinical utility is likely to be limited because of the difficulty of the delivery of protein drugs. Based on our extensive research in the field of immunosuppressive drugs, we have been able to generate a large number of compounds, known as neurophilin ligands, that trigger nerve growth activity. Extensive IN VITRO and IN VIVO studies conducted with a reference compound designed by Vertex support the broad potential of our neurophilin ligands in the treatment of degenerative central nervous system and peripheral nervous system diseases. Our clinical neurophilin ligand candidate, timcodar, has demonstrated potent activity in accelerating recovery of nerve function following injury and reversing experimental nerve damage in preclinical studies. Our researchers are still seeking to determine the mechanism of action of neurophilin ligands.

BACKGROUND TO DRUG DISCOVERY

Drugs are natural or synthetic compounds that interact with a target molecule, typically a protein, either to induce or to inhibit that molecule's function within the human body. Traditionally, pharmaceutical products have been discovered through screening thousands of compounds in predictive assays for a chosen disease target.

The drug discovery process is complex and involves multiple steps and disciplines. The key steps in the discovery and development of a compound for human testing (a drug candidate) typically include:

- identification of a drug target;

- development of a relevant biological assay;

- selection of compounds for screening;

- identification of a lead molecule;

- optimization of a lead molecule; and

- preclinical development.

Qualities that are critical to the successful development of an oral small molecule include sufficient potency, oral bioavailability, adequate pharmacokinetics, and safety. Failure to achieve any one of these parameters is a major reason for a molecule failing early in the development process.

OUR INTEGRATED APPROACH TO DRUG DISCOVERY

We use a broad-based, proprietary approach to drug design that integrates multiple advanced technologies early in the drug design process, to increase the speed and certainty of drug development. We have consistently shown the ability of our approach to advance drug candidates directed at biologically complex targets. We believe that our track record compares favorably with industry standards. Our drug discovery platform integrates advanced biology, biophysics chemistry and information technologies in a coordinated and simultaneous fashion throughout the discovery process. We employ a variety of technologies to accelerate the drug discovery process and to provide a more certain outcome in clinical development, including:

FUNCTIONAL GENOMICS. We use a number of functional genomics techniques, such as gene knock-out mice, to help guide target selection and test the potential of its compounds in disease models. We also use techniques such as site-directed mutagenesis to identify critical residues for drug interaction in the active site of a molecular target.

BIOPHYSICS. A core strength of Vertex is the generation of atomic structural information on molecular targets using x-ray crystallography and nuclear magnetic resonance (NMR) spectroscopy to guide design of optimization of lead classes of drugs. Our scientists have also pioneered innovative NMR techniques, including a proprietary technology called NMR SHAPES which can screen molecular subunits for weak affinity to a molecular target. This initial screening can quickly identify lead classes of molecules for further evaluation.

COMPUTER-BASED MODELING. We apply advanced, proprietary computational modeling tools to guide early evaluation of compounds. During initial virtual compound screening ("IN SILICO"), we can evaluate 10(14) compounds in one day to select 100 or 1,000 compounds for synthesis and traditional screening, and repeat the cycle on subsequent days based on initial results. By using proprietary algorithms to sort and filter compounds for specific properties, our scientists can efficiently focus on compounds that are more likely to be useful leads.

MEDICINAL AND COMBINATORIAL CHEMISTRY. Medicinal chemistry expertise is a key part of our drug discovery process. Medicinal chemists visually evaluate each compound which emerges through IN SILICO screening process and provide insight into the creation of focused libraries for screening. We use combinatorial chemistry to design diverse libraries based on promising early leads.

PHARMACOLOGY. We employ a number of approaches designed to provide predictive information on the bioavailability and pharmacokinetic profile of potential compounds at the earliest stages of the drug discovery process. These approaches, which include IN VITRO metabolism and toxicological studies and IN

VIVO assessment of leads in predictive animal models, provide greater certainty that a compound will have properties desired of an oral drug.

RESEARCH PROGRAMS

SINGLE TARGET PROGRAMS
HEPATITIS C VIRUS PROGRAMS

We are conducting two discovery research programs to develop compounds to treat hepatitis C. Identified in 1989, the hepatitis C virus (HCV) causes chronic inflammation in the liver. In a majority of patients, HCV establishes a chronic infection that can persist for decades and eventually lead to cirrhosis, liver failure and liver cancer. HCV infection represents a significant medical problem worldwide for which there is inadequate or no therapy for a majority of patients. Sources at the CDC have estimated that approximately 2.7 million Americans, or more than 1% of the population, are chronically infected with HCV, and the WHO estimates that there are more than 170 million chronic carriers of the virus worldwide. Currently, there is no vaccine available to prevent hepatitis C infection. The only drugs approved for the treatment of hepatitis C are interferon alpha and ribavirin. Combination therapy with interferon alpha and ribavirin is the most successful treatment currently available, but over 50% of patients still failed to show long-term sustained response to that combination, and safe and effective treatments for HCV infection are needed.

HEPATITIS C PROTEASE

The hepatitis C NS3-4A serine protease is a virally encoded enzyme generally believed to be essential for replication of HCV. Under an agreement signed during 1997, we are collaborating with Eli Lilly and Company on the research, development and commercialization of novel, orally active HCV protease inhibitors for the treatment of hepatitis C infection. This research derives heavily from detailed structural information about the protease, discovered and developed by our researchers.

HEPATITIS C HELICASE

We are also conducting discovery research to design orally deliverable drugs to inhibit the hepatitis C virus helicase. The NS3 helicase enzyme is believed to play an essential role in the infectious cycle of the hepatitis C virus by aligning viral DNA in its proper configuration for replication. Therefore, the HCV helicase represents an attractive target for drug discovery.

Researchers from Vertex solved the three-dimensional atomic structure of the hepatitis C virus NS3 helicase. We are using this structural information to identify and optimize inhibitors of the enzyme, employing structure-based techniques, including cluster-based screening, and computational, combinatorial, and medicinal chemistry, to design novel small molecule inhibitors of the HCV helicase for clinical development as new antiviral drugs to treat HCV infection.

DISCOVERY OPPORTUNITY: CHEMOGENOMICS

Genomics and related biological approaches are producing a wealth of information on new molecular targets. New drugs, however, have not emerged at the same rate as new targets, since the technological and organizational advances in potential target identification have proceeded much faster industrywide compared to advances in drug discovery. The number of new targets now emerging is outpacing the capability of pharmaceutical research and development groups to discover efficiently drugs based on those targets. We believe that those companies that can best utilize genomic information will be the ultimate beneficiaries of the genomics revolution. Vertex is uniquely positioned to translate genomics information into targeted drug candidates.

Our approach to drug discovery to date has focused on discrete and unrelated molecular targets, such as HIV protease, IMPDH, and ICE. We are now engaged in a discovery approach designed to generate drugs directed at structurally related molecular targets in protein families. This approach applies our integrated strategy across a range of molecular targets to pursue rapid and simultaneous generation of lead compounds.

We believe that our skills in designing drugs based on the atomic structure of a molecular target's active site will allow us to:

- efficiently design multiple chemical scaffolds that bind to many different related proteins and

- rapidly identify appropriate chemical side chains for these scaffolds that will provide specificity for a particular target of interest within a group of related proteins.

This strategy has already enabled us to describe large numbers of lead classes of novel chemical compounds directed at the caspase and kinase protein families, and to describe the interactions of these compounds with a variety of molecular targets in these families.

We use the term CHEMOGENOMICS to describe this discovery approach. Chemogenomics is the discovery and description of all possible drug compounds directed at all possible drug targets. We believe that we will be able to use our integrated technological approach to describe many, and in some cases, all of the possible novel chemical classes of compounds and their interactions with specific molecular targets in protein families of our choosing. We will seek intellectual property protection for compound classes not previously described for a given target. We believe that the chemogenomics approach will accelerate drug discovery directed at important novel targets as well as provide the company with broad and enabling intellectual property. We also believe that our chemogenomics strategy will create opportunities for broad corporate partnerships directed at the discovery of new drugs.

To further accelerate this strategy, on February 28, 2000, we entered into an agreement with Incyte Pharmaceuticals to gain access to its Lifeseq Gold database, a comprehensive portfolio of genomic information. We anticipate integrating such information, as well as information from both public and private databases, to further our chemogenomics approach.

MULTI-TARGET RESEARCH PROGRAMS

CASPASE INHIBITORS PROGRAM

We are designing novel small molecule inhibitors of selected caspase enzyme targets to treat a variety of diseases in which apoptosis, or programmed cell death, plays a role. Our scientists are leveraging the expertise gained through our successful design and optimization of inhibitors of ICE (caspase-1). In November 1999, we began collaborating with Taisho Pharmaceutical Co., Ltd. to discover, develop, and commercialize caspase inhibitors in Japan and certain Far East markets. We retain exclusive rights to the caspase program in the United States, Europe and the rest of the world.

All cells have the ability to self-destruct via a tightly-regulated pathway known as apoptosis in response to certain signals. Apoptosis is an essential component of numerous biological processes, including tissue remodeling and immune system regulation. When not properly regulated, apoptosis can have damaging effects and contribute to a variety of diseases. Caspases are a family of 11 structurally related human enzymes which play specific roles in apoptosis and inflammation. Our discovery effort is focused on the design of small molecules for inhibiting caspase-mediated apoptotic processes, thereby exerting a protective effect on cells in specific tissues. Potential indications include tissue damage related to acute conditions such as stroke and myocardial ischemia, and neurodegenerative disorders such as Alzheimer's Disease and Parkinson's Disease.

In our caspase inhibitors program, we are implementing our strategy for exploiting emerging genomic information by targeting large families of structurally-related proteins for drug discovery. Different

caspases share similar structural features, and by using parallel structural approaches combined with new medicinal and computational chemistry tools, our scientists have been able to make rapid progress in the design and synthesis of multiple lead classes of compounds. Our scientists 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. Through gene knockout studies, our scientists have been able to gain important insight into the biological role of different caspases in the activation of apoptosis in specific cells and tissues. We intend to use this information to design novel small molecule caspase inhibitors for development and commercialization in several indications in collaboration with Taisho.

MAP KINASE INHIBITORS PROGRAM

We have undertaken a broad-based drug discovery effort targeting MAP kinase intracellular signaling pathways. Human mitogen-activated protein (MAP) kinases form a group of structurally-related enzymes that include extracellular-signal regulated kinase (ERK), p38 MAP kinase, and Jun N-terminal kinase (JNK). In response to specific biological and chemical signals, MAP kinases become activated by specific upstream kinases, called MAP kinase kinases (MKK). The activated MAP kinases in turn activate other downstream kinases, transcription factors, and translation factors, resulting in cellular responses including apoptosis, cell proliferation and cytokine release.

We are currently focused on discovery and development of inhibitors of MAP kinases, including JNK and ERK, as well as other related kinases. As a neuronal-specific isoform of JNK, JNK3 is a member of the MAP kinase family and is implicated as a key mediator of signal transduction pathways central to the pathogenesis of certain neurological diseases involving apoptosis-driven neurodegeneration. Recent findings suggest that JNK3 plays an important role in central nervous system disorders such as epilepsy, stroke and Alzheimer's Disease. Our scientists are leveraging the expertise gained through our p38 MAP kinase program. We have

identified several novel classes of JNK3 MAP kinase inhibitors and are currently using advanced drug discovery technology to move lead compounds toward clinical candidate status.

We are also engaged in the discovery of inhibitors of the enzyme ERK2, which plays a role in the activation of enzymes and other factors involved in cell division. We believe that ERK2 inhibitors may have a role in the treatment of cancer. We are also applying our discovery expertise in the MAP kinase area to the discovery of inhibitors targeting a wide variety of structurally related kinases.

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.

GLAXO WELLCOME PLC.

In December 1993, we entered into a collaboration with Glaxo Wellcome covering the development and commercialization of Agenerase (amprenavir) and its prodrug, VX-175 (also referred to as GW433908). Glaxo Wellcome has exclusive rights to develop and commercialize our HIV protease inhibitors in all parts of the world except the Far East and pays us a royalty on sales. We have retained certain bulk drug manufacturing rights and certain co-promotion rights in the territories licensed to Glaxo Wellcome. Under the collaborative agreement, Glaxo Wellcome agreed to pay us up to $42 million, comprised of a $15 million license payment paid in December 1993, $14 million of product research funding over five years and $13 million of development and commercialization milestone payments for an initial drug candidate. Glaxo Wellcome is also obligated to pay us additional development and commercialization milestone payments for subsequent drug candidates, including VX-175. From the inception of the

agreement in December 1993 through December 31, 1999, we recognized $40 million as revenue. We have received the full amount of research funding specified under the agreement. In addition, Glaxo Wellcome is required to bear the costs of development in its territory under the collaboration. During 1999, we received a $5 million milestone payment from Glaxo Wellcome for Agenerase marketing approval in the United States.

Glaxo Wellcome has the right to terminate its agreement with us without cause upon twelve months' notice. Termination by Glaxo Wellcome of the agreement will relieve Glaxo Wellcome of its obligation to make further commercialization and development milestone and royalty payments, and will end any license granted to Glaxo Wellcome by us.

We and Glaxo Wellcome have a non-exclusive, worldwide license under certain Searle patent applications claiming HIV protease inhibitors to permit Vertex and Glaxo Wellcome to develop, manufacture and market Agenerase free of the risk of intellectual property claims by Searle. The terms of the license require us to pay Searle a royalty on net sales.

KISSEI PHARMACEUTICAL CO., LTD.

HIV PROTEASE INHIBITORS. In April 1993, we entered into a collaboration with Kissei covering the development of amprenavir, our HIV protease inhibitor. Kissei has exclusive rights to develop and commercialize amprenavir in Japan and will pay us a royalty on sales. Kissei also has an exclusive option to develop and commercialize the amprenavir prodrug VX-175 in Japan. We are responsible for the manufacture of bulk product for Kissei. Under the collaborative agreement, Kissei agreed to pay to us up to $20 million, comprised of $9.8 million of product research funding over three years, $7 million of development and commercialization milestone payments and a $3.2 million equity investment. From the inception of the agreement in April 1993 through December 31, 1999, $15.6 million has been recognized as revenue. In addition, $4 million has been recognized related to reimbursements of certain development costs. We have received the full amount of research funding specified under the agreement.

P38 MAP KINASE. In September 1997, we entered into a collaboration with Kissei to identify and develop compounds that target p38 MAP kinase, including VX-745. We will collaborate with Kissei in the development and commercialization of novel, orally active p38 MAP kinase inhibitors as drugs for the treatment of inflammatory and neurological diseases. Kissei will have the right to develop and commercialize these compounds in its licensed territories. Kissei has exclusive rights to p38 MAP kinase compounds 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. Under the terms of the agreement, Kissei agreed to pay us up to $22 million, comprised of a $4 million license payment paid in September 1997, $11 million of product research funding over three years and $7 million of development and commercialization milestone payments. Additionally, Kissei agreed to pay certain costs. From the inception of the agreement in September 1997 through December 31, 1999, $15 million

has been recognized as revenue. Kissei has the right to terminate the agreement without cause upon six months' notice.

BIOCHEM PHARMA INC.

In May 1996, we entered into a collaboration with BioChem for the development and commercialization in Canada of Incel, our cancer multidrug resistance inhibitor. From the inception of the agreement in May 1996 through December 31, 1998, we recognized $0.8 million as revenue. BioChem also paid certain costs of development of Incel in Canada. We have received the full amount of research funding specified under the agreement, and BioChem has no further license rights with respect to Incel.

AVENTIS S.A.

In September 1, 1999, we entered into an expanded agreement with HMR covering the development of HMR 3480/VX-740. HMR and Rhone-Poulenc Rorer merged to form Aventis in December 1999. Aventis has an exclusive worldwide license to develop, manufacture and market VX-740, as well as an exclusive option for all other compounds discovered as part of the research collaboration between Vertex and HMR that ended in 1997. Aventis will fund the development of VX-740. 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 agreed to pay us $20 million for prior research costs, and $62 million in milestone payments for successful development by Aventis of VX-740 in rheumatoid arthritis, the first targeted indication, as well as similar milestone payments for each additional indication. Aventis has the right to terminate this agreement without cause upon six months' written notice.

ELI LILLY & COMPANY

In June 1997, we entered into a collaboration with Lilly covering the development of novel small molecule compounds to treat hepatitis C infection. Vertex and Lilly will jointly manage the research, development, manufacturing and marketing of drug candidates emerging from the collaboration. We will have primary responsibility for drug design, process development and pre-commercial drug substance manufacturing, and Lilly will have primary responsibility for formulation, preclinical and clinical development and global marketing. We have the option to supply 100% of Lilly's commercial drug substance supply needs. We will receive royalties on future product sales, if any. If we exercise our commercial supply option, we will receive drug supply payments in addition to royalties on future product sales, if any. Under the terms of the agreement, Lilly will pay us up to $51 million, comprised of a $3 million payment paid in June 1997, $33 million of product research funding over six years and $15 million of development and commercialization milestone payments. From the inception of the agreement in June 1997 through December 31, 1999, $16.2 million has been recognized as revenue. Lilly has the right to terminate the agreement without cause upon six months' notice.

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 will have an equal role in management of neurophilin ligand research and product development. In North America, we will have manufacturing rights, and we will share equally with Schering AG in the marketing expenses and profits from commercialized compounds. In addition to having manufacturing rights in North America, we retain the option to manufacture bulk drug substance for sales and marketing in territories outside Europe, the Middle East and Africa. Schering AG will have the right to manufacture and market any commercialized compounds in Europe, the Middle East and Africa, and pay us a royalty on product sales. Under the terms of the agreement, Schering AG will pay us up to $88 million, comprised of $6 million paid upon signing in September 1998, $22 million of product research funding over five years and $60 million of development and commercialization milestone payments. From the inception of the agreement in August 1998 through December 31, 1999, $14 million has been recognized as revenue. After December 2000, Schering AG has the right to terminate without cause upon six months' written notice.

TAISHO PHARMACEUTICAL CO., LTD.

In November 1999, we entered into a collaboration with Taisho covering the discovery, development, and commercialization of caspase inhibitors for the treatment of cerebrovascular, cardiovascular and neurodegenerative diseases. Taisho will have an option to obtain marketing rights in Japan and certain Far East markets for any compounds arising from the collaboration. Under the agreement, Taisho agreed to pay us up to $43 million comprised of research funding, milestone payments, including $4.5 million for

prior research costs. These amounts are based on the development of two compounds. We will also receive royalties on future product sales, if any. In addition, Taisho will also pay for certain costs of developing compounds that emerge from the caspase research program. From inception of the agreement in November 1999 through December 31, 1999, $3.9 million has been recognized as

revenue.

INTELLECTUAL PROPERTY

We vigorously pursue patents to protect our intellectual property. As of February 25, 2000, we have 69 issued U.S. patents and have 108 pending U.S. patent applications covering proprietary technologies and intellectual property within our discovery and development programs, as well as foreign counterparts in many other countries.

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 using such compounds, we have several pending patent applications directed to proprietary elements of our drug discovery platform. These include patent applications on our SHAPES approach to NMR-based screening and on the use of a protein or a mutant of that protein to design inhibitors of other related proteins. We have also filed patent applications related to the three-dimensional atomic structures of targets of interest, the use of those structures to design drugs, classes of compounds that bind to a target of interest, and the interactions required between a compound and a target of interest.

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, advisors and collaborators to enter into confidentiality agreements that prohibit the disclosure of confidential information to anyone outside Vertex. These agreements require disclosure and assignment to Vertex of ideas, developments, discoveries and inventions made by employees, consultants, advisors and collaborators.

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 commercialized 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, pharmaceutical formulations containing amprenavir and methods of using of amprenavir to treat HIV infection or AIDS-related central nervous system disorders. Another issued United States patent covers processes for preparing synthetic intermediates useful in the synthesis of a class of compounds that includes amprenavir. We have a non-exclusive, worldwide license under certain Searle patent applications claiming HIV protease inhibitors. We also have applications pending in the United States and other countries claiming VX-175 and related compounds.

- an issued United States patent which covers a class of chemical compounds, pharmaceutical compositions containing such compounds, and methods of using those compounds to treat or prevent IMPDH-mediated diseases. The class of compounds covered by this patent includes VX-497.

- issued United States patents claiming Incel and structurally related compounds, VX-853 and structurally related compounds, and other compounds for treating multidrug resistance, as part of our MDR research and development program.

- issued United States patents covering the active metabolite of VX-740, several different classes of compounds useful as inhibitors of ICE, pharmaceutical compositions containing those compounds and methods of using those compounds to treat ICE-related diseases. We have also received a Notice of Allowance in an application claiming VX-740. These patents and applications also include a series of patents and applications purchased from Sanofi S.A., in July 1997. We also have a United States patent obtained from Sanofi S.A. that covers DNA sequences encoding ICE.

- an issued patent that covers a class of chemical compounds that includes VX-745, as well as applications claiming VX-745 specifically, compositions comprising those compounds and the use of those compounds to treat p38-related disorders, as part of our p38 MAP kinase research and development program.

- issued United States patents covering various classes of chemical compounds and their use to treat a wide variety of neurological disorders. One of these patents specifically covers the use of timcodar to treat neurological disorders, as part of our neurophilin research and development program.

- an issued United States patent covering an assay useful to evaluate potential inhibitors of hepatitis C protease. Other applications cover hepatitis C protease and hepatitis C helicase inhibitors and 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.

- filed applications claiming classes of caspase inhibitors and a caspase target discovered under our caspase inhibitors program.

- filed applications claiming inhibitors of JNK and ERK, in addition to p38 MAP kinase, as part of our kinase research programs.

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 uncertain. We also cannot be sure that we will be able to avoid infringing, and thus having to negotiate a license under, any patents issued to others, or that a license to such patents would be available on commercially acceptable terms, if at all. (See "Risk Factors--Our patents may not protect our products, and our products may infringe third-party patents".)

MANUFACTURING

We rely on third party manufacturers and collaborative partners to produce our compounds for preclinical and clinical purposes and may do so for commercial production of any compounds that are approved for marketing. Commercial manufacturing of Agenerase is being done by Glaxo Wellcome. We retain the option to manufacture a portion of Glaxo Wellcome's requirements for bulk drug substance for Agenerase and its prodrug. If we were to exercise that option, we would rely upon one or more contract manufacturers to manufacture the bulk drug substance on our behalf.

We have established a quality assurance program, including a set of standard operating procedures, 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 existing compounds 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 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 its potential products. However, in the event that 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 such 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 compounds 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 compounds for us. In addition, a contract manufacturer may develop process technology related to the manufacture of our compounds that the manufacturer owns either independently or jointly with us. This would increase our reliance on such manufacturer or require us to obtain a license from such 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 that 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 are currently marketing their drugs. In the field of HIV protease inhibition, Merck & Co., Inc., Abbott Laboratories, Inc., Hoffmann-La Roche, and Warner Lambert have other

HIV protease inhibitor drugs on the market. Many of our competitors have substantially greater financial, technical and human resources than ours and more experience 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.

As an initial step in the FDA regulatory approval process, preclinical studies are typically 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 would be available until such compounds progress to human clinical trials.

Clinical trials are typically 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 compound will be 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 preclinical testing and clinical trials are submitted to the FDA in a New Drug Application (NDA) for marketing approval. The process of completing 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, monies 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.

Even after initial FDA approval has been obtained, further studies, including post-marketing 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-marketing reporting to monitor the side effects of the drug. Results of post-marketing programs may limit or expand further marketing of the products. 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.

The Orphan Drug Act provides incentives to drug manufacturers to develop and manufacture drugs for the treatment of diseases or conditions that affect fewer than 200,000 individuals in the United States. Orphan drug status can also be sought for diseases or conditions that affect more than 200,000 individuals in the United States if the sponsor does not realistically anticipate its product becoming profitable from sales in the United States. Under the Orphan Drug Act, a manufacturer of a designated orphan product can seek tax benefits, and the holder of the first FDA approval of a designated orphan product will be granted a seven-year period of marketing exclusivity for that product for the orphan indication. While the marketing exclusivity of an orphan drug would prevent

other sponsors from obtaining approval of the same compound for the same indication, it would not prevent other types of drugs from being approved for the same use. We may apply for orphan drug status for certain indications of MDR in cancer.

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, 1999, we had 353 full-time employees, including 240 in research and development, 53 in support services and 60 in general and administrative functions. 31 of these employees were located at our U.K. research and development facility. Our scientific staff members (132 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.	48	Chairman, President and Chief Executive Officer
Richard H. Aldrich	45	Senior Vice President and Chief Business Officer
Vicki L. Sato, Ph.D.	51	Senior Vice President of Research and Development and Chief Scientific Officer; Chair of the Scientific Advisory Board
John J. Alam, M.D.	38	Vice President of Clinical Development
Iain P. M. Buchanan	46	Vice President of European Operations; Managing Director of Vertex Pharmaceuticals (Europe) Limited
Thomas G. Auchincloss, Jr.	38	Vice President of Finance and Treasurer
Barry M. Bloom	70	Director
Roger W. Brimblecombe, Ph.D., D.Sc.	69	Director
Donald R. Conklin	62	Director
Charles A. Sanders, M.D.	67	Director
Elaine S. Ullian	51	Director
Bruce I. Sachs	40	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. Boger is a founder of Vertex and was our President and Chief Scientific Officer from our inception in 1989 until May 1992, when he became President and Chief Executive Officer. In 1997, Dr. Boger became Chairman, President and Chief Executive Officer. 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 is also a Director of Millennium Pharmaceuticals, Inc. Dr. Boger holds a B.A. in chemistry and philosophy from Wesleyan University and M.S. and Ph.D. degrees in chemistry from Harvard University.

Mr. Aldrich served as Vice President of Business Development of Vertex from June 1989 to May 1992, when he became Vice President and Chief Business Officer. In December 1993, Mr. Aldrich was promoted to Senior Vice President and Chief Business Officer. He joined Vertex from Integrated Genetics, where he headed that company's business development group. Previously, he served as Program Executive at Biogen, Inc., where he coordinated worldwide commercial development of several biopharmaceuticals, and as Licensing Manager at Biogen S.A. in Geneva, Switzerland, where he managed European and Far Eastern licensing. Mr. Aldrich previously worked at the Boston Consulting Group, an international management consulting firm. Mr. Aldrich received a B.S. degree from Boston College and an M.B.A. from the Amos Tuck School of Business, Dartmouth College.

Dr. Sato joined Vertex in September 1992 as Vice President of Research and was appointed Senior Vice President of Research and Development in September 1994. 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 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. Sato is also a Director of Mitotix, Inc.

Dr. Alam has served as Vice President of Clinical Development since joining Vertex in October 1997. 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 Brigham and Women's Hospital in Boston. Dr. Alam holds an M.D. from Northwestern University Medical School and a B.S. in Chemical Engineering from the Massachusetts Institute of Technology.

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 since 1987. He previously held the position of Marketing Director of Biogen, Inc. 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. Auchincloss joined Vertex in October 1994 after serving as an investment banker at Bear, Stearns & Co. Inc. since 1988, most recently as Associate Director of the Corporate Finance Department. Prior to Bear Stearns, Mr. Auchincloss was a financial analyst for PaineWebber, Inc. Mr. Auchincloss holds a B.S. from Babson College and an M.B.A. from The Wharton School, University of Pennsylvania.

Dr. Bloom has served as our director since 1994. He was formerly with Pfizer Inc. as Executive Vice President of Research and Development from 1992 to 1993, and as Vice President from 1990 to 1992, and a director since 1973. He also serves as a director of Catalytica Pharmaceuticals, Cubist Pharmaceuticals Inc., Incyte Genomics Inc., Neurogen Corporation and MICROBIA, Inc.

Dr. Brimblecombe has served as our director since 1993. He has served as Chairman of Vanguard Medica Ltd. since 1991 and of Core Group plc since 1997. He also served as Non-Executive Chairman of Oxford Asymmetry International plc since 1997. 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 Ontogeny, Inc. and several other companies located in the United Kingdom.

Mr. Conklin has served as our director since 1994. He served as Vice President of Schering Plough from 1986 to 1996 and subsequently retired at the end of 1996. He also serves as a director of AlfaCell Inc. and BioTransplant 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. Has served on the boards of Merrill Lynch, Reynolds Metals and Morton International Inc. He is currently a director of Biopure Corporation, Genentech, Inc., Kendle International Inc., Magainin

Pharmaceuticals Inc., Pharmacopeia Inc., Scios, Inc., Staffmark Inc., Trimeris Inc.

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 President and Chief Executive Officer of Faulkner Hospital. She also serves as a director of Hologics Inc.

Mr. Sachs has served as our director since 1998. He currently serves as a General Partner at Charles River Ventures. From 1998 to 1999, he served as Executive Vice President and General Manager of Ascend Communications, Inc. From 1997 until 1998, Mr. Sachs served as President and CEO of Stratus Computer, Inc. From 1995 to 1997, he served as Executive Vice President and General Manager of the Internet Telecom Business Group at Bay Networks, Inc. From 1993 to 1995, he served as Chief Executive Officer at Xylogics, Inc. Mr. Sachs also serves as a director of Media 100 Inc.

SCIENTIFIC ADVISORY BOARD

Vertex's Scientific Advisory Board consists of individuals with demonstrated expertise in various fields who advise us concerning long-term scientific planning, research and development. The Scientific Advisory

Board also evaluates our research programs, recommends personnel to us and advises us on technological matters. The members of the Scientific Advisory Board, which is chaired by Dr. Vicki L. Sato, are:

Vicki L. Sato, Ph.D.....	Senior Vice President of Research and Development and Chief Scientific Officer, Vertex Pharmaceuticals Incorporated.
Steven J. Burakoff, M.D.....	Chair, Department of Pediatric Oncology, Dana-Farber Cancer Institute; Margaret M. Dyson Professor of Pediatrics, Harvard Medical School.
Eugene H. Cordes, Ph.D.....	Professor of Pharmacy and Chemistry, University of Michigan at Ann Arbor.
Jerome E. Groopman, M.D.....	Chief, Division of Experimental Medicine, Beth Israel Deaconess Medical Center; Recanati Chair of Medicine and Professor of Medicine, Harvard Medical School.
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....	Dean of the Faculty of Arts and Sciences and Amory Houghton Professor of Chemistry and Biochemistry, Harvard University.
Robert T. Schooley, M.D.....	Tim Gill Professor of Medicine and Head of Infectious Disease, University of Colorado Health Sciences Center.

Other than 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 HOW SUCCESSFUL AGENERASE WILL BE IN THE MARKET.

Agenerase was launched less than a year ago and is currently awaiting marketing approval by regulatory authorities in a number of major markets, including the EU. It is too early to predict the extent to which Agenerase will be successful in the market. Four other HIV protease inhibitors are on the market, as well as a number of other products for the treatment of HIV infection and AIDS. In

addition, other drugs are still in development by our competitors, which may have more efficacy, fewer side effects, easier administration and/or lower costs than Agenerase. HIV has been shown to develop resistance to antiviral drugs, including currently marketed HIV protease inhibitors. We cannot be sure whether such disease resistance or other factors may limit the efficacy of Agenerase. Although we co-promote Agenerase in the U.S. and intend to co-promote it in Europe, most of the marketing and sales efforts are being made by Glaxo Wellcome, and we will have little control over the success of those efforts. Glaxo Wellcome has the right to terminate its agreement with us without cause upon twelve months' notice.

WE DO NOT KNOW WHETHER DEVELOPMENT OF OUR DRUG PIPELINE WILL BE SUCCESSFUL.

The products that we are pursuing will require extensive additional development, testing and investment, as well as regulatory approvals, prior to commercialization. We cannot be sure whether our product development efforts will be successful, that required regulatory approvals will be obtained or that any products, if introduced, will 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. We cannot be sure that clinical trials of products under development will demonstrate the safety and efficacy of such products or will result in a marketable product. 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 our company. In addition, the FDA may require additional clinical trials, which could result in increased costs and significant development delays. Commercial formulation and manufacturing processes have yet to be developed for our drug candidates other than Agenerase. We or our collaborators may encounter difficulties in manufacturing process development and formulation activities that could result in delays in clinical trials, regulatory submissions, regulatory approvals, and commercialization of our products, or cause negative financial and competitive consequences.

DEVELOPMENT PROGRESS MAY BE SLOWED BY CLINICAL TRIAL DELAYS.

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 planned patient enrollment in clinical trials may result in increased costs, program delays or both, which could have a material adverse effect on our company. We cannot be certain that if clinical trials are completed, we will be able to submit an NDA or that any such application will be reviewed and approved by the FDA in a timely manner, if at all.

WE MAY NOT OBTAIN REGULATORY APPROVAL FOR OUR PRODUCTS ON A TIMELY BASIS, OR AT ALL.

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 takes several years or longer and may vary substantially based upon the type, complexity and novelty of the pharmaceutical product. Data obtained from preclinical 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 clinical trials or marketing of our products, if any are developed and submitted for approval, for a considerable period of time, to impose costly procedures upon our activities and to 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 compound may be marketed.

OUR PRODUCTS, EVEN IF APPROVED BY THE FDA OR FOREIGN REGULATORY AUTHORITIES, MAY NOT BE ACCEPTED BY PHYSICIANS, INSURERS OR PATIENTS.

If any of our products after receiving FDA or other foreign regulatory approval fails to achieve market acceptance, our ability to become profitable in the future could be adversely affected. We believe that market acceptance depends on our ability to provide acceptable evidence of safety, efficacy and cost-effectiveness, among other factors.

WE DEPEND ON COLLABORATIVE PARTNERS FOR THE DEVELOPMENT AND COMMERCIALIZATION OF OUR

PRODUCTS.

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 have rights to control the planning and execution of product development and clinical programs. The corporate 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 our corporate collaborators were to terminate its relationship with us, it could have a material adverse effect on our ability 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 develop and commercialize our products in the future. We cannot be certain that we will be able to establish acceptable collaborative arrangements in the future or that such collaborative arrangements will be successful.

IT IS POSSIBLE THAT WE MAY LOSE OUR TECHNOLOGICAL ADVANTAGE BECAUSE PHARMACEUTICAL RESEARCH TECHNOLOGIES CHANGE RAPIDLY.

The pharmaceutical research field is characterized by rapid technological progress and intense competition. Further, we believe that interest in the application of structure-based drug design and related technologies may continue and may accelerate as the technologies 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. We cannot be certain that we will be able to access the same technologies at an acceptable price, or at all.

OUR COMPETITORS MAY BRING SUPERIOR PRODUCTS TO MARKET OR MAY BRING THEIR PRODUCTS TO MARKET BEFORE WE DO.

We do not know whether our products in development will 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. In order to compete successfully in these areas, we must demonstrate improved safety, efficacy, ease of manufacturing and market acceptance over competing products which have received regulatory approval and are currently marketed. Many of our competitors 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, only highly qualified and trained scientists 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. We face intense competition for these professionals from our competitors, our collaborative partners and other companies throughout our industry. Our 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.

IF WE FAIL TO MANAGE OUR GROWTH EFFECTIVELY, OUR BUSINESS MAY SUFFER.

Our ability to commercialize our products, achieve our expansion objectives and manage our growth effectively depends on a variety of factors. Key factors include our ability to develop products internally, enter into strategic partnerships with collaborators, attract and retain skilled employees and effectively expand our internal organization to accommodate anticipated growth. If we are unable to manage growth effectively, there could be a material adverse effect on our business, financial condition and results of operations.

WE DEPEND ON THIRD PARTY MANUFACTURERS.

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 currently do not have the capacity to manufacture drugs in large-scale quantities. We depend on third party manufacturers or collaborative partners for the production of our compounds for preclinical research, clinical trial purposes

and commercial production. If we are not able to obtain contract manufacturing on commercially reasonable terms, we may not be able to conduct or complete clinical trials or commercialize our products as planned. We have no experience in manufacturing pharmaceutical or other products, and we do not know whether we will be able to develop such capabilities. Some of our current corporate partners have manufacturing rights with respect to our products under development. If those partners do not either supply products to us promptly and on acceptable terms or transfer the manufacturing technology to us, we may not be able to conduct our development programs and commercialize any resulting products in a timely and efficient manner.

OUR PATENTS MAY NOT PROTECT OUR PRODUCTS, AND OUR PRODUCTS MAY INFRINGE THIRD-PARTY PATENTS.

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. We are currently contesting a suit filed by Chiron Corporation claiming infringement of three U.S. patents issued to Chiron. Although we believe that the ultimate outcome of the action will not have a material impact on our consolidated financial position, defense and prosecution of patent claims, including those at issue in the Chiron case, 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 the affected products, any of which could have a material adverse effect on our company.

WE EXPECT TO INCUR FUTURE LOSSES AND CANNOT BE CERTAIN THAT WE WILL BECOME A PROFITABLE COMPANY.

We have incurred significant operating losses each year since our inception and expect to incur a significant operating loss in 2000. We believe that operating losses will continue beyond 2000, even if significant royalties are realized on Agenerase sales, because we are planning to make significant investments in research and development, and will incur significant selling, general, and administrative expenses for our other 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 be certain that we will ever achieve and sustain profitability.

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:

- Agenerase royalty revenue;

- future product sales to the extent that we market products directly;

- future payments under our collaborative agreements;

- existing cash reserves, together with interest earned on those reserves;

- facilities and equipment financing; and

- additional collaborative agreements.

If funds from these sources are not sufficient to fund our activities, 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 which, among other things, restrict

our ability to pay dividends and interest (although we do not intend to pay dividends for the foreseeable future). 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. We cannot know whether additional financing will be available on acceptable terms, if at all.

GOVERNMENT AND PRIVATE INSURANCE PLANS MAY NOT PAY FOR OUR PRODUCTS.

The success of our products in the United States and other significant markets will depend, in part, upon the extent to which a consumer will be able to obtain reimbursement for the cost of such products from government health administration authorities, third-party payors and other organizations. We cannot always determine in advance the reimbursement status of newly approved therapeutic products. Even if a product is approved for marketing, we cannot be sure that adequate reimbursement will be available. Also, future legislation or regulation relating to the health care industry or third-party coverage and reimbursement may affect our business. In particular, legislation or regulation limiting consumers' reimbursement rights could have a material adverse effect on our company.

OUR SALES AND MARKETING EXPERIENCE IS LIMITED.

We currently 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. In the territories where we retain marketing and co-promotion rights, we may not be able to develop successfully our own sales and marketing force. We do not know whether we will be able to enter into marketing and sales agreements with others on acceptable terms, if at all. 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. To the extent that our collaborative partners have commercial rights to our products, any revenues we receive from those

products will depend on the sales and marketing efforts of others, and we do not know how successful those efforts will be.

WE MAY INCUR PRODUCT LIABILITY EXPENSES.

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 do not know whether we will be able to maintain our existing levels of product liability insurance or be able to obtain or maintain any additional insurance we may need in the future on acceptable terms. Nor can we be sure that our existing insurance or any such additional insurance will provide adequate coverage against potential liabilities.

SOME OF OUR OPERATIONS INVOLVE HAZARDOUS MATERIALS, WHICH COULD SUBJECT US TO SIGNIFICANT LIABILITY.

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.

EVENTS WITH RESPECT TO OUR SHARE CAPITAL COULD CAUSE THE PRICE OF OUR COMMON STOCK TO DECLINE.

Sales of substantial amounts of our common stock in the open market, or the availability of such shares for sale, could adversely affect the price of our common stock. As of December 31, 1999, we had 25,685,364 shares of common stock outstanding, excluding shares reserved for issuance upon the exercise of outstanding stock options, employee stock purchase and 401(k) plans. We have granted stock options to purchase 6,744,000 shares of our common stock at a weighted average exercise price of approximately $23.50 per share (subject to adjustment in certain circumstances). Of this total, 3,440,000 are currently exercisable at an average exercise price of approximately $20.57 per share. The shares of our common stock that may be issued under the options are either currently registered with the SEC, or will be registered with the SEC before the shares are purchased by the holders of the options.

WE HAVE ADOPTED ANTI-TAKEOVER PROVISIONS THAT MAY DISCOURAGE A CHANGE OF CONTROL.

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 (a "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.

ADOPTION OF SAB 101 MAY INCREASE OUR REPORTED NET LOSSES.

In December 1999, the SEC issued Staff Accounting Bulletin 101, "Revenue Recognition in Financial Statements" (SAB 101), which provides guidance related to revenue recognition and disclosure. We plan to

adopt SAB 101 in the first quarter of 2000, and we are currently determining what impact this will have on our financial statements. We cannot be certain that our adoption of SAB 101 will not materially increase our reported net losses in the quarter ended March 31, 2000.

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 last 12 months our common stock has traded between $19.38 and $82.56. 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. Fluctuations in the trading price of our common stock will affect the trading price of the notes. The future market price of our securities could be significantly and adversely affected by factors such as:

- announcements of results of clinical trials;

- 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;

- patent or proprietary rights; and

- developments and market conditions for pharmaceutical and biotechnology stocks, in general.

ITEM 2. PROPERTIES

PROPERTIES

We lease an aggregate of approximately 179,000 square feet of laboratory and office space in seven facilities in Cambridge, Massachusetts. The leases have expiration dates ranging from December 2000 to 2009. 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. We have also entered into an agreement to lease an additional 192,000 square feet of laboratory and office space presently under construction adjacent to our headquarters. That lease will expire in 2010 with the option to extend the lease for up to two additional terms, ending in 2030.

We lease approximately 21,000 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

Chiron Corporation ("Chiron") filed suit on July 30, 1998 against Vertex and Eli Lilly and Company in the United States District Court for the Northern District of California, alleging infringement by the defendants of three U.S. patents issued to Chiron. The infringement action relates to research activities by the defendants in the hepatitis C viral protease field and the alleged use of inventions claimed by Chiron in connection with that research. Chiron has requested damages in an unspecified amount, as well as an order permanently enjoining the defendants from unlicensed use of the claimed Chiron inventions. During 1999, Chiron requested and was granted a reexamination by the U.S. Patent and Trademark Office of all three of the patents in suit. Chiron also requested and, over the opposition of Vertex and Lilly, was granted a stay in the infrignement lawsuit, pending the outcome of the patent reexamination. While the length of the stay, the outcome of the reexamination, the effect of that outcome on the lawsuit and the final outcome of the

lawsuit cannot be determined, Vertex maintains that the plaintiff's claims are without merit and intends to defend the lawsuit, if and when it resumes, vigorously.

ITEM 4. SUBMISSION OF MATTERS TO SECURITY HOLDERS

There were no matters submitted to a vote of security holders during the fourth quarter of the fiscal year ended December 31, 1999.

PART II

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

Our common stock trades on the Nasdaq National Market ("Nasdaq") under the symbol "VRTX." The following table sets forth the high, low and last sale prices of each quarter for the common stock as reported on the Nasdaq:

YEAR ENDED DECEMBER 31, 1998:	HIGH	LOW	CLOSE
First quarter	$40 3/8	$31 1/4	$31 15/16
Second quarter	33 7/8	21 1/2	22 1/2
Third quarter	27 7/8	14 1/2	23
Fourth quarter	30	20	29 3/4
YEAR ENDED DECEMBER 31, 1999:			
First quarter	$32 1/2	$22 1/2	$25 1/4
Second quarter	26 3/8	19 3/8	24 1/8
Third quarter	34 13/16	22 1/8	31 1/16
Fourth quarter	37 1/4	23 3/8	35
YEAR ENDED DECEMBER 31, 2000:			
First quarter (through March 3, 2000)	$82 9/16	$32 1/2	--

The last sale price of the common stock on February 28, 2000, as reported by Nasdaq, was $62.00 per share. As of February 28, 2000, there were 213 holders of record of the common stock (approximately 6,500 beneficial holders).

Vertex has never declared or paid any cash dividends on its Common Stock and currently expects that future earnings, if any, will be retained for use in its business.

RECENT SALES OF UNREGISTERED SECURITIES

None

ITEM 6. SELECTED CONSOLIDATED FINANCIAL DATA

The following selected consolidated financial data for each of the five years in the period ended December 31, 1999 are derived from our Consolidated Financial Statements. This data should be read in

conjunction with our audited financial statements and related notes, and "Management's Discussion and Analysis of Financial Condition and Results of Operations."

	YEAR ENDED DECEMBER 31,				
	1999	1998	1997	1996	1995
	(IN THOUSANDS, EXCEPT PER SHARE AMOUNTS)				
Consolidated Statement of Operations Data:					
Revenues:					
Royalties and product sales	$ 8,053	--	--	--	--
Collaborative and other research and development revenues	42,507	$ 29,055	$ 29,926	$ 13,341	$ 22,081
Investment income	11,088	15,343	13,873	5,257	5,453
Total revenues	61,648	44,398	43,799	18,598	27,534
Costs and expenses:					
Royalties and product costs	2,925	--	--	--	--
Research and development	72,180	58,668	51,624	35,212	41,512
General and administrative	26,131	18,135	11,430	7,929	7,069
License payment	--	--	--	15,000	--
Loss in equity affiliate	724	--	--	--	--
Interest	654	681	576	462	481
Total costs and expenses	102,614	77,484	63,630	58,603	49,062
Net loss	$ (40,966)	$(33,086)	$(19,831)	$(40,005)	$(21,528)
Basic and diluted net loss per common share	$ (1.61)	$ (1.31)	$ (0.82)	$ (2.13)	$ (1.25)
Basic and diluted weighted average number of common shares outstanding	25,518	25,299	24,264	18,798	17,231

	DECEMBER 31,				
	1999	1998	1997	1996	1995
Consolidated Balance Sheet Data:					
Cash, cash equivalents and investments	$ 187,802	$ 245,652	$ 279,671	$130,359	$ 86,978
Total assets	232,445	266,346	295,604	143,499	98,981
Obligations under capital leases and debt, excluding current portion	4,693	7,032	5,905	5,617	4,912
Accumulated deficit	(190,827)	(149,861)	(116,775)	(96,944)	(56,939)
Total stockholders' equity	209,234	246,212	276,001	130,826	85,272

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

THIS DISCUSSION CONTAINS FORWARD-LOOKING STATEMENTS, WHICH ARE SUBJECT TO CERTAIN RISKS AND UNCERTAINTIES THAT CAN CAUSE ACTUAL RESULTS TO DIFFER MATERIALLY FROM THOSE DESCRIBED. FACTORS THAT MAY CAUSE SUCH DIFFERENCES INCLUDE BUT ARE NOT LIMITED TO THOSE DESCRIBED IN THE SECTION ENTITLED "RISK FACTORS." READERS ARE CAUTIONED NOT TO PLACE UNDUE RELIANCE ON THESE FORWARD-LOOKING STATEMENTS, WHICH SPEAK ONLY AS OF THE DATE HEREOF. WE UNDERTAKE NO OBLIGATION TO PUBLICLY UPDATE OR REVISE THESE FORWARD-LOOKING STATEMENTS TO REFLECT EVENTS OR CIRCUMSTANCES AFTER THE DATE HEREOF.

We discover, develop and market small molecule drugs that address major medical needs. We have seven drug candidates in clinical development to treat viral diseases, inflammation, cancer, autoimmune

diseases and neurological disorders. We have created our pipeline using a proprietary approach, information-driven drug design, that

integrates multiple technologies in biology, chemistry and biophysics aimed at increasing the speed and success rate of drug discovery.

Our first approved product is Agenerase-TM- (amprenavir), an HIV protease inhibitor, which we co-promote with Glaxo Wellcome plc ("Glaxo Wellcome"). We earned a royalty from Glaxo Wellcome from sales of Agenerase in 1999. Agenerase received U.S. Food and Drug Administration ("FDA") approval through an expedited review process for the treatment of HIV infection. Agenerase has also received approval in other countries, including Japan where the drug is sold under the trade name Prozei-TM-. Approval of Agenerase is pending in other countries, including the European Union, where the drug is being made available through early access programs.

We have incurred operating losses since our inception and expect to incur a loss in 2000. We believe that operating losses will continue beyond 2000, even if significant royalties are realized on Agenerase sales, as we are planning to make significant investments in research and development for our other potential products. We expect that losses will fluctuate from year to year and that such fluctuations may be substantial.

RESULTS OF OPERATIONS

YEAR ENDED DECEMBER 31, 1999 COMPARED WITH YEAR ENDED DECEMBER 31, 1998

The net loss for 1999 was $40,966,000 or $1.61 per share compared to $33,086,000 or $1.31 per share in 1998.

Our total revenues increased to $61,648,000 in 1999 from $44,398,000 in 1998. In 1999, royalty and product sales revenue was $8,053,000, collaborative and other research and development revenue was $42,507,000, and investment income was $11,088,000. Revenue in 1998 consisted of $29,055,000 in collaborative and other research and development and $15,343,000 in investment income.

Royalties and product sales consist of Agenerase royalty revenue of $7,461,000 from Glaxo Wellcome as well as initial sales of commercial drug substance to Kissei in Japan. Agenerase royalty revenue from Glaxo Wellcome was recognized for the first time in 1999 and is based upon worldwide net sales of Agenerase as provided by Glaxo Wellcome. These sales reflect prescriptions as well as initial trade stocking which is expected to be consistent with demand.

The growth in collaborative and other research and development revenue in 1999, as compared with 1998, is largely due to new collaborative agreements and larger milestone payments during the year. In April of 1999, we earned a $5,000,000 milestone payment from Glaxo Wellcome for U.S. FDA approval of Agenerase. We recorded $15,000,000 in collaborative revenue from Aventis S.A. ("Aventis"), formerly Hoechst Marion Roussel Deutschland GmbH, in October of 1999, upon entering into an expanded agreement covering the development of VX-740, an orally active inhibitor of interleukin-1 beta converting enzyme (ICE). This consisted of a $10,000,000 payment for prior research costs and a $5,000,000 milestone payment for entering Phase II clinical trials. In November 1999, we agreed with Taisho Pharmaceutical Co., Ltd. of Japan to collaborate to discover, develop and commercialize caspase inhibitors for the treatment of cerebrovascular, cardiovascular and neurodegenerative diseases. In connection with this contract, we recognized $3,000,000 for prior research costs and approximately $900,000 in product research funding. Included in 1998 collaborative and other research and development revenue is a $6,000,000 payment from Schering A.G. earned in connection with the signing of a new collaborative agreement for our neurophilins ligand program and a $3,000,000 milestone payment from Glaxo Wellcome for the NDA filing for Agenerase. Research funding decreased from all collaborative partners, by approximately $1,380,000 in 1999 primarily because the research funding requirements under the Glaxo Wellcome agreement ended on December 31, 1998.

Interest income decreased in 1999 compared with 1998 due to a lower level of cash and investments throughout the year as well as lower yields earned on investment securities.

Total costs and expenses increased to $102,614,000 in 1999 from $77,484,000 in 1998. Royalties and product costs of $2,925,000 in 1999 consist of royalty payments to G.D. Searle & Co. ("Searle") and the cost of commercial drug substance sold to Kissei. Under the terms of the 1996 license agreement between Glaxo Wellcome, Searle and us, we agreed to pay Searle a royalty on the sales of Agenerase.

Research and development expenses increased to $72,180,000 in 1999 from $58,668,000 in 1998 principally due to the continued expansion of our research and development operations. Our UK subsidiary expanded from a business development operation to include scientific research and development staff in the second half of 1998. Related to our expansion were increases in facilities expenses, lab supplies and increased equipment depreciation. Additionally, there was an increase in development expenses due to the commencement of clinical trials in the second half of 1998 and the increase in other development activities associated with our

IMPDH inhibitor, VX-497, for psoriasis and hepatitis C, our neurophilins drug candidate, timcodar, for diabetic neuropathy, and our p38 MAP kinase inhibitor, VX-745, for inflammatory diseases. We anticipate research and development expenses to continue to increase as personnel are added and additional research and development activities are expanded to accommodate our existing collaborations and additional commitments we may undertake in the future.

Sales, general and administrative expenses increased to $26,131,000 in 1999 from $18,135,000 in 1998 primarily as a result of increased personnel and professional expenses associated with the marketing of Agenerase-TM- and related corporate advertising activities. Legal and patent expenses increased as we continue to protect our intellectual property and contest a suit filed by Chiron Corporation ("Chiron") claiming infringement of three U.S. patents issued to Chiron. While the final outcome of the litigation with Chiron cannot be determined, we believe, based on information currently available, that the ultimate outcome of the action will not have a material impact on our consolidated financial position. We expect sales, general and administrative expenses to continue to increase as we continue to grow and enter our first full year of Agenerase sales.

In February 1999, we restructured our investment in Altus Biologics ("Altus"), which was a wholly owned subsidiary. As part of the transaction, we provided Altus $3,000,000 of cash and surrendered our shares in Altus preferred stock in exchange for two new classes of preferred stock and warrants. Altus now operates independently from us. At December 31, 1999, we had a 29.5% equity investment in Altus of approximately $2,276,000. For the year ending December 31, 1999, we recorded $724,000 as our share of Altus' losses. Altus is expected to incur additional losses in 2000 and we will record our proportionate share of losses against the investment balance.

YEAR ENDED DECEMBER 31, 1998 COMPARED WITH YEAR ENDED DECEMBER 31, 1997

The net loss for 1998 was $33,086,000 or $1.31 per share compared to $19,831,000 or $0.82 per share in 1997.

Our total revenues were $44,398,000 in 1998 as compared to $43,799,000 in 1997. In 1998, revenues consisted of $27,939,000 under our collaborative agreements, $15,343,000 in investment income and $1,116,000 in government grants and other income. Collaborative revenue in 1998 included a $6,000,000 payment from Schering AG associated with the signing of a collaborative agreement for our neurophilin ligand program and $4,000,000 of research funding from Schering AG, a $2,000,000 milestone payment from Kissei for the acceptance of VX-745 as the lead development candidate for our p38 MAP kinase program, and a $3,000,000 milestone payment from Glaxo Wellcome for the NDA filing of Agenerase-TM-. Other collaborative revenue in 1998 included $3,738,000 from Kissei, $3,457,000 from Glaxo Wellcome, $5,193,000 from Eli Lilly and Company ("Lilly") and $551,000 from others. In 1997, revenues consisted of $27,703,000 under our collaborative agreements, $13,873,000 in investment income, and $2,223,000 in government grants and other income. Revenue from collaborative agreements in 1997 consisted of

$3,275,000 from Glaxo Wellcome, $8,660,000 from HMR, $9,810,000 from Kissei, $5,694,000 from Lilly and $264,000 from others.

Total costs and expenses increased to $77,484,000 in 1998 from $63,630,000 in 1997. Research and development expenses increased to $58,668,000 in 1998 from $51,624,000 in 1997. We increased research staffing, including opening a research site in the U.K., to fully staff a higher number of discovery programs. In addition, we expanded our development infrastructure. General and administrative expenses increased in 1998 to $18,135,000 from $11,430,000 in 1997 primarily as a result of headcount growth to handle the administrative requirements of our growing research and development operation, legal expenses associated with expansion of our intellectual property position and marketing expenses associated with the anticipated launch of Agenerase-TM- and our co-promotion preparations. Interest expense increased in 1998 to $681,000 from $576,000 in 1997 due to higher levels equipment financing during 1998.

LIQUIDITY AND CAPITAL RESOURCES

Our operations have been funded principally through strategic collaborative agreements, public offerings and private placements of our equity securities, equipment financing, government grants and investment income. With the approval and launch of Agenerase, we began receiving product royalty revenues in 1999. We have continued to increase and advance the products in our research and development pipeline. Consequently, we expect to incur increased research and development and related supporting expenses and are likely to continue experiencing losses on a quarterly and annual basis as we continue to develop existing and future compounds and to conduct clinical trials of potential drugs. We also expect to incur substantial administrative and commercialization expenditures in the future and additional expenses related to the filing, prosecution, defense and enforcement of patent and other intellectual property rights.

We expect to finance these substantial cash needs with royalties from the sales of Agenerase, our existing cash and investments of approximately $187,802,000 at December 31, 1999 and investment income earned thereon, future payments under our existing and

new collaborative agreements, facilities and equipment financing and to the extent available, by raising additional funds through public offerings or private placements of securities or other methods of financing. There can be no assurance that such financing will be available on acceptable terms, if at all. In December of 1999, we obtained a $20,000,000 line of credit. The purpose of the line of credit is to fund equipment and leasehold improvement expenditures in connection with the expansion of facilities. No amounts were outstanding as of December 31, 1999. We believe that our existing cash and investments should be sufficient to meet our anticipated requirements for at least the next two years.

Our aggregate cash and investments decreased in 1999 by $57,850,000 to $187,802,000 at December 31, 1999. Cash used by operations in 1999, principally to fund research and development activities, was $31,806,000. Property and equipment expenditures were $16,210,000 in 1999, $7,901,000 in 1998 and $6,020,000 in 1997. The expenditures were principally for research equipment and leasehold improvements to new and existing facilities. In 1999, we entered in new operating lease agreements for additional space and facilities in the U.S. In connection with the new leases, we were required to provide security deposits in the form of stand-by letters of credit in the amount of $7,472,000, which is reflected in the increase of restricted cash. We intend to make significant investments in equipment and leasehold improvements in the future to support research and development activities. At December 31, 1999, we leased approximately 179,000 square feet of office and research space in the U.S. and 21,000 square feet in the U.K. We have also entered into an agreement to lease an additional 192,000 square feet of new facilities presently under construction. The leases have expiration dates ranging from December 2000 to 2009--subject to extension for additional terms ending in 2015. In addition, our liability for capitalized equipment lease obligations and other equipment financing totaled approximately $7,059,000 at December 31, 1999. During 1999, we repaid $2,725,000 of our lease obligations.

During 1999, we entered into two new collaborative agreements. In September 1999, we entered into an expanded agreement with Aventis covering the development of VX-740, an orally active inhibitor of interleukin-1 beta converting enzyme (ICE). Under the terms of the agreement Aventis agreed to pay us $20,000,000 for prior research costs, up to $62,000,000 of development and commercialization milestone payments, and royalties on sales, if any.

In November 1999, we entered into an agreement with Taisho Pharmaceutical Co., LTD ("Taisho") to collaborate on the discovery, development and commercialization of caspase inhibitors for the treatment of cerebrovascular, cardiovascular and neurdegenerative diseases. Under the agreement, Taisho agreed to pay us up to $43,000,000 in pre-commercial payments, comprised of research funding, milestone payments and $4,500,000 in payments for prior research costs. These amounts are based on the development of two compounds. In addition, Taisho will also pay for certain of the costs of developing compounds that emerge from the caspase research program.

RECENT ACCOUNTING PRONOUNCEMENTS

In December 1999, the Securities and Exchange Commission issued Staff Accounting Bulletin No. 101, "Revenue Recognition in Financial Statements," ("SAB 101") which is effective no later than the quarter ending March 31, 2000. SAB 101 clarifies the Securities and Exchange Commission's views related to revenue recognition and disclosure. We will adopt SAB 101 in the first quarter of 2000 and are presently determining the effect it will have on our financial statements, although the amount could be material to net financial results.

In June 1998, the Financial Accounting Standards Board issued SFAS 133, "Accounting for Derivative Instruments and Hedging Activities." The effective date of this statement was deferred to fiscal years beginning after June 15, 2000. This statement requires the recognition of all derivative instruments as either assets or liabilities in the statement of financial position and the measurement of those instruments at fair value. The Company does not expect the adoption of this statement to have a material impact on its financial statements.

YEAR 2000

Beginning in late 1998, we conducted a program to address the impact of the Year 2000 on the processing of date sensitive information by our computer systems and software ("IT Systems"), embedded systems in our non-computer equipment ("Non-IT Systems") and relationships with certain third parties.

In the first stage of the program, we determined which IT Systems, Non-IT Systems and third party relationships were critical to our business.

Assessment, testing, and remediation of our critical IT Systems and Non-IT Systems for Year 2000 compliance were completed by mid-November, 1999. Some non-critical Non-IT Systems were non-compliant and, because of the age of those systems or other factors, could not be made compliant. We formulated contingency plans for each of those systems.

We also contacted third parties that provide goods, services and information that were deemed critical to our business. Based on our review of the responses and Year 2000 website statements of those entities, we assessed our Year 2000 compliance. We formulated contingency plans for the services provided by third parties that were found to be non-compliant, or where we were unable to determine whether a third party was compliant. However, it has not proven necessary to implement any of the contingency plans, since there have been no significant Year 2000 disruptions to the goods, services and information provided by critical third parties.

We used both internal and external resources to conduct our Year 2000 program. The total costs, both out-of pocket and internal, of our Year 2000 program were not material. Other IT Systems projects were not significantly deferred as a result of our Year 2000 program, because we were able to integrate much of

our Year 2000 assessment and remediation efforts into our routine maintenance and upgrade programs. We funded the Year 2000 costs through available cash and have no remaining costs.

We have not to date experienced any significant problems with our own IT and Non-IT Systems or third party relationships as a result of the January 1, 2000 date change. There has been no material adverse effect on our results of operations as a result of Year 2000 computer problems or the assessment, testing, and remediation program.

ITEM 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

Vertex owns financial instruments that are sensitive to market risks as part of its investment portfolio. 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 own 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 and money market instruments. These investments are denominated in U.S. dollars. These bonds are subject to interest rate risk, and could decline in value if interest rates fluctuate. Vertex's investment portfolio includes only marketable securities with active secondary or resale markets to help ensure portfolio liquidity and Vertex has implemented guidelines limiting the duration of investments. 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 Item 8 is contained on pages F-1 through F-21 of this Report.

ITEM 9. CHANGES IN AND DISAGREEMENTS WITH ACCOUNTANTS ON ACCOUNTING AND FINANCIAL DISCLOSURE

Not applicable.

PART III

ITEM 10. DIRECTORS AND EXECUTIVE OFFICERS OF THE REGISTRANT

The information regarding directors required by this Item is included in the definitive Proxy Statement for Vertex's 2000 Annual Meeting of Stockholders, to be filed with the Commission on or about April 11, 2000 (the "2000 Proxy Statement"), under "Election of Directors" and is incorporated herein by reference. The information regarding executive officers required by this Item is included in Part I of this Annual Report on Form 10-K.

ITEM 11. EXECUTIVE COMPENSATION

The information required by this Item is included in the 2000 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 2000 Proxy Statement, which shall not be deemed incorporated herein).

ITEM 12. SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT

The information required by this Item is included in the 2000 Proxy Statement under "Security Ownership of Certain Beneficial Owners and Management" and is incorporated herein by reference.

ITEM 13. CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS

Not applicable.

PART IV

ITEM 14. 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
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. 0-19319) 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. 0-19319) 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. 0-19319) and incorporated herein by reference).
3.4	By-laws of Vertex (filed as Exhibit 3.2 to Vertex's Registration Statement on Form S-1 (Registration No. 33-43874) 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. 0-19319) and incorporated herein by reference).
10.1	1991 Stock Option Plan, as amended and restated as of September 14, 1999 (filed herewith).*
10.2	1994 Stock and Option Plan, as amended and restated as of September 14, 1999 (filed herewith).*
10.3	1996 Stock and Option Plan, as amended and restated as of September 14, 1999 (filed herewith).*
10.4	Non-Competition and Stock Repurchase Agreement between Vertex and Joshua Boger, dated April 20, 1989 (filed as Exhibit 10.2 to Vertex's Registration Statement on Form S-1 (Registration No. 33-40966) or amendments thereto and incorporated herein by reference).*
10.5	Form of Employee Stock Purchase Agreement (filed as Exhibit 10.3 to Vertex's Registration Statement on Form S-1 (Registration No. 33-40966) or amendments thereto and incorporated herein by reference).*
10.6	Form of Employee Non-Disclosure and Inventions Agreement (filed as Exhibit 10.4 to Vertex's Registration Statement on Form S-1 (Registration No. 33-40966) or amendments thereto and incorporated herein by reference).
10.7	Form of Executive Employment Agreement executed by Richard H. Aldrich, Joshua S. Boger, and Vicki L. Sato (filed as Exhibit 10.6 to Vertex's 1994 Annual Report on Form 10-K (File No. 0-19319) and incorporated herein by reference).*

EXHIBIT NUMBER	EXHIBIT DESCRIPTION
10.9	Lease dated October 1, 1992 between C. Vincent Vappi and Vertex relating to the premises at 40 Allston Street, 618 Putnam Street, 228 Sidney Street, and 240 Sidney Street (filed as Exhibit 10.14 to Vertex's Annual Report on Form 10-K for the year ended December 31, 1992 (File No. 0-19319) and incorporated herein by reference).
10.10	First Amendment as of March 1, 1995 to the lease between C. Vincent Vappi and Vertex (filed as Exhibit 10.2 to Vertex's Quarterly Report on Form 10-Q for the quarter ended June 30, 1995 (File No. 0-19319) and incorporated herein by reference).
10.11	Second Amendment as of February 12, 1997 to Lease between C. Vincent Vappi and Vertex (filed as Exhibit 10.14 to Vertex's Annual Report on Form 10-K for the year ended December 31, 1996 (File No. 0-19319) and incorporated herein by reference).
10.12	Lease dated March 1, 1993, between Fort Washington Realty Trust and Vertex, relating to the premises at 625 Putnam Avenue, Cambridge, MA (filed as Exhibit 10.10 to Vertex's Annual Report on Form 10-K for the year ended December 31, 1993 (File No. 0-19319) and incorporated herein by reference).
10.13	First Amendment, dated 1 December 1996, to Lease between Fort Washington Realty Trust and Vertex dated 1 March 1993 (filed as Exhibit 10.16 to Vertex's Annual Report on Form 10-K for the year ended December 31, 1996 (File No. 0-19319) and incorporated herein by reference).
10.14	Second Amendment, dated 1 February 1998, to Lease between Fort Washington Realty Trust and Vertex dated 1 March 1993 (filed as Exhibit 10.17 to Vertex's 1997 Annual Report on Form 10-K (File No. 0-19319) and incorporated herein by reference).
10.15	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. 0-19319) and incorporated herein by reference).
10.16	First Amendment to Lease dated March 3, 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. 0-19319) and incorporated herein by reference).
10.17	Second Amendment to Lease and Option Agreement dated June 12, 1997 between Fort Washington Realty Trust and Vertex (filed herewith).
10.18	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 herewith)
10.19	Lease by and between Trustees of Fort Washington Realty Trust, Landlord, and the Company as Tenant, executed September 17, 1999 (filed as Exhibit 10.27 to Vertex's Quarterly Report on Form 10-Q for the quarter ended

EXHIBIT NUMBER	EXHIBIT DESCRIPTION
10.22	License Agreement and Supply Agreement, both dated May 9, 1996, between Vertex and BioChem Pharma (International) Inc. (with certain confidential information deleted) (filed as Exhibit 10.1 to Vertex's Quarterly Report on 10-Q for the quarter ended March 31, 1996 (File No. 0-19319) and incorporated herein by reference).
10.23	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, and incorporated herein by reference).
10.24	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, and incorporated herein by reference).
10.25	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, and incorporated herein by reference).
10.26	License, Development and Commercialization Agreement between the Company and Hoechst Marion Roussel Deutschland GmbH dated September 1, 1999 (filed as Exhibit 10.27 to Vertex's Quarterly Report on Form 10-Q for the quarter ended September 30, 1999, with certain confidential information deleted (File No. 0-19319), and incorporated herein by reference).
10.27	Collaboration and Option Agreement between Vertex and Taisho Pharmaceutical Co., Ltd. dated November 30, 1999 (with certain confidential information deleted) (filed herewith).
10.28	Credit Agreement between Vertex and Fleet National Bank (filed herewith).
21	Subsidiaries of Vertex (filed herewith).
23	Consent of Independent Accountants (filed herewith).
27	Financial Data Schedule (submitted as an exhibit only in the electronic format of this Annual Report on Form 10-K submitted to the Securities and Exchange Commission).

* Compensatory plan or agreement applicable to management and employees.

(b) Reports on Form 8-K. No reports on Form 8-K were filed by Vertex during the quarter ended December 31, 1999.

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

By: /s/ JOSHUA S. BOGER
Joshua S. Boger
PRESIDENT AND CHIEF EXECUTIVE OFFICER

February 29, 1999

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed below by the following persons on behalf of the registrant and in the capacities and on the dates indicated.

NAME	TITLE	DATE
/s/ JOSHUA S. BOGER Joshua S. Boger	Director, Chairman, President and Chief Executive Officer (Principal Executive Officer)	February 29, 1999
/s/ THOMAS G. AUCHINCLOSS, JR. Thomas G. Auchincloss, Jr.	Vice President of Finance and Treasurer (Principal Financial and Accounting Officer)	February 29, 1999
/s/ BARRY M. BLOOM Barry M. Bloom	Director	February 29, 1999
/s/ ROGER W. BRIMBLECOMBE Roger W. Brimblecombe	Director	February 29, 1999
/s/ DONALD R. CONKLIN Donald R. Conklin	Director	February 29, 1999
/s/ BRUCE I. SACHS Bruce I. Sachs	Director	February 29, 1999
/s/ CHARLES A. SANDERS Charles A. Sanders	Director	February 29, 1999
/s/ ELAINE S. ULLIAN Elaine S. Ullian	Director	February 29, 1999

EXHIBIT INDEX

10.1	1991 Stock Option Plan, as amended and restated as of September 14, 1999 (filed herewith).
10.2	1994 Stock and Option Plan, as amended and restated as of September 14, 1999 (filed herewith).
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VERTEX PHARMACEUTICALS INCORPORATED
INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

REPORT OF INDEPENDENT ACCOUNTANTS

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, stockholders'

equity and cash flows present fairly, in all material respects, the financial position of Vertex Pharmaceuticals Incorporated and its subsidiaries at December 31, 1999 and 1998, and the results of their operations and their cash flows for each of the three years in the period ended December 31, 1999 in conformity with generally accepted accounting principles in the United States. 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, 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 the opinion expressed above.

PricewaterhouseCoopers LLP

Boston, Massachusetts
February 16, 2000, except as to the information in Note R for which the date is
February 28, 2000

CONSOLIDATED BALANCE SHEETS

VERTEX PHARMACEUTICALS INCORPORATED

	DECEMBER 31,	
	1999	1998
	(DOLLARS IN THOUSANDS)	
ASSETS		
Current assets:		
Cash and cash equivalents	$ 31,548	$ 24,169
Investments	156,254	221,483
Accounts receivable	5,956	1,462
Prepaid expenses	1,439	1,594
Total current assets	195,197	248,708
Restricted cash	9,788	2,316
Property and equipment, net	24,480	14,476
Investment in equity affiliate	2,276	--
Other assets	704	846
Total assets	$ 232,445	$ 266,346
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	$ 2,979	$ 2,808
Accrued expenses	11,173	7,542
Deferred revenue	2,000	--
Obligations under capital lease and debt	2,366	2,752
Total current liabilities	18,518	13,102
Obligations under capital lease and debt, excluding current portion	4,693	7,032
Total liabilities	23,211	20,134
Commitments (Note I)		
Stockholders' equity:		
Preferred stock, $.01 par value; 1,000,000 shares authorized; none issued		
Common stock, $.01 par value; 100,000,000 shares authorized; 25,685,364 and 25,358,559 shares issued and outstanding in 1999 and 1998, respectively	257	254
Additional paid-in capital	400,888	395,332
Deferred compensation	(114)	(167)
Accumulated other comprehensive income (loss)	(970)	654
Accumulated deficit	(190,827)	(149,861)
Total stockholders' equity	209,234	246,212
Total liabilities and stockholders' equity	$ 232,445	$ 266,346

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

CONSOLIDATED STATEMENTS OF OPERATIONS

VERTEX PHARMACEUTICALS INCORPORATED

	YEARS ENDED DECEMBER 31,		
	1999	1998	1997
	(IN THOUSANDS, EXCEPT PER SHARE DATA)		
Revenues:			
Royalties and product sales	$ 8,053	--	--
Collaborative and other research and development	42,507	$ 29,055	$ 29,926
Investment income	11,088	15,343	13,873
Total revenues	61,648	44,398	43,799
Costs and expenses:			
Royalties and product costs	2,925	--	--
Research and development	72,180	58,668	51,624
Sales, general and administrative	26,131	18,135	11,430
Loss in equity affiliate	724	--	--
Interest	654	681	576
Total costs and expenses	102,614	77,484	63,630
Net loss	$(40,966)	$(33,086)	$(19,831)
Basic and diluted loss per common share	$ (1.61)	$ (1.31)	$ (0.82)
Basic and diluted weighted average number of common shares outstanding	25,518	25,299	24,264

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

CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY
VERTEX PHARMACEUTICALS INCORPORATED

	COMMON STOCK		ADDITIONAL PAID-IN CAPITAL	DEFERRED COMPENSATION	ACCUMULATED DEFICIT	ACCUMULATED OTHER COMPREHENSIVE INCOME (LOSS)
	SHARES	AMOUNT				
				(IN THOUSANDS)		
Balance, December 31, 1996	21,097	$211	$227,557	$ (47)	$ (96,944)	$ 49
Net change in unrealized holding gains/losses on investments						115
Translation adjustments						(12)
Net loss					(19,831)	
Comprehensive loss						
Issuances of common stock:						
Public offering of common stock	3,450	34	148,776			
Private placement of common stock	264	3	9,997			
Benefit plans	405	4	6,115			
Equity compensation for services rendered			44	(82)		
Amortization of deferred compensation				12		
Balance, December 31, 1997	25,216	252	392,489	(117)	(116,775)	152
Net change in unrealized holding gains/losses on investments						502
Translation adjustments						
Net loss					(33,086)	
Comprehensive loss						
Issuances of common stock:						
Benefit plans	143	2	2,784			
Equity compensation for services rendered			59	(82)		
Amortization of deferred compensation				32		
Balance, December 31, 1998	25,359	254	395,332	(167)	(149,861)	654
Net change in unrealized holding gains/losses on investments						(1,672)
Translation adjustments						48
Net loss					(40,966)	
Comprehensive loss						
Issuances of common stock:						
Benefit plans	326	3	5,497			
Equity compensation for services rendered			59			
Amortization of deferred compensation				53		
Balance, December 31, 1999	25,685	$257	$400,888	$(114)	$(190,827)	$ (970)

	COMPREHENSIVE INCOME (LOSS)	TOTAL STOCKHOLDERS' EQUITY
		(IN THOUSANDS)
Balance, December 31, 1996		$130,826
Net change in unrealized holding gains/losses on investments	$ 115	115
Translation adjustments	(12)	(12)
Net loss	(19,831)	(19,831)
Comprehensive loss	(19,728)	
Issuances of common stock:		
Public offering of common stock		148,810
Private placement of common stock		10,000
Benefit plans		6,119
Equity compensation for services rendered		(38)
Amortization of deferred compensation		12
Balance, December 31, 1997		276,001
Net change in unrealized holding gains/losses on investments	502	502
Translation adjustments		
Net loss	(33,086)	(33,086)
Comprehensive loss	(32,584)	
Issuances of common stock:		
Benefit plans		2,786
Equity compensation for services rendered		(23)
Amortization of deferred compensation		32
Balance, December 31, 1998		246,212
Net change in unrealized holding gains/losses on investments	(1,672)	(1,672)
Translation adjustments	48	48
Net loss	(40,966)	(40,966)
Comprehensive loss	(42,590)	
Issuances of common stock:		
Benefit plans		5,500
Equity compensation for services rendered		59
Amortization of deferred compensation		53
Balance, December 31, 1999		$209,234

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

CONSOLIDATED STATEMENTS OF CASH FLOWS

	YEARS ENDED DECEMBER 31,		
	1999	1998	1997
	(IN THOUSANDS)		
Cash flows from operating activities:			
Net loss	$ (40,966)	$ (33,086)	$ (19,831)
Adjustment to reconcile net loss to net cash used by operating activities:			
Depreciation and amortization	6,206	4,520	3,588
Amortization of deferred compensation	53	32	12
Equity compensation for services rendered	59	59	44
Realized (gains)/losses on investments	655	(547)	--
Loss in equity affiliate	724	--	--
Changes in assets and liabilities:			
Accounts receivable	(4,494)	--	--
Prepaid expenses	155	(1,104)	(161)
Accounts payable	171	(1,439)	2,856
Accrued expenses	3,631	1,157	3,630
Deferred revenue	2,000	(556)	556
Net cash (used) by operating activities	(31,806)	(30,964)	(9,306)
Cash flows from investing activities:			
Purchases of investments	(365,970)	(507,540)	(303,599)
Sales and maturities of investments	428,872	495,323	191,005
Expenditures for property and equipment	(16,210)	(7,901)	(6,020)
Restricted cash	(7,472)	--	--
Investment in equity affiliate	(3,000)	--	--
Other assets	142	(276)	(200)
Net cash provided (used) by investing activities	36,362	(20,394)	(118,814)
Cash flows from financing activities:			
Repayment of capital lease obligations and debt	(2,725)	(2,716)	(3,104)
Proceeds from equipment sale/leaseback	--	--	1,179
Proceeds from debt	--	4,085	1,813
Proceeds from public offerings of common stock	--	--	148,810
Proceeds from private placement of common stock	--	--	10,000
Proceeds from other issuances of capital stock	5,500	2,704	6,037
Net cash provided by financing activities	2,775	4,073	164,735
Effect of exchange rates on cash	48	--	(12)
Increase (decrease) in cash and cash equivalents	7,379	(47,285)	36,603
Cash and cash equivalents at beginning of year	24,169	71,454	34,851
Cash and cash equivalents at end of year	$ 31,548	$ 24,169	$ 71,454

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

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

A. THE COMPANY

Vertex Pharmaceuticals Incorporated ("Vertex" or the "Company") uses a range of drug discovery technologies to discover, develop and market small molecule drugs that address major medical needs. The Company is headquartered in Cambridge, Massachusetts and operates primarily in the U.S. Vertex also has a research facility in the U.K. The Company has seven drug candidates in clinical

development. The Company's first product, the HIV protease inhibitor Agenerase-TM- (amprenavir), received accelerated approval from the U.S. Food and Drug Administration and was launched in May 1999. Agenerase is marketed in the U.S. by Glaxo Wellcome plc ("Glaxo Wellcome") and is co-promoted in the U.S. by Vertex. The Company expects to incur operating losses over the next two years and possibly longer, as a result of expenditures for its research and development programs.

The consolidated financial statements include the accounts of the Company and the following subsidiaries: Vertex Securities Corp., Vertex Pharmaceuticals (Europe) Limited and Altus Biologics, Inc. ("Altus"), until January, 1999. All material intercompany transactions are eliminated. The Company restructured its majority ownership investment in Altus during 1999. As a result of the transaction, Vertex accounts for its investment in Altus under the equity method.

The Company 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, uncertainty of protection of proprietary technology, clinical trial uncertainty, dependence on collaborative partners, share price volatility, the possible 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 for compliance with government regulations.

B. ACCOUNTING POLICIES

USE OF ESTIMATES

The preparation of financial statements in conformity with generally accepted accounting principles 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 financial statements and the reported amounts of revenues and expenses during the reported period. Actual results could differ from those estimates.

RECLASSIFICATION IN THE PREPARATION OF FINANCIAL STATEMENTS

Certain reclassifications have been made to prior year data to conform to the current presentation.

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.

INVESTMENTS

Investments consist of marketable securities, which are classified as available for sale. Investments are stated at fair value with unrealized gains and losses included as a component of accumulated other comprehensive income (loss) until realized. The fair value of these securities is based on quoted market

prices. Realized gains and losses are determined on the specific identification method and are included in investment income.

CONCENTRATION OF CREDIT RISK

Financial instruments, which 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 losses in such accounts and does not believe it is exposed to any significant credit risk on these funds.

Two collaborative partners represented approximately 52% and 29%, respectively, of the Company's accounts receivable balance at December 31, 1999, which potentially exposes the Company to a concentration of credit risk. At December 31, 1998, three

collaborative partners represented approximately 14%, 14% and 15%, respectively, of the Company's accounts receivable balance. Management believes that credit risks associated with these 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 or five years for equipment and furniture and three years for computers and purchased software. Leasehold improvements are amortized over the life of the leases. 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 income (loss).

STOCK-BASED COMPENSATION

In accounting for its stock-based compensation plans, the Company applies Accounting Principles Board Opinion No. 25 ("APB 25") and related interpretations for all awards granted to employees. Under APB 25, 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. For stock options granted to nonemployees, the Company recognizes compensation costs in accordance with the requirements of Statement of Financial Accounting Standards No. 123, "Accounting for Stock-Based Compensation" ("SFAS 123"). SFAS 123 requires that companies recognize compensation expense for grants of stock, stock options and other equity instruments based on fair value.

REVENUE RECOGNITION

Revenue under research and development arrangements is recognized as earned under the terms of the respective agreements. License payments are recorded as revenue when payment is assured and contractual obligations have been met. Product research funding is recorded as revenue, generally on a quarterly basis, as research effort is incurred. Deferred revenue arises from payments received that have not yet been earned under research and development arrangements. The Company recognizes milestone payments when the milestones are achieved. Royalty revenue is recognized based on net sales

of licensed products in licensed territories, as provided by the collaborative partner. Product sales revenue is recorded upon shipment.

RESEARCH AND DEVELOPMENT

All research and development costs are expensed as incurred.

ADVERTISING

All advertising costs are expensed as incurred.

INCOME TAXES

Deferred tax assets and liabilities are recognized for the expected future tax consequences, using current tax rates, 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.

BASIC AND DILUTED LOSS PER COMMON SHARE

Basic earnings per share is based upon the weighted average number of common shares outstanding during the period. Diluted earnings 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 assumed exercise of outstanding stock options, the proceeds of which are then assumed to have been used to

repurchase outstanding stock using the treasury stock method. Common equivalent shares have not been included in the net loss per share calculations as the effect would be anti-dilutive. Potential common equivalent shares consist of 6,744,000 stock options outstanding with a weighted average exercise price of $23.50 as of December 31, 1999.

SEGMENT INFORMATION

The Company is in one business segment under the management approach, the business of discovery, development and marketing of small molecule drugs that address major medical needs.

NEW ACCOUNTING PRONOUNCEMENTS

In December 1999, the Securities and Exchange Commission issued Staff Accounting Bulletin No. 101, "Revenue Recognition in Financial Statements," ("SAB 101") which is effective no later than the quarter ending March 31, 2000. SAB 101 clarifies the Securities and Exchange Commission's views regarding recognition of revenue. The Company will adopt SAB 101 in the first quarter of 2000 and is presently determining the effect it will have on the financial statements, although the amount could be material to net financial results.

In June 1998, the Financial Accounting Standards Board issued SFAS 133, "Accounting for Derivative Instruments and Hedging Activities." The effective date of this statement was deferred to fiscal years beginning after June 15, 2000. This statement requires the recognition of all derivative instruments as either assets or liabilities in the statement of financial position and the measurement of

B. ACCOUNTING POLICIES (CONTINUED)

those instruments at fair value. The Company does not expect the adoption of this statement to have a material impact on its financial statements.

C. INVESTMENTS

Investments consist of the following at December 31 (in thousands):

	1999		1998	
	COST	FAIR VALUE	COST	FAIR VALUE
Cash and cash equivalents				
Cash and money market funds	$ 27,339	$ 27,339	$ 20,888	$ 20,888
Corporate debt securities	4,209	4,209	3,281	3,281
Total cash and cash equivalents	$ 31,548	$ 31,548	$ 24,169	$ 24,169
Investments				
US government securities				
Due within 1 year	$ 12,318	$ 12,292	$ 18,383	$ 18,363
Due within 1 to 5 years	18,054	17,702	28,734	28,834
Due over 5 years	--	--	3,048	3,037
Corporate debt securities				
Due within 1 year	71,807	71,788	21,684	21,638
Due within 1 to 5 years	31,647	31,304	133,039	133,665
Due over 5 years	23,450	23,168	15,945	15,946
Total Investments	$157,276	$156,254	$220,833	$221,483

Gross unrealized holding gains and losses at December 31, 1999 were approximately $112,000 and $1,134,000, respectively, and at December 31, 1998 were $911,000 and $261,000, respectively. Gross realized gains and losses for 1999 were $106,000 and $761,000, respectively. Gross realized gains and losses for 1998 were $852,000 and $305,000, respectively. The effect of gross realized gains and losses on the financial statements for 1997 was immaterial. Maturities stated are effective maturities.

D. RESTRICTED CASH

In accordance with operating lease agreements, at December 31, 1999 and 1998 the Company held in deposit approximately $9,788,000 and $2,316,000, respectively, with its bank to collateralize conditional, stand-by letters of credit in the name of the landlord. In 1999, the Company entered into new operating leases for additional space and facilities. In connection with these leases the Company was required to provide security deposits in the form of stand-by letters of credit. The letters of credit are redeemable only if the Company defaults on the leases under specific criteria. These funds are restricted from the Company's use during the lease period, although the Company is entitled to all interest earned on the funds.

E. PROPERTY AND EQUIPMENT

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

	1999	1998
Leasehold improvements	$15,851	$ 7,804
Furniture and equipment	15,215	9,847
Computers	3,190	1,223
Software	4,053	3,276
Equipment under capital lease	20,522	20,471
	58,831	42,621
Less accumulated depreciation and amortization	34,351	28,145
	$24,480	$14,476

The net book value of equipment under capital lease was $2,018,000 and $3,687,000 at December 31, 1999 and 1998, respectively.

Financial information relating to the Company's operations by geographic area was as follows (in thousands):

	LONG-LIVED ASSETS	
	1999	1998
United States	$51,903	$41,712
United Kingdom	6,928	909
Consolidated	$58,831	$42,621

F. INVESTMENT IN AFFILIATE

In February 1999, Vertex restructured its investment in Altus, which was a wholly owned subsidiary, so that Altus operates independently from Vertex. As part of the transaction, Vertex provided Altus $3,000,000 of cash and surrendered its shares in Altus preferred stock in exchange for two new classes of preferred stock and warrants. At December 31, 1999, Vertex had a 29.5% equity

investment in Altus of approximately $2,276,000. For the year ending December 31, 1999, Vertex recorded $724,000 as its share of Altus' losses.

G. ACCRUED EXPENSES

Accrued expenses consist of the following at December 31 (in thousands):

	1999	1998
Professional fees	$ 3,005	$2,134
Development contract costs	3,331	2,391
Payroll and benefits	1,822	1,239
Other	3,015	1,778
	$11,173	$7,542

H. CAPITAL LEASES AND DEBT OBLIGATIONS

At December 31, 1999, long-term capital lease and debt obligations were due as follows (in thousands):

YEAR ENDED DECEMBER 31,	CAPITAL LEASES	DEBT	TOTAL
2000	$1,492	$1,027	$2,519
2001	1,335	1,114	2,449
2002	89	1,351	1,440
2003	--	873	873
Total	2,916	4,365	7,281
Less amount representing interest payments	222	--	222
Present value of minimum lease and debt payments	2,694	4,365	7,059
Less current portion	1,339	1,027	2,366
	$1,355	$3,338	$4,693

During 1997, the Company financed under capital lease arrangements an aggregate of $1,179,000 of asset cost under master lease agreements. At the end of the lease term, the Company has the right to either return the equipment to the lessor or purchase the equipment for fair market value at that time. These agreements have a term of five years and require that the Company maintain a certain level of cash and investments.

During 1998, the Company financed under a master debt agreement, assets with a cost of $1,574,000, $1,506,000 and $1,005,000 with interest rates of 7.89%,
8.06% and 8.08%, respectively. During 1997, the Company financed under a master debt agreement assets with a cost of $676,000 and $1,137,000 with the interest rates of 8.59% and 8.38%, respectively. The Company has certain equipment with a net book value of $3,765,000 designated as collateral under these agreements at December 31, 1999. These agreements have a term of five years, and

require that the Company maintain a certain level of cash and investments. The carrying value of these debt obligations approximates fair value.

In December 1999, the Company obtained a line of credit allowing for borrowings in aggregate of up to $20,000,000 for equipment and leasehold improvement expenditures. As of December 31, 1999, no amounts were outstanding and $20,000,000 was available under the line of credit.

Interest paid under capital leases and debt was $654,000, $681,000 and $576,000 in 1999, 1998 and 1997, respectively.

I. COMMITMENTS

The Company leases its facilities and certain equipment under operating leases. The Company's leases have terms through the year 2009. In 1999, the Company entered into new operating lease commitments for additional space and facilities in the U.S.

I. COMMITMENTS (CONTINUED)

At December 31, 1999, future minimum commitments under leases with non-cancelable terms of more than one year are as follows (in thousands):

YEAR	OPERATING LEASES
2000	$ 7,502
2001	$ 11,975
2002	$ 11,258
2003	$ 11,258
2004	$ 10,840
Thereafter	$ 50,714
Total	$103,547

Rental expense was $6,235,000, $4,358,000 and $3,363,000 in 1999, 1998 and 1997, respectively.

The Company has certain license and maintenance contracts that contain future, committed payments for the support and upgrade of specific software programs currently used in research. For the years 2000 and 2001 the amounts committed under these contracts are $811,000 and $766,000, respectively.

J. INCOME TAXES

The Company's federal statutory income tax rate for 1999, 1998 and 1997 was 34%. The Company recorded no income tax benefit for 1999, 1998 and 1997 and recorded a full valuation allowance against net operating losses due to uncertainties related to 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 the deferred taxes at December 31 were as follows (in thousands):

	1999	1998
Net operating loss	$66,001	$57,295
Tax credits carryforward	13,464	10,958
Property, plant and equipment	676	1,345
Other	411	572
Gross deferred tax asset	80,552	70,170
Valuation allowance	(80,552)	(70,170)
Net deferred tax balance	$ --	$ --

For federal income tax purposes, as of December 31, 1999, the Company has net operating loss carryforwards of approximately $162,776,000 and $9,331,000 of tax credits, which may be used to offset future income. These net operating loss carryforwards expire beginning in 2005, and the tax credit carryforwards begin to expire in 2004. The 1999 deferred tax asset has been adjusted in connection with the restructuring of the Company's investment in Altus. A valuation allowance has been established for the full amount of the deferred tax asset since it is more likely than not that the deferred tax asset will not be realized.

J. INCOME TAXES (CONTINUED)

The amount of tax credits and net operating loss carryforwards that the Company may utilize in any one year is limited in accordance with Internal Revenue Code Section382. This limitation arises whenever a cumulative change in ownership in excess of 50% occurs. A change of ownership has occurred which will limit the amount of net operating loss and tax credits available prior to the change. There may also be further changes of ownership subsequent to 1999, which may also limit the amount of net operating loss and tax credit utilization in a subsequent year.

K. COMMON AND PREFERRED STOCK

COMMON STOCK

In March 1997, the Company completed a public offering of 3,450,000 shares of its common stock at a price of $45.50 per share with net proceeds to the Company of approximately $148,810,000. In June 1997, Eli Lilly and Company ("Lilly") purchased 263,922 shares of the Company's common stock for $10,000,000.

During 1997, the Company increased the authorized number of shares of common stock by 50,000,000 shares to 100,000,000 shares. In May 1999, the shareholders approved an amendment to the Company's 1996 Stock and Option Plan and the Employee Stock Purchase Plan authorizing the addition of 1,250,000 and 200,000 shares to the plans, respectively. At December 31, 1999, 8,873,000 shares of the Company's common stock were reserved for exercise of common stock options granted or to be granted under its 1991 Stock Option Plan, 1994 Stock and Option Plan, and 1996 Stock and Option Plan; 43,000 shares were reserved for exercise of certain other options granted in 1991; approximately 57,000 shares of common stock were reserved for issuance under the Company's 401(k) Plan, and approximately 224,000 shares of common stock were reserved for issuance under the Company's Employee Stock Purchase Plan.

STOCK 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"). Under the 1994 Plan and the 1996 Plan, stock rights, which are either
(i) incentive stock options when Internal Revenue Code requirements are met,
(ii) non-qualified stock options ("NQSOs"), or (iii) award 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), consultants, advisors and non-employee directors (NQSOs and stock awards only). 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 periods, generally four or five years, are determined by the Compensation Committee. Incentive stock options granted under the Plans must expire not more than ten

years from the date of grant. At December 31, 1999, the Company had 2,173,000 shares of common stock available for future grant under its stock option plans.

The Company issued options to purchase 20,000 shares of common stock in 1998 and 1997, at exercise prices below the fair market value of the common stock on the date of grant. The Company recorded an increase to additional paid in capital and a corresponding charge to deferred compensation to recognize the aggregate difference between the exercise price and the fair market value of the common stock in the amount of $82,000 and $82,000 for 1998 and 1997, respectively. Deferred compensation is being amortized over the option vesting period. Amortization of deferred compensation expense of $53,000, $32,000 and $12,000 was recognized during 1999, 1998 and 1997, respectively.

K. COMMON AND PREFERRED STOCK (CONTINUED)

Compensation cost recognized in connection with the issuance of stock options to nonemployees was $59,000, $59,000 and $44,000 in 1999, 1998 and 1997, respectively.

Stock option activity for the years ended December 31, 1999, 1998 and 1997 is as follows (shares in thousands):

	1999		1998		1997	
	SHARES	WEIGHTED AVERAGE EXERCISE PRICE	SHARES	WEIGHTED AVERAGE EXERCISE PRICE	SHARES	WEIGHTED AVERAGE EXERCISE PRICE
Outstanding at beginning of year.....	5,837	$22.62	4,702	$22.03	4,033	$18.98
Granted.....	1,315	$25.99	1,341	$24.57	1,257	$29.78
Exercised.....	(244)	$15.24	(78)	$14.89	(375)	$13.97
Canceled.....	(164)	$27.17	(128)	$25.90	(213)	$23.99
Outstanding at end of year.....	6,744	$23.50	5,837	$22.62	4,702	$22.03
Options exercisable at year-end.....	3,440	$20.57	2,758	$18.76	1,944	$16.50
Weighted average fair value of options granted during the year.....		$13.05		$11.68		$13.94

The fair value of each option granted during 1999, 1998 and 1997 was estimated on the date of grant using the Black-Scholes option-pricing model with the following weighted average assumptions:

	1999	1998	1997
Expected life (years).....	5.5	5.11	5.18
Expected volatility.....	45%	46.5%	44.7%
Risk free interest rate.....	6.20%	4.86%	5.5%
Dividend yield.....	0	0	0

The following table summarizes information about stock options outstanding and exercisable at December 31, 1999 (shares in thousands):

RANGE OF EXERCISE PRICES	OPTIONS OUTSTANDING NUMBER OUTSTANDING	WEIGHTED AVERAGE REMAINING CONTRACTUAL LIFE	WEIGHTED AVERAGE EXERCISE PRICE	OPTIONS EXERCISABLE NUMBER EXERCISABLE	WEIGHTED AVERAGE EXERCISE PRICE
$ 7.25-$15.75	1,535	3.96	$13.33	1,527	$13.32
$15.88-$26.22	2,445	8.50	$22.80	726	$19.63
$26.31-$27.34	1,438	8.36	$27.27	456	$27.29
$27.37-$48.81	1,317	7.31	$32.35	726	$32.38
$49.13-$49.13	9	7.45	$49.13	5	$49.13
$ 7.25-$49.13	6,744	7.20	$23.50	3,440	$20.57

EMPLOYEE STOCK PURCHASE PLAN

Under the Company's Employee Stock Purchase Plan, substantially all permanent employees may, through payroll withholdings, purchase shares of the Company's common stock at a price of 85% of the

K. COMMON AND PREFERRED STOCK (CONTINUED)

lesser of fair market value at the beginning or end of each six-month withholding period. During 1999, 1998 and 1997 the following was issued under the plan:

	1999	1998	1997
Number of shares	51,529	38,170	26,213
Average price paid	$19.37	$22.66	$28.00

Had the Company adopted SFAS 123, the weighted average fair value of each purchase right granted during 1999, 1998 and 1997 would have been $6.63, $7.65 and $9.16, 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: (1) expected life of one half year for all years (2) expected volatility of 45%, 52% and 51% for 1999, 1998 and 1997, respectively (3) risk-free interest rate of 5.72%, 4.70% and 5.43% for 1999, 1998 and 1997, respectively, and (4) no dividend yield.

PRO FORMA DISCLOSURES

Had compensation cost for the Company's grants for stock-based compensation plans been determined consistent with SFAS 123, the Company's net loss and net loss per share would approximate the pro forma amounts below (in thousands except per share data):

		1999	1998	1997
Net Loss	As reported	$(40,966)	$(33,086)	$(19,831)
	Pro forma	$(52,997)	$(41,542)	$(25,154)
Basic and diluted loss per share	As reported	$ (1.61)	$ (1.31)	$ (0.82)
	Pro forma	$ (2.08)	$ (1.64)	$ (1.04)

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 one-hundredth of a share of Series A junior participating preferred

stock, $.01 par value (the "Junior Preferred Shares"), of the Company at a price of $270 per one 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 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 $.01 per Right.

L. COLLABORATIVE RESEARCH AND DEVELOPMENT AGREEMENTS

In November 1999, the Company and Taisho Pharmaceutical Co., LTD ("Taisho") entered into an agreement to collaborate on the discovery, development and commercialization of caspase inhibitors for the treatment of cerebrovascular, cardiovascular and neurdegenerative diseases. Under the agreement, Taisho agreed to pay the Company up to $43,000,000 in pre-commercial payments, comprised of research funding, milestone payments and $4,500,000 for prior research costs. These amounts are based on the development of two compounds. Vertex received and recognized $3,000,000 in the fourth quarter of 1999 for prior research costs and will receive $1,500,000 in November 2000. In addition, Taisho will also pay for certain costs of developing compounds that emerge from the caspase research program. From the inception of the agreement in November 1999 through December 1999, $3,900,000 has been recognized as revenue. Taisho will have an option to obtain marketing rights in Japan and certain Far East markets for any compounds arising from the collaboration.

In September 1999, the Company and Aventis S.A. ("Aventis"), formerly Hoechst Marion Roussel Deutschland GmbH ("HMR"), entered into an expanded agreement covering the development of VX-740, an orally active inhibitor of interleukin-1 beta converting enzyme ("ICE"). Under the agreement, Aventis agreed to pay the Company $20,000,000 for prior research costs, and up to $62,000,000 in milestone payments for successful development by Aventis of VX-740 in rheumatoid arthritis, the first targeted indication, as well as similar milestones for each additional indication. Vertex received $10,000,000 in the fourth quarter of 1999 for prior research costs and will receive $10,000,000 in the second quarter of 2000. Aventis has an exclusive worldwide license to develop, manufacture and market VX-740, as well as an exclusive option for all other compounds discovered as part of the research collaboration between the Company and HMR that ended in 1997 under which the Company received research funding. Aventis will fund the development of VX-740. Vertex may co-promote the product in the U.S. and Europe and will receive royalties on global sales, if any. Aventis may terminate this agreement without cause upon six months' written notice. Revenues earned under the 1999 agreement were $15,000,000. Revenues earned under the previous agreement were $120,000, $460,000 and $8,660,000 in 1999, 1998 and 1997, respectively.

The Company and Schering AG, Germany ("Schering AG") are collaborating on 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. Under the terms of the agreement, Schering AG agreed to pay the Company up to $88,000,000 comprised of $6,000,000 paid upon signing in September 1998, $22,000,000 of product research funding over five years and $60,000,000 of development and commercialization milestone payments. From the inception of the agreement in August 1998 through December 31, 1999, $14,000,000 has been recognized as revenue. Under terms of the agreement, Vertex and Schering AG will have an equal role in management of neurophilin ligand research and product development. In North America, Vertex will have manufacturing rights, and Vertex and Schering AG will share equally in the marketing expenses and profits from commercialized compounds. In addition to having manufacturing rights in North America, the Company retains the option to manufacture bulk drug substance for sales and marketing in territories outside Europe, the Middle East and Africa. Schering AG will have the right to manufacture and market any commercialized compounds in Europe, the Middle East and Africa, and pay Vertex a royalty on product sales, if any. After December 2000, Schering AG has the right to terminate without cause upon a six months' written notice. Revenues earned from Schering AG under the neurophilin ligand agreement were $4,000,000 and $10,000,000 in 1999 and 1998, respectively.

The Company and Kissei Pharmaceutical Co., Ltd. ("Kissei") are collaborating to design inhibitors of p38 MAP kinase and to develop them as novel, orally active drugs for the treatment of inflammatory and neurological diseases. Under the terms of the agreement, Kissei agreed to pay the Company up to

L. COLLABORATIVE RESEARCH AND DEVELOPMENT AGREEMENTS (CONTINUED) $22,000,000 composed of a $4,000,000 license payment, $11,000,000 of product research funding over three years and $7,000,000 of development and commercialization milestone payments. From the inception of the agreement in September 1997 through December 31, 1999, $15,000,000 has been recognized as revenue. Kissei will have the right to develop and commercialize these compounds in its licensed territories. Kissei has exclusive rights to p38 MAP kinase compounds in Japan and certain Southeast Asian countries and semi-exclusive rights in China, Taiwan and South Korea. The Company retains exclusive marketing rights in the United States, Canada, Europe and the rest of the world. In addition, the Company will have the right to supply bulk drug material to Kissei for sale in its territory and will receive royalties and drug supply payments on future product sales, if any. Kissei has the right to terminate the agreement without cause upon six months' notice. Additionally, Kissei agreed to pay certain development costs. Revenues earned from Kissei under the p38 MAP kinase agreement were $6,286,000, $5,521,000 and $5,500,000 in 1999, 1998 and 1997, respectively.

The Company and Eli Lilly and Company ("Lilly") are collaborating on designing inhibitors of the hepatitis C protease enzyme and developing them as novel drugs to treat hepatitis C infection. Under the terms of the agreement, Lilly agreed to pay the Company up to $51,000,000 composed of a $3,000,000 payment paid in June 1997, $33,000,000 of product research funding over six years and $15,000,000 of development and commercialization milestone payments. From the inception of the agreement in June 1997 through December 31, 1999, $16,209,000 has been recognized as revenue. The Company has the option to supply 100 percent of Lilly's commercial drug substance supply needs. The Company will receive royalties on future product sales, if any. If the Company exercises its commercial supply option, the Company will receive drug supply payments in addition to royalties on future product sales, if any. Lilly has the right to terminate the agreement without cause upon six months' notice. In connection with this collaboration, Lilly purchased 263,922 shares of the Company's common stock for $10,000,000 in June 1997. Revenues earned from Lilly were $5,452,000, $5,193,000 and $5,694,000 in 1999, 1998 and 1997, respectively.

The Company and BioChem Pharma ("BioChem") collaborated on the development and commercialization in Canada of Incel-TM- (VX-710), Vertex's lead multidrug resistance reversal agent. Under the development agreement, BioChem agreed to pay Vertex an initial licensing fee of $500,000 and development and commercialization milestone payments. From the inception of the agreement in May 1996 through the year ended December 31, 1999, $750,000 has been recognized as license and research revenue. BioChem also funded certain development activities for Incel in Canada. The Company has received the full amount of research funding specified under the agreement and BioChem has no further license rights with respect to Incel. No revenues were earned from BioChem in 1999. Revenues earned from BioChem were $56,000 and $251,000 in 1998 and 1997, respectively.

The Company and Glaxo Wellcome are collaborating on the development and commercialization of Agenerase (amprenavir) and its prodrug VX-175. Under the collaborative agreement, for research and development of HIV protease inhibitors, Glaxo Wellcome agreed to pay the Company up to $42,000,000 comprised of a $15,000,000 license payment paid 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. Glaxo Wellcome is also obligated to pay additional development and commercialization milestone payments for subsequent drug candidates, including VX-175. From the inception of the agreement in December 1993 through the year ended December 31, 1999, $40,000,000 has been recognized as revenue. Research funding under this agreement ended on December 31, 1998. In addition, Glaxo Wellcome is required to bear the costs of development in its territory of drug candidates under the collaboration. Glaxo Wellcome has exclusive rights to develop and commercialize Vertex HIV protease inhibitors in all parts of the world except the Far East and will pay Vertex a royalty on sales. The Company has retained certain bulk drug manufacturing rights and certain

L. COLLABORATIVE RESEARCH AND DEVELOPMENT AGREEMENTS (CONTINUED)

co-promotion rights in territories licensed to Glaxo Wellcome. Glaxo Wellcome has the right to terminate its arrangement without cause upon twelve months' notice given at any time. Termination by Glaxo Wellcome of the agreement will relieve it of its obligation to make further commercialization and development milestone and royalty payments and will end any license granted to Glaxo Wellcome by Vertex thereunder. In 1999, the Company began earning a royalty from Glaxo Wellcome from sales of Agenerase. Revenues and royalties earned from Glaxo Wellcome were $13,927,000, $6,457,000 and $3,275,000 for 1999, 1998 and 1997, respectively.

In June 1996, the Company and Glaxo Wellcome obtained a worldwide, non-exclusive license under certain G.D. Searle & Co. ("Searle") patent applications in the area of HIV protease inhibition. Vertex paid $15,000,000 and Glaxo Wellcome paid $10,000,000 to Searle for the license. Based on sales of Agenerase in 1999, the Company also began to pay Searle a royalty.

The Company and Kissei are collaborating on the development and commercialization of amprenavir. Under the collaborative agreement, Kissei agreed to pay the Company up to $20,000,000, comprised of $9,800,000 of product research funding through 1995, $7,000,000 of development milestone and territory option payments and a $3,200,000 equity investment. From the inception of the agreement in April 1993 through the year ended December 31, 1999, $15,642,000 has been recognized as revenue. During 1997, the

Company also received $4,000,000 related to reimbursements of certain development costs. The Company has received the full amount of research funding specified under the agreement. Under the collaboration, Kissei has exclusive rights to develop and commercialize amprenavir in Japan and will pay Vertex a royalty on sales, if any. Vertex is responsible for the manufacture of bulk product for Kissei. Kissei also has an exclusive option to develop and commercialize the amprenavir prodrug VX-175 in Japan. Revenues earned under this Kissei agreement were $1,000,000, $217,000 and $4,310,000 in 1999, 1998 and 1997, respectively.

M. EMPLOYEE BENEFITS

The Company has a 401(k)-retirement plan in which substantially all of its permanent employees are eligible to participate. Participants may contribute up to 15% of their annual compensation to the plan, subject to statutory limitations. For 1999, the Company declared discretionary matching contributions to the plan in the aggregate amount of $866,000, payable in the form of shares of the Company's common stock. Of these shares, 23,854 were issued as of December 31, 1999 with approximately 6,700 issuable in 2000. For 1998, the Company declared discretionary matching contributions to the plan in the aggregate amount of $672,000, payable in the form of shares of the Company's common stock. Of these shares, 19,419 were issued as of December 31, 1998 with the remaining 7,195 issued in 1999. For 1997, the Company declared discretionary matching contributions to the plan in the aggregate amount of $482,000, payable in the form of shares of the Company's common stock. Of these shares, 6,458 were issued as of December 31, 1997 with the remaining 7,113 issued in 1998.

N. RELATED PARTY

A sibling of the Company's Chairman and Chief Executive Officer is a partner in the law firm representing the Company to which $480,000, $333,000 and $394,000 in legal fees were paid in 1999, 1998 and 1997, respectively.

O. LEGAL PROCEEDINGS

Chiron Corporation ("Chiron") filed suit on July 30, 1998 against Vertex and Eli Lilly and Company in the United States District Court for the Northern District of California, alleging

O. LEGAL PROCEEDINGS (CONTINUED)

infringement by the defendants of three U.S. patents issued to Chiron. The infringement action relates to research activities by the defendants in the hepatitis C viral protease field and the alleged use of inventions claimed by Chiron in connection with that research. Chiron has requested damages in an unspecified amount, as well as an order permanently enjoining the defendants from unlicensed use of the claimed Chiron inventions. During 1999, Chiron requested and was granted a reexamination by the U.S. Patent and Trademark Office of all three of the patents in suit. Chiron also requested and, over the opposition of Vertex and Lilly, was granted a stay in the infringement lawsuit, pending the outcome of the patent reexamination. While the length of the stay, the outcome of the reexamination, the effect of that outcome on the lawsuit and the final outcome of the lawsuit cannot be determined, Vertex maintains that the plaintiff's claims are without merit and intends to defend the lawsuit, if and when it resumes, vigorously.

P. ACCUMULATED OTHER COMPREHENSIVE INCOME (LOSS)

Accumulated other comprehensive income (loss) consists of the following (in thousands):

	CUMULATIVE TRANSLATION ADJUSTMENT	UNREALIZED GAIN/(LOSS) ON INVESTMENTS	ACCUMULATED OTHER COMPREHENSIVE INCOME (LOSS)
Balance as of December 31, 1997	$ 4	$ 148	$ 152
Unrealized gains/(losses) on securities:			
Unrealized holding gains arising during the period	--	1,049	1,049
Less: reclassification adjustment for gains Included in net loss		(547)	(547)
Balance as of December 31, 1998	4	650	654
Foreign currency translation adjustment	48		48
Unrealized gains/(losses) on securities:			
Unrealized holding gains arising during the period		(1,672)	(1,672)
Balance as of December 31, 1999	$ 52	$(1,022)	$ (970)

Q. QUARTERLY FINANCIAL DATA (UNAUDITED)

(IN THOUSANDS, EXCEPT PER SHARE)

	FIRST QUARTER	SECOND QUARTER	THIRD QUARTER	FOURTH QUARTER	TOTAL YEAR
1999					
Total revenues	$ 7,129	$ 15,328	$ 9,561	$ 29,630	$ 61,648
Total expenses	24,683	26,169	23,847	27,915	102,614
Net loss	(17,554)	(10,841)	(14,286)	1,715	(40,966)
Basic earnings per share	(.69)	(.43)	(.56)	.07	(1.61)
Diluted earnings per share	(.69)	(.43)	(.56)	.06	(1.61)
1998					
Total revenues	$ 7,169	$ 7,152	$ 18,417	$ 11,660	$ 44,398
Total expenses	15,583	16,954	20,690	24,257	77,484
Net loss	(8,414)	(9,802)	(2,273)	(12, 597)	(33,086)
Basic and diluted earnings per share	(0.33)	(0.39)	(0.09)	(0.50)	(1.31)

R. SUBSEQUENT EVENT

On February 28, 2000, the Company entered into an agreement with Incyte Pharmaceuticals, Inc. to gain access to one of Incyte's databases of genomic information. Under the agreement, Vertex must make certain payments, including milestone payments and royalties on sales of products developed with Incyte technology, if any.

EXHIBIT 10.1

VERTEX PHARMACEUTICALS INCORPORATED

1991 STOCK OPTION PLAN

As amended and restated as of September 14, 1999

1. PURPOSE OF PLAN.

The purpose of this 1991 Stock Option Plan (the "Plan") is to promote the interests of Vertex Pharmaceuticals Incorporated, a Massachusetts corporation (the "Company," including for the purposes of this paragraph any affiliated companies), by providing a method whereby employees of the Company, and others providing material assistance to the Company, may be given compensation or additional compensation for their efforts on behalf of or assistance to the Company, and to aid the Company in attracting and retaining capable personnel.

2. SCOPE AND DURATION OF THE PLAN.

Options granted under this Plan may contain such terms as will qualify the options as incentive stock options ("ISOs") within the meaning of Section
422(b) of the Internal Revenue Code of 1986, as amended (the "Code"), or in the form of non-statutory stock options ("NSOs"). Unless otherwise indicated, references in this Plan to "options" include ISOs and NSOs. Subject to adjustment as provided in Section 11 hereof, the maximum number and kind of shares of the Company's capital stock with respect to which options may be granted under this Plan shall be 2,000,000 shares of Common Stock, $.01 par value per share ("Common Stock"). Until termination of this Plan, the Company shall at all times reserve a sufficient number of shares to meet the requirements of the Plan. Such shares may be authorized and unissued shares or shares held in the Company's treasury.

There shall become available for subsequent grants under this Plan any shares of Common Stock underlying an option which cease for any reason to be subject to purchase under such option. No ISO shall be granted under this Plan more than 10 years after adoption of the Plan by the Board of Directors.

3. ADMINISTRATION OF PLAN.

The Compensation Committee or any successor thereto (the "Committee") appointed by the Company's Board of Directors shall administer this Plan. The Committee shall have full power and authority to: (i) designate the employees and other persons to whom options shall be granted; (ii) designate options or any portion thereof as ISOs; (iii) determine the number of shares of Common Stock for which options may be granted and the option price or prices; (iv) determine the other terms and provisions of option agreements (which need not be identical) including, but not limited to, provisions concerning the time or times when and the extent to which the options may be exercised and the nature and duration of restrictions as to transferability or constituting substantial risks of forfeiture, provided that with respect to ISOs such time or times shall not occur before approval of this Plan by the stockholders of the Company in the manner provided under Section 15 below; (v) amend or modify any option, with the consent of the holder thereof; (vi) accelerate the right of an optionee to exercise in whole or in part any previously granted option; and (vii) interpret the provisions and supervise the administration of this Plan.

Options may be granted singly or in combination. The Committee shall have the authority to grant in its discretion to the holder of an outstanding option in exchange for the surrender and

cancellation of such option, a new option in the same or a different form and containing such terms as the Committee may deem appropriate, including without limitation a price which is different (either higher or lower) than any price provided in the option so surrendered and cancelled.

In connection with the grant of an NSO, the Committee may in its discretion, concurrently or after grant of the NSO, grant or agree to grant a tax offset bonus to the optionee to offset in whole or in part the tax liability of the optionee realized upon exercise of the NSO.

All decisions and selections made by the Committee pursuant to the provisions of this Plan shall be made by a majority of its members. Any decision reduced to writing and signed by all of the members of the Committee who are authorized to make such decision shall be as fully effective as if it had been made by a majority at a duly held meeting of the Committee.

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

4. DESIGNATION OF PARTICIPANTS.

Options may be granted only to employees, including officers who are employees, of the Company or any parent or subsidiary of the Company, and other individuals, including consultants, who are determined by the Committee to contribute, or have the potential to contribute, materially to the success of the Company or any parent or subsidiary, provided that ISOs shall be granted only to persons who are employees of the Company or any parent or subsidiary of the Company.

5. OPTION PRICE.

(a) The purchase price of each share of Common Stock subject to an option or any portion thereof which has been designated as an ISO shall not be less than 100% (or 110%, if at the time of grant the optionee owns or under
Section 424(d) of the Code is deemed to own more than 10% of the total combined voting power of all classes of stock of the Company or any parent or subsidiary corporation) of the fair market value of such share on the date the option is granted, determined without regard to any restriction other than a restriction which, by its terms, will never lapse. The purchase price of each share of Common Stock subject to an NSO shall be such price as the Committee shall determine in its sole discretion.

(b) The fair market value of a share of Common Stock on a particular date shall be the mean between the highest and lowest quoted selling prices on such date (the "valuation date") on the securities market where the Common Stock of the Company is traded, or if there were no sales on the valuation date, on the next preceding date within a reasonable period (as determined in the sole discretion of the Committee) on which there were sales. In the event that there were no sales

in such a market within a reasonable period, the fair market value shall be as determined in good faith by the Board of Directors in its sole discretion.

6. TERM AND EXERCISE OF OPTIONS.

(a) The term of each ISO granted under this Plan shall be not more than ten years from the date of grant, or five years from the date of grant if at the time of grant the optionee owns (or under Section 424(d) of the Code is deemed to own) more than 10% of the total combined voting power of all classes of stock of the Company or any parent or subsidiary corporation. The term of each NSO granted under this Plan shall be such period of time as the Committee shall determine in its sole discretion.

(b) An option shall be exercisable at such time or times as shall be determined by the Committee. An option may be exercised only by written notice of intent to exercise such option with respect to a specified number of shares of Common Stock and payment to the Company of the amount of the option price for the number of shares of Common Stock as to which such notice applies. Payment for such shares shall be paid at the time of purchase (i) in cash, (ii) with shares of Common Stock that have been held for at least six months, to be valued at the fair market value thereof on the date of such exercise, determined as provided in Section 5(b), (iii) by any other means, including the promissory note of the holder of the option, which the Committee determines to be consistent with the purpose of this Plan and applicable law, or (iv) a combination of the foregoing. Upon receipt of payment, the Company shall deliver to the person exercising such option a certificate or certificates for such shares. It shall be a condition of the Company's obligation to issue Common Stock upon exercise of an option that the person exercising the option pay, or make provision satisfactory to the Company for the payment of, any taxes which the Company is obligated to collect with respect to the transfer of Common Stock upon such exercise or (in the case of an ISO) with respect to the disposition of such Common Stock.

The Committee may establish a program through which optionees can borrow funds with which to purchase Common Stock pursuant to exercise of an option.

(c) The proceeds of the sale of Common Stock subject to options are to be added to the general funds of the Company and used for its general corporate purposes.

7. INCENTIVE STOCK OPTIONS. [Intentionally omitted.]

8. TRANSFER OF OPTIONS.

An option or portion thereof designated as an ISO shall not be transferable by an optionee otherwise than by will or the laws of descent and distribution, and shall be exercisable during his lifetime only by him. An NSO shall not be transferable by an optionee otherwise than by will or the laws of descent and distribution, or pursuant to a qualified domestic relations order as defined by the Code or Title I of the Employee Retirement Income Security Act or the rules thereunder, except as otherwise provided by the Committee. Notwithstanding the foregoing, the designation of a beneficiary of an option by an optionee shall not be deemed a transfer prohibited by this Section.

9. TERMINATION OF EMPLOYMENT.

(a) If the employment of an optionee terminates for any reason other than for cause or by reason of death, or disability (as may be determined by the Committee under Section 9(c) below), the optionee may for a period of three months after the date of termination of employment (unless a longer period is allowed by the Committee) exercise options held by the optionee to the extent he or she was entitled to exercise such options on the date when his or her employment

terminated. In no event, however, may such optionee exercise an option at a time when the option would not be exercisable had the optionee remained an employee. For purposes of this Section 9, an optionee's employment will not be considered terminated (i) if the Committee in the exercise of its discretion shall so determine in the case of sick leave or other bona fide leave of absence approved by the Company or any parent or subsidiary company or (ii) in the case of a transfer by such optionee to the employment of an affiliated company of the employing company.

(b) If an optionee dies at a time when he or she is entitled to exercise an option, then at any time or times within one year after death, such option may be exercised, as to all or any of the shares which the optionee was entitled to purchase immediately prior to his death,

by the optionee's executor or administrator or the person or persons to whom the option is transferred by will or the applicable laws of descent and distribution. In no event, however, may any option be exercised after the expiration of such option by its terms, except as the Committee may otherwise allow for a period up to one year after such optionee's death.

(c) If an optionee becomes disabled at a time when he or she is entitled to exercise an option, then at any time or times within one year after the date of such disability, he or she may exercise such option as to all or any of the shares which he or she was entitled to purchase under such option immediately prior to his or her disability. In no event, however, may any option be exercised after the expiration of such option by its terms. The Committee shall have authority to determine whether or not an optionee has become disabled (as such term may be used in the Code); and its determination shall be binding on all concerned.

(d) If termination of employment of an optionee shall be for cause or in violation of an agreement by the optionee to remain in the employ of the Company or any parent or subsidiary company, the options held by such optionee shall terminate forthwith. If an optionee shall breach in a material respect an agreement to refrain from competition with the Company or any parent or subsidiary company, or to refrain from solicitation of the Company's customers, suppliers or employees of the Company or any parent or subsidiary company, the options, and any shares of Common Stock issued pursuant to the exercise of options, held by such optionee shall at the option of the Company be forfeited by the optionee and deemed not to be outstanding.

10. RIGHTS OF STOCKHOLDERS.

The holders of options shall not be or have any of the rights or privileges of stockholders of the Company in respect of any shares of Common Stock purchasable upon the exercise of any option until such option shall have been validly exercised.

11. ADJUSTMENTS.

Notwithstanding any other provision of this Plan, the Committee may at any time make or provide for such adjustments to this Plan, to the number and class of shares available hereunder or to any outstanding options, as it shall deem appropriate to prevent dilution or enlargement of rights, including adjustments in the event of distributions to holders of Common Stock of other than a normal cash dividend, changes in the outstanding Common Stock by reason of stock dividends, split-ups, recapitalizations, mergers, consolidations, combinations or exchanges of shares, separations, reorganizations, liquidations and the like. In the event of any general offer to holders of Common Stock relating to the acquisition of their shares, the Committee may make such adjustment as it deems equitable in respect of outstanding options, including in the Committee's discretion revision of outstanding options, so that they may be exercisable for the consideration payable in the acquisition transaction. Any such determination by the Committee shall be conclusive.

12. AMENDMENTS OR TERMINATION.

The Company's Board of Directors or the Committee may amend, alter, or discontinue this Plan, except that no amendment or alteration requiring stockholder approval pursuant to the Code's provisions with respect to ISOs shall be made without the approval of the Company's stockholders.

13. FOREIGN NATIONALS.

The Committee may in order to fulfill the purposes of this Plan modify grants to participants who are foreign nationals or employed outside the United States to accommodate differences in applicable law, tax policy, or custom.

14. GOVERNING LAW.

This Plan shall be governed by and construed and enforced in accordance with the laws of the Commonwealth of Massachusetts to the extent that such laws, as applicable to the Plan, are not superseded by or inconsistent with Federal law.

15. EFFECTIVE DATE.

This Plan is effective as of May 24, 1991, the date of its adoption by the Company's Board of Directors and Shareholders.

16. CONSOLIDATIONS OR MERGERS. In the event of a consolidation or merger in which the Company is not the surviving corporation or which results in the acquisition of substantially all the Company's outstanding stock by a single person or entity or by a group of persons and/or entities acting in concert, or in the event of the sale or transfer of substantially all the Company's assets (any of the foregoing, an "Acquisition"), all then outstanding Options shall terminate unless assumed pursuant to clause (i) below; provided, that either (i) the Committee shall provide for the surviving or acquiring entity or an affiliate thereof to assume the outstanding Options

or grant replacement options in lieu thereof, any such replacement to be upon an equitable basis as determined by the Committee, or (ii) if there is no such assumption or substitution, all outstanding Options shall become immediately and fully exercisable immediately prior to the Acquisition, notwithstanding any restrictions or vesting conditions set forth therein.

rev.11/18/99/SPC

EXHIBIT 10.2

VERTEX PHARMACEUTICALS INCORPORATED

1994 STOCK AND OPTION PLAN

(as amended as of September 14, 1999 and restated)

1. DEFINITIONS

Unless otherwise specified or unless the context otherwise requires, the following terms, as used in this Vertex Pharmaceuticals Incorporated 1994 Stock and Option Plan, have the following meanings:

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

BOARD OF DIRECTORS means the Board of Directors of the Company.

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

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

COMMON STOCK means shares of the Company's common stock, $.01 par value.

COMPANY means Vertex Pharmaceuticals Incorporated, a Massachusetts corporation.

DISABILITY or DISABLED means permanent and total disability as defined in Section 22(e)(3) of the Code.

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

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

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

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

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

NON-EMPLOYEE DIRECTOR means a member of the Board of Directors who is not an employee of the Company or any Affiliate.

OPTION means an ISO or NQSO granted under the Plan.

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

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

PLAN means this Vertex Pharmaceuticals Incorporated 1994 Stock and Option Plan, as amended from time to time.

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

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

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

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

2. PURPOSES OF THE PLAN

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

3. SHARES SUBJECT TO THE PLAN

The number of Shares subject to this Plan as to which Stock Rights may be granted from time to time shall be 2,000,000 plus the number of shares of Common Stock previously reserved for the granting of options under the Vertex Pharmaceuticals Incorporated 1991 Stock Option Plan but not granted thereunder, or the equivalent of such number of Shares after the Committee, in its sole discretion, has interpreted the effect of any stock split, stock dividend, combination, recapitalization or similar transaction in accordance with Section 17 of this Plan.

If an Option granted hereunder or any option granted under the 1991 Stock Option Plan ceases to be "outstanding", in whole or in part, or if the Company shall reacquire any Shares issued pursuant to Stock Awards, the Shares which were subject to such Option and any Shares so reacquired by the Company shall also be available for the granting of other Stock Rights under the Plan. Any Stock Right shall be treated as "outstanding" until such Stock Right is exercised in full,

or terminates or expires under the provisions of the Plan, or by agreement of the parties to the pertinent Stock Agreement, without having been exercised in full.

4. ADMINISTRATION OF THE PLAN

The Plan shall be administered by the Committee.

Subject to the provisions of the Plan, the Committee is authorized to:

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

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

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

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

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

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

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

5. ELIGIBILITY FOR PARTICIPATION

The Committee shall, in its sole discretion, name the Participants in the Plan, provided, however, that each Participant must be a Key Employee, Non-Employee Director, consultant or advisor of the Company or of an Affiliate at the time a Stock Right is granted. Notwithstanding the foregoing, the Committee may authorize the grant of a Stock Right to a person not then an employee, Non-Employee Director, consultant or advisor of the Company or of an Affiliate; PROVIDED, HOWEVER, that the actual grant of such Stock Right shall be conditioned upon such person becoming eligible to become a Participant at or prior to the time of execution of the Stock Agreement evidencing such Stock Right. The granting of any Stock Right to any individual shall neither entitle that individual to, nor disqualify him or her from, participation in other grants of Stock Rights.

6. TERMS AND CONDITIONS OF OPTIONS

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

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

6.2.1 ISO Option Price: The Option price per Share of the Shares subject to an ISO shall not be less than one hundred percent (100%) of the Fair Market Value per share of the Common Stock on the date of grant of the ISO; provided, however that the Option price per

share of the Shares subject to an ISO granted to a Participant who owns, directly or by reason of the applicable attribution rules in Code Section 424(d), more than ten percent (10%) of the total combined voting power of all classes of share capital of the Company or an Affiliate, shall not be less than one hundred ten percent (110%) of the said Fair Market Value on the date of grant.

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

6.2.3 Limitation on Grant of ISOs: No ISOs shall be granted after December 8, 2004, the date which is ten (10) years from the earlier of the date of the adoption of this Plan and the date of the approval of the Plan by the shareholders of the Company.

6.3 LIMITATION ON NUMBER OF OPTIONS GRANTED. Notwithstanding anything in this Plan to the contrary, no Participant shall be granted Options in any calendar year for the purchase of more than 200,000 Shares (subject to adjustment pursuant to Section 17 to the extent consistent with Section 162(m) of the Code).

7. TERMS AND CONDITIONS OF STOCK AWARDS

Each Stock Award shall be set forth in a Stock Agreement, duly executed by the Company and, to the extent required by law or requested by the Company, by the Participant. The Stock Agreement shall be in the form approved by the Committee, with such changes and modifications to such form as the Committee, in its discretion, shall approve with respect to any particular Participant or Participants. The Stock Agreement shall contain terms and conditions which the Committee determines to be appropriate and in the best interest of the Company; PROVIDED, HOWEVER, that the purchase price per share of the Shares covered by each Stock Award shall not be less than the par value per Share. Each Stock Agreement shall state the number of Shares to which the Stock Award pertains, the date prior to which the Stock Award must be exercised by the Participant, and the terms of any right of the Company to reacquire the Shares subject to the Stock Award, including the time and events upon which such rights shall accrue and the purchase price therefor, and any restrictions on the transferability of such Shares.

8. EXERCISE OF STOCK RIGHTS AND ISSUANCE OF SHARES

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

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

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

9. RIGHTS AS A SHAREHOLDER

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

10. ASSIGNABILITY AND TRANSFERABILITY OF STOCK RIGHTS

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

11. EFFECT OF TERMINATION OF SERVICE

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

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

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

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

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

12. EFFECT OF TERMINATION OF SERVICE FOR "CAUSE"

Except as otherwise provided in the pertinent Stock Agreement, in the event of a Termination of Service of a Participant "for cause" all outstanding and unexercised Stock Rights as of the date the Participant is notified his or her service is terminated "for cause" will immediately be forfeited.

For purposes of this Section 12, "cause" shall include (and is not limited to) dishonesty with respect to the Company and its Affiliates, insubordination, substantial malfeasance or non-feasance of duty, unauthorized disclosure of confidential information, conduct substantially prejudicial to the business of the Company or any Affiliate, and termination by the Participant in violation of an agreement by the Participant to remain in the employ of the Company of an Affiliate. The determination of the Committee as to the existence of cause will be conclusive on the Participant and the Company. "Cause" is not limited to events which have occurred prior to a Participant's Termination of Service, nor is it necessary that the Committee's finding of "cause" occur prior to termination. If the Committee determines, subsequent to a Participant's Termination of Service but prior to the exercise of a Stock Right, that either prior or subsequent to the Participant's termination the Participant engaged in conduct which would constitute "cause," then the right to exercise any Stock Right shall be forfeited. Any definition in an agreement between a Participant and the Company or an Affiliate which contains a conflicting definition of "cause" for termination and which is in effect at the time of such termination shall supersede the definition in this Plan with respect to that Participant.

13. EFFECT OF TERMINATION OF SERVICE FOR DISABILITY

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

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

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

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

15. PURCHASE FOR INVESTMENT

Unless the offering and sale of the Shares to be issued upon the particular exercise of an Stock Right shall have been effectively registered under the Securities Act of 1933, as now in force

or hereafter amended (the "1933 Act"), the Company shall be under no obligation to issue the Shares covered by such exercise unless and until the following conditions have been fulfilled:

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

"The shares represented by this certificate have been taken for investment and they may not be sold or otherwise transferred by any person, including a pledgee, unless (1) either (a) a Registration Statement with respect to such shares shall be effective under the Securities Act of 1933, as amended, or (b) the Company shall have received an opinion of counsel satisfactory to it that an exemption from registration under such Act is then available, and (2) there shall have been compliance with all applicable state securities laws.

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

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

16. DISSOLUTION OR LIQUIDATION OF THE COMPANY

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

17. ADJUSTMENTS

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

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

17.2 CONSOLIDATIONS OR MERGERS. In the event of a consolidation or merger in which the Company is not the surviving corporation or which results in the acquisition of substantially all the

Company's outstanding stock by a single person or entity or by a group of persons and/or entities acting in concert, or in the event of the sale or transfer of substantially all the Company's assets (any of the foregoing, an "Acquisition"), all then outstanding Options shall terminate unless assumed pursuant to clause (i) below; provided, that either (i) the Committee shall provide for the surviving or acquiring entity or an affiliate thereof to assume the outstanding Options or grant replacement options in lieu thereof, any such replacement to be upon an equitable basis as determined by the Committee, or
(ii) if there is no such assumption or substitution, all outstanding Options shall become immediately and fully exercisable immediately prior to the Acquisition, notwithstanding any restrictions or vesting conditions set forth therein.

17.3 RECAPITALIZATION OR REORGANIZATION. In the event of a recapitalization or reorganization of the Company (other than a transaction described in Section 17.2 above) pursuant to which securities of the Company or of another corporation are issued with respect to the outstanding shares of Common Stock, a Participant upon exercising a Stock Right shall be entitled to receive for the purchase price paid upon such exercise the securities he or she would have received if he or she had exercised such Stock Right prior to such recapitalization or reorganization.

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

18. ISSUANCES OF SECURITIES

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

19. FRACTIONAL SHARES

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

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

Any Options granted under this Plan which do not meet the requirements of the Code for ISOs shall automatically be deemed to be NQSOs without further action on the part of the Committee. The Committee, at the written request of any Participant, may in its discretion take such actions as may be necessary to convert such Participant's ISOs (or any portion thereof) that have not been exercised on the date of conversion into NQSOs at any time prior to the expiration of such ISOs, regardless of whether the Participant is an employee of the Company or an Affiliate at the time of such conversion. Such actions may include, but not be limited to, extending the exercise period or reducing the exercise price of the appropriate installments of such Options. At the time of such conversion, the Committee (with the consent of the Participant) may impose such

conditions on the exercise of the resulting NQSOs as the Committee in its discretion may determine, provided that such conditions shall not be inconsistent with this Plan. Nothing in the Plan shall be deemed to give any Participant the right to have such Participant's ISOs converted into NQSOs, and no such conversion shall occur until and unless the Committee takes appropriate action. The

Committee, with the consent of the Participant, may also terminate any portion of any ISO that has not been exercised at the time of such termination.

21. WITHHOLDING

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

22. NOTICE TO COMPANY OF DISQUALIFYING DISPOSITION

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

23. EFFECTIVE DATE; TERMINATION OF THE PLAN

The Plan shall be effective on December 8, 1994, the date it is approved by the Board of Directors. The Plan will terminate on December 8, 2004, the date which is ten (10) years from the earlier of the date of its adoption or the date of its approval by the stockholders of the Company. The Plan may be terminated at an earlier date by vote of the stockholders of the Company; provided, however, that any such earlier termination will not affect any Stock Rights granted or Stock Agreements executed prior to the effective date of such termination.

24. AMENDMENT OF THE PLAN; AMENDMENT OF STOCK RIGHTS

The Plan may be amended by the stockholders of the Company. The Plan may also be amended by the Board of Directors or the Committee, including, without limitation, to the extent necessary to qualify any or all outstanding Stock Rights granted under the Plan or Stock Rights to be granted under the Plan for favorable federal income tax treatment (including deferral of taxation

upon exercise) as may be afforded incentive stock options under Section 422 of the Code, to the extent necessary to ensure that Stock Rights granted or to be granted under the Plan are in accordance with Rule 16b-3 under the Exchange Act, and to the extent necessary to qualify the shares issuable upon exercise of any outstanding Stock Rights granted, or Stock Rights to be granted, under the Plan for listing on any national securities exchange or quotation in any national automated quotation system of securities dealers. Any amendment approved by the Board of Directors or the Committee which is of a scope that requires stockholder approval in order to ensure favorable federal income tax treatment for any ISOs or Section 162(m) of the Code shall be subject to obtaining such stockholder approval. No modification or amendment of the Plan shall adversely affect a Participant's rights under a Stock Right previously granted to the Participant without such Participant's consent.

In its discretion, the Committee may amend any term or condition of any outstanding Stock Right, PROVIDED, (i) such term or condition as amended is permitted by the Plan, (ii) if the amendment is adverse to the Participant, such amendment shall be made only with the consent of the Participant, (iii) any such amendment of any ISO shall be made only after the Committee determines whether such amendment would constitute a "modification" of any Stock Right which is an ISO (as that term is defined in Section 424(h) of the Code) or would cause any adverse tax consequences for the holder of such ISO, and (iv) with respect to any Stock Right held by any Participant who is subject to the provisions of

Section 16(a) of the Exchange Act, any such amendment shall be made only after the Committee determines whether such amendment would constitute the grant of a new Stock Right.

25. EMPLOYMENT OR OTHER RELATIONSHIP

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

26. GOVERNING LAW

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

rev. 11/18/99/SPC

EXHIBIT 10.3

VERTEX PHARMACEUTICALS INCORPORATED

1996 STOCK AND OPTION PLAN

(as amended on September 14, 1999 and restated)

1. DEFINITIONS

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

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

BOARD OF DIRECTORS means the Board of Directors of the Company.

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

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

COMMON STOCK means shares of the Company's common stock, $.01 par value.

COMPANY means Vertex Pharmaceuticals Incorporated, a Massachusetts corporation.

DISABILITY or DISABLED means permanent and total disability as defined in Section 22(e)(3) of the Code.

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

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

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

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

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

NON-EMPLOYEE DIRECTOR means a member of the Board of Directors who is not an employee of the Company or any Affiliate.

OPTION means an ISO or NQSO granted under the Plan.

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

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

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

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

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

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

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

2. PURPOSES OF THE PLAN

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

3. SHARES SUBJECT TO THE PLAN

The number of Shares subject to this Plan as to which Stock Rights may be granted from time to time shall be 4,500,000 plus the number of shares of Common Stock previously reserved for the granting of options under the Vertex Pharmaceuticals Incorporated 1991 Stock Option Plan and 1994 Stock and Option Plan but not granted thereunder, or the equivalent of such number of Shares after the Committee, in its sole discretion, has interpreted the effect of any stock split, stock dividend, combination, recapitalization or similar transaction in accordance with Section 17 of this Plan.

If an Option granted hereunder or any option granted under the 1991 Stock Option Plan or 1994 Stock and Option Plan ceases to be "outstanding", in whole or in part, or if the Company shall reacquire any Shares issued pursuant to Stock Awards, the Shares which were subject to such Option and any Shares so reacquired by the Company shall also be available for the granting of other Stock Rights under the Plan. Any Stock Right shall be treated as "outstanding" until such Stock Right is exercised in full, or terminates or expires under the provisions of the Plan, or by

agreement of the parties to the pertinent Stock Agreement, without having been exercised in full.

4. ADMINISTRATION OF THE PLAN

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

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

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

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

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

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

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

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

5. ELIGIBILITY FOR PARTICIPATION

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

6. TERMS AND CONDITIONS OF OPTIONS

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

for the Company and its other shareholders, including requirements that the Participant's or the Participant's Survivors' right to sell or transfer the Shares may be restricted, and the Participant or the Participant's Survivors may be required to execute letters of investment intent and to acknowledge that the Shares will bear legends noting any applicable restrictions.

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

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

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

6.2.3 LIMITATION ON GRANT OF ISOS: No ISOs shall be granted after December 8, 2004, the date which is ten (10) years from the earlier of the date of the adoption of this Plan and the date of the approval of the Plan by the shareholders of the Company.

6.3 NON-EMPLOYEE DIRECTORS' OPTIONS. Each Non-Employee Director, upon first being elected or appointed to the Board of Directors, shall be granted an NQSO to purchase 20,000 Shares. Each such Option shall (i) have an exercise price equal to the Fair Market Value (per share) on the date of grant of the Option, (ii) have a term of ten (10) years, and (ii) shall become cumulatively exercisable in sixteen (16) equal quarterly installments, upon completion of each full quarter of service on the Board of Directors after the date of grant. In addition, on June 1 of each year, each Non-Employee Director shall be granted a NQSO to purchase 5,000 shares. Each such Option shall (i) have an exercise price equal to the Fair Market Value (per share) on the date of grant of such Option, (ii) have a term of ten (10) years, and (iii) be exercisable in full immediately on the date of grant. Any director entitled to receive an Option grant under this Section may elect to decline the Option. Notwithstanding the provisions of Section 24 concerning amendment of the Plan, the provisions of this Subsection shall not be amended more than once every six months, other than to comport with changes in the Code, the Employee Retirement Income Security Act, or the rules thereunder. Notwithstanding anything to the contrary contained in any other provisions of this Plan, the Committee shall have no discretion to vary the terms of Options granted under this Section 6.3 from those set forth herein. The provisions of Sections 11, 13 and 14 below shall not apply to Options granted pursuant to this Subsection.

6.4 LIMITATION ON NUMBER OF OPTIONS GRANTED. Notwithstanding anything in this Plan to the contrary, no Participant shall be granted Options in any calendar year for the purchase of more than 200,000 Shares (subject to adjustment pursuant to Section 17 to the extent consistent with Section 162(m) of the Code).

7. TERMS AND CONDITIONS OF STOCK AWARDS

Each Stock Award shall be set forth in a Stock Agreement, duly executed by the Company and, to the extent required by law or requested by the Company, by the Participant. The Stock Agreement shall be in the form approved by the Committee, with such changes and modifications to such form as the Committee, in its discretion, shall approve with respect to any particular Participant or Participants. The Stock Agreement shall contain terms and conditions which the Committee determines to be appropriate and in the best interest of the Company; PROVIDED, HOWEVER, that the purchase price per share of the Shares covered by each Stock Award shall not be less than the par value per Share. Each Stock Agreement shall state the number of Shares to which the Stock Award pertains, the date prior to which the Stock Award must be exercised by the Participant, and the terms of any right of the Company to reacquire the Shares subject to the Stock Award, including the time and events upon which such rights shall accrue and the purchase price therefor, and any restrictions on the transferability of such Shares.

8. EXERCISE OF STOCK RIGHTS AND ISSUANCE OF SHARES

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

any representation required by the Plan or the Stock Agreement.

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

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

9. RIGHTS AS A SHAREHOLDER

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

10. ASSIGNABILITY AND TRANSFERABILITY OF STOCK RIGHTS

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

11. EFFECT OF TERMINATION OF SERVICE

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

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

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

11.4 Absence from work with the Company or an Affiliate because of temporary disability or a leave of absence for any purpose, shall not, during the period of any such absence in accordance with Company policies, be deemed, by virtue of such absence alone, a

Termination of Service, except as the Committee may otherwise expressly provide.

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

12. EFFECT OF TERMINATION OF SERVICE FOR "CAUSE"

Except as otherwise provided in the pertinent Stock Agreement, in the event of a Termination of Service of a Participant "for cause" all outstanding and unexercised Stock Rights as of the date the Participant is notified his or her service is terminated "for cause" will immediately be forfeited.

For purposes of this Section 12, "cause" shall include (and is not limited to) dishonesty with respect to the Company and its Affiliates, insubordination, substantial malfeasance or non-feasance of duty, unauthorized disclosure of confidential information, conduct substantially prejudicial to the business of the Company or any Affiliate, and termination by the Participant in violation of an agreement by the Participant to remain in the employ of the Company of an Affiliate. The determination of the Committee as to the existence of cause will be conclusive on the Participant and the Company. "Cause" is not limited to events which have occurred prior to a Participant's Termination of Service, nor is it necessary that the Committee's finding of "cause" occur prior to termination. If the Committee determines, subsequent to a Participant's Termination of Service but prior to the exercise of a Stock Right, that either prior or subsequent to the Participant's termination the Participant engaged in conduct which would constitute "cause," then the right to exercise any Stock Right shall be forfeited. Any definition in an agreement between a Participant and the Company or an Affiliate which contains a conflicting definition of "cause" for termination and which is in effect at the time of such termination shall supersede the definition in this Plan with respect to that Participant.

13. EFFECT OF TERMINATION OF SERVICE FOR DISABILITY

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

The Committee shall make the determination both of whether Disability has occurred and of the date of its occurrence (unless a procedure for such determination is set forth in another

agreement between the Company and such Participant, in which case such procedure shall be used for such determination). If requested, the Participant shall be examined by a physician selected or approved by the Committee, the cost of which examination shall be paid for by the Company.

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

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

15. PURCHASE FOR INVESTMENT

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

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

"The shares represented by this certificate have been taken for investment and they may not be sold or otherwise transferred by any

person, including a pledgee, unless (1) either (a) a Registration Statement with respect to such shares shall be effective under the Securities Act of 1933, as amended, or (b) the Company shall have received an opinion of counsel satisfactory to it that an exemption from registration under such Act is then available, and (2) there shall have been compliance with all applicable state securities laws.

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

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

16. DISSOLUTION OR LIQUIDATION OF THE COMPANY

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

17. ADJUSTMENTS

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

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

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

17.3 RECAPITALIZATION OR REORGANIZATION. In the event of a recapitalization or reorganization of the Company (other than a transaction described in Section 17.2 above) pursuant to which securities of the Company or of another corporation are issued with respect to the outstanding shares of Common Stock, a Participant upon exercising a Stock Right shall be entitled to receive for the purchase price paid upon such exercise the securities he or she would have received if he or she had exercised such Stock Right prior to such recapitalization or reorganization.

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

18. ISSUANCES OF SECURITIES

Except as expressly provided herein, no issuance (including for this purpose the delivery of shares held in treasury) by the Company of shares of stock of any class, or securities convertible into shares of stock of any class, shall affect, and no adjustment by reason thereof

shall be made with respect to, the number or price of Shares subject to Options. Except as expressly provided herein, no adjustments shall be made for dividends paid in cash or in property (including without limitation, securities) of the Company.

19. FRACTIONAL SHARES

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

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

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

21. WITHHOLDING

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

22. NOTICE TO COMPANY OF DISQUALIFYING DISPOSITION

Each Key Employee who receives an ISO must agree to notify the Company in writing immediately after the Key Employee makes a "Disqualifying Disposition" of any Shares acquired pursuant to the exercise of an ISO. A Disqualifying Disposition is any disposition (as defined in Section 424(c) of the Code) of such shares before the later of (a) two years from the date the Key Employee was granted the ISO, or (b) one year after the date the Key Employee acquired Shares

by exercising the ISO. If the Key Employee has died before such Shares are sold, the notice provisions of this Section 22 shall not apply.

23. EFFECTIVE DATE; TERMINATION OF THE PLAN

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

24. AMENDMENT OF THE PLAN; AMENDMENT OF STOCK RIGHTS

The Plan may be amended by the stockholders of the Company. The Plan may also be amended by the Board of Directors or the Committee, including, without limitation, to the extent necessary to qualify any or all outstanding Stock Rights granted under the Plan or Stock Rights to be granted under the Plan for favorable federal income tax treatment (including deferral of taxation upon exercise) as may be afforded incentive stock options under Section 422 of the Code, to the extent necessary to ensure that Stock Rights granted or to be granted under the Plan are in accordance with Rule 16b-3 under the Exchange Act, and to the extent necessary to qualify the shares issuable upon exercise of any outstanding Stock Rights granted, or Stock Rights to be granted, under the Plan for listing on any national securities exchange or quotation in any national automated quotation system of securities dealers. No modification or amendment of the Plan shall adversely affect a Participant's rights under a Stock Right previously granted to the Participant without such Participant's consent.

In its discretion, the Committee may amend any term or condition of any outstanding Stock Right, PROVIDED, (i) such term or condition as amended is permitted by the Plan, (ii) if the amendment is adverse to the Participant, such amendment shall be made only with the consent of the Participant, (iii) any such amendment of any ISO shall be made only after the Committee determines whether such amendment would constitute a "modification" of any Stock Right which is an ISO (as that term is defined in Section 424(h) of the Code) or would cause any adverse tax consequences for the holder of such ISO, and (iv) with respect to any Stock Right held by any Participant who is subject to the provisions of
Section 16(a) of the Exchange Act, any such amendment shall be made only after the Committee determines whether such amendment would constitute the grant of a new Stock Right.

25. EMPLOYMENT OR OTHER RELATIONSHIP

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

26. GOVERNING LAW

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

rev. 11/18/99/SPC

EXHIBIT 10.27
(WITH CERTAIN CONFIDENTIAL INFORMATION DELETED AND MARKED WITH BRACKETED **ASTERIKS)**

Collaboration and Option Agreement

BETWEEN

Vertex Pharmaceuticals Incorporated

AND

Taisho Pharmaceutical Co., Ltd

November 30, 1999

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COLLABORATION AND OPTION AGREEMENT

AGREEMENT made and effective this 30th day of November, 1999, between VERTEX PHARMACEUTICALS INCORPORATED, a corporation duly organized and existing under the laws of the Commonwealth of Massachusetts with its principal place of business at 130 Waverly Street, Cambridge, Massachusetts 02139-4242, U.S.A. ("Vertex"), and TAISHO PHARMACEUTICAL CO., LTD., a corporation duly organized and existing under the laws of Japan with its principal place of business at 24-1, Takata 3-Chome, Toshima-ku, Tokyo 170-8633, Japan ("Taisho").

INTRODUCTION

A. Vertex is engaged in the discovery, development and commercialization of novel, small molecule pharmaceuticals using advanced biology, biophysics, chemistry and information technologies. The Company has been involved for some time in research aimed at designing certain caspase inhibitors for acute intervention in stroke and other therapeutic indications.

B. Taisho is a diversified pharmaceutical company with substantial expertise in the areas of research, product development, the conduct of preclinical and clinical trials, sales and marketing, and is interested in the research, development, marketing and sale of pharmaceuticals for acute intervention in stroke and other therapeutic indications.

C. Both parties desire to enter into a collaboration specifically targeting an area in which Vertex has been working for some time -- the development of small molecule inhibitors of certain caspases -- applying the complementary skills and strengths which each party brings to the transaction.

D. The purpose of this Agreement is to set forth the terms upon which Vertex, together with Taisho, will attempt to design and develop novel, small molecule inhibitors of certain caspases for acute intervention in stroke and other therapeutic indications, with the financial and technical assistance of Taisho, for development, formulation, marketing and sale by Taisho and/or sublicensees in the Territory (as defined below) upon the terms set forth herein and in the License and Development Agreement attached as ExhibitA hereto.

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

ARTICLE I

DEFINITIONS

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

The term "control" means the possession, direct or indirect, of the power to direct or cause the direction of the management and policies of a Person, whether through the ownership of voting securities, by contract or otherwise. Control will be presumed if one Person owns, either of record or beneficially, fifty percent (50%) or more of the voting stock of any other Person.

1.2 "PERSON" shall mean any individual, corporation, partnership, association, limited liability company, trust, unincorporated organization or government or political subdivision thereof.

1.3 "CASPASES" are
[**********
****
**********].

1.4 "COMPOUND" shall mean a small molecule inhibitor of a Caspase, synthesized (a) by Vertex, prior to the Effective Date of this Agreement in the course of its research program directed toward the discovery of Caspase inhibitors; or (b) by Vertex, Taisho, or Vertex together with Taisho, in the course of the Research Program to which this Agreement relates. The term "Compound" shall, however, exclude
[**********
****
****
****
****
**********]

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

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

1.7 "FIELD" shall mean the treatment or prevention of diseases in humans using pharmaceutical products which inhibit one or more Caspases.

1.8 "LICENSE AGREEMENT" shall mean a License and Development Agreement substantially in the form attached hereto as Exhibit A which shall become effective as set forth in Article IV hereof.

1.9 "LICENSED COMPOUND" shall mean any Compound which becomes the subject of Taisho's rights upon exercise of its license and development option or is selected by the JDC (as defined in Article IV (c)) in accordance with the provisions of Article IV hereof.

1.10 "LICENSED PATENTS" shall mean any Vertex Patents which become the subject of Taisho's rights upon exercise of its license

and development option or is selected by the JDC in accordance with the provisions of Article IV hereof.

1.11 "PATENTS" shall mean all existing patents and patent applications and all patent applications hereafter filed, including any continuations, continuations-in-part, divisionals, provisionals or any substitute applications, any patent issued with respect to any such patent applications, any reissue, reexamination, renewal or extension (including any supplemental patent certificate) of any such patent, and any confirmation patent or registration patent or patent of addition based on any such patent, and all foreign counterparts of any of the foregoing.

1.12 "VERTEX PATENTS" shall mean any Patents Controlled by Vertex (or any of its Affiliates) claiming (i) a Compound or a method of using a Compound (a "method of using" being deemed to refer, here and hereafter in this Agreement, to a use patent), or (ii) a Compound formulation or a manufacturing process or packaging invention related to a Compound or (iii) an improvement to the subject matter of a Patent covering a Compound or a method of using a Compound or a manufacturing process or packaging invention related to a Compound. A list of Vertex Patents is appended hereto as Schedule 1.12 and will be updated periodically to reflect additions thereto during the course of this Agreement.

1.13 "TAISHO PATENTS" shall mean any Patents Controlled by Taisho (or any of its Affiliates), excluding patent applications or patents which Taisho has assigned to Vertex under Section 2.6 hereof, claiming (i) a Compound or a method of using a Compound or (ii) a Compound formulation or a manufacturing process or packaging invention related to a Compound or (iii) an improvement to the subject matter of a Patent covering a Compound or a method of using a Compound or a manufacturing process or packaging invention related to a Compound. A list of Taisho Patents is appended hereto as Schedule 1.13 and will be updated periodically to reflect additions thereto during the course of this Agreement.

1.14 "KNOW-HOW" shall mean all proprietary and confidential material and information including data, technical information, know-how, experience, inventions, discoveries, trade secrets, compositions of matter and methods, whether currently existing or developed or obtained during the course of this Agreement and whether or not patentable, that are Controlled by a party hereto or its Affiliates and that relate to the development, utilization, manufacture or use of any Compound, including but not limited to processes, techniques, methods, products, materials and compositions.

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

1.16 "TAISHO KNOW-HOW" shall mean all Know-How of Taisho.

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

1.18 "TAISHO TECHNOLOGY" shall mean all Taisho Patents and Taisho Know-How.

1.19 "RESEARCH PROGRAM" shall mean research activities associated with discovery or creation of Compounds hereunder, including IN VITRO studies of Compounds, IN VIVO animal studies for research purposes only (rather than for the generation of data for regulatory submission), and related activities, as described in the Summary of Research Activities attached hereto as Schedule 1.19, as that Summary may be revised from time to time by the Joint Research Committee.

1.20 "TERRITORY" shall mean those countries listed in Schedule 1.2 hereto.

1.21 "THIRD PARTY" shall mean any Person other than Vertex, Taisho or their respective Affiliates or sublicensees of rights conveyed under this Agreement.

ARTICLE II

RESEARCH PROGRAM

2.1 COMMENCEMENT. Vertex shall commence the Research Program promptly upon the Effective Date and shall use its reasonable best efforts to diligently conduct the Research Program during the term of this Agreement in accordance with the provisions hereof. The Research Program will continue for [*******] after the Effective Date, and may be extended for a further period by written agreement of the parties hereto.

2.2 JOINT RESEARCH COMMITTEE. Upon the execution of this Agreement, Vertex and Taisho will establish a Joint Research Committee (the "JRC") under the leadership of Vertex which shall consist of three (3) persons designated from time to time by Vertex

and three (3) persons designated from time to time by Taisho, or such additional number as may be mutually agreed. The initial members of the JRC shall be those persons designated on Schedule 2.2 hereto. The JRC shall operate by consensus and in accordance with agreed joint resolutions, but in the event of disagreement which cannot be resolved by discussion among the parties, [**********]The JRC shall meet formally at least semi-annually, or with such other frequency, and at such time and location, as may be established by the JRC, for the following purposes:

(a) To receive and review reports by Vertex (and by Taisho if it is conducting activities under the Research Program), which shall be prepared and submitted to the JRC on a quarterly basis within thirty (30) days after the end of the quarter, setting forth in general terms the results of work performed by the reporting party and its Affiliates and sublicensees during the preceding calendar quarter under the Research Program, including any planned or filed Patents covering Compounds;

(b) To advise Vertex and Taisho concerning research strategy, goals and activities, and to consider whether redirection of the Research Program should be recommended to Vertex and Taisho under Section 2.4 of this Agreement;

(c) To assist in coordinating scientific interactions between Vertex and Taisho during the course of the Research Program;

(d) To discuss matters relating to Vertex Patents and Taisho Patents (other than [**********
**********]

2.3 EXCHANGE OF INFORMATION. Vertex and Taisho will meet informally on a regular basis to discuss the Research Program, and each party will freely share with the other party, technical and commercial information Controlled by the disclosing party which is relevant to the subject matter of the Research Program and the license and development option referenced in Article IV hereof. Vertex will provide quarterly written reports on the progress of the Research Program, including information regarding possible Compound candidates, to Taisho and to the JRC, within thirty (30) days after the end of each calendar quarter during the term of the Research Program. Taisho will make similar reports if it has conducted activities in connection with the Research Program during the reporting period. Each party will enable any of the other party's representatives on the JRC, or other authorized representatives, to review the ongoing research being conducted by it under the Research Program and to discuss that research with its officers, all at such reasonable times and as often as may be reasonably requested. Any representatives of Vertex or Taisho receiving information from representatives of the other party shall sign appropriate agreements ensuring that information disclosed to them is held in confidence as required under Article V, or shall be subject to similar obligations of confidentiality and non-use which cover the information disclosed. In the event that Taisho is required under any provision hereof to disclose to or provide Vertex with data or information generated by Taisho, or at its direction, during the Research Program, concerning a Compound, Taisho shall provide a summary of that data and information, in English, sufficient for Vertex to understand the general content and significance of that data and information, [**********
****
**********].

2.4 REDIRECTION OF RESEARCH PROGRAM. The primary focus of the Research Program is to design Compounds having activity in the inhibition of Caspases, for [**********]. If at any time during the term of this Agreement, the JRC shall determine in good faith that the Research Program or any portion thereof cannot be successfully completed, or if so completed will not produce a Compound that is commercially viable, or that the goal of the Research Program has been attained prior to the end of its [******], the JRC may suggest revision or reorientation of the Research Program to each party's own top management, and upon mutual consent Vertex and Taisho shall thereafter promptly modify their respective activities in connection with the Research Program accordingly.

2.5 TAISHO RESEARCH. Taisho will not be obligated to conduct any part of the Research Program, and [**********
**********]. If Taisho is conducting activities under the Research Program pursuant to the foregoing, Vertex will supply Taisho with such amounts of bulk Compound as shall be reasonably necessary for any small-scale preclinical activities being undertaken by Taisho hereunder, at [**********].

2.6 IMPROVEMENT. Taisho shall use its reasonable best efforts to keep Vertex promptly and fully informed of any Compounds designed or discovered by Taisho or any of its Affiliates, sublicensees and subcontractors as a result of work under the Research Program ("Taisho Research Compounds"), and any improvements other than the Formulation and Use Inventions defined in Section 6.1 hereof, made by Taisho or its Affiliates or sublicensees relating to Compounds and Know-How during the term of the Research

Program, whether patentable or not ("Taisho Improvements"). Upon Vertex's written request which shall be required to be made within three (3) months from Taisho's notification, Taisho shall [**********]. Vertex shall use its reasonable best efforts to keep Taisho promptly and fully informed of any Compounds designed or discovered by Vertex or any of its Affiliates, sublicensees and subcontractors as a result of work under the Research Program ("Vertex Research Compound"), and any improvements made by Vertex or any of its Affiliates, sublicensees and subcontractors relating to Compound and Know-How during the term of the Research Program, whether patentable or not ("Vertex Improvement"). Such Vertex Research Compound and Vertex Improvement shall be subject to Taisho's rights under Article IV hereof. [**********].Vertex will not [**********].

2.7 EXCLUSIVITY. During the term of this Agreement, [**********] other than under the terms of this Agreement. The foregoing provision shall only be applicable to the research, development, manufacture or sale of small molecule compounds, or pharmaceutical products containing small molecule compounds, for which Caspase inhibition is a principal mode of therapeutic action. Notwithstanding the foregoing, this Section 2.7 shall

not apply to [**********].

ARTICLE III

PAYMENTS BY TAISHO

3.1 REIMBURSEMENT. Taisho will make reimbursement to Vertex as follows, on the dates referenced below, of certain of Vertex's past research costs, in recognition of Vertex's research program in the Field having achieved certain research milestones through the Effective Date:

1. Not more than fifteen (15) [****] business days after the later of the Effective Date or the date upon which the last party hereto executes this Agreement:

2. On the first anniversary of the [****] Effective Date: TOTAL [****]

At Taisho's request Vertex will provide Taisho with documentation which support characterization of the payments made by Taisho under this Section 3.1 as reimbursement for research expenditures made by Vertex.

3.2 RESEARCH PAYMENT. Taisho will make research payment for Vertex's research activities under the Research Program in the form of the following payments to Vertex.

Research Year 1.	October 1, 1999 - September 30, 2000
[****]	
Research Year 2.	October 1, 2000 - September 30, 2001
[****]	
Research Year 3.	October 1, 2001 - September 30, 2002
[****]	

	TOTAL
[****]	

The payments referenced in this paragraph shall be made in equal quarterly installments of [***], each of which will be due not later than
[**********]the commencement of each three (3) month period (October 1, January 1, April 1 and July 1) during the referenced Research Year. The first payment due for the period October 1 - December 31, 1999 shall be made not more than
[**********]the later of the Effective Date or the date upon which the last party

hereto executes this Agreement. A "business day" for purposes of this Agreement shall mean a day that is not a weekend day or a legal holiday in Boston, Massachusetts or Tokyo, Japan or is customarily specified as a holiday by Vertex or Taisho. All payments shall be made by wire transfer in United States dollars to the credit of such bank account as may be designated by Vertex in writing to Taisho. Any payment which falls due on a date which is not a business day may be made on the next succeeding business day. Taisho's obligation to make any of the foregoing payments which are due and payable on the effective date of any termination of this Agreement pursuant to Section 8.1 hereof shall survive termination.

3.3 RESEARCH RECORDS; EXPENDITURE REPORTS. Each researcher performing work under this Agreement, whether employed directly by Vertex or Taisho or one of its Affiliates, or subcontractors, shall keep and properly maintain a laboratory notebook in which all work and experiments performed by him are entered and kept separate and distinct from all other work not related to this Agreement. Vertex shall provide to Taisho, annually during the term of the Research Program, a research expenditure report in the form attached hereto as Schedule
3.3, which shall be delivered to Taisho within ninety (90) days following December 31 of each year of the Research Program. The books and records of Vertex relating to such research expenditures will be subject to inspection at all reasonable times by Taisho with reasonable notice, for the purpose of verifying the accuracy of the research expenditure report referenced above. The books and records relating to a reported research expenditure shall be retained by Vertex for a period of not less than five (5) full fiscal years after the year in which the research expenditure occurred.

ARTICLE IV

LICENSE AND DEVELOPMENT OPTION

Taisho has the exclusive license and development option to the Compounds and by exercising its option may obtain an exclusive license to one or more Licensed Compounds which Taisho is interested in developing, marketing and selling in the Territory subject to the following terms and conditions.

(a) (i) During the course of the Research Program
[**********]Vertex will notify Taisho in writing if and when Vertex has selected a Compound for development in the Field outside the Territory. Taisho shall have a period of [**********](an "Option Exercise Period") after receipt of such written notice from Vertex in which to exercise its option to obtain a license and to develop that Compound as a Licensed Compound under the License Agreement, by written notice to Vertex. Taisho shall use good faith efforts to decide as early as possible within the
[****] Option Exercise Period whether to exercise its option in each case, and will communicate that decision to Vertex as soon as it is made. Taisho's option with respect to a particular Compound shall expire if the option is not exercised within the associated Option Exercise Period.

(ii) If during the term of the Research Program Vertex does not designate any Compounds for development in the Field outside the Territory, or if there are no Compounds under development outside the Territory on the date the Research Program terminates, then Taisho shall have an option exercisable during the [*******] after termination of the Research Program to obtain a license and to develop any Compound as a Licensed Compound under the License Agreement, whether or not thereafter selected by Vertex for development outside the Territory, upon written notice to Vertex. Vertex shall not be obligated in such event to develop that Compound, and if it chooses not to do so, the full cost of development of that Compound in the Territory shall be borne by Taisho.

(b) Promptly upon exercise of any such option by notice in writing from Taisho to Vertex, the parties shall execute a License Agreement covering the Licensed Compound to which the option exercise was directed, substantially identical in form and substance to the form of License Agreement attached hereto as Exhibit A. Subsequent Licensed Compounds, if any, as to which Taisho exercises its option shall be added to the License Agreement as contemplated therein. Taisho will develop that Compound as a Licensed Compound in the Territory in accordance with the terms of the License Agreement.

(c) Taisho's option rights under this Article IV shall expire upon the later of [**********provided that, even after [**********]and so long as the option has previously been exercised with respect to a Licensed Compound and development or commercialization of that Licensed Compound is proceeding in accordance with the terms of the License Agreement, Taisho may propose to the Joint Development Committee (the "JDC," a committee established under the License Agreement, details of which are provided in the License Agreement), at any time during the [**********that the JDC select any other Compound for development under the License Agreement from among those Compounds that were synthesized or had shown activity as Caspase inhibitors in the Research Program. Any Compound so proposed by Taisho and selected by the JDC will be developed by Taisho under the License Agreement, except that Vertex shall not be obligated in such event to develop that Compound, and if it chooses not to do so, the full cost of development of that Compound in the Territory shall be borne by Taisho. Without reference to the previously mentioned [*****] limitation or provisions of Article IV (d), [**********
**********]with respect to a Licensed Compound shall be exercisable for a period ending ninety (90) days after the earlier of termination of the development of that Licensed Compound or [********** *******] in the Territory with respect to that Licensed Compound. The option shall also continue to be exercisable, [**********
****
**********]with respect to that Licensed Compound, after which it will expire. For purposes of the foregoing: (i) a [****** ******] shall mean a Phase II Clinical Trial which contains one or more studies aimed at yielding preliminary data on the efficacy of a Compound in a tested indication. ; (ii) a Designated Substitute Compound for a Licensed Compound shall be those one or more Compounds

(presumptively one Compound, but more than one upon a demonstration that more than one is reasonably necessary) selected by the JDC which in the opinion of the JDC are the Compound or Compounds, if any, most likely on a scientific and commercial basis to be selected for development as substitutes for a Licensed Compound if development of that Licensed Compound should be terminated prior to regulatory approval in Japan for the sale of a Drug Product containing that Licensed Compound. If the JDC is unable to reach consensus on whether a Compound so proposed by Taisho should be selected for development, or whether a Compound should be substituted for a Licensed Compound the development of which has been terminated, or which if any Compound should be selected as Designated Substitute Compound for a Licensed Compound, [**********
**********].

(d) After the expiration of the [*****] period referenced in (c) above, and so long as Taisho is developing or commercializing a Licensed Compound in accordance with the terms of the License Agreement, Vertex will attempt in good faith to negotiate with Taisho the terms under which Taisho might obtain a license, to develop and commercialize in the Territory any Compound in the Field, before Vertex shall license or otherwise transfer rights to that Compound in the Territory to a Third Party. Notwithstanding the foregoing, Vertex shall not license or otherwise transfer rights to any Compound to a Third Party without adequate provisions to ensure that those Compounds remain subject to Taisho's option or the JDC's option of substitution referenced in (c) above, so long as that option is exercisable with respect to those Compounds.

(e) Upon exercise by Taisho or the JDC of the option under Article IV to develop a Compound, Taisho will be entitled to the exclusive right to that Compound in the Territory under the terms of the License Agreement, which right includes [**********
**********].

ARTICLE V

CONFIDENTIALITY

5.1 UNDERTAKING. During the term of this Agreement, each party shall keep confidential, and other than as provided herein shall not use or disclose, directly or indirectly, any trade secrets, confidential or proprietary information (including information embodied in sample materials), or any other knowledge, information, documents or materials, owned, developed or possessed by the other party, whether in tangible or intangible form, the confidentiality of which such other party takes reasonable measures to protect, including but not limited to Vertex Technology and Taisho Technology. Each party shall take any and all lawful measures to prevent the unauthorized use and disclosure of such information, and to prevent unauthorized persons or entities from obtaining or using such information. Each party further agrees to refrain from directly or indirectly taking

any action which would constitute or facilitate the unauthorized use or disclosure of such information. Each party may disclose such information to its directors, officers, employees, consultants and agents, and in the case of Vertex, to its licensees and subcontractors in the Field outside the Territory, and in case of Taisho, to sublicensees under the License Agreement, if any, and to subcontractors in connection with the research, development or manufacture of Compounds, to the extent necessary to enable such parties to perform their obligations or exercise their rights hereunder or under the applicable sublicense or subcontract, as the case may be; provided, that such directors, officers, employees, consultants, agents, licensees, sublicensees and subcontractors have entered into appropriate confidentiality agreements for secrecy and non-use of such information which by their terms shall be enforceable by injunctive relief at the instance of the disclosing party. Each party shall be liable for any unauthorized use and disclosure of such information by its directors, officers, consultants, employees and agents and any such licensees, sublicensees and subcontractors. Taisho may also provide a copy of this Agreement to the Bank of Japan, Japan's Ministry of Finance, Ministry of Health and Welfare, National Tax Office and other governmental agencies, all as and only to the extent required under applicable Japanese laws or government regulations.

5.2 EXCEPTIONS. Notwithstanding the foregoing, the provisions of
Section 5.1 hereof shall not apply to knowledge, information, documents or materials which the receiving party can conclusively establish: (i) have entered the public domain without such party's breach of any obligation owed to the disclosing party; (ii) have become known to the receiving party prior to the disclosing party's disclosure of such information to such receiving party; (iii) are permitted to be disclosed by the prior written consent of the disclosing party; (iv) have become known to the receiving party from a source other than the disclosing party other than by breach of an obligation of confidentiality owed to the disclosing party;
(v) are disclosed by the disclosing party to a Third Party without restrictions on its disclosure; (vi) are independently developed by the receiving party without breach of this Agreement; or (vii) are required to be disclosed by the receiving party to comply with applicable laws, to defend or prosecute litigation or to comply with governmental regulations, provided that the receiving party provides prior written notice of such disclosure to the disclosing party and takes reasonable and lawful actions to avoid or minimize the degree of such disclosure.

5.3 PUBLICITY. The timing and content of any press releases or other public communications relating to the Agreement and the transactions contemplated herein will, except as otherwise required by law, be determined jointly by Taisho and Vertex.

5.4 SURVIVAL. The provisions of this Article V shall survive the termination of this Agreement.

ARTICLE VI

PATENTS

6.1 PREPARATION. Vertex will be responsible for the preparation, filing, prosecution and maintenance of any and all Patents in the Territory included in Vertex Patents,
[**********
**********]. Taisho will be responsible for the preparation, filing, prosecution and maintenance of any and all Patents in the Territory included in the Taisho Patents
[**********
**********]including without limitation any such Patents covering formulations
[**********].Vertex and Taisho shall each furnish to the other party copies of significant documents relevant to any such preparation, filing, prosecution or maintenance. Vertex

and Taisho shall cooperate fully in the preparation, filing, prosecution and maintenance of all Vertex Patents and Taisho Patents, executing all papers and instruments so as to enable the responsible party to apply for, prosecute, and to maintain patent applications and patents in its name in any country in the Territory. The parties acknowledge the importance of maintaining the confidentiality of any inventions or other information relating to potential patent claims prior to the filing of patent applications with respect thereto. Each party shall provide to the other prompt notice as to all matters which may affect the preparation, filing, prosecution or maintenance of any such patent applications or patents.

6.2 COST REIMBURSEMENT. Taisho shall reimburse Vertex for the following direct costs with respect to Vertex Patents [**********
**********] for the preparation, filing, prosecution and maintenance of Vertex Patents in the Territory. "General patent preparation and maintenance costs" shall include the direct costs of preparation, filing and prosecution of any patent application contained in Vertex Patents from which a patent application filed in any country of the Territory claims priority, and any patent application filed under the Patent Cooperation Treaty (PCT). Vertex shall notify Taisho in writing from time to time of its plans with respect to the preparation, filing, prosecution and maintenance of Vertex Patents in each country in the Territory which are, or have not yet become, Licensed Patents, together with Vertex's estimate of the costs of such preparation, filing, prosecution and maintenance and an estimate of Vertex's general patent preparation and maintenance costs. Taisho shall reimburse Vertex for
[**********
**********] In any event, the provisions of Section 6.3 will apply to any patent which is the object of the

foregoing notice from Taisho and which Vertex continues to prosecute or maintain.

6.3 FAILURE TO REIMBURSE. If Taisho shall fail, without good reason hereunder, to reimburse Vertex as required under Section 6.2 above with respect to a patent application or patent included within the Vertex Patents within sixty (60) days after receipt of a written request for payment from Vertex, Vertex may terminate Taisho's rights with respect to that patent or patent application upon thirty (30) days written notice thereof to Taisho, unless Taisho during such 30-day period shall have submitted payment pursuant to the aforementioned request for payment.

6.4 LICENSE TO FORMULATIONS AND USE INVENTIONS. The license to the Formulations and Use Inventions granted to Vertex under
Section 8.2 of the License Agreement shall be effective hereunder subject to the limitations set forth in Section 8.2 of the License Agreement.

ARTICLE VII

INFRINGEMENT

Either party shall notify the other party promptly of any possible infringements, imitations or unauthorized possession, knowledge or use of the intellectual property embodied in any of the Vertex Technology by Third Parties in any country in the Territory, of which it becomes aware. Either party shall promptly furnish the other party with full details of such infringements, imitations or unauthorized possession, knowledge or use, and shall assist in preventing any recurrence thereof.

[**********
**********].
Such suit may not be settled by Taisho without Vertex's consent, which shall not be unreasonably withheld. Damages recovered in any actions referenced hereunder shall be divided [**********] to Taisho and [********] to Vertex after reimbursement to each party of their respective expenses in prosecuting such actions as provided hereunder.

ARTICLE VIII

TERM AND TERMINATION

8.1 TERM OF AGREEMENT. This Agreement will extend until the later of the expiration of Taisho's option rights or JDC's option right under Article IV hereof, unless earlier terminated by either party hereto in accordance with other applicable provisions of this Agreement. Taisho may elect to extend the term of the Research Program and this Agreement by written notice given to Vertex not less than [**********] prior to the expiration of the Research Program, upon

terms and conditions to be negotiated in good faith and agreed upon in writing by the parties.

8.2 TERMINATION OF RESEARCH PROGRAM BY TAISHO FOR CAUSE. Upon written notice to Vertex, Taisho may at its sole option terminate the Research Program and this Agreement upon the occurrence of any of the following events:

(a) Vertex shall materially breach this Agreement, which shall include a failure to use its reasonable best efforts to pursue the Research Program diligently (provided, however, that this provision shall not be construed as a guarantee by Vertex that the Research Program will be successfully completed or any Compounds successfully developed), and such material failure to perform shall not have been remedied or steps initiated to remedy the same to Taisho's reasonable satisfaction, within [**********] days after Taisho sends written notice of failure to perform to Vertex; or

(b) Vertex shall cease to function as a going concern by suspending or discontinuing its business for any reason except for interruptions caused by strike, labor dispute or any other events over which it has no control (unless termination of this Agreement is permitted under Section 10.3 hereof); or

(c) A receiver for Vertex shall be appointed or applied for, or a general assignment shall be made for the benefit of its creditors or any proceeding involving Vertex shall be voluntarily commenced by it under any bankruptcy, reorganization, insolvency, readjustment of debt, dissolution or liquidation law or statute of the United States or any state thereof or such proceedings shall be involuntarily instituted against it, and Vertex by any action shall indicate its approval of or consent to, or acquiescence therein, or the same shall remain undismissed for [*******].

In the event of any valid termination under this Section 8.2, Taisho shall not be required to make any payments under Section 3.2 hereof which are not due and payable prior to receipt by Vertex of the notice of failure to perform referenced under Section 8.2(a), receipt by Vertex of the notice of termination pursuant to Section 8.2(b), or the occurrence of the event referenced in Section 8.2(c), as the case may be. Notwithstanding the foregoing, any License Agreement then in effect under the provisions of Article IV of this Agreement shall continue in effect in accordance with its terms.

8.3 TERMINATION BY VERTEX FOR CAUSE. In addition to rights of termination which may be granted to Vertex under other provisions of this Agreement, upon written notice to Taisho, Vertex may at its sole option terminate this Agreement upon the occurrence of any of the following events:

(a) Taisho shall materially breach this Agreement, and such material failure to perform shall not have been remedied or steps initiated to remedy the same to Vertex's reasonable satisfaction, within [**********] after Vertex sends written notice of failure to perform to Taisho; or

(b) Taisho shall cease to function as a going concern by suspending or discontinuing its business for any reason except for interruptions caused by strike, labor dispute or any other events over which it has no control (unless termination of this Agreement is permitted under Section 10.3 hereof); or

(c) A receiver for Taisho shall be appointed or applied for, or a general assignment shall be made for the benefit of its creditors or any proceeding involving Taisho shall be voluntarily commenced by it under any bankruptcy, reorganization, insolvency, readjustment of debt, dissolution or liquidation law of Japan or such proceedings shall be involuntarily instituted against it, and Taisho by any action shall indicate its approval of or consent to, or acquiescence therein, or the same shall remain undismissed for [**********].

8.4 TERMINATION. If the parties shall determine in good faith (as evidenced by a writing signed by each party), that there is no further scientific basis to pursue research and development of Compounds in the Field, and if either party shall propose, in writing, to the JRC and the other party that the parties consider redirection of the Research Program under Section 2.4 of this Agreement, and if within [*******] after such proposal is received by the other party and the JRC, the Research Program has not been redirected, then either party may terminate this Agreement on [**********] written notice to the other party. On or after the effective date of any such termination no further payments shall become due and payable hereunder by one party to the other, except pursuant to obligations which have accrued hereunder prior to the effective date of such termination.

8.5 EFFECT OF TERMINATION OR EXPIRATION. Termination of this Agreement for any reason, or expiration of this Agreement, will not affect: (i) obligations which have accrued as of the date of termination or expiration, and (ii) obligations and rights under the following provisions, which shall survive termination or expiration of this Agreement: the last sentence of both Sections 3.2 and 3.3; Articles IV(d), V and IX.

ARTICLE IX

DISPUTE RESOLUTION

9.1 GOVERNING LAW, AND JURISDICTION. This Agreement shall be governed and construed in accordance with the [**********]Both parties agree that any legal proceedings between the parties relating to this Agreement other than a proceeding to which Section 9.2 is applicable, shall be brought in the state or prefecture of the principal office of the defendant party; provided that a proceeding to enforce an arbitration award may be brought in the state or prefecture of the plaintiff's principal office, and each party agrees to submit to personal jurisdiction and to accept venue in the courts of such state or prefecture solely for the purpose of enforcement of any such award.

9.2 ARBITRATION. In the event of any controversy or claim arising out of or relating to any provision of this Agreement or the breach thereof, the parties shall try to settle their differences amicably between themselves. Any such controversy or claim which the parties are unable to resolve shall, upon the written request for arbitration of one party delivered to the Secretariat of the International Court of Arbitration (the "Court"), be submitted to and be settled by arbitration [**********
**********]in accordance with the Rules of Arbitration of the International Chamber of Commerce (the "Rules") then in effect (except as hereinafter stated), and enforcement of the award rendered by the arbitrators may be entered in any court having jurisdiction thereof and shall be final and conclusive upon both parties hereto. Notwithstanding anything to the contrary which may be contained in the Rules of the Court, the parties further agree as follows:

(i) [**********
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(ii) The arbitrators will consider the nature of the dispute, the availability of information upon which resolution of the dispute may be fairly based, and in view of those considerations and such other facts and circumstances as they may deem appropriate, shall determine the application of discovery and, if decided it is applied, shall determine the nature, scope and timing of any discovery which will be permitted to the parties to any proceeding hereunder, and that determination of the arbitrators shall be binding on such parties. The costs of arbitration to each party will be determined in accordance with Articles 30 and 31 of the Rules.

(iii) The arbitrators shall state the reasons upon which any award is based. The arbitrators shall not be authorized to award punitive damages to either party.

(iv) Upon receipt of the arbitrator's statement, either party will have the right, within [**********]thereof, to apply to the Secretariat for a correction and/or an interpretation of the award, and the arbitrators thereupon will reconsider the issues raised by said application and either confirm or alter their decision, which will then be final and conclusive upon both parties hereto.

ARTICLE X

MISCELLANEOUS PROVISIONS

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

10.2 WAIVER. Any waiver by either party of the breach of any term or condition of this Agreement will not be considered as a waiver of any subsequent breach of the same or any other term or condition hereof.

10.3 FORCE MAJEURE. Neither party will be in breach hereof by reason of its delay in the performance of, or failure to perform any of its obligations hereunder, if that delay or failure is caused by strikes, acts of God or the public enemy, riots, incendiaries, interference by civil or military authorities, compliance with governmental priorities for materials, or any fault beyond its control or without its fault or negligence. In the event that any delay or failure to perform by Vertex by reason of force majeure shall extend [**********]Taisho may suspend any payment which would otherwise become due and payable to Vertex during

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10.4 SEVERABILITY. Should one or more provisions of this Agreement be or become invalid, then the parties hereto shall attempt in good faith to agree upon valid provisions in substitution for the invalid provisions, which in their economic effect come so close to the invalid provisions that it can be reasonably assumed that the parties would have accepted this Agreement with those new provisions. If the parties are unable to agree on such valid provisions, the invalidity of such one or more provisions of this Agreement shall nevertheless not affect the validity of this Agreement as a whole.

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

10.6 GOVERNMENT APPROVALS. Taisho or its sublicensees will, if necessary, obtain any government approval required in the Territory to enable this Agreement to become effective, or to enable any payment hereunder to be made, or any other

obligation hereunder to be observed or performed. Taisho will keep Vertex informed of progress in obtaining any such government approval, and Vertex will cooperate with Taisho in any such efforts.

10.7 EXPORT CONTROLS. This Agreement is made subject to any restrictions concerning the export of Compounds or Vertex Technology from the United States which may be imposed upon or related to either party to this Agreement from time to time by the Government of the United States. Furthermore, Taisho will not export, directly or indirectly, any Vertex Technology or any Compounds utilizing such Technology to any countries for which the United States Government or any agency thereof at the time of export requires an export license or other governmental approval, without first obtaining the written consent to do so (of which Taisho will promptly inform Vertex) from the Department of Commerce or other agency of the United States Government when required by applicable statute or regulation. As of the date hereof Vertex warrants that current US export control regulations do not prohibit the disclosure or delivery to Taisho of information, data, compounds, or other materials required to be provided by Vertex to Taisho hereunder, and if such regulations should become applicable, Vertex will forthwith notify Taisho.

10.8 NO WARRANTY. Vertex makes no warranty of any kind whatsoever, either express or implied, to Taisho, or any customer of Taisho, as to the ability of Taisho to understand and utilize the Vertex Technology. Taisho makes no warranty of any kind whatsoever, either express or implied, to Vertex, or to any customer of Vertex, as to the ability of Vertex to understand and utilize the Taisho Technology.
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**********].Should a party becomes aware of any unexpected serious adverse reactions to any Compounds, Licensed Compounds or Drug Products administered to humans or animals, the party shall promptly notify the other and/or make a report to the U.S. Food and Drug Administration ("FDA") or the Japanese Ministry of Health and Welfare as required by applicable governmental regulations.

10.9 THIRD PARTY ACTIONS. (a) To Vertex's knowledge
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**********].Nevertheless, each party will promptly notify the other in the event any relevant Third Party patents come to its notice. Neither party gives a warranty to the other regarding the infringement of Third Party rights by the development, manufacture, use or sale of the Licensed Compounds or the practice of the Vertex Technology or the Taisho Technology, and gives no indemnity against costs, damages, expenses or other losses arising out of proceedings brought against the other party or any other Person by any Third Party.

(b) In the event that the development of a Compound in any country necessarily involves working within the scope of a Third Party's patent, which would otherwise be infringed by the practice of a Vertex Patent in connection with such development, then
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**********]. If the terms of a required license under a Third Party patent do not meet the foregoing requirements and Vertex therefore elects not to assume its share of any financial obligation, [**********
**********]. If the required license is either unavailable or its terms are unacceptable both to Vertex and to Taisho, then Taisho may elect in its sole discretion to discontinue sales of the Drug Product in such country or at its sole expense to undertake the defense of a patent infringement action or the prosecution of a declaratory judgment action with respect to the Third Party patents.

(c) In the event Taisho is sued for infringement of any rights of any Third Party in the course of its development of the Compounds or its use of Vertex Technology in connection therewith, Vertex shall extend to Taisho good faith assistance and support in defending such action, and may participate in the conduct of, and in discussions regarding strategic and business responses to, the suit. Damages and out-of-pocket legal fees and expenses (including legal fees and expenses of Taisho and Vertex) arising from such a legal action shall be borne [**********
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10.11 ASSIGNMENT. This Agreement may not be assigned or otherwise transferred by either party without the prior written consent of the other party; PROVIDED, HOWEVER, that either party may assign this Agreement, WITHOUT the consent of the other party,

(i) to any of its Affiliates, if the assigning party guarantees the full performance of its Affiliates' obligations

hereunder, or (ii) in connection with the transfer or sale of all or substantially all of its assets or business or in the event of its merger or consolidation with another Person. Any purported assignment in contravention of this section shall, at the option of the nonassigning party, be null and void and of no effect. No assignment shall release either party from responsibility for the performance of any accrued obligations of such party hereunder.

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

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

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

if to Taisho, at: Taisho Pharmaceutical Co., Ltd.
24-1, Takata 3-Chome
Toshimaku, Tokyo, 170-8633, Japan
Attention: General Manager, Licensing Division

with a copy to:

General Manager, Legal Division

if to Vertex, at: 130 Waverly Street
Cambridge, MA 02139-4242
Attention: Richard H. Aldrich
Senior Vice President and Chief Business Officer
cc: Corporate Counsel

with a copy to:

Kirkpatrick & Lockhart LLP
75 State Street
Boston, MA 02109
Attention: Kenneth S. Boger, Esquire
Fax: 617-951-9151

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

10.16 AUTHORITY. The undersigned represent that they are authorized to sign this Agreement on behalf of the parties hereto. The parties each represent that no provision of this Agreement will violate any other agreement that a party may have with any Third Party. Each party has relied on that representation in entering into this Agreement.

10.17 ENTIRE AGREEMENT. This Agreement contains the entire understanding of the parties relating to the matters referred to herein, and may only be amended by a written document, duly executed on behalf of the respective parties.

VERTEX PHARMACEUTICALS INCORPORATED

By:

Title:

Date of Signature:

TAISHO PHARMACEUTICAL CO., LTD.

By:
Akira Uehara

Title: PRESIDENT
Date of Signature:

SCHEDULE 1.4

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SCHEDULE 1.12

LIST OF VERTEX PATENTS

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SCHEDULE 1.13

LIST OF TAISHO PATENTS

NONE

SCHEDULE 1.19

SUMMARY OF RESEARCH ACTIVITIES

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SCHEDULE 1.20

COUNTRIES IN THE TERRITORY

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SCHEDULE 2.2

INITIAL MEMBERS OF JOINT RESEARCH COMMITTEE

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SCHEDULE 3.3

ANNUAL REPORT OF RESEARCH EXPENDITURES

VERTEX/TAISHO CASPASE PROGRAM

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EXHIBIT A TO COLLABORATION AND OPTION AGREEMENT

License and Development Agreement

BETWEEN

Vertex Pharmaceuticals Incorporated

AND

Taisho Pharmaceutical Co., Ltd

November 30, 1999

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SCHEDULE 1.9 -- LICENSED COMPOUNDs

LICENSE AND DEVELOPMENT AGREEMENT

This Agreement is made and entered into as of _____ between VERTEX PHARMACEUTICALS INCORPORATED, a corporation duly organized and existing under the laws of the Commonwealth of Massachusetts with its principal place of business at 130 Waverly Street, Cambridge, Massachusetts 02139-4242, U.S.A. (hereinafter "Vertex"), and TAISHO PHARMACEUTICAL CO., LTD., a corporation duly organized and existing under the laws of Japan with its principal place of business at 24-1, Takata 3-Chome, Toshima-ku, Tokyo 170-8633, Japan (hereinafter "Taisho").

INTRODUCTION

WHEREAS, Vertex and Taisho are parties to the Collaboration Agreement (as defined below) under which Vertex is engaged in the design and discovery of certain novel small molecule inhibitors of caspases, with the financial and technical assistance of Taisho; and

WHEREAS, Taisho has exercised its option under the Collaboration Agreement to develop and commercialize one or more Licensed Compounds in the Territory.

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

ARTICLE I

DEFINITIONS

1.1. "AFFILIATE" shall mean, with respect to any Person, any other Person which directly or indirectly, by itself or through one or more intermediaries, controls, is controlled by or is under direct or indirect common control with, such Person. The term "control" means the possession, direct or indirect, of the power to direct or cause the direction of the management and policies of a Person, whether through the ownership of voting securities, by contract or otherwise. Control will be presumed if one Person owns, either of record or beneficially, fifty percent (50%) or more of the voting stock of any other Person.

1.2. "COLLABORATION AGREEMENT" shall mean that certain Collaboration and Option Agreement dated November 30, 1999 by and between Vertex and Taisho.

1.3. "CORE DEVELOPMENT PLAN," "CORE DEVELOPMENT ACTIVITIES" and "CORE DEVELOPMENT COSTS" shall have the meanings ascribed to them in Section 3.1 hereof.

1.4. "DEVELOPMENT PROGRAM" shall mean activities associated with development of Licensed Compounds for sale as Drug Products in the Territory, including but not limited to (a) formulation of Licensed Compounds for use in preparation for

preclinical studies; (b) preclinical animal studies performed in accordance with "Good Laboratory Practices" (or the applicable equivalent) in preparation for the filing of an Investigational New Drug Application (or the applicable equivalent); (c) formulation and manufacture of Licensed Compounds for preclinical and clinical studies; (d) planning, implementation, evaluation and administration of human clinical trials; (e) manufacturing process development and scale-up for the manufacture of bulk Licensed Compound and Drug Product; (f) preparation and submission of applications for regulatory approval; and (g) post-market surveillance of approved drug indications, as required or agreed as part of a marketing approval by any governmental regulatory authority.

1.5. "DRUG PRODUCT" shall mean a product prepared from bulk Licensed Compound in finished dosage form ready for administration to the ultimate consumer as a

pharmaceutical.

1.6. "COMMENCEMENT DATE" shall mean, with respect to the application of this Agreement to a Licensed Compound, the date on which Taisho exercises its option under Article IV of the Collaboration Agreement with respect to that Licensed Compound.

1.7. "CASPASES" are[**********
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1.8. "FIELD" shall mean the treatment or prevention of diseases in humans using pharmaceutical products which inhibit one or more Caspases.

1.9. "LICENSED COMPOUNDS" shall mean any Compounds as to which the option rights granted under Article IV of the Collaboration Agreement have been exercised in accordance therewith by Taisho as identified on Schedule 1.9 hereto, as Schedule 1.9 may be updated from time to time by reason of the subsequent exercise by Taisho or the JDC of such option rights with respect to additional Compounds. "Compounds" shall have the meaning ascribed to it in the Collaboration Agreement, and the "JDC" shall have the meaning ascribed to it in Section 3.1 hereof.

1.10. "LICENSED PATENTS" shall mean any Vertex Patents which become the subject of Taisho's rights under Article II of this Agreement upon exercise of its license and development option or selection by the JDC in accordance with the provisions of Article IV of the Collaboration Agreement.

1.11. "PATENTS" shall mean all existing patents and patent applications and all patent applications hereafter filed, including any continuations, continuations-in-part, divisionals, provisionals or any substitute applications, any patent issued with respect to any such patent applications, any reissue reexamination, renewal or extension (including any supplemental patent certificate) of any such patent, and

any confirmation patent or registration patent or patent of addition based on any such patent, and all foreign counterparts of any of the foregoing.

1.12. "VERTEX PATENTS" shall mean any Patents Controlled by Vertex (or any of its Affiliates) claiming (i) a Compound or a method of using a Compound (a "method of using" being deemed to refer, here and hereafter in this Agreement, to a use patent), or (ii) a method of formulating, manufacturing, process development or packaging related to a Compound or (iii) an improvement to the subject matter of a Patent covering a Compound or a method of using a Compound or a method of manufacturing, process development or packaging related to a Compound. A list of Vertex Patents is appended hereto as Schedule 1.12 and will be updated periodically to reflect additions thereto during the course of this Agreement.

1.13. "TAISHO PATENTS" shall mean any Patents Controlled by Taisho (or any of its Affiliates) excluding patent applications or patents which Taisho has assigned to Vertex under Section 2.6 of the Collaboration Agreement, claiming (i) a Compound or a method of using a Compound or (ii) a method of formulating, manufacturing, process development or packaging related to a Compound or (iii) an improvement to the subject matter of a Patent covering a Compound or a method of using a Compound or a method of manufacturing, process development or packaging related to a Compound. A list of Taisho Patents is appended hereto as Schedule 1.13 and will be updated periodically to reflect additions thereto during the course of this Agreement.

1.14. "KNOW-HOW" shall mean all proprietary and confidential material and information including data, technical information, know-how, experience, inventions, discoveries, trade secrets, compositions of matter and methods, whether currently existing or developed or obtained during the course of this Agreement, and whether or not patentable, that are controlled by a party hereto or its Affiliates and that relate to the development, utilization, manufacture or use of any Compound, including but not limited to processes, techniques, methods, products, materials and compositions.

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

1.16. "TAISHO KNOW-HOW" shall mean all Know-How of Taisho.

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

1.18. "TAISHO TECHNOLOGY" shall mean all Taisho Patents and Taisho Know-How.

1.19. "NET SALES" shall mean, with respect to a Drug Product, the gross amount invoiced by Taisho and any Taisho Affiliate, sublicensee or marketing partner to Third Party customers for the Drug Product, less:

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1.20. "RESEARCH PROGRAM" shall have the meaning ascribed to it in the Collaboration Agreement.

1.21. "PERSON" shall mean any individual, corporation, partnership, association, limited liability company, trust, unincorporated organization or government or political subdivision thereof.

1.22. "PHASE II CLINICAL TRIALS" shall mean human clinical trials conducted for inclusion in (i) that portion of the FDA submission and approval process which provides for trials of a Drug Product on a limited number of patients for the purposes of collecting data on dosage, evaluating safety and collecting preliminary information regarding efficacy in the proposed therapeutic indication, as more fully defined in 21 C.F.R.
Section 312.21(b), and (ii) equivalent submissions with similar requirements in other countries in the Territory.

1.23. "PHASE III CLINICAL TRIALS" shall mean human clinical trials conducted for inclusion in (i) that portion of the FDA submission and approval process which provides for the continued trials of a Drug Product on sufficient numbers of patients to generate safety and efficacy data to support Regulatory Approval in the proposed therapeutic indication, as more fully defined in 21 C.F.R. Section 312.21(c), and (ii) equivalent submissions with similar requirements in other countries in the Territory.

1.24. "REGULATORY APPROVAL" shall mean, with respect to a country in the Territory, all authorizations by the appropriate governmental entity or entities necessary for commercial sale of a Drug Product in that country including, without limitation and where applicable, approval of labeling, price, reimbursement and manufacturing.

1.25. "THIRD PARTY" shall mean any Person other than Vertex, Taisho or their respective Affiliates or sublicensees of rights conveyed under this Agreement.

1.26. "LIVE CLAIM" shall mean a claim of any issued, unexpired Patent which shall not have been withdrawn, canceled or disclaimed, nor held invalid or unenforceable by a court of competent jurisdiction in an unappealed or unappealable decision.

1.27. "GMP" shall mean the current Good Manufacturing Practice regulations promulgated by the FDA, published at 21 CFR Part 210 et seq., as such regulations may be amended, and such equivalent foreign regulations or standards as may be applicable with respect to bulk Licensed Compound or Drug Product(s) manufactured or sold outside the United States.

1.28. "FIRST COMMERCIAL SALE" shall mean the first shipment of a Drug Product to a Third Party by Taisho or an Affiliate or sublicensee of Taisho in a country in the Territory following applicable Regulatory Approval of the Drug Product in such country.

1.29. "TERRITORY" shall mean those countries listed in Schedule 1.29 hereof.

ARTICLE II

RIGHTS AND LICENSES

2.1. TAISHO RIGHTS.

2.1.1. EXCLUSIVE LICENSE. Subject to the other provisions of this Agreement (including the rights of Vertex under Articles III and V hereof), Vertex grants to Taisho an ----------exclusive license, with the right to sublicense, under the Vertex Technology to develop, use, sell, have sold, export (within the Territory) and import the Licensed Compounds and to develop, make, have made, use, market, sell, have sold, export (within the Territory) and import for sale Drug Products in each country in the Territory, except in [**********].Vertex hereby grants to Taisho a semi-exclusive license (exclusive except as to Vertex or Vertex's other permitted licensees hereunder) under the Vertex Technology in [**********]as set forth in Section
2.1.2 below. The foregoing licenses shall not extend to the sale of Licensed Compounds in bulk form for purposes other than manufacturing Drug Product. Taisho shall have the right to grant sublicenses as stated above in each country in the Territory, under terms not inconsistent with this Agreement, and subject in each case to prior written notification to Vertex. Any such sublicense shall

be entered into by Taisho and the sublicensee on an arms-length basis. In the event the sublicensee breaches the sublicense, Taisho shall promptly take all reasonable steps to enforce the same. In the event of a continuing breach Taisho shall, if so requested by Vertex, terminate that sublicense in accordance with the procedures prescribed therein.

2.1.2. [**********]. Vertex and Taisho shall have semi-exclusive rights in [**********]under the Vertex Technology to develop, make, have made, use, market and sell, have sold, export (within the Territory) and import for sale Drug Products. Vertex and Taisho each may further license its semi-exclusive rights in [**********],to not more than one licensee (in the case of Taisho, such license being a sublicense subject to the terms and conditions

of this Agreement governing sublicensees). Either party shall notify the other party of its grant of any such license in advance, together with the name and address of any such licensee.

2.2. IMPROVEMENTS. Taisho shall use its reasonable best efforts to keep Vertex promptly and fully informed of any improvements (other than improvements made solely by Taisho which are Formulation and Use Inventions under Section 8.1 hereof) relating to Licensed Compounds, made by Taisho or its Affiliates or sublicensees during the term of the Development Program, whether those improvements are patentable or not ("Taisho Improvements"). Upon Vertex's written request which shall be required to be made within three (3) months from Taisho's notification, Taisho shall
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**********]Vertex shall use its reasonable best efforts to keep Taisho promptly and fully informed of any improvement relating to Licensed Compounds, made by Vertex or any of its Affiliates, sublicensees and subcontractors as a result of activities hereunder, and such improvement shall be included in the Vertex Technology and shall be subject to Taisho's rights under Section 2.1 hereof. [**** **********
**********]. Vertex will not
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2.3. EXCLUSIVITY. During the period ending
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**********]other than under the terms of this Agreement.
[**********
**********]. The foregoing provisions shall only be applicable to small molecule compounds, or pharmaceutical products containing small molecule compounds, for which Caspase inhibition is a principal mode of therapeutic action, and
[**********]If this Agreement is validly terminated by Vertex under Section 10.3 hereof, then Taisho and its Affiliates will refrain from any of the foregoing activity for a period of [*******] after such termination.

ARTICLE III

DEVELOPMENT

3.1. JOINT DEVELOPMENT COMMITTEE. As soon as practicable after the Commencement Date with respect to a Licensed Compound, Vertex and Taisho shall establish a Joint Development Committee (the "JDC") comprised of an equal number of representatives. The JDC shall coordinate the development efforts of both parties with respect to development of a Licensed Compound, will review the Core Development Plan submitted by Vertex as specified below, and will review and approve the Taisho Development Plan. When appropriate, Vertex and Taisho will seek to form a committee or other group, with members representing each party, to coordinate the development activities, worldwide, being conducted with respect to Licensed Compounds by Vertex, Taisho and any of its or their Affiliates, licensees or sublicensees. The JDC shall operate by consensus and in accordance with agreed joint resolutions, but in the event of disagreement which cannot be resolved by discussions among the parties, decisions shall be made as follows:

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3.2. CORE DEVELOPMENT ACTIVITIES. Vertex and/or its licensees, if any, will be undertaking development activities, including preclinical and clinical studies and process development, which Vertex deems necessary or appropriate in order to obtain Regulatory Approval for the sale of Drug Products outside the Territory from the U.S. FDA and the EMEA of the European Union (the "Core Development Activities"). Vertex expects the Core Development Activities will be undertaken applying standards which will allow the results of those activities to be used by Taisho in its regulatory filings in the Territory. If drug development standards and practices in the Territory are substantially at variance with usual and customary practices in the United States or the European Union in connection with Core Development Activities proposed to be conducted by Vertex, Taisho shall so inform Vertex on a timely basis. Vertex shall create a development plan for Core Development Activities with respect to Licensed Compounds (the "Core

Development Plan"), which shall be provided to the JDC and Taisho in advance for its review and comment. **
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3.3. DEVELOPMENT ACTIVITIES EXCLUSIVELY FOR THE TERRITORY. Taisho and/or its sublicensees, if any, will be responsible for and, except as otherwise provided below with ** respect to development activities by Vertex in [**********],shall bear the cost of the Development Program for Licensed Compound(s) in the Territory. The Taisho Development Program shall be conducted in accordance with a development plan (the "Taisho Development Plan") provided in advance to and reviewed and approved by the JDC. The Taisho Development Plan shall include, without limitation, the design and conduct of all preclinical and clinical studies required to obtain regulatory approval for Drug Products in the Territory that are not otherwise required as part of the Core Development Plan outside the Territory. The Taisho Development Plan may provide for the conduct of development activities in countries outside the Territory, as may be reasonably necessary or appropriate in connection with Regulatory Approval in the Territory, so long as those activities have been coordinated and are consistent with the Core Development Plan and have been approved by the JDC.[**********
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**********].

3.4. DEVELOPMENT ACTIVITIES IN [**********]. Vertex and Taisho will attempt to coordinate their respective development activities in [***] but shall have the right to pursue development of Licensed Compounds independently [*********] if effective coordination is not achieved. Absent any agreement to the contrary, each party will bear the cost of its own activities which are undertaken exclusively for Regulatory Approval in [*****]. Either party shall be free to use any data and information generated by the other party and its sublicensees, as permitted by law,

in connection with development activities in the Field for Licensed Compounds [******] for the purpose of developing Licensed Compounds in their respective territory.

3.5. INFORMATION TRANSFER. Vertex shall deliver to Taisho all information (including raw data from clinical studies of Licensed Compounds conducted by Vertex and its other licensees outside the Territory) which is necessary or useful for further development of the Licensed Compound, and for manufacture, commercial exploitation and distribution of the Drug Product in the Territory, to the extent that such information is not subject to restrictions imposed by a Third Party on disclosure to or use by the other party. Such information shall include a summary of all material written communications (copies of which Vertex will provide to Taisho at Taisho's request and expense) between Vertex or (to the extent available to Vertex) its other licensees and the U.S. FDA concerning Licensed Compounds. This information shall also include copies of all patents, patent applications, copyrights, copyright registrations and applications therefor and all other manifestations of the intellectual property embodied in the Licensed Compounds, whether in human or machine readable form.

3.6. BULK SUPPLY FOR DEVELOPMENT. Vertex will provide Taisho with bulk Licensed Compound for development in the Territory,
[**********].For purposes hereof
[**********
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**********].

3.7. REGULATORY APPROVALS. Taisho will be responsible for all required Regulatory Approvals in the Territory, including all interaction with Koseisho (Ministry of Health and Welfare) in Japan. All filings with Koseisho will be made by Taisho and approvals will be held in the name of Taisho. Taisho will keep Vertex informed about the substance of all material written communication between Taisho and Koseisho (copies of which communications Taisho will provide to Vertex at Vertex's request and expense) and may at Vertex's request attend meetings between Taisho and Koseisho representatives. Taisho shall have the right to cross-reference information and regulatory filings arising out of development work which has been conducted by Vertex and its Affiliates, licensees and sublicensees outside the Territory, for the purpose of regulatory filings in the Territory. Vertex and its licensees shall have the reciprocal right to cross reference all information and regulatory filings arising out of development work conducted by Taisho and its Affiliates and sublicensees hereunder. Taisho will supply Vertex at its request with data based on all raw data from clinical

studies conducted by Taisho and any of its sublicensees with respect to Licensed Compounds. In the event that Taisho is required subject to any provision hereof to disclose or provide Vertex with data or information generated by it during the Development Program, concerning a Licensed Compound or a Drug Product, Taisho shall provide a summary of that data and information, in English, sufficient for Vertex to understand the general content and significance of that data and information,
[**********
**********].

3.8. DUE DILIGENCE. Promptly upon exercise of its option with respect to a Compound, Taisho shall commence the Development Program in the Territory with respect to that Licensed Compound and shall use its reasonable best efforts to effect introduction of the Drug Product into the commercial market in the Territory as soon as practicable, consistent with the requirements of the Development Program and sound and reasonable business practices and judgment. After the date of the first Regulatory Approval for the sale of the Drug Product(s) in the Territory, Taisho shall use reasonable best efforts to effect introduction of the Drug Product(s) into commercial use in the other countries of the Territory, and following initial product introduction in each country shall keep the Drug Product(s) reasonably available to the public therein. In the normal course of development, a certain Licensed Compound may be dropped from development and replaced within a reasonable time with another Licensed Compound, and such occurrence in the Development Program shall not constitute a failure of due diligence. After Regulatory Approval thereof and until the expiration of this Agreement, Taisho shall endeavor to keep Drug Products reasonably available to the public throughout the commercial market in the Territory.

ARTICLE IV

MILESTONE PAYMENTS

Taisho shall make the following milestone payments with respect to each Licensed Compound developed hereunder. Milestone

payments shall be payable
[**********
**********].If two (2) (or more) Licensed Compounds are being developed at the same time, the milestones specified below will be applicable to each such Licensed Compound; PROVIDED, that [**********].On the date any one of the milestone payments set forth below is earned with respect to a particular Licensed Compound, any of the other lower numbered milestones which have not yet been earned with respect to that Licensed Compound shall be deemed to have been achieved and therefore payable with respect to that Licensed Compound.

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ARTICLE V

SUPPLY LICENSED COMPOUND

5.1. SUPPLY. Vertex shall manufacture or have manufactured and supply Taisho, its Affiliates and its sublicensees with their entire commercial requirements for bulk Licensed Compound in the Territory. Taisho shall purchase all of the requirements (including those of its Affiliates and sublicensees) of bulk Licensed Compound from Vertex for manufacture of Drug Products containing the Licensed Compounds for sale in the Territory. If Vertex shall be in material default of its supply obligations hereunder, it will immediately meet with Taisho at Taisho's request, and the parties shall agree on an alternative supply arrangement, which shall include manufacture of bulk Licensed Compound by Taisho, and shall consider whether that arrangement shall apply for the long term or until such time as the causes for Vertex's default have been cured.

5.2. SUPPLY PRICE. The supply price for a unit of bulk Licensed Compound supplied by Vertex for the manufacture of a Drug Product sold in the Territory shall be determined [***** **********
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5.3. FORECASTS AND ADJUSTMENTS.
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5.4. SUPPLY AGREEMENT. All bulk Licensed Compound supplied by Vertex to Taisho hereunder shall be provided under the terms of a supply agreement containing terms and ** conditions, in addition to those provided herein, which are usual and customary in the trade, as shall be agreed in good faith between the parties hereto.

5.5. PRICE REVISION. If Taisho produces and submits to Vertex supportive materials that show, with reference to market pricing and/or cost factors (as appropriate), that Taisho is unable to achieve a reasonable margin on sales of a Drug Product, then it will notify Vertex and the parties shall meet to discuss the matter. If it ** appears, as a result of those discussions, that the cost to Vertex of producing the Licensed Compound being sold to Taisho is significantly low in relation to the ** supply price to Taisho under the circumstances of this Agreement, then Vertex will consider reducing the supply price. Similarly, Taisho shall consider upward ** revisions of the supply price in the event that Vertex produces and submits to Taisho supportive materials that show, with reference to market pricing and/or cost ** factors (as appropriate), that Vertex is unable to obtain a reasonable margin on sales of Licensed Compound to Taisho.

5.6. UNPATENTED PRODUCT. In the event that [**********
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**********] Vertex shall reduce the Applicable Percentage of Net Sales, for Net Sales in that country, that is used to compute the supply price under Section 5.2 above for the ** Licensed Compound which is incorporated in the Drug Product, by [**********].

5.7. TAXES. The amounts payable under this Article V are net of any applicable duties, government charges, or similar items, if any, all of which shall be paid by ** Taisho.

5.8. CO-LABELING. All Drug Products sold in the Territory shall bear reference to Taisho's and Vertex's logos and trademarks with equal prominence or to the extent not ** prohibited by local law. Vertex's name, where it shall appear, will be written in the English language.

ARTICLE VI **

REPORTING **

6.1. DEVELOPMENT REPORTS. Taisho shall prepare and submit to Vertex, on a quarterly basis, reports which set forth in reasonable detail the progress of the Development ** Program in the Territory and the results of work performed thereunder during the preceding quarter. Vertex shall also report to Taisho on a quarterly basis the ** results of any development work which it may have undertaken with respect to Licensed Compounds during the preceding quarter.

6.2. SALES REPORTS AND RECORDS. During the term of this Agreement and after the First Commercial Sale of a Drug Product, Taisho shall deliver to Vertex within forty five (45) days after the end of each calendar quarter a written report showing actual Net Sales of Drug Products by Taisho, its Affiliates and sublicensees in each ** country in the Territory during such calendar quarter, and any revision of the supply price for bulk Licensed Compound to be recommended by Taisho, based on the ** information in that report. All Net Sales shall be divided in each such report into sales by Taisho and each Affiliate and sublicensee, as well as on a ** country-by-country basis, shall be stated in U.S. dollars, and shall state the rates of exchange used to convert the amounts into United States dollars from the ** currency in which such amounts are received by Taisho, using Taisho's then-current standard exchange rate methodology applied in its external reporting for the ** translation of foreign currency sales into U.S. dollars. Taisho will keep complete, true and accurate books of account and records for the purpose of showing the ** derivation of Net Sales and all amounts payable to Vertex under this Agreement. Such books and records will be kept at Taisho's principal place of business for at ** least three (3) years following the end of the calendar quarter to which they pertain, and will be open at all reasonable times and agreed by Taisho for inspection ** and copying by representatives of Vertex for the purpose of verifying Taisho's sales reports, or Taisho's compliance in other respects with this Agreement. Such ** inspections shall be at the expense of Vertex, unless a variation or error

exceeding
[**********]or the equivalent, is discovered in the course of any such ** inspection, whereupon the costs relating thereto shall be for the account of Taisho. Taisho will promptly pay to Vertex the full amount of any

underpayment, together with interest thereon at the rate of
[**********]assessed from the date payment was due.

6.3. PAYMENT DELAY. In case of a delay in any payments due from Taisho to Vertex hereunder not occasioned by force majeure, interest at the rate of [**********],assessed from the thirty-first day after the due date of the said payment, shall be due by Taisho without any special notice.

ARTICLE VII

CONFIDENTIALITY

7.1. UNDERTAKING. During the term of this Agreement, each party shall keep confidential, and other than as provided herein shall not use or disclose, directly or indirectly, any trade secrets, confidential or proprietary information (including information embodied in sample materials), or any other knowledge, information, documents or materials, owned, developed or possessed by the other party, whether in tangible or intangible form, the confidentiality of which such other party takes reasonable measures to protect, including but not limited to Vertex Technology and Taisho Technology. Each party shall take any and all lawful measures to prevent the unauthorized use and disclosure of such information, and to prevent unauthorized persons or entities from obtaining or using such information. Each party further agrees to refrain from directly or indirectly taking any action which would constitute or facilitate the unauthorized use or disclosure of such information. Each party may disclose such information to its directors, officers, employees, consultants and agents, (and in the case of Vertex, to its licensees in the Field outside the Territory, and in case of Taisho, to sublicensees under this Agreement, if any), and to subcontractors in connection with the development or manufacture of Licensed Compounds and Drug Products, to the extent necessary to enable such parties to perform their obligations hereunder or under the applicable sublicense or subcontract, as the case may be; provided, that such directors, officers, employees, consultants, agents, licensees, sublicensees and subcontractors have entered into appropriate confidentiality agreements for secrecy and non-use of such information which by their terms shall be enforceable by injunctive relief at the instance of the disclosing party. Each party shall be liable for any unauthorized use and disclosure of such information by its directors, officers, consultants, employees and agents and any such sublicensees and subcontractors. Taisho may also provide a copy of this Agreement to the Bank of Japan, Japan's Ministry of Finance, Ministry of Health and Welfare, National Tax Office and other governmental agencies, all as and only to the extent required under applicable Japanese laws or government regulations.

7.2. EXCEPTIONS. Notwithstanding the foregoing, the provisions of section 7.1 hereof shall not apply to knowledge, information, documents or materials which the

receiving party can conclusively establish: (i) have entered the public domain without such party's breach of any obligation owed to the disclosing party; (ii) have become known to the receiving party prior to the disclosing party's disclosure of such information to such receiving party; (iii) are permitted to be disclosed by the prior written consent of the disclosing party; (iv) have become known to the receiving party from a source other than the disclosing party other than by breach of an obligation of confidentiality owed to the disclosing party; (v) are disclosed by the disclosing party to a Third Party without restrictions on its disclosure; (vi) are independently developed by the receiving party without breach of this Agreement; or (vii) are required to be disclosed by the receiving party to comply with applicable laws, to defend or prosecute litigation or to comply with governmental regulations, provided that the receiving party provides prior written notice of such disclosure to the other party and takes reasonable and lawful actions to avoid or minimize the degree of such disclosure.

7.3. PUBLICITY. The timing and content of any press releases or other public communications relating to the Agreement and the transactions contemplated herein will, ** except as otherwise required by law, be determined jointly by Vertex and Taisho.

7.4. SURVIVAL. The provisions of this Article VII shall survive the termination of this Agreement.

ARTICLE VIII

PATENTS

8.1. PREPARATION. Vertex will be responsible for the preparation, filing, prosecution and maintenance of any and all Patents in the

Territory included in Vertex Patents,[**********]. Taisho will be responsible for the preparation, filing, prosecution and maintenance of any and all Patents in the Territory included in the Taisho Patents
[**********
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**********] including without limitation any such Patents covering formulations [**********
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**********]Vertex and Taisho shall each furnish to the other party copies of significant documents relevant to any such preparation, filing, prosecution or maintenance. Vertex and Taisho shall cooperate fully in the preparation, filing, prosecution and maintenance of all Vertex Patents and Taisho

Patents, executing all papers and instruments so as to enable the responsible party to apply for, to prosecute and to maintain patent applications and patents in its name in any country in the Territory. The parties acknowledge the importance of maintaining the confidentiality of any inventions or other information relating to potential patent claims prior to the filing of patent applications with respect hereto. Each party shall provide to the other prompt notice as to all matters which may affect the preparation, filing, prosecution or maintenance of any such patent applications or patents.

8.2. LICENSE TO FORMULATION AND USE INVENTIONS. Taisho shall use its reasonable best efforts to keep Vertex promptly (but not before filing of any planned patent application) and fully informed, of any Formulation and Use Inventions. Upon Vertex's written request which shall be required to be made within three (3) months from Taisho's notice to Vertex, Vertex shall have, and Taisho hereby grants to Vertex, a royalty-free, exclusive license (with the right to sublicense) under Patents covering the Formulation and Use Inventions to make, have made, use, import for sale, sell and have sold, Compounds and pharmaceutical products incorporating Compounds worldwide outside the Territory. The foregoing license will continue following expiration or termination (excluding the case of Section 10.2) of this Agreement, and will extend thereafter to the Territory. Provided, however, Vertex may license or otherwise transfer its rights to apply the Formulation and Use Inventions to the development and sale in the Field of a Compound in the Territory, only after any and all Taisho's rights to that Compound hereunder have terminated.

8.3. COST REIMBURSEMENT. Taisho shall reimburse Vertex for the following patent direct costs with respect to Vertex Patents
[**********
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**********] for the preparation, filing, prosecution and maintenance of Vertex Patents in the Territory. "General patent preparation and maintenance direct costs" shall include the costs of preparation, filing and prosecution of any patent application from which a patent application filed in any country of the Territory claims priority, and any patent application filed under the Patent Cooperation Treaty (PCT). Vertex shall notify Taisho in writing from time to time of its plans with respect to the preparation, filing, prosecution and maintenance of Vertex Patents in each country in the Territory, together with its estimate of the costs of such preparation, filing, prosecution and maintenance and an estimate of Vertex's general patent preparation and maintenance costs. Taisho shall reimburse Vertex for
[**********
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**********]In any event, the provisions of Section 8.3 will apply to any patent which is the object of the

foregoing notice from Taisho and which Vertex continues to prosecute or maintain.

8.4. FAILURE TO REIMBURSE. If Taisho shall fail, without good reason hereunder, to reimburse Vertex as required under Section 8.3 above with respect to a patent application or patent included within the Vertex Patents within sixty (60) days after receipt of a written request for payment from Vertex, Vertex may terminate Taisho's rights with respect to that patent or patent application upon thirty (30) days written notice thereof to Taisho, unless Taisho during such thirty (30) day period shall have submitted payment pursuant to the aforementioned request for payment.

8.5. COST REIMBURSEMENT FOR THE PATENTS COVERING THE FORMULATION AND USE INVENTIONS. In the event that Vertex is granted a license to the Patents covering the Formulation and Use Inventions under Section 8.2, Vertex shall reimburse Taisho for the following patent direct costs with respect to such licensed Formulation and Use Inventions: (a) two-thirds (2/3) of all of Taisho's "general patent preparation and maintenance direct costs;" and (b) all of the reasonable expenses (other than "general patent

prosecution and maintenance" costs) which Taisho has incurred, or may in the future incur, for the preparation, filing, prosecution and maintenance of the Patents covering the Formulation and Use Inventions outside the Territory. Taisho shall notify Vertex in writing from time to time of its plans with respect to the preparation, filing, prosecution and maintenance of the Patents covering the Formulation and Use Inventions in each country outside the Territory, together with its estimate of the costs of such preparation, filing, prosecution and maintenance and an estimate of general patent preparation and maintenance costs of the Patents covering the Formulation and Use Inventions.
Section 8.4 shall be applied mutatis mutandis to this Section 8.5

ARTICLE IX

INFRINGEMENT

Either party shall notify the other party promptly of any possible infringements, imitations or unauthorized possession, knowledge or use of the intellectual property embodied in any of the Licensed Patents and Vertex Know-How or Taisho Know-How related to the manufacture or use of Licensed Compounds and Drug Products by Third Parties in any country in the Territory, of which it becomes aware. Either party shall promptly furnish the other party with full details of such infringements, imitations or unauthorized possession, knowledge or use, and shall assist in preventing any recurrence thereof.
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**********] Such suit may not be settled by Taisho without Vertex's consent, which shall not be unreasonably withheld. Damages recovered in any actions referenced hereunder shall be

divided [**********]to Taisho and [**********]to Vertex after reimbursement to each party of their respective expenses in prosecuting such actions as provided hereunder.

ARTICLE X

TERM AND TERMINATION

10.1. TERM. The term of this Agreement with respect to any Licensed Compound or Drug Product incorporating that Licensed Compound shall extend in each country of the Territory until the later of the last to expire in that country of any substance Patent or use Patent which are Licensed Patents covering the Licensed Compound or Drug Product, or [*****] from the date of First Commercial Sale of the Drug Product in that country .

10.2. TERMINATION OF RESEARCH PROGRAM BY TAISHO FOR CAUSE. Upon written notice to Vertex, Taisho may at its sole option terminate this Agreement with respect to a Licensed Compound upon the occurrence of any of the following events:

(a) Vertex shall materially breach this Agreement, which shall include a failure to use its reasonable best efforts to pursue the Development Program diligently (provided, however, that this provision shall not be construed as a guarantee by Vertex that the Development Program will be successfully completed or any Licensed Compounds successfully developed), and such material failure to perform shall not have been remedied or steps initiated to remedy the same to Taisho's reasonable satisfaction, within [**********] after Taisho sends written notice of failure to perform to Vertex; or

(b) Vertex shall cease to function as a going concern by suspending or discontinuing its business for any reason except for interruptions caused by strike, labor dispute or any other events over which it has no control (unless termination of this Agreement is permitted under Section 12.6 hereof); or

(c) A receiver for Vertex shall be appointed or applied for, or a general assignment shall be made for the benefit of its creditors or any proceeding involving Vertex shall be voluntarily commenced by it under any bankruptcy, reorganization, insolvency, readjustment of debt, dissolution or liquidation law or statute of the United States or any state thereof or such proceedings shall be involuntarily instituted against it, and Vertex by any action shall indicate its approval of or consent to, or acquiescence therein, or the same shall remain undismissed for [**********].

In the event of any valid termination under this Section 10.2, Taisho shall not be required to make any payments under Article IV hereof which are not due and payable prior to receipt by Vertex of the notice of failure to perform referenced under Section 10.2(a), receipt by Vertex of the notice of termination pursuant to Section 10.2(b), or the occurrence of the event referenced in Section 10.2(c), as the case may be. Notwithstanding the foregoing, any License

Agreement then in effect covering another Licensed Compound shall continue in accordance with its terms.

10.3. TERMINATION BY VERTEX FOR CAUSE. In addition to rights of termination which may be granted to Vertex under other provisions of this Agreement with respect to a Licensed Compound, upon written notice to Taisho, Vertex may at its sole option terminate this Agreement upon the occurrence of any of the following events:

(a) Taisho shall materially breach this Agreement, and such material failure to perform shall not have been remedied or steps initiated to remedy the same to Vertex's reasonable satisfaction, [**********]after Vertex sends written notice of failure to perform to Taisho; or

(b) Taisho shall cease to function as a going concern by suspending or discontinuing its business for any reason except for interruptions caused by strike, labor dispute or any other events over which it has no control (unless termination of this Agreement is permitted under Section 12.6 hereof); or

(c) A receiver for Taisho shall be appointed or applied for, or a general assignment shall be made for the benefit of its creditors or any proceeding involving Taisho shall be voluntarily commenced by it under any bankruptcy, reorganization, insolvency, readjustment of debt, dissolution or liquidation law of Japan or such proceedings shall be involuntarily instituted against it, and Taisho by any action shall indicate its approval of or consent to, or acquiescence therein, or the same shall remain undismissed for [**********].

10.4. TERMINATION. If the parties shall determine in good faith (as evidenced by a writing signed by each party), that there is no further scientific basis to pursue research and development of a Licensed Compound in the Field, and if either party shall thereafter propose, in writing, to the JDC and the other party that the parties consider redirection of the Development Program for such Licensed Compound, and if within [**********]after such proposal is received by the other party and the JDC, the Development Program has not been redirected, then either party may terminate the License Agreement regarding such Licensed Compound on [**********]written notice to the other party. On or after the effective date of any such termination no further payments shall become due and payable hereunder by one party to the other, except pursuant to obligations which have accrued hereunder prior to the effective date of such termination.

10.5. EFFECT OF TERMINATION AND EXPIRATION. Termination of this Agreement for any reason, or expiration of this Agreement, will not affect: (i) obligations, including the payment of any milestones or royalties, which have accrued as of the date of termination or expiration, and (ii) rights and obligations under the following provisions of this Agreement, which shall survive termination or expiration of this Agreement: the last sentence of Section 2.3, and Articles VII, XI and the last

sentence of Section 12.4. Following termination of this Agreement under Section 10.1 hereof with respect to a particular country, Taisho shall have a fully paid license under the Vertex Technology to make, have made, use, sell, have sold, and import for sale the Licensed Compound and Drug Product in that country in the Territory.

ARTICLE XI

DISPUTE RESOLUTION

11.1. GOVERNING LAW, AND JURISDICTION. This Agreement shall be governed and construed in accordance with the [**********]Both parties agree that any legal proceedings between the parties relating to this Agreement other than a proceeding to which Section 9.2 is applicable, shall be brought in the state or prefecture of the principal office of the defendant party; provided that a proceeding to enforce an arbitration award may be brought in the state or prefecture of the plaintiff's principal office, and each party agrees to submit to personal jurisdiction and to accept venue in the courts of such state or prefecture solely for the purpose of enforcement of any such award.

11.2. ARBITRATION. In the event of any controversy or claim arising out of or relating to any provision of this Agreement or the breach thereof, the parties shall try to settle their differences amicably between themselves. Any such controversy or claim which the parties are unable to resolve shall, upon the written request for arbitration of one party delivered to the Secretariat of the International Court of Arbitration (the "Court"), be submitted to and be settled by arbitration [**********in

accordance with the Rules of Arbitration of the International Chamber of Commerce (the "Rules") then in effect (except as hereinafter stated), and enforcement of the award rendered by the arbitrators may be entered in any court having jurisdiction thereof and shall be final and conclusive upon both parties hereto. Notwithstanding anything to the contrary which may be contained in the rules of the Court, the parties further agree as follows:

(i)

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(ii) The arbitrators will consider the nature of the dispute, the availability of information upon which resolution of the dispute may be fairly based, and in view of those considerations and such other facts and circumstances as they may deem appropriate, shall determine the application of discovery and, if decided it is applied, shall determine the nature, scope and timing of any discovery which will be permitted to the parties to any proceeding hereunder, and that determination of the arbitrators shall be binding on such parties. The costs of arbitration to each party will be determined in accordance with Articles 30 and 31 of the Rules.

(iii) The arbitrators shall state the reasons upon which any award is based. The arbitrators shall not be authorized to award punitive damages to either party.

(iv) Upon receipt of the arbitrator's statement, said written opinion, either party will have the right, within [**********]thereof, to apply to the Secretariat for a correction and/or an interpretation of the award, and the arbitrators thereupon will reconsider the issues raised by said application and either confirm or alter their decision, which will then be final and conclusive upon both parties hereto.

ARTICLE XII

MISCELLANEOUS PROVISIONS

12.1. NO WARRANTY. Vertex makes no warranty of any kind whatsoever, either express or implied, to Taisho, or any customer of Taisho, as to the ability of Taisho to understand and utilize the Vertex Technology. Taisho makes no warranty of any kind whatsoever, either express or implied, to Vertex, or to any customer of Vertex, as to the ability of Vertex to understand and utilize the Taisho Technology. [**********
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**********]. Should a party becomes aware of any unexpected serious adverse reactions to any Licensed Compounds or Drug Products administered to humans or

animals, the party shall promptly notify the other and/or make a report to U.S. FDA or MHW as required by applicable governmental regulations.

12.2. THIRD PARTY ACTIONS. (a) To Vertex's knowledge, [**********

**********]Nevertheless, each party will promptly notify the other in the event any relevant Third Party patents come to its notice. Neither party gives a warranty to the other regarding the infringement of Third Party rights by the development, manufacture, use or sale of the Licensed Compounds or the practice of the Vertex Technology or the Taisho Technology, and gives no indemnity against costs, damages, expenses or other losses arising out of proceedings brought against the other party or any other Person by any Third Party.

(b) In the event that the development of a Licensed Compound or the sale of a Drug Product in any country necessarily involves working within the scope of a Third Party's patent, which would otherwise be infringed by the practice of a Vertex Patent in connection with such development or sale, [******
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**********]If the terms of a required license under a Third Party patent do not meet the foregoing requirements and Vertex therefore elects not to assume its share of any financial obligation,
[**********]If the required license is either unavailable or its terms are unacceptable both to Vertex and to Taisho, then Taisho may elect in its sole discretion to discontinue sales of the Drug Product in such country or at its sole expense to undertake the defense of a patent infringement action or the prosecution of a declaratory judgment action with respect to the Third Party patents.

(c) In the event Taisho is sued for infringement of any rights of any Third Party in the course of its development, manufacture, marketing and sale of Licensed Compounds or Drug Products or its use of Vertex Technology in connection therewith, Vertex shall extend to Taisho good faith assistance and support in defending such action, and may participate in the conduct of, and in discussions regarding strategic and business responses to, the suit. Damages and out-of-pocket legal fees and expenses (including legal fees and expenses of Taisho and Vertex) arising from such a legal action shall be borne
[**********
**********]

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

12.4. TAX. [**********
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**********]At Taisho's request Vertex will provide Taisho with such documentation as may be reasonably available to it which support characterization of the payments made by Taisho

12.5. WAIVER. Any waiver by either party of the breach of any term or condition of this Agreement will not be considered as a waiver of any subsequent breach of the same or any other term or condition hereof.

12.6. FORCE MAJEURE. Neither party will be in breach hereof by reason of its delay in the performance of or failure to perform any of its obligations hereunder, if that delay or failure is caused by strikes, acts of God or the public enemy, riots, incendiaries, interference by civil or military authorities, compliance with governmental priorities for materials, or any fault beyond its control or without its fault or negligence. In the event that any delay or failure to perform by Vertex by reason of force majeure shall extend beyond six (6) months, Taisho may terminate this Agreement upon notice in writing to Vertex; provided that Taisho's right to terminate hereunder shall end, if not exercised, at such time as Vertex shall have eliminated any material delay or failure to perform giving rise to the Taisho's termination right under this Section 12.5, if Taisho does not exercise its right to terminate this Agreement under this Section 10.3 within fifteen (15) days after the conclusion of the twelve
(12) month period.

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

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

12.9. GOVERNMENT APPROVALS. Taisho or its sublicensees will, if necessary, obtain any government approval required in the Territory to enable this Agreement to become effective, or to enable any payment hereunder to be made, or any other obligation hereunder to be observed or performed. Taisho will keep Vertex informed of progress in obtaining any such government approval, and Vertex will cooperate with Taisho in any such efforts.

12.10. EXPORT CONTROLS. This Agreement is made subject to any restrictions concerning the export of Licensed Compounds or Vertex Technology from the United States which may be imposed upon or related to either party to this Agreement from time to time by the Government of the United States. Furthermore, Taisho will not export, directly or indirectly, any Vertex Technology or any Licensed Compounds utilizing such Technology to any countries for which the United States Government or any agency thereof at the time of export requires an export license or other governmental approval, without first obtaining the written consent to do so (of which Taisho will promptly inform Vertex) from the Department of Commerce or other agency of the United States Government when required by applicable statute or regulation.

12.11. ASSIGNMENT. This Agreement may not be assigned or otherwise transferred by either party without the prior written consent of the other party; PROVIDED, HOWEVER, that either party may assign this Agreement, WITHOUT the consent of the other party, (i) to any of its Affiliates, if the assigning party guarantees to full performance of its Affiliates' obligations hereunder, or (ii) in connection with the transfer or sale of all or substantially all of its assets or business or in the event of its merger or consolidation with another company. Any purported assignment in contravention of this section shall, at the option of the nonassigning party, be null and void and of no effect. No assignment shall release either party from responsibility for the performance of any accrued obligations of such party hereunder.

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

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

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

if to Taisho, at: Taisho Pharmaceutical Co., Ltd.
24-1, Takata 3-Chome
Toshimaku, Tokyo, 170-8633, Japan
Attention: General Manager, Licensing Division

with a copy to:

General Manager, Legal Division

if to Vertex, at: 130 Waverly Street
Cambridge, MA 02139-4242
Attention: Richard H. Aldrich
Senior Vice President and Chief Business Officer
cc: Corporate Counsel

with a copy to:

Kirkpatrick & Lockhart LLP
75 State Street
Boston, MA 02109
Attention: Kenneth S. Boger, Esquire
Fax: 617-951-9151

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

12.16. AUTHORITY. The undersigned represent that they are authorized to sign this Agreement on behalf of the parties hereto. The parties each represent that no provision of this Agreement will violate any other agreement that a party may have with any Third Party . Each party has relied on that representation in entering into this Agreement.

12.17. ENTIRE AGREEMENT. This Agreement contains the entire understanding of the parties relating to the matters referred to herein, and may only be amended by a written document, duly executed on behalf of the respective parties.

VERTEX PHARMACEUTICALS INCORPORATED

By:_____

Title:_____

Date of Signature:_____

TAISHO PHARMACEUTICAL CO., LTD.

By:_____

Title:_____

Date of Signature:_____

SCHEDULE 1.9

LICENSED COMPOUNDS

EXHIBIT 10.28

(WITH CERTAIN CONFIDENTIAL INFORMATION DELETED AND MARKED WITH BRACKETED **ASTERISKS)**

CREDIT AGREEMENT

BETWEEN

VERTEX PHARMACEUTICALS INCORPORATED

AND

FLEET NATIONAL BANK

DATED AS OF DECEMBER 21, 1999

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CREDIT AGREEMENT

CREDIT AGREEMENT dated as of December 21, 1999 between VERTEX PHARMACEUTICALS INCORPORATED, a Massachusetts corporation ("Borrower"), and FLEET NATIONAL BANK, a national banking association ("Lender").

WHEREAS, Borrower has requested that Lender provide it with a term loan facility;

WHEREAS, Lender is willing, on the terms and subject to the conditions in this Agreement, to make such a credit facility available to Borrower;

NOW, THEREFORE, in consideration of the mutual promises contained herein and other good and valuable consideration, the receipt and sufficiency of which are acknowledged, Lender and Borrower agree as follows:

ARTICLE 1. - DEFINITIONS

1.1 DEFINED TERMS. Unless otherwise defined herein, the capitalized terms, as used in this Agreement, shall have the meanings as set forth on SCHEDULE 1 hereto.

1.2 ACCOUNTING TERMS. All accounting terms not specifically defined herein shall be interpreted and all financial statements and reports as to financial matters required to be delivered to Lender hereunder shall be prepared in accordance with GAAP consistently applied with those used in the preparation of the audited and quarterly financial statements furnished to Lender in connection with the initial Loans issued on the Initial Borrowing Date.

ARTICLE 2. - TERM LOANS

2.1 TERM LOAN COMMITMENT. Subject to the terms and conditions hereof, Lender agrees to make the Term Loans to the Borrower from time to time during the Term Loan Commitment Period, provided, however, that, except as provided in the Term Note, each Term Loan request shall be in a minimum amount of $250,000 and shall not exceed the Purchased Equipment Cost. Not more than one such Term Loan request shall be made in each calendar quarter (except for any Term Loan request that equals or exceeds $500,000), and the aggregate principal amount of all Term Loans shall not exceed the Term Loan Limit.

2.2 TERM LOAN BORROWING REQUEST. Subject to the terms and conditions hereof and the Term Note, Borrower may borrow under the Term Loan Commitment during the Term Loan Commitment Period on any Business Day. Borrower may request Term Loans from time to time by submitting irrevocable Loan requests in such form and manner as Lender may require or permit signed by an Authorized Representative of Borrower, specifying the amount to be borrowed, the requested Borrowing Date and, if such Term Loan is to be made after the Initial Borrowing Date, together with a completed Notice of Selection (as defined in the Term Note), and

copies of invoices and such information Lender may reasonably request concerning the Purchased Equipment or Build-Out Fees, as the case may be, for which invoices are being submitted for reimbursement with the proceeds of such Term Loan. Except as otherwise agreed

by Lender, the proceeds of all Term Loans will be made available to Borrower by Lender by crediting Borrower's deposit account(s) with Lender.

2.3 TERM LOAN PREPAYMENT. Amounts borrowed as Term Loans which are paid or prepaid by the Borrower may not be reborrowed. Term Loans may be prepaid to the extent and in the manner permitted under the Term Note.

2.4 TERM NOTE AND RECORDS. The Term Loans shall be evidenced by the Term Note and shall bear interest and be payable as set forth therein. Lender shall maintain records of each (i) Term Loan and (ii) payments of principal balance of Term Loans. The Lender's records shall constitute PRIMA FACIE evidence of the accuracy of the information recorded therein and in the event that Borrower fails to object, within thirty (30) days of receipt of Lender's periodic reports to Borrower with respect to Term Loans, the information in such reports shall be conclusive and binding as against Borrower; PROVIDED, HOWEVER, that any failure by Lender to maintain such records or furnish such reports shall not affect the obligations of Borrower under the Note or this Agreement.

2.5 TERM LOAN PROCEEDS. Borrower shall use the proceeds of the Term Loans to acquire Purchased Equipment and to pay Build-Out Fees (in each case, in compliance with all applicable legal and regulatory requirements, including, without limitation, Regulations U and X and the Securities Act of 1933 and the Securities Exchange Act of 1934); PROVIDED that Lender shall have no responsibility as to the use of any of such proceeds.

2.6 REDUCTION OR TERMINATION OF TERM LOAN COMMITMENT.

(a) The Borrower may permanently reduce, from time to time, the Term Loan Limit by giving Lender not less than ten (10) Business Days prior notice and prior to the reduction date prepay the Term Loans to the extent the outstanding amount of the Term Loans exceed the reduced Term Loan Limit, provided, however, that, (i) each such reduction shall be an amount that is at least $500,000 or any greater multiple thereof, and (ii) no reduction shall be effective if the amount of the Term Loans as of the proposed reduction date exceeds the amount of the proposed reduced Term Loan Limit.

(b) To terminate the Term Loan Commitment, Borrower shall give Lender not less than ten (10) Business Days prior notice and on the termination date prepay in full all Term Loans together with accrued interest, fees, and charges thereon to the date of prepayment, including, without limitation, any loss, cost or expense including yield maintenance fees (as defined in the Note) due hereunder or under the Note. As set forth in Article 7, the Term Loan Commitment may be terminated by Lender or shall terminate automatically as set forth therein.

2.7 FACILITY FEE. Borrower shall pay to Lender a Term Loan facility fee as provided in the facility fee letter between Borrower and Lender dated as of December 21, 1999, which facility fee shall be fully earned and paid on the date hereof.

2.8 DEBIT OF ACCOUNTS. Lender may, at its election, without any obligation on the part of the Lender, effect payment of all amounts due, or any portion thereof, from Borrower under

this Agreement, the Note or the other Loan Documents, by debiting from time to time any of the Borrower's deposit or other accounts maintained at the Lender.

ARTICLE 3. - REPRESENTATIONS AND WARRANTIES

In order to induce Lender to enter into this Agreement and to make the Loans, Borrower represents and warrants to Lender, except as otherwise set forth in a schedule attached hereto and made a part hereof, that:

3.1 FINANCIAL CONDITION. The financial statements previously delivered to Lender and listed on SCHEDULE 3.1 present fairly the Consolidated financial position of Borrower and its Subsidiaries as of the dates thereof and its and their results of operations, shareholders' equity and cash flows for the periods then ended. All such financial statements and information, including any related schedules and notes, and any other financial information or statements furnished in accordance herewith, have been prepared in accordance with GAAP, subject only in the case of unaudited interim financial statements to normal year-end audit adjustments and the absence of footnotes. In the case of each Loan, the representations and warranties in this Section shall be deemed to have been made in respect of the then most recent financial statements of Borrower furnished to Lender pursuant to Section 4.1.

3.2 ORGANIZATION, EXISTENCE, GOOD STANDING. Each of Borrower and VSC:
(i) is duly organized, validly existing and in good standing as a corporation under the laws of the Commonwealth of Massachusetts (ii) has obtained all licenses, permits, approvals and consents and has filed all registrations necessary for the lawful operation of its business, (iii) has the corporate power and authority and the legal right to own, lease and operate its property and to conduct the business in which it is currently engaged, and (iv) is duly qualified to do business and is licensed and in good standing as a foreign corporation under the laws of each jurisdiction where its ownership, lease or operation of property or the conduct of its business requires such qualification, except where the failure to be so qualified would not have a Material Adverse Effect.

3.3 SUBSIDIARIES; CAPITALIZATION. Except as set forth on SCHEDULE 3.3, Borrower has no Subsidiaries, Investments or Joint Ventures in or with any other Person. As of the date hereof, except as set forth on SCHEDULE 3.3, no other Person owns beneficially or of record more than fifty percent (50%) of the issued and outstanding voting common stock of the Borrower and, to Borrower's knowledge, no other Person owns beneficially or of record more than five percent (5%) of the issued and outstanding voting common stock of the Borrower. Borrower owns all of the issued and outstanding shares of capital stock or other equity securities of VSC.

3.4 POWER AND AUTHORITY. Borrower has (i) full corporate power, authority and legal right to execute, deliver and perform its obligations under the Loan Documents to which it is a party and to borrow hereunder, (ii) taken all necessary actions to authorize the execution, delivery and performance by it of each Loan Document to which it is a party and to authorize its borrowings hereunder, and (iii) caused to be duly executed and delivered on behalf of the Borrower each of the Loan Documents to which Borrower is a party.

3.5 LEGAL, VALID, BINDING OBLIGATION. Each of the Loan Documents and each agreement, certificate, document, instrument or other paper delivered pursuant thereto, to which Borrower is a party, constitutes the legal, valid, and binding obligation of Borrower enforceable against Borrower in accordance with its terms.

3.6 CONSENTS. No consent, permit, license, approval, authorization or other action of, or registration, declaration or filing with or notice to, any governmental authority, bureau or agency or any other Person is required in connection with the execution, delivery or performance by Borrower, or the validity or enforceability against Borrower, of any Loan Document to which it is a party, except for the consents and approvals set forth on SCHEDULE 3.6, all of which have been obtained.

3.7 NO LEGAL BAR. The execution, delivery and performance by Borrower of the Loan Documents, and each agreement, certificate, document, instrument or other paper delivered pursuant thereto, to which Borrower is a party, does not and will not conflict with or cause a breach of any provision of any existing law, rule or regulation, order, judgment, award or decree of any court, arbitrator or governmental authority, bureau or agency, or of the Articles of Organization or Bylaws of, or any security issued by, Borrower or VSC, as the case may be, or of any material mortgage, deed of trust, indenture, lease, contract or other agreement or undertaking to which Borrower or VSC, as the case may be, is a party or by which any of the properties or VSC, as the case may be, may be bound, and will not result in the creation or imposition of any Lien on any of its revenues or properties, except in favor of Lender.

3.8 NO LITIGATION. Except as set forth on SCHEDULE 3.8, no litigation, investigation or other proceeding of or before any court, arbitrator or governmental authority is currently pending nor, to the knowledge of Borrower, threatened against Borrower, any of its Subsidiaries or its properties which, if adversely determined, could reasonably be expected to have a Material Adverse Effect.

3.9 NO DEFAULT. Neither Borrower nor any of its Subsidiaries is in default in any respect in the payment or performance of any of its obligations for monies borrowed or under any material mortgage, deed of trust, indenture, lease, contract or other agreement or undertaking to which it is a party or by which it or any of its property may be bound or affected and no Default or Event of Default has occurred and is continuing. Neither Borrower nor any of its Subsidiaries is in default under any order, award or decree of any court, arbitrator or governmental authority binding upon or affecting it or by which any of its property may be bound or affected, and no such order, award or decree has or could reasonably be expected to have a Material Adverse Effect.

3.10 ASSETS, NO LIENS. Borrower and each of its Subsidiaries has good and marketable title to, or valid leasehold interest in, all of its real property and good title to all its personal property, including assets carried on its books and reflected in the financial statements furnished to Lender herewith, subject to no Liens except for (i) Liens permitted under Section 5.3 hereof, or (ii) inventory sold or otherwise disposed of in the ordinary course of its business.

3.11 NO BURDENSOME RESTRICTIONS. Except as set forth in SCHEDULE 3.11, neither

Borrower nor any of its Subsidiaries is a party to or bound by any contract, agreement or instrument or subject to any corporate

restriction (including any restriction set forth in its charter or Bylaws) or subject to any legal requirement or restriction that would have a Material Adverse Effect.

3.12 TAXES. All federal, state, local and other tax reports and returns which are required to be filed by Borrower and its Subsidiaries have been filed, except where extensions have been properly obtained, and Borrower and its Subsidiaries have paid or made adequate provision for all taxes, interest and penalties shown to be due and payable on such returns or on any assessments made against it or any of its property and all other taxes, fees or other charges imposed on it or any of its property by any governmental authority, including, without limitation, all payroll withholding taxes, have been paid and no tax liens have been filed and no claims are being asserted with respect to any such taxes, fees or other charges.

3.13 REGULATION U, ETC. Neither Borrower nor any of its Subsidiaries is engaged or will engage, principally or as one of its important activities, in the business of extending credit for the purpose of "purchasing" or "carrying" any "margin stock" (within the respective meanings of each of the quoted terms under Regulations U, T, or X of the Board of Governors of the Federal Reserve System and any successors thereto as now and from time to time hereafter in effect), and the proceeds of any Loan hereunder shall not be used for "purchasing" or "carrying" any "margin stock" as so defined, or for any purpose which violates, or which would be inconsistent with, the provisions of Regulation U of the Federal Reserve Board.

3.14 ERISA. The Borrower, all Commonly Controlled Entities, and all their Plans are and have been in substantial compliance with the provisions of, to the extent applicable, ERISA, the qualification requirements of IRC Section 401(a), and the published interpretations thereunder. No notice of intent to terminate any such Plan has been filed under Section 4041 of ERISA, nor has any such Plan been terminated under Section 4041(e) of ERISA which resulted in substantial liability to Borrower or any of its Commonly Controlled Entities. The PBGC has not instituted proceedings to terminate, or appoint a trustee to administer, any such Plan and no event has occurred or condition exists which might constitute grounds under Section 4042 of ERISA for the termination of, or the appointment of a trustee to administer any such Plan. Neither Borrower nor any Commonly Controlled Entities would be liable for any amount pursuant to Sections 4063 or 4064 of ERISA if all such Plans terminated as of the most recent valuation dates of such Plans. Neither Borrower nor any Commonly Controlled Entities have: withdrawn from a Multiemployer Plan during a plan year for which it was a substantial employer, as defined in Section 4001(a)(2) of ERISA; or failed to make a payment to a Plan required under Section 302(f)(1) of ERISA such that security would have to be provided pursuant to Section 307 of ERISA. No lien upon the assets of Borrower or any of its Subsidiaries has arisen with respect to any such Plan. To the best knowledge of Borrower, no Prohibited Transaction or Reportable Event has occurred with respect to any such Plan. Borrower and each Commonly Controlled Entity has each made all contributions required to be made by them to any such Plan or Multiemployer Plan when due. There is no accumulated funding deficiency in any such Plan, whether or not waived.

3.15 INVESTMENT COMPANY ACT, ETC. Neither Borrower nor any of its Subsidiaries is an "investment company" registered or required to be registered under the Investment Company Act of 1940, or a company "controlled" (within the meaning of such Investment Company Act) by such an "investment company". Neither Borrower nor any of its Subsidiaries is subject to regulation under the Public Utility Holding Company Act of 1935, the Federal Power Act, the Interstate Commerce Act or to any other federal or state statute or regulation limiting its ability to incur indebtedness for money borrowed.

3.16 INDEBTEDNESS. Neither Borrower nor any of its Subsidiaries has any Indebtedness of any type except Indebtedness incurred under this Agreement and that which is permitted under Section 5.1 of this Agreement. All credit and loan agreements, indentures, commitments, notes and other agreements, instruments and documents pursuant to which Borrower or any of it Subsidiaries, as the case may be, has incurred or has the right to borrow or incur Indebtedness are set forth on SCHEDULE 5.1.

3.17 CONTINGENT LIABILITIES. Except as set forth in SCHEDULE 5.2, neither Borrower nor any of its Subsidiaries has any material Contingent Liabilities.

3.18 CHIEF PLACE OF BUSINESS; LOCATIONS OF BOOKS AND RECORDS; LOCATIONS OF ASSETS. The chief executive office of Borrower is located at 130 Waverly Street, Cambridge, Massachusetts 02139, all books and records of Borrower are located at that address, and the Borrower and its Subsidiaries have no property located at any other location, except as set forth on SCHEDULE 3.18.

3.19 LAWS INCLUDING ENVIRONMENTAL AND SAFETY MATTERS. Borrower and each of its Subsidiaries is in compliance in all material respects with all laws, statutes, rules, regulations ordinances, orders of court or other governmental authorities, and other valid requirements of governmental authorities applicable to it including, without limitation, all environmental, health and safety statutes and regulations and specifically the Federal Resource Conservation and Recovery Act, the Federal Comprehensive Environmental Response, Compensation and Liability Act, the Federal Clean Water Act, the Clean Air Act, the requirements and regulations of the Nuclear Regulatory Commission, the Federal Occupational Safety and Health Act and the Federal Food, Drug and

Cosmetic Act, and the regulations promulgated thereunder. Neither Borrower nor any of its Subsidiaries is subject to any judicial or administrative proceedings alleging the violation of any applicable law or regulation which could reasonably be expected to have a Material Adverse Effect. Neither Borrower nor any of its Subsidiaries is the subject of any federal, state or local investigation regarding, among other matters, the release of any Hazardous Material into the environment, the results of which could reasonably be expected to have a Material Adverse Effect. Neither Borrower nor any of its Subsidiaries has filed any notice under any applicable law indicating past or present treatment, storage, disposal, generation, transportation or reporting a spill or release into the environment of any Hazardous Material which could reasonably be expected to have a Material Adverse Effect. Neither Borrower nor any of its Subsidiaries has placed or disposed of, used, generated or transported any Hazardous Material in violation of any applicable law or regulation, upon or over any real property owned or leased by Borrower and any of its Subsidiaries and neither Borrower nor any of its

Subsidiaries has knowledge of such Hazardous Material on such real property.

3.20 INTELLECTUAL PROPERTY; FRANCHISES; PERMITS. Except as set forth on SCHEDULE 3.20 hereto, (a) the Borrower and its Subsidiaries own or license all material Intellectual Property necessary for the conduct of their business as presently conducted; (b) all material agreements pursuant to which the Borrower and its Subsidiaries license the manufacture, marketing or sale of products employing its Intellectual Property, and all non-governmental permits and franchises material to the proper conduct of their business, are in full force and effect; (c) no claims, demands, suits, or proceedings are pending or, to the knowledge of the Borrower and its Subsidiaries, threatened which might impair their rights in any material Intellectual Property used in the conduct of their business or any material agreement relating thereto; and (d) the Borrower and its Subsidiaries have not infringed (without any license therefor) any Intellectual Property of any other Person, and the present conduct of the Borrower's and its Subsidiaries' business does not infringe any such rights in any way which would have a Material Adverse Effect.

3.21 NEGATIVE PLEDGES. Neither Borrower nor any of its Subsidiaries is a party to or bound by any agreement, indenture, or other instrument which prohibits the creation, incurrence or allowance to exist of any mortgage, deed of trust, pledge, lien, security interest or other encumbrance or conveyance upon Borrower's or any Subsidiary's properties, except as disclosed on SCHEDULE 3.21 hereto or in favor of the Lender.

3.22 YEAR 2000 COMPLIANCE. The Borrower has taken all necessary action to access and evaluate all of the hardware, software, embedded microchips and other processing capabilities it uses and which is used in the products it sells, directly or indirectly, and has made inquiry of the Borrower's and its Subsidiaries' material suppliers and vendors, to be able to ensure that the Borrower and its Subsidiaries and each product they sell will be able to function accurately and without interruption using date information before, during and after January 1, 2000. Any reprogramming of any computer systems or equipment required to permit the proper functioning of the Borrower and its Subsidiaries and its business and each product it sells following January 1, 2000 and any testing of such systems and equipment and each product it sells was completed by September 30, 1999, and the cost of such reprogramming and testing has not and will not result in a material adverse change in the operations, business, financial condition or prospects of the Borrower and its Subsidiaries.

3.23 FULL DISCLOSURE. The financial statements referred to in Section 3.1, the Schedules hereto, the Loan Documents and any list, certificate, written statement, instrument, paper or other information furnished by Borrower to Lender in connection with the Loan Documents do not contain any untrue statement of a material fact or omit to state any material fact necessary to make the statements contained therein and herein, in light of the circumstances in which they are made, not misleading.

ARTICLE 4. - AFFIRMATIVE COVENANTS

Borrower covenants and agrees that so long as any Commitment remains in effect, any Note remains outstanding and unpaid, in whole or in part, or any other amount is owing to

Lender hereunder:

4.1 FINANCIAL STATEMENTS AND OTHER DOCUMENTS. Borrower shall furnish or cause to be furnished to Lender:

(a) QUARTERLY FINANCIAL STATEMENTS. As soon as available and in any event within 45 days after the end of each of the first three quarterly fiscal periods of the Borrower, Consolidated statements of earnings, shareholders' equity, and cash flows of the Borrower and its Subsidiaries for such period and for the period from the beginning of the respective fiscal year to the end of such period, and the related Consolidated balance sheets of the Borrower and its Subsidiaries as at the end of such period, setting forth in each case in comparative form, the corresponding Consolidated figures for the corresponding periods in the preceding fiscal year

accompanied by a certificate of the chief financial officer of the Borrower, which certificate shall state that said Consolidated financial statements present fairly in all material respects the Consolidated financial position and results of operations of the Borrower and its Subsidiaries, in accordance with GAAP, as at the end of, and for, such period (subject to normal year-end audit adjustments);

(b) ANNUAL FINANCIAL STATEMENTS. As soon as available and in any event within 90 days after the end of each fiscal year of the Borrower, Consolidated statements of earnings, shareholders' equity and cash flows of the Borrower and its Subsidiaries for such fiscal year and the related Consolidated balance sheets of the Borrower and its Subsidiaries as at the end of such fiscal year, setting forth in each case in comparative form, to the extent such figures appear therein, the corresponding Consolidated figures for the preceding fiscal year, and accompanied by a report thereon of independent certified public accountants satisfactory to the Lender, which report shall state that said Consolidated financial statements present fairly in all material respects the Consolidated financial position and results of operations of the Borrower and its Subsidiaries as at the end of, and for, such fiscal year in accordance with GAAP, consistently applied;

(c) PERIODIC SEC REPORTS; COMPLIANCE CERTIFICATE. Simultaneously with the delivery of the financial statements required under Section 4.1(a) and (b) above, (i) a copy of the Borrower's Form 10-Q or 10-K filing made for the periods covered by such financial statements, together with (ii) a properly completed Compliance Certificate as of the date of such financial statements, in the form attached as EXHIBIT B hereto;

(d) OTHER SEC REPORTS. Promptly upon their becoming available, copies of all (i) regular, periodic and special reports that the Borrower shall have filed with the Securities and Exchange Commission (or any governmental agency substituted therefor) pursuant to the Securities Exchange Act of 1934, as amended, (ii) financial statements, reports, notices or proxy or other statements sent to shareholders of the Borrower, and (iii) press releases and other statements generally made available by the Borrower to the public concerning material developments in the business of the Borrower;

(e) ERISA NOTICES. As soon as possible and in any event within five (5) days after any officer of Borrower obtains knowledge thereof: (i) notice of Borrower's failure to make any required payment to any Plan in sufficient amount to comply with ERISA and the Code on or before the due date for such payment;
(ii) notice of the occurrence or expected occurrence of any

"Reportable Event" under ERISA, "Prohibited Transaction" or "Accumulated Funding Deficiency" with respect to any Plan; and (iii) notice of receipt by Borrower of any notice (A) from a Multiemployer Plan regarding the imposition of withdrawal liability; or (B) of the institution, or expectancy of the institution, of any proceeding or any other action which may result in the termination of any Plan, or Borrower's withdrawal or partial withdrawal from any Plan;

(f) NOTICE OF DEFAULT. Promptly after the Borrower knows that any Default has occurred, a notice of such Default describing the same in reasonable detail and, together with such notice or as soon thereafter as possible, a description of the action that the Borrower has taken or proposes to take with respect thereto (a "Notice of Default");

(g) PROJECTIONS; MANAGEMENT LETTER. (a) With the delivery of the Borrower's 10-K annual report, the Borrower's quarterly projections (income statements and balance sheets) for the then current fiscal year of the Borrower, as approved by the Board of Directors of the Borrower and (b) as soon as available, but in any event within 120 days after the end of each fiscal year of the Borrower, a copy of any letter from the Borrower's auditors to Borrower's management prepared in connection with the audited financial statements of the Borrower; and

(h) OTHER INFORMATION. From time to time such other information regarding the property, operations, business, financial condition or prospects of the Borrower or any of its Subsidiaries as the Lender may reasonably request.

4.2 EXISTENCE; COMPLIANCE WITH LAWS; ETC.. Borrower shall and shall cause each Subsidiary to:

(a) CORPORATE EXISTENCE. Preserve and keep in full force and effect its corporate existence and all franchises, licenses and permits issued by governmental agencies material to the proper conduct of its business;

(b) COMPLIANCE WITH APPLICABLE LAWS. Comply with and duly observe all applicable laws, statutes, regulations, rules, ordinances, orders of court or governmental authorities, and requirements of governmental authorities the breach of which could reasonably be expected to have a Material Adverse Effect, except when contested with due diligence, in good faith and in proper proceedings. Borrower shall also pay and cause all of its Subsidiaries to pay all of their other Indebtedness and obligations promptly and in accordance with normal terms and trade practices.

(c) PAYMENT OF TAXES. File or cause to be filed all tax returns and reports which are required by law to be filed by it, and pay and discharge all taxes, assessments and governmental charges or levies imposed on it or on its income or profits or on any of its property prior to the date on which penalties attached thereto, except for any such tax, assessment, charge or levy the payment of which is being contested in good faith and by proper proceedings and against which adequate reserves are being maintained in accordance with GAAP.

(d) RECORDS. Keep adequate records and books of account, in which complete entries

will be made in accordance with GAAP; and

(e) ACCESS. Permit representatives of Lender, upon reasonable advance notice to the Borrower and during normal business hours, to examine, copy and make extracts from its books and records, to inspect any of its properties, including, without limitation, any Purchased Equipment, and to discuss its business and affairs with its officers, all to the extent reasonably requested by Lender.

4.3 MAINTAIN PROPERTY. Borrower shall, and Borrower shall cause each of its Subsidiaries to, keep and maintain all property useful and necessary in its business in good operating condition and repair, ordinary wear and tear excepted.

4.4 INSURANCE. Borrower shall keep adequately insured by financially sound and responsible insurers (a) all property owned or leased by it and its Subsidiaries and all property of an insurable nature, such insurance to be in at least such amounts and covering loss or damage from at least such risks and hazards (including, without limitation, business interruption insurance and use and occupancy insurance) as are usually insured against in the same geographic areas by companies engaged in similar businesses, and (b) all liabilities of Borrower and its Subsidiaries for damage to property, death or bodily injury, including without limitation insurance required under all applicable workmen's compensation laws, and insurance for such liabilities resulting from, caused by or arising out of any product sold by any predecessor of Borrower or by Borrower or any Subsidiary, all such insurance to be in at least such amounts as are usually insured against by companies engaged in the same or similar businesses.

4.5 NOTICE OF MATERIAL EVENTS. Borrower will, promptly upon any officer of Borrower obtaining knowledge thereof, give notice to Lender of (i) any material casualty, loss or depreciation to any inventory or other property of Borrower or any Subsidiary or any litigation, investigation or other proceeding against or involving Borrower or any Subsidiary the result of any of which might have a Material Adverse Effect; (ii) any litigation, investigation (other than in the ordinary course of business), other proceeding or dispute affecting Borrower (A) which relates, in whole or in part, to any of the transactions contemplated by any of the Loan Documents, (B) which involves an amount in excess of $1,000,000, or (C) which may exist between Borrower or any Subsidiary and any governmental body; or (iii) any release of any Hazardous Materials at any location owned or leased by Borrower or any Subsidiary or any investigation or proceeding by any governmental body alleging or relating to the violation by Borrower or any Subsidiary of any law or regulation. Borrower will furnish to Lender from time to time all information which Lender shall reasonably request with respect to the status of any litigation, investigation, other proceeding or dispute to which Borrower is a party.

4.6 DEPOSIT ACCOUNTS. Borrower shall maintain with Lender bank accounts to be used as its principal depository and operating account(s).

ARTICLE 5. - NEGATIVE COVENANTS

Borrower covenants and agrees that, so long as any Commitment is in effect, any Note remains outstanding and unpaid, in whole or in part, or any other amount is owing to Lender

hereunder, Borrower will not, directly or indirectly, and Borrower will not permit any of its Subsidiaries to:

5.1 INDEBTEDNESS. Create, incur, assume or allow to exist any Indebtedness, except:

(a) LOAN DOCUMENT INDEBTEDNESS. Indebtedness evidenced by the Note and any other Indebtedness owing to or held by Lender arising under any of the Loan Documents;

(b) DISCLOSED INDEBTEDNESS. Indebtedness of Borrower existing on the Initial Borrowing Date and disclosed in SCHEDULE 5.1 (including, without limitation, all Capital Lease Obligations and purchase money financings existing on the Initial Borrowing Date); PROVIDED, HOWEVER, that, without the prior written consent of Lender, none of such Indebtedness shall be renewed, extended or otherwise modified in any material respect and may be extended by Borrower only on substantially the same terms and conditions as in effect on the date hereof;

(c) UNSECURED CURRENT LIABILITIES. Unsecured current liabilities (not the result of borrowing) incurred in the ordinary course of business which are not evidenced by notes or instruments and which are not more than sixty (60) days overdue from the original due dates thereof (unless and to the extent only that any such liability is contested by Borrower in good faith by appropriate proceedings and adequate reserves have been set aside with respect thereto in accordance with GAAP);

(d) ADDITIONAL CAPITAL LEASES AND PURCHASE MONEY FINANCINGS. Capital Leases and purchase money financings incurred in the ordinary course of business by Borrower for the lease or purchase of Capital Equipment provided that the aggregate outstanding amount of all Capital Leases and purchase money financings existing on the Initial Borrowing Date plus all additional Capital Leases and purchase money financings incurred after the Initial Borrowing Date shall not exceed $20,000,000, the amount of each such Capital Lease or purchase money financing does not exceed 100% of the lesser of the cost or fair market value of such Capital Equipment (and Borrower agrees to furnish copies of the documentation for its outstanding Capital Leases and purchase money financings to Lender from time to time upon request);

(e) INDEBTEDNESS AMONG SUBSIDIARIES. Indebtedness existing as of the date hereof and disclosed on Schedule 5.1 of (i) Subsidiaries of the Borrower to the Borrower, (ii) the Borrower to any of its Subsidiaries, or (iii) Subsidiaries to Subsidiaries, provided that any such Indebtedness of the Borrower to its Subsidiaries is subordinated as to payment of the Obligations in a manner satisfactory to Lender; and

(f) APPROVED INDEBTEDNESS. Indebtedness for borrowed money incurred after the Initial Borrowing Date with prior notice to and the written consent of Lender.

5.2 CONTINGENT LIABILITIES. Except for Contingent Liabilities existing on the Initial Borrowing Date and disclosed on SCHEDULE 5.2, create, incur, assume or allow to exist any Contingent Liabilities in excess of $500,000, in the aggregate, except for Contingent Liabilities arising out of the endorsement of instruments for deposit or collection in the ordinary course of business.

5.3 LIMITATION ON LIENS. Create, incur, assume or allow to exist, any Lien upon any of its property, income or profits, whether now owned or held or hereafter acquired, including attachment, levy, garnishment or other judicial process relating to such property, except:

(a) Liens in existence on the date hereof and listed on SCHEDULE 5.3 hereof;

(b) Liens imposed by any governmental authority for taxes, assessments or charges not yet due or that are being contested in good faith and by appropriate proceedings if adequate reserves with respect thereto are maintained on the books of the Borrower, in accordance with GAAP;

(c) carriers', warehousemen's, mechanics', materialmen's, repairmen's or other like Liens arising in the ordinary course of business that are not overdue or that are being contested in good faith and by appropriate proceedings if adequate reserves with respect thereto are maintained or the books of the Borrower, in accordance with GAAP;

(d) pledges or deposits under worker's compensation, unemployment insurance and other social security legislation;

(e) deposits to secure the performance of bids, trade contracts (other than for Indebtedness), leases, statutory obligations, surety and appeal bonds, performance bonds and other obligations of a like nature incurred in the ordinary course of business;

(f) easements, rights-of-way, restrictions and other similar encumbrances incurred in the ordinary course of business and encumbrances consisting of zoning restrictions, easements, licenses, restrictions on the use of property or imperfections in title thereto that, in the aggregate, are not material in amount, and that do not in any case materially detract from the value of the property subject thereto or interfere with the ordinary conduct of the business of the Borrower or any of its Subsidiaries;

(g) Liens upon Capital Equipment to secure purchase money Indebtedness or Capital Lease of the Borrower or a Subsidiary permitted under Section 5.1(a); PROVIDED, THAT, (i) such Lien does not extend to or cover any other property of the Borrower or such Subsidiary and (ii) such Lien does not secure any Indebtedness other than the Indebtedness so incurred;

(h) Liens arising from or upon any judgment or award, provided that such judgment or award does not exceed $50,000 and is being contested in good faith by proper appeal proceedings, such judgment or award is not secured by any Lien which is not discharged within thirty (30) days, and only so long as execution thereon shall be stayed; and

(i) Liens now or hereafter granted to the Lender under the Loan Documents.

5.4 MERGERS; DISSOLUTION; DISPOSALS; OR ACQUISITIONS. (a) Enter into any transaction of merger or consolidation or amalgamation; (b) liquidate, wind-up or dissolve itself; (c) convey, sell, issue, exchange, lease, assign, transfer or otherwise dispose of all or any material portion of its business or property or the business, property or stock of any Subsidiary (other than sales of

inventory in the ordinary course of business and obsolete equipment or equipment no longer used or useful in the business of Borrower); or (d) without the prior written consent of the Lender, make any Investment in or purchase, lease or otherwise acquire all or any material portion of the business or property of any other Person or enter into any Joint Venture or any exclusive licensing agreement for any of its material Intellectual Property; PROVIDED, HOWEVER, that notwithstanding the foregoing so long as no Default or Event of Default exists, the Borrower may enter into agreements, including licensing agreements, relating to the research, development, marketing and sale of its products and Intellectual Property in the ordinary course of its business and on reasonable and appropriate terms and conditions including the payment of fair and reasonable compensation to the Borrower.

5.5 INVESTMENTS AND LOANS. Except as permitted by Section 5.1(e) make any Investment in or make any loan or other advances of money to any Person, including, without limitation, any Subsidiary, except for loans and advances to employees for salary, travel advances, advances against commissions and similar advances in the ordinary course of BUSINESS or pursuant to the investment policy attached hereto as SCHEDULE 5.5.

5.6 DIVIDENDS. Pay or set aside any amount to pay any Dividends.

5.7 TRANSACTIONS WITH AFFILIATES. Enter into or be a party to any agreement or transaction with any Affiliate, except in the ordinary course of Borrower's business and pursuant to reasonable requirements of Borrower's business and upon fair and reasonable terms and conditions which are fully disclosed to Lender and are no less favorable to Borrower than would obtain in a comparable arm's length transaction with a person not an Affiliate of Borrower.

5.8 NEGATIVE PLEDGE. Directly or indirectly, enter into any agreement, indenture, or other instrument which prohibits the creation, incurrence or allowance to exist of any mortgage, deed of trust, pledge, lien, security interest or other encumbrance or conveyance upon any of Borrower's or its Subsidiaries' property, except for negative pledges in connection with Indebtedness incurred under Capital Leases and purchase money financings permitted under Section 5.1(d) hereof, provided that such negative pledges apply only to the Capital Equipment purchased or leased pursuant thereto and not to any other property.

5.9 MINIMUM LIQUIDITY RATIO. Permit the Borrower's Liquidity Ratio, on a Consolidated basis, to be less than [***] to 1.0 at any time.

5.10 MINIMUM TANGIBLE CAPITAL BASE. Permit the Borrower's Tangible Capital Base, on a Consolidated Basis, to be less than [********]at any time.

5.11 MINIMUM DEBT SERVICE TEST/MINIMUM CASH AND CASH EQUIVALENTS. Permit, for any fiscal quarter, the Borrower's Debt Service Coverage Ratio, on a Consolidated basis, to be less than [***] to 1.0, for the period of the four consecutive fiscal quarters ending with such fiscal quarter; UNLESS the sum of the Borrower's Unrestricted Cash on a Consolidated basis, is not less than the GREATER of: (x) the sum of (1) the product of the net loss, as determined in accordance with GAAP excluding all extraordinary and nonrecurring gains and losses (the "Net Loss") for such fiscal quarter, MULTIPLIED BY four, PLUS (2) Funded Indebtedness; or (y) the sum of

(1) the Net Loss for the period of the four consecutive fiscal quarters ending with such fiscal quarter, PLUS (2) Funded Indebtedness.

5.12 LINES OF BUSINESS. Engage to any significant extent, or permit any Subsidiary to engage to any significant extent, in any line or lines of business activity other than the biotechnology or pharmaceutical businesses.

5.13 TANGIBLE CAPITAL BASE. Permit, at any time, (a) the sum of the Tangible Capital Base of Borrower alone and VSC alone (in each case, exclusive of any investment in Subsidiaries and any Indebtedness owed by any Subsidiary to the Borrower) to be less than 90% of the Tangible Capital Base of the Borrower and its Subsidiaries.

ARTICLE 6. - CONDITIONS PRECEDENT

6.1 CONDITIONS OF INITIAL EXTENSION OF CREDIT. The obligation of Lender to make a Term Loan on the Initial Borrowing

Date is subject to the satisfaction of the condition precedent that Lender shall have received on or before such date, the following items in form and substance satisfactory to Lender and its counsel executed where appropriate by a duly authorized officer of Borrower:

LOAN DOCUMENTS

(a) CREDIT AGREEMENT. This Agreement;

(a) TERM NOTE. The Term Note; and

(b) PLEDGE AGREEMENT. The Pledge Agreement, together with originals of all share certificates of capital stock of VSC, accompanied by an executed, undated stock power with respect to such shares.

CORPORATE DOCUMENTS:

(d) CORPORATE RESOLUTIONS. Copies of resolutions of the Board of Directors (and, if necessary, the Stockholders) of Borrower, authorizing the execution, delivery and performance of the Loan Documents to which Borrower is a party, and the transactions contemplated thereby, certified as of the Initial Borrowing Date by the Secretary/Clerk or Assistant Secretary/Clerk of Borrower (which certificate shall state that such resolutions have not been amended, modified, revoked or rescinded as of such date);

(e) CORPORATE INCUMBENCY CERTIFICATE. Certificate of the Secretary/Clerk or Assistant Secretary/Clerk of Borrower, dated as of the Initial Borrowing Date, certifying the names and titles of the officers authorized to execute the Loan Documents to which Borrower is a party and any other documents related to any thereof, together with specimen signatures of such officers;

(f) CHARTER DOCUMENTS. Copies of (i) the charter documents and all amendments thereto of Borrower and VSC, currently certified by the Office of the Secretary of State for the Commonwealth of Massachusetts, and (ii) the By-Laws of Borrower and VSC certified as of the Initial Borrowing Date by the Secretary/Clerk or Assistant Secretary/Clerk of the Borrower;

(g) LEGAL GOOD STANDING CERTIFICATES. For each of Borrower and VSC, a certificate of legal existence and good standing issued by the Office of the Secretary of State for the Commonwealth of Massachusetts and a certificate of foreign qualification and good standing issued by the Secretary of State of each state of foreign qualification or authorization, all of which shall be dated currently;

(h) TAX GOOD STANDING CERTIFICATES. For each of Borrower and VSC, a certificate of tax good standing currently dated from each jurisdiction in which such party is obliged to file tax returns and pay taxes (or, to the extent any such certificates are unobtainable, because it is not the practice of the taxing authority to issue such certificate, or because of time delays in the issuance of such certificate attributable to such taxing authority, a letter from Borrower's or VSC's, as the case may be, chief financial officer setting forth the nature of the tax obligation and the relevant jurisdiction, and certifying that all required returns have been duly filed and all required taxes shown thereon paid);

MISCELLANEOUS DOCUMENTS:

(i) UCC AND OTHER SEARCHES. Copies of UCC, tax lien, judgment, bankruptcy and other searches reasonably requested by Lender of all appropriate filing offices relating to the Borrower and its Subsidiaries;

(j) TERMINATIONS AND DISCHARGES. Termination Statements, mortgage discharges and other discharges of all Liens other than those permitted under Section 5.3 hereof;

(k) LEGAL OPINIONS. Written opinions of counsel for Borrower and VSC in form and content satisfactory to Lender, dated the Initial Borrowing Date, addressed to Lender and covering such matters related to the Borrower and VSC and the transactions contemplated hereby as Lender may request;

(l) CONSENTS. Copies of all consents or approvals of any Person that may be required in connection with the transactions contemplated by the Loan Documents;

(m) FEES. Execution of the facility fee letter referenced under Section 2.7 hereof, and payment of the facility fee set forth therein, together with the estimated fees and disbursements of Lender's counsel in connection with the Loan Documents and the transactions contemplated hereby; and

(n) ADDITIONAL CLOSING AGENDA ITEMS. Fulfillment, to Lender's satisfaction, of each of the additional items set forth on the closing agenda for this transaction.

6.2 CONDITIONS OF ALL LOANS. The Lender's obligation to make any Loan is subject to the fulfillment of the following additional conditions precedent:

(a) REPRESENTATIONS. The representations and warranties made by any party to any Loan Document (other than Lender) in any Loan Document or in any certificate, document or financial or other statement furnished at any time under or in connection therewith shall be true and correct on and as of the Borrowing Date for such Loan as if made on and as of such date, provided that, if any such representation or warranty is expressly required herein or therein to be made only as of a specific date, such representation or warranty shall be true or correct as of such date;

(b) NO DEFAULT. No Default or Event of Default shall have occurred and be continuing on the Borrowing Date for such Loan either before or after giving effect to the Loan made on such date; and

(c) NO MATERIAL ADVERSE EFFECT. There shall have occurred no event or change in circumstances having a Material Adverse Effect since the date of the most recent financial statements delivered by Borrower to Lender.

Each request for a Loan by Borrower hereunder shall constitute a representation and warranty by Borrower as of the date of such request or application that the conditions contained in paragraphs (a) through (c) of this Section 6.2 have been satisfied.

ARTICLE 7. - EVENTS OF DEFAULT

7.1 EVENTS OF DEFAULT. The occurrence of any of the following shall constitute an Event of Default:

(a) FAILURE OF PAYMENT. If Borrower fails to pay any principal, interest or other amount due, under this Agreement or with respect to any Loan on the date due (whether on a scheduled payment date or otherwise) and in the manner provided herein;

(b) MISSTATEMENTS. If any representation, warranty or other statement made herein or in any other Loan Document or otherwise in writing by or on behalf of Borrower or any Subsidiary in connection herewith proves to be or to have been incorrect or misleading in any material respect as of the date at which it is made or deemed to be made;

(c) PERFORMANCE OF OTHER COVENANTS. If Borrower defaults in the due performance or observance of:

(i) any covenant contained in Sections 4.1, 4.2(a) or 4.4 or Article 5 or

(ii) any other covenant, condition or provision to be performed or observed by it hereunder or under any of the Loan Documents (other than a payment or covenant default the performance or observance of which is dealt with specifically elsewhere in this Section 7.1) and the breach of

such other provision is not cured to Lender's satisfaction within thirty (30) days after the sooner to occur of Borrower's receipt of notice of such breach from Lender or the date on which such failure or neglect first becomes known to any officer of Borrower.

(d) OTHER INDEBTEDNESS. If Borrower or any Subsidiary defaults, which default continues after any applicable grace or cure period, in any payment of principal of or interest on any Indebtedness for borrowed money in excess of $1,000,000, including, without limitation, on any Capital Lease or any other default occurs with respect to any Indebtedness for borrowed money in excess of $1,000,000 giving the holder thereof the right to accelerate the payment thereof or require such Indebtedness to be paid before its stated maturity or before any regularly scheduled date of prepayment;

(e) MATERIAL CONTRACTS. Any default occurs under any material contract of Borrower or any Subsidiary which default gives any other party to such contract the right to terminate such contract or exercise remedies and such termination or remedies are reasonably likely to have a Material Adverse Effect;

(f) JUDGMENTS. If Borrower or any Subsidiary permits any judgment against it in excess of $1,000,000 to remain undischarged for a period of more than thirty (30) days unless (i) during such period such judgment is effectively stayed or bonded, on appeal or otherwise; or (ii) such judgment is insured, subject only to the Borrower's or Subsidiary's regular deductible amount, without

exception;

(g) LEVY, ATTACHMENTS. If any levy, seizure, attachment, execution or similar process shall be issued on any of the Borrower's or its Subsidiaries' cash, accounts or any material property and, with respect to attachments only, such attachment is not voided or removed within 10 days of such issuance;

(h) VOLUNTARY BANKRUPTCY. If Borrower or any Subsidiary (i) commences a voluntary case under the Bankruptcy Code (as now or hereafter in effect); or (ii) files a petition or commences any case, proceeding, or action in bankruptcy or seeking reorganization, liquidation, dissolution, winding-up, arrangement, composition, readjustment of its debts or any other relief under any other bankruptcy, insolvency, reorganization, liquidation, dissolution, arrangement, composition, readjustment of debt or similar act or law of any jurisdiction, now or hereafter existing; or (iii) takes any action indicating its consent to, approval of, or acquiescence in, any such case, proceeding or other action; or (iv) applies for a receiver, trustee or custodian of it or for all or a substantial part of its property; or (v) makes an assignment for the benefit of creditors; or (vi) is unable to pay its debts as they mature or admits in writing such inability; or (vii) is adjudicated insolvent or bankrupt;

(i) INVOLUNTARY BANKRUPTCY. (i) If there is commenced against Borrower or any Subsidiary (1) an involuntary case under the Bankruptcy Code (as now or hereafter in effect); or (2) any case or proceeding or any other action in bankruptcy or seeking reorganization, liquidation, dissolution, winding-up, arrangement, composition, readjustment of its debts or any other relief under any other bankruptcy, insolvency, reorganization, liquidation, dissolution,

arrangement, composition, readjustment of debt or similar act or law of any jurisdiction, now or hereafter existing, or seeking appointment of a receiver, trustee or custodian of Borrower or any Subsidiary or for all or a substantial part of the property of either of them, and any of the foregoing cases, proceedings, or actions is not dismissed within sixty (60) days; or (ii) if an order, judgment or decree approving any of the foregoing is entered or a warrant of attachment, execution or similar process against any substantial part of the property of Borrower or any Subsidiary is issued, and such order, judgment, decree, warrant, execution or similar process is not vacated or stayed within sixty (60) days; or (iii) if an order for relief under the Bankruptcy Code (as now or hereafter in effect) is entered against Borrower or any Subsidiary;

(j) CHANGE IN CONTROL OF BORROWER. A Change in Control shall occur; or

(k) MATERIAL ADVERSE EFFECT. Any event or change in circumstances having a Material Adverse Effect.

7.2 LENDER'S REMEDIES. Upon the occurrence of any such Event of Default, Lender may, at Lender's option, immediately exercise one or more of the following rights: (a) declare all obligations of Lender to Borrower, including, without limitation, the Commitments to be terminated, whereupon such obligations shall immediately terminate; (b) declare all obligations of Borrower to Lender, including, without limitation, the Loans and all other amounts owing under this Agreement and the Note to be immediately due and payable, whereupon they shall immediately become due and payable without presentment, demand, protest or notice of any kind, all of which are hereby expressly waived; and (c) exercise any and all rights and remedies of the Lender under Section 11 of the Pledge Agreement; PROVIDED, however, that upon the occurrence of any such Event of Default specified in Sections 7.1(h) or 7.1(i), the Commitments shall immediately terminate and all obligations of Borrower to Lender, including, without limitation, Loans and all other amounts owing under this Agreement and the Note shall immediately become due and payable without presentment, further demand, protest or notice of any kind, all of which are hereby expressly waived.

7.3 CROSS DEFAULT It is agreed by Borrower that any Event of Default under this Agreement will constitute an event of default under all Loans and all of the Loan Documents and all other agreements and evidences of Indebtedness between Borrower and Lender, whether now existing or hereafter executed and whether or not such is an event of default therein.

7.4 SETOFF. Borrower hereby grants to Lender a lien, security interest and right of set off as security for all liabilities and obligations to Lender, whether now existing or hereafter arising, upon and against all deposits, credits, collateral and property, now or hereafter in the possession, custody, safekeeping or control of Lender or any entity under the control of Fleet Financial Group, Inc., or in transit to any of them. At any time, without demand or notice, Lender may set off the same or any part thereof and apply the same to any liability or obligation of Borrower even though unmatured and regardless of the adequacy of any other collateral securing the Loans. ANY AND ALL RIGHTS TO REQUIRE LENDER TO EXERCISE ITS RIGHTS OR REMEDIES WITH RESPECT TO ANY OTHER COLLATERAL WHICH SECURES THE LOANS, PRIOR TO EXERCISING ITS RIGHT OF SETOFF WITH

RESPECT TO SUCH DEPOSITS, CREDIT OR OTHER PROPERTY OF THE BORROWER ARE HEREBY KNOWINGLY, VOLUNTARILY AND IRREVOCABLY WAIVED.

ARTICLE 8. - MISCELLANEOUS

8.1 NOTICES. Except as otherwise specified herein, all notices to or upon the parties hereto shall be in writing (including teletransmissions), shall be given or made to the party to which such notice is required or permitted to be given or made under this Agreement at the address or telex or telecopier number set forth below or at such other address or telex or telecopier number as any party hereto may hereafter specify to the others in writing, and (unless otherwise specified herein) shall be deemed delivered on receipt, if teletransmitted or delivered by hand, or three (3) Business Days after mailing, and all mailed notices shall be by registered or certified mail, postage prepaid:

If to Borrower to:

Vertex Pharmaceuticals Incorporated
130 Waverly Street
Cambridge, MA 02139
Attention: Thomas G. Auchincloss, Jr., Vice President of Finance
Fax No. (617) 577-6680

With a copy to:

Vertex Pharmaceuticals Incorporated 130 Waverly Street
Cambridge, MA 02139
Attention: Sarah P. Cecil, Esquire, Corporate Counsel Fax No. (617) 577-6680

If to Lender to:

Fleet National Bank
High Technology Division One Federal Street
Boston, MA 02110
Attention: Kimberly A. Martone, Senior Vice President Fax No. 617-346-0151

With a copy to:

Brown, Rudnick, Freed & Gesmer, P.C.
One Financial Center
Boston, MA 02111
Attention: Jeffery L. Keffer, Esquire

Facsimile No. (617) 856-8201

8.2 NO WAIVER OF RIGHTS. No failure to exercise nor any delay in exercising, on the part of Lender, any right, remedy, power or privilege under the Loan Documents shall operate as a waiver thereof; nor shall any single or partial exercise of any right, remedy, power, or privilege operate as a waiver of any further or complete exercise thereof. No waiver shall be effective unless in writing. No waiver or condonation of any breach on one occasion shall be deemed a waiver or condonation on any other occasion.

8.3 OBLIGATIONS ABSOLUTE; CUMULATIVE REMEDIES. All payments to be made by the Borrower hereunder and under the Note and other Loan Documents shall be made in immediately available funds and shall be absolute and unconditional and shall not be subject to set off, recoupment or counterclaim of any kind. Each of the Loan Documents and the obligations of Borrower thereunder are in addition to and not in substitution for any other obligations or security interests now or hereafter held by Lender and shall not operate as a merger of any contract or debt or suspend the fulfillment of or affect the rights, remedies, powers, or privileges of Lender in respect of any obligation or other security interest held by it for the fulfillment thereof. The rights and remedies provided in the Loan Documents are cumulative and not exclusive of any other rights or remedies provided by law.

8.4 SUCCESSORS. This Agreement shall be binding upon and inure to the benefit of Borrower, Lender and all future holders of the Note, and their respective successors and assigns, except that Borrower may not assign or transfer its rights or obligations hereunder without the prior written consent of Lender. Lender shall have the unrestricted right at any time or from time to time, and without Borrower's consent, to assign all or any portion of its rights and obligations hereunder to one or more banks or other financial institutions (each, an "Assignee"), and Borrower agrees that it shall execute, or cause to be executed, such documents, including

without limitation, amendments to this Agreement and to any other documents, instruments and agreements executed in connection herewith as Lender shall deem necessary to effect the foregoing. In addition, at the request of Lender and any such Assignee, Borrower shall issue one or more new promissory notes, as applicable, to any such Assignee and, if Lender has retained any of its rights and obligations hereunder following such assignment, to Lender, which new promissory notes shall be issued in replacement of, but not in discharge of, the liability evidenced by the Note held by Lender prior to such assignment and shall reflect the amount of the respective Commitments and Loans held by such Assignee and Lender after giving effect to such assignment. Upon the execution and delivery of appropriate assignment documentation, amendments and any other documentation required by Lender in connection with such assignment, and the payment by Assignee of the purchase price agreed to by Lender, and such Assignee, such Assignee shall be a party to this Agreement and shall have all of the rights and obligations of Lender hereunder (and under any and all other guaranties, documents, instruments and agreements executed in connection herewith) to the extent that such rights and obligations have been assigned by Lender pursuant to the assignment documentation between Lender and such Assignee, and Lender shall be released from its obligations hereunder and thereunder to a corresponding extent. Lender may furnish any information concerning Borrower in its possession from time to time to prospective Assignees, provided that Lender shall require any

such prospective Assignee to agree in writing to maintain the confidentiality of such information.

8.5 PARTICIPANTS.

(a) LENDER'S RIGHTS. Lender shall have the unrestricted right at any time and from time to time, and without the consent of or notice to Borrower or any guarantor, to grant to one or more banks or other financial institutions (each, a "Participant") participating interests in Lender's obligation to lend under the Loan Documents and/or any or all of the loans held by Lender hereunder. In the event of any such grant by Lender of a participating interest to a Participant, whether or not upon notice to Borrower, Lender shall remain responsible for the performance of its obligations under the Loan Documents and Borrower shall continue to deal solely and directly with Lender in connection with Lender's rights and obligations hereunder and thereunder. Lender may furnish any information concerning Borrower in its possession from time to time to prospective participants, provided that Lender shall require any such prospective participant to agree in writing to maintain the confidentiality of such information.

(b) QUALIFYING PARTICIPATION EVENT. A "Qualifying Participation Event" shall be deemed to have occurred upon the occurrence of all of the following on or before December 31, 2000: (i) a Participant who is a non-affiliate of the Lender and who is satisfactory in all respects to the Lender in its discretion purchasing a participation interest in Lender's obligation to lend under the Loan Documents and/or any or all of the loans held by Lender hereunder in the amount of not less than $5,000,000; (ii) the execution and delivery of such a Participant's written agreement that the Amortization Number (as defined in the Term Note) may be increased to forty (40); and (iii) the execution and delivery by such a Participant of any and all documents evidencing such purchase in form and substance satisfactory to the Lender. The Borrower agrees that: (i) the Lender has no obligation to solicit potential Participants; and (ii) the Lender has no obligation to require or persuade potential Participants to agree to increase the Amortization Number to forty (40) as a pre-condition to becoming a Participant.

8.6 GOVERNING LAW. This Agreement, the Note and other Loan Documents shall be governed by, and construed and interpreted in accordance with, the laws of the Commonwealth of Massachusetts.

8.7 SUBMISSION TO JURISDICTION; WAIVER OF TRIAL BY JURY.

(a) For purposes of any action or proceeding involving the Loan Documents or any other agreement or document referred to therein, Borrower hereby submits to the jurisdiction of all federal and state courts located in the Commonwealth of Massachusetts and consents that any order, process, notice of motion or other application to or by any of said courts or a judge thereof may be served within or without such court's jurisdiction by registered mail or by personal service, PROVIDED a reasonable time for appearance is allowed (but not less than the time otherwise afforded by any law or rule).

(b) THE BORROWER AND LENDER MUTUALLY HEREBY KNOWINGLY,

VOLUNTARILY AND INTENTIONALLY WAIVE THE RIGHT TO A TRIAL BY JURY IN RESPECT OF ANY CLAIM BASED HEREON, ARISING OUT OF, UNDER OR IN CONNECTION WITH THIS AGREEMENT OR ANY OTHER LOAN DOCUMENTS CONTEMPLATED TO BE EXECUTED IN CONNECTION HEREWITH OR ANY COURSE OF CONDUCT, COURSE OF DEALINGS, STATEMENTS (WHETHER VERBAL OR WRITTEN) OR ACTIONS OF ANY PARTY. THIS WAIVER CONSTITUTES A MATERIAL INDUCEMENT FOR LENDER TO ACCEPT THIS AGREEMENT AND MAKE THE LOANS.

8.8 COMPLETE AGREEMENT, AMENDMENTS. This Agreement, together with the Note and other Loan Documents contains the entire agreement between the parties with respect to the transactions contemplated hereby, and supersedes all negotiations, presentations, warranties, commitments, offers, contracts and writings prior to the date hereof relating to the subject matter. This Agreement may only be amended, modified, waived, discharged or terminated by a writing signed by the party to be charged with such amendment, modification, waiver, discharge or termination.

8.9 EXPENSES. The Borrower shall pay on demand, regardless of whether any Default or Event of Default has occurred or whether any proceeding to enforce any Loan Document has been commenced, all out-of-pocket expenses (including, without limitation, the reasonable fees and disbursements of counsel to Lender) incurred by Lender in connection with (a) the negotiation, preparation, filing or recording of the Loan Documents, and any future requests for amendments or waivers of the Loan Documents (whether or not the transactions contemplated thereby shall be consummated), (b) the collection of the Loans and any and all other obligations of Borrower to Lender whether now existing or hereafter arising, or with the preservation, exercise or enforcement of Lender's rights and remedies under or in connection with the Loan Documents, including, without limitation, any and all expenses incurred by Lender in or in connection with any case commenced by or against Borrower under the Bankruptcy Code, and
(c) any claim or liability for any stamp, excise or other similar taxes and any penalties or interest with respect thereto that may be levied, collected, withheld or assessed by any jurisdiction in connection with the execution and delivery of the Loan Documents or any modification thereof. This covenant shall survive payment of the Loans and termination of this Agreement. Borrower hereby authorizes Lender to debit Borrower's deposit accounts if Borrower fails to pay such amount promptly after demand.

8.10 INDEMNIFICATION. Borrower agrees to indemnify and hold Lender harmless from and against any and all loss, liability, obligations, damages, penalties, judgments, actions, investigations, claims, costs and expenses
(including, without limitation, reasonable attorneys' fees and disbursements) now or in the future incurred by or asserted against Lender by any Person arising out of or in connection with any past, present, or future action or inaction by Lender or Borrower in connection with any Loan Document, or any transaction contemplated thereby, except any action or inaction arising out of Lender's gross negligence or willful misconduct as determined by a court of competent jurisdiction in an order binding on Lender and not subject to appeal.

8.11 SURVIVAL OF AGREEMENTS. All covenants, agreements, representations and warranties made herein and in the certificates delivered pursuant hereto shall survive the making of Loans and the execution and delivery to Lender of the Note and shall continue in full force and effect so long as any Note is outstanding and unpaid or this Agreement remains in effect. All agreements, obligations and liabilities of Borrower under this Agreement concerning the payment of money to Lender, other than the obligation to pay principal of and interest on Loans, shall survive the payment in full of Loans and termination of this Agreement.

8.12 SEVERABILITY. Any provision hereof that is prohibited or unenforceable in any jurisdiction shall, as to such jurisdiction, be ineffective to the extent of such prohibition or unenforceability without invalidating the remaining provisions hereof, and any such prohibition or unenforceability in any jurisdiction shall not invalidate or render unenforceable such provision in any other jurisdiction.

8.13 DESCRIPTIVE HEADINGS. The Table of Contents and the captions in this Agreement are for convenience of reference only and shall not define or limit the provisions hereof.

8.14 COUNTERPARTS. This Agreement may be executed by one or more of the parties on any number of separate counterparts, and all of said counterparts taken together shall be deemed to constitute one and the same instrument.

8.15 PLEDGE TO FEDERAL RESERVE. Lender may at any time pledge all or any portion of its rights under the Loan Documents including any portion of the Note to any of the twelve (12) Federal Reserve Banks organized under Section 4 of the Federal Reserve Act, 12 U.S.C. Section 341. No such pledge or enforcement thereof shall release Lender from its obligations under any of the Loan Documents.

8.16 LOST NOTE. Upon receipt of an affidavit of an officer of Lender as to the loss, theft, destruction or mutilation of the Note or any other Loan Documents which is not of public record, and, in the case of any such loss, theft, destruction or mutilation, upon receipt of an affidavit of surrender and cancellation of such Note or other Loan Document, Borrower will issue, in lieu thereof, a replacement Note or other Loan Document in the same principal amount thereof and otherwise of like tenor.

[REMAINDER OF PAGE INTENTIONALLY BLANK]

IN WITNESS WHEREOF, the parties hereto have caused this Agreement to be executed as an instrument under seal by their respective duly authorized officers as of the date first written above.

WITNESS: VERTEX PHARMACEUTICALS INCORPORATED

_____ By: _____ Name: Thomas G. Auchincloss, Jr.
Title: Vice President, Finance

FLEET NATIONAL BANK

_____ By: _____ Name: Kimberly A. Martone Title: Senior Vice President

SCHEDULE 1

DEFINITIONS

"ACCUMULATED FUNDING DEFICIENCY" - the amount referred to by such term as defined in Section 302(a)(2) of ERISA.

"AFFILIATE" - as to any Person (a) any other Person which, directly or indirectly, is in control of, is controlled by, or is under common control with such Person, or (b) any other Person who is an officer or director of such Person, or (c) any Person described in clause (a) above (other than any Subsidiary all of the capital stock of which is owned by Borrower).

"AUTHORIZED REPRESENTATIVE" - any person holding the position of President, Treasurer or Vice President of Finance of the Borrower at any time.

"BANKRUPTCY CODE" - The Bankruptcy Reform Act of 1978, as heretofore and hereafter amended, and codified as 11 U.S.C. Sections 101, et seq.

"BORROWING DATE" - the Business Day on which any Loan is made.

"BUILD-OUT FEES" - the fees earned and reimbursable expenses incurred by architects, contractors, and engineers for their services in connection with the build-out of the Borrower's premises at 200 Sidney Street, Cambridge, Massachusetts.

"BUSINESS DAY" - any day other than a Saturday, Sunday or day on which shall be in the Commonwealth of Massachusetts a legal holiday or a day on which banking institutions in Boston, Massachusetts are required or authorized to close.

"CAPITAL EQUIPMENT" - equipment that in accordance with GAAP is required or permitted to be depreciated or amortized on Borrower's balance sheet.

"CAPITAL EXPENDITURES" - for any period, the sum of (i) all expenditures that, in accordance with GAAP, are required to be included in land, property, plant or equipment or similar fixed asset account (whether involving real or personal property) and (ii) Capital Lease Obligations incurred during such period (excluding renewals of Capital Leases).

"CAPITAL LEASE" - any capital lease, conditional sales contract or other title retention agreement relating to the acquisition of Capital Equipment.

"CAPITAL LEASE OBLIGATIONS" - the aggregate capitalized amount of the obligations of Borrower under all Capital Leases.

"CASH EQUIVALENTS" - (a) securities with maturities of 180 days or less from the date of acquisition issued or fully guaranteed or insured as to payment of principal and interest by the United States or any agency thereof, (b) certificates of deposit with maturities of 365 days or less

from the date of acquisition issued by Lender or any domestic commercial bank having capital and surplus reasonably acceptable to Lender and (c) commercial paper of a domestic issuer rated at least either A-1 by Standard & Poor's or B-1 by Moody's Investors

Service with maturities of 180 days or less from the date of acquisition.

"CHANGE IN CONTROL" - at any time that any Person, together with the affiliates and associates of such Person within the meaning of Rule 12b-2 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), shall acquire beneficial ownership within the meaning of Rule 13d of the Exchange Act of fifty (50%) percent or more of the voting stock or total equity of the Borrower, or if a change in the Board of Directors of Borrower in which the individuals who constituted the Board of Directors at the beginning of the two (2) year period immediately preceding such change (together with any other director whose election by the Board of Directors was approved by at least two-thirds of the directors then in office at the beginning of such period) cease for any reason to constitute a majority of the directors of the Borrower then in office.

"COMMITMENTS" - the Term Loan Commitment.

"COMMONLY CONTROLLED ENTITY" - an entity, whether or not incorporated, which is under common control with Borrower within the meaning of Section 414(b) or (c) of the IRC.

"CONSOLIDATED" - when used with reference to any term, that term as applied to the accounts of the Borrower and all of its Subsidiaries, consolidated in accordance with GAAP.

"CONTINGENT LIABILITY" - any obligation of Borrower guaranteeing or in effect guaranteeing any Indebtedness, leases, dividends or other obligations ("primary obligations") of any other Person (the "primary obligor") in any manner, whether directly or indirectly.

"DEBT SERVICE COVERAGE RATIO" - for any period, the quotient of: (i) the sum of (a) net earnings (loss) as determined in accordance with GAAP excluding all extraordinary and nonrecurring gains, PLUS (b) the sum of interest, taxes, depreciation, and amortization (to the extent that any of the foregoing were deducted in calculating net earnings (loss)); DIVIDED BY (ii) the sum of (a) current maturities of long-term Indebtedness, PLUS (ii) interest expense, PLUS (iii) non-financed Capital Expenditures.

"DEFAULT" - any event specified in Article 7, whether or not any requirement for the giving of notice or lapse of time or any other condition has been satisfied.

"DIVIDENDS" means, for any applicable period, the aggregate of all amounts paid or payable (without duplication) as dividends (exclusive of dividends payable solely in capital stock of Borrower), distributions or owner withdrawals with respect to Borrower's shares of capital stock, whether now or hereafter outstanding and includes any purchase, redemption or other retirement of any shares of the Borrower's stock, directly or indirectly.

"DOLLARS" and "$" - lawful money of the United States. Any reference to payment means payment in lawful money of the United States in immediately available funds.

"ELIGIBLE ACCOUNTS" - shall mean accounts receivable of the Borrower arising from the sale of inventory or provision of services in the ordinary course of business, that are unpaid less than 90 days from the invoice date, that are not subject to counterclaim, setoff or other claim of any kind, and that are otherwise reasonably acceptable to Lender.

"ERISA" - the Employee Retirement Income Security Act of 1974, as amended from time to time, including all regulations promulgated under such Act.

"EVENT OF DEFAULT" - any event specified in Article 7, PROVIDED that any requirement for the giving of notice or lapse of time or any other condition has been satisfied.

"FUNDED INDEBTEDNESS" - shall mean all obligations of the Borrower for borrowed money including, without limitation, all Capital Lease Obligations and all obligations in respect of advances made or to be made under letters of credit issued for such Person's account and in respect of acceptance of drafts drawn by such Person.

"GAAP" - those generally accepted accounting principles set forth in Statements of the Financial Accounting Standards Board and in Opinions of the Accounting Principles Board of the American Institute of Certified Public Accountants or which have other substantial authoritative support in the United States and are applicable in the circumstances, as applied on a consistent basis. As used in the preceding sentence "consistent basis" shall mean that the accounting principles observed in the current period are comparable in all material respects to those applied in the preceding period.

"HAZARDOUS MATERIAL" - any hazardous waste, toxic substance hazardous chemical, radioactive material, hazardous material, oil or gasoline, under any applicable federal or state statute, county or municipal law or ordinance, including (without limitation) any substance defined as a "hazardous substance" or "toxic substance" (or comparable term) in the Comprehensive Environmental Response, Compensation and Liability Act, as amended (42 U.S.C. 9601, ET SEQ.), the Hazardous Materials Transportation Act (49 U.S.C. 1802), or the Resource Conservation and Recovery Act (42 U.S.C. 6901, ET SEQ.).

"INDEBTEDNESS" - with respect to any Person, any item that would properly be included as a liability on the liability side of a balance sheet of such Person as of any date as of which Indebtedness is to be determined and includes (but is not limited to) (a) all obligations for borrowed money including all Loans, (b) all obligations evidenced by bonds, debentures, notes or other similar instruments, (c) all obligations to pay the deferred purchase price of property or services, (d) all Capital Lease Obligations, (e) all Contingent Liabilities, and (e) all obligations in respect of advances made or to be made under letters of credit issued for such Person's account and in respect of acceptances of drafts drawn by such Person.

"INITIAL BORROWING DATE" - the date of this Agreement.

"INTANGIBLE ASSETS" - all intangible assets of the Borrower including, without limitation, all deferred assets, patents, copyrights, trademarks, non-compete agreements and similar intangibles, good will, unamortized debt discount and expenses, and all investments other than

Marketable Investments.

"INTELLECTUAL PROPERTY" - shall mean "Intellectual Property," as defined in Section 101(35A) of the Bankruptcy Code, now or hereafter owned by Borrower or any of its Subsidiaries, together with all of the following property now or hereafter owned by Borrower or any of its Subsidiaries: all domestic and foreign patents and patent applications; inventions, discoveries and improvements, whether or not patentable; trademarks, trademark applications and registrations; service marks, service mark applications and registrations; copyrights, copyright applications and registrations; all licenses therefor; trade secrets and all other proprietary information.

"INVESTMENT" - any transfers of property to, contribution to capital of, acquisition of stock, other securities or evidences of indebtedness of, acquisition of businesses of, or acquisition of property of, any Person, other than in the ordinary course of business.

"IRC" - the Internal Revenue Code of 1986, as amended from time to time and including all regulations promulgated thereunder.

"JOINT VENTURE" - a single-purpose corporation, partnership, limited liability company, joint venture or other similar legal arrangement (whether created by contract or conducted through a separate legal entity) now or hereafter formed by Borrower or any of its Subsidiaries with another Person in order to conduct a common venture or enterprise with such Person.

"LIEN" - any mortgage, deed of trust, pledge, hypothecation, assignment, deposit arrangement, encumbrance (including, without limitation, any easement, right-of-way, zoning or similar restriction or title defect), lien (statutory or other) or preference, priority or other security agreement or preferential arrangement of any kind or nature whatsoever (including, without limitation, any conditional sale or other title retention agreement, any financing lease having substantially the same economic effect as any of the foregoing and the filing of any financing statement under the UCC or comparable law of any jurisdiction).

"LIQUIDITY RATIO" - at any date, the quotient of: (a) the sum of Unrestricted Cash, PLUS Marketable Investments, PLUS Eligible Accounts; DIVIDED BY (b) all Indebtedness of the Borrower.

"LOAN" or "LOANS" - any Term Loan.

"LOAN DOCUMENTS" - this Agreement, the Term Note, and all other instruments and documents executed in connection with the Indebtedness covered hereby and thereby.

"MARKETABLE INVESTMENTS" - any interest-bearing debt obligations owned by Borrower (excluding directors' qualifying shares and items included as Cash Equivalents) which meet the definition of marketable securities under GAAP. Such amounts shall exclude common or preferred stock. Such securities shall include obligations issued by the U.S. Treasury and other agencies of the U.S. government, corporate bonds, bank notes, mortgage and asset backed securities, finance company securities and auction rate preferred stocks. Such securities shall be rated investment grade (BBB or better for bonds or similar securities, A1/P1 for commercial

paper and notes) and shall otherwise be liquid investments as reasonably determined by Lender.

"MATERIAL ADVERSE EFFECT" - means a material adverse effect, as reasonably determined by the Lender, on (a) the property, business, operations, financial condition, liabilities or capitalization of Borrower or of Borrower and its Subsidiaries taken as a whole; or (b) the validity or enforceability of any of the Loan Documents.

"MULTIEMPLOYER PLAN" - a Plan which is a multiemployer plan as defined in Section 3(37)(A) of ERISA or Section 414(f) of the IRC.

"NOTE" - the Term Note.

"OBLIGATIONS" means all loans, advances, interest, fees, debts, guaranties, liabilities, obligations (including without limitation the Loans and contingent obligations under guarantees), agreements, undertakings, covenants and duties owing or to be performed or observed by Borrower to or in favor of Lender, of every kind and description (whether or not evidenced by any note or other instrument; for the payment of money; arising out of the Loans, this Agreement or any other agreement between Lender and Borrower or any other instrument of Borrower in favor of Lender; arising out of or relating or similar to transactions described herein; or contemplated as of the Initial Borrowing Date), direct or indirect, absolute or contingent, due or to become due, now existing or hereafter arising, including without limitation all interest, fees, charges, and amounts chargeable to Borrower under this Agreement.

"PBGC" - the Pension Benefit Guaranty Corporation established pursuant to Subtitle A of Title IV of ERISA.

"PERSON" - an individual, partnership, corporation, business trust, joint stock company, trust, unincorporated association, joint venture, governmental authority or other entity of whatever nature.

"PLAN" - any pension plan, as defined in Section 3(2) of ERISA and any welfare plan, as defined in Section 3(1) of ERISA, which is sponsored, maintained or contributed to by Borrower or any Commonly Controlled Entity, or in respect of which Borrower or a Commonly Controlled Entity is an "employer" as defined in Section 3(5) of ERISA.

"PLEDGE AGREEMENT" - the Pledge Agreement in the form of EXHIBIT C hereto, as it may be amended, supplemented or otherwise modified, from time to time.

"PROHIBITED TRANSACTION" - any of the transactions set forth in Section 406 of ERISA to the extent not exempt under Section 408 of ERISA.

"PURCHASED EQUIPMENT" - the equipment and fixtures at 200 Sidney Street, Cambridge, Massachusetts 02139 purchased by Borrower.

"PURCHASED EQUIPMENT COST" - the amount paid by Borrower to purchase the Purchased

Equipment or to pay Build-Out Fees.

"QUALIFYING PARTICIPATION EVENT" - has the meaning set forth in Section 8.5 hereof.

"REPORTABLE EVENT" - any of the events set forth in Section 4043(b) of **ERISA.**

"SUBORDINATED DEBT" - Indebtedness of Borrower and its Subsidiaries that by its terms is fully subordinated to the payment and enforcement of the Loans in a manner satisfactory to the Lender.

"SUBSIDIARY" - with respect to any Person, any corporation, partnership, trust or other organization, whether or not incorporated, the majority of the voting stock or voting rights of which is owned or controlled, directly or indirectly, by such Person.

"TANGIBLE CAPITAL BASE" - the sum of shareholders' equity, PLUS Subordinated Debt, LESS Intangible Assets.

"TERM LOAN" - any loan made pursuant to Section 2.1.

"TERM LOAN COMMITMENT" - the commitment by the Lender to make Term Loans pursuant to Section 2.1.

"TERM LOAN COMMITMENT PERIOD" - the period from and including the Initial Borrowing Date to and including December 31, 2000.

"TERM LOAN LIMIT" - $20,000,000, less the aggregate principal amount of all Term Loans made to Borrower.

"TERM NOTE" - a promissory note of Borrower made to evidence the Term Loans in the form of EXHIBIT A, as it may be amended, supplemented or otherwise modified, from time to time.

"TERMINATION DATE" - the earlier of (a) December 30, 2005, and (b) the date the Lender's commitment to make Loans is terminated pursuant to Section 7.2 of Article 7.

"UNRESTRICTED CASH" - cash and Cash Equivalents of the Borrower or VSC that are readily available to Borrower or VSC, as the case may be, and not subject to any lien or limitation or restriction on their use by the Borrower or VSC, as the case may be.

"VSC" - Vertex Securities Corp., a Massachusetts corporation.

SCHEDULE 3.1

FINANCIAL STATEMENTS OF BORROWER PROVIDED

Year 2000 Forecasted Statement of Operations:

- Summary Income Statement
- Major Expense Groupings
- Forecasted Balance Sheets

SCHEDULE 3.3

SUBSIDIARIES, INVESTMENTS AND +5% SHAREHOLDERS

SUBSIDIARIES:

Vertex Securities Corp. (incorporated in Massachusetts) (wholly-owned)

Vertex Pharmaceuticals (Europe) Limited (incorporated in England) (wholly-owned)

INVESTMENTS:

Altus Biologics Inc. (incorporated in Massachusetts). At December 31, 1998, Vertex owned approximately 70% of the capital stock of Altus. On February 5, 1999, Vertex restructured its investment in Altus. As part of the transaction, Vertex provided Altus $3,000,000 of cash in exchange for preferred stock and warrants. The preferred stock provides Vertex with a minority ownership position in Altus, and the warrants become exercisable upon certain events. As a result of the transaction, Altus now operates independently from Vertex. In addition, Vertex has retained a non-exclusive royalty-free right to use Altus' technology for discovering, developing and manufacturing small molecule drugs. Vertex records its percentage of Altus' net income and losses using the equity method of accounting.

Versal Technologies Inc. (incorporated in Massachusetts). Vertex owns less than 20% of total Versal shares outstanding.

PRINCIPAL SHAREHOLDERS

As of 12/17/99, based solely upon information filed by shareholders with the S.E.C.:

Name	Shares Beneficially Owned	Percentage of Total
Wellington Management Company LLP	2,704,200	10.7%
Trimark Financial Corporation	2,102,000	8.3%
Bluewater Fund	1,370,000	5.4%

SCHEDULE 3.6

CONSENTS AND APPROVALS REQUIRED

None

SCHEDULE 3.8

LITIGATION

Chiron Corporation ("Chiron") filed suit on July 30, 1998 against the Company and Eli Lilly and Company in the United States District Court for the Northern District of California, alleging infringement by the defendants of various U.S. patents issued to Chiron. The infringement action relates to research activities by the defendants in the hepatitis C viral protease field and the alleged use of inventions claimed by Chiron in connection with that research and development. Chiron has requested damages in an unspecified amount, as well as an order permanently enjoining the defendants from unlicensed use of Chiron inventions. While the final outcome of these actions cannot be determined, the Company believes that the plaintiff's claims are without merit and intends to defend the actions vigorously.

SCHEDULE 3.11

BURDENSOME RESTRICTIONS

None

SCHEDULE 3.18

LOCATION OF ASSETS

130 Waverly Street, Cambridge, MA, USA (includes buildings located at 40 Allston Street, 228 and 240 Sidney Street, 62 Hamilton Street, and 625 Putnam Street, Cambridge, Massachusetts)

88 Milton Park, Abingdon, Oxon OX14 4RY, U.K.

Items in storage in leased premises at 345 Vassar Street and 21 Erie Street, Cambridge, MA, and in contracted warehouse storage at 134 Mass. Ave. (Metropolitan Storage), Cambridge, and 41 Atlantic Ave in Woburn (Sacco's Storage Warehouse).

Office equipment and related property maintained by medical liaison field staff based in 12 locations in the U.S., Germany, France and

Italy (1 employee in each location)

In addition, from time to time Vertex compounds and other research and development materials are sent to contract testing laboratories and process development contractors for testing, scale-up and manufacture. Some clinical trial materials may be located in off-site storage facilities.

The Purchased Equipment will be located at 200 Sidney Street, Cambridge, MA.

SCHEDULE 3.20

INTELLECTUAL PROPERTY DISCLOSURE

See Schedule 3.8

In addition, an opposition to one of Vertex's patents in the EPO has been filed by another pharmaceutical company.

SCHEDULE 3.21

NEGATIVE PLEDGES

None

SCHEDULE 5.1

INDEBTEDNESS

Capital Leases
- BankBoston Balance at 11/30/99 = $1,848,807 - GE Capital Balance at 11/30/99 = $4,447,321 - Lasalle Balance at 11/30/99=$886,717 - Apple Comm Credit Balance at 11/30/99 = $87,926

Operating Leases
- Fort Washington Realty Trust lease expires 1/1/01 - Fort Washington Limited Partnershipleases expire12/31/09 & 12/31/05 - Fort Washington Limited Partnership (new building) lease expires 5/1/10 - Hybridon lease expires 10/01/00 - Sidney Street Enterprises lease expires 12/1/00 - C. Vincent Vappi lease expires 12/31/03 - Milton Park Limited (UK) lease expires 12/31/09

Purchase Commitments
- Silicon Graphics - Supercomputer lease through 2001 - Various Software - approx. $350,000 per year for 2000 & 2001

SCHEDULE 5.2

CONTINGENT LIABILITIES

None

SCHEDULE 5.3

DISCLOSED LIENS

PRECISION CORPORATE SERVICES, INC.

October 12, 1999

SUBJECT: VERTEX PHARMACEUTICALS INCORPORATED

SEARCH REQUEST: UCC - CAMBRIDGE CITY CLERK, MA

THROUGH DATE: OCTOBER 4, 1999 Page 1 of 5

File Date	File Number	Type	Description
Mar. 23, 1992	#055544		SNET Credit Inc. North Haven, CT 06473
		Assignment	Filed 07-16-93
		Assignment	Filed 08-09-95
		Continuation	Filed 10-02-96
Apr. 13, 1992	#055593		SNET Credit, Inc. North Haven, CT 06473
		Assignment	Filed 07-16-93
		Assignment	Filed 08-09-95
		Continuation	Filed 10-15-96
Jun. 05, 1992	#055728		SNET Credit, Inc. North Haven, CT 06473
		Assignment	Filed 07-16-93
		Assignment	Filed 08-09-95
		Continuation	Filed 12-10-96
Aug. 26, 1992	#055976		SNET Credit, Inc. North Haven, CT 06473
		Assignment	Filed 08-09-95
		Continuation	Filed 01-02-97
Oct. 14, 1992	#056113		General Electric Capital Corporation Hunt Valley, MD
	#056113	Continuation	Filed 04-24-97

PRECISION CORPORATE SERVICES, INC.

October 12, 1999

SUBJECT: VERTEX PHARMACEUTICALS INCORPORATED

SEARCH REQUEST: UCC - CAMBRIDGE CITY CLERK, MA

THROUGH DATE: OCTOBER 4, 1999 Page 2 of 5

File Date	File Number	Type	Description
Jan. 21, 1993	#056399		General Electric Capital Corporation Hunt Valley, MD
		Continuation	Filed 07-23-97
Oct. 07, 1993	#057220		General Electric Capital Corporation Hunt Valley, MD 21031
		Continuation	Filed 04-16-98
Jan. 13, 1994	#057551		General Electric Capital Corporation Hunt Valley, MD 21031
		Continuation	Filed 07-24-98
Jan. 20, 1995	#058888		BayBank Boston, N.A. Boston, MA 01803
		Assignment	Filed 08-28-97
		Amendment	Filed 09-26-97
Apr. 27, 1995	#059248		BayBank Boston, N.A. Boston, MA 02110
		Assignment	Filed 09-26-97
		Amendment	Filed 09-26-97
Jun. 28, 1995	#059459		BayBank Boston, N.A.

PRECISION CORPORATE SERVICES, INC.

October 12, 1999

SUBJECT: VERTEX PHARMACEUTICALS INCORPORATED

SEARCH REQUEST: UCC - CAMBRIDGE CITY CLERK, MA

THROUGH DATE: OCTOBER 4, 1999 Page 3 of 5

File Date	File Number	Type	Description
			Boston, MA 02110
		Assignment	Filed 09-26-97
		Amendment	Filed 09-26-97
Sep. 20, 1995	#059731		BayBank Boston, N.A. Boston, MA 02110
		Assignment	Filed 09-26-97
		Amendment	Filed 09-26-97
Dec. 29, 1995	#060100		BayBank , N.A. Boston, MA 02110
		Assignment	Filed 09-26-97
		Amendment	Filed 09-26-97
Apr. 30, 1996	#060550		BayBank, N.A. Burlington, MA 01803
		Assignment	Filed 09-26-97
		Amendment	Filed 09-26-97
		Assignment	Filed 10-09-97
Jul. 02, 1996	#060862		BayBank, N.A. Burlington, MA 01803
		Assignment	Filed 09-26-97
		Amendment	Filed 09-26-97

PRECISION CORPORATE SERVICES, INC.

October 12, 1999

SUBJECT: VERTEX PHARMACEUTICALS INCORPORATED

SEARCH REQUEST: UCC - CAMBRIDGE CITY CLERK, MA

THROUGH DATE: OCTOBER 4, 1999 Page 4 of 5

File Date	File Number	Type	Description
		Assignment	Filed 10-09-97
Oct. 15, 1996	#061251		BayBank, N.A. Burlington, MA 01803
		Assignment Amendment Assignment	Filed 09-26-97 Filed 09-26-97 Filed 10-09-97
Jan. 15, 1997	#061671		BayBank Burlington, MA 01803
		Assignment Amendment	Filed 09-26-97 Filed 09-26-97
Feb. 11, 1997	#061786		BayBank, N.A. Burlington, MA 01803
		Assignment Amendment Assignment	Filed 09-26-97 Filed 09-26-97 Filed 10-09-97
May 08, 1997	#062107		BayBank, N.A. Burlington, MA
		Assignment Amendment Assignment	Filed 09-26-97 Filed 09-26-97 Filed 10-09-97
Aug. 05, 1997	#062498		BancBoston Leasing Inc. Burlington, MA 01803

PRECISION CORPORATE SERVICES, INC.

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SUBJECT: VERTEX PHARMACEUTICALS INCORPORATED

SEARCH REQUEST: UCC - CAMBRIDGE CITY CLERK, MA

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File Date	File Number	Type	Description
		Amendment	Filed 09-26-97
Oct. 03, 1997	#062753		General Electric Capital Corporation Hunt Valley, MD
		Amendment	Filed 06-18-98
Nov. 13, 1997	#062933		Silicon Graphics, Inc. Mountain View, CA
Jan. 05, 1998	#063181		General Electric Capital Corporation Hunt Valley, MD
Apr. 09, 1998	#063544		General Electric Capital Corporation Hunt Valley, MD 21030
Jul. 10, 1998	#063965		General Electric Capital Corporation Hunt Valley, MD 21030
Nov. 03, 1998	#064537		General Electric Capital Corporation Hunt Valley, MD 21030

PRECISION CORPORATE SERVICES, INC.

October 6, 1999

SUBJECT: VERTEX PHARMACEUTICALS INCORPORATED

SEARCH REQUEST: UCC - MASSACHUSETTS SECRETARY OF STATE

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File Date	File Number	Type	Description
Mar. 25, 1992	#081823		SNET Credit, Inc. North Haven, CT 06473
	#176429	Assignment	Filed 07-28-93
	#330976	Assignment	Filed 08-09-95
	#420394	Continuation	Filed 10-02-96
Apr. 13, 1992	#085553		SNET Credit, Inc. North Haven, CT 06473
	#174092	Assignment	Filed 07-16-93
	#330975	Assignment	Filed 08-09-95
	#423008	Continuation	Filed 10-15-96
Jun. 05, 1992	#096063		SNET Credit, Inc. North Haven, CT 06473
	#174067	Assignment	Filed 07-16-93
	#330974	Assignment	Filed 08-09-95
	#434738	Continuation	Filed 12-10-96
June. 26, 1992	#100038		SNET Credit, Inc. North Haven, CT 06473
	#174069	Assignment	Filed 07-16-93
	#330978	Assignment	Filed 08-09-95
	#439923	Continuation	Filed 01-02-97
Sep. 08, 1993	#112691		SNET Credit, Inc. North Haven, CT 06473
	#174070	Assignment	Filed 07-16-93

PRECISION CORPORATE SERVICES, INC.

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File Date	File Number	Type	Description
	#330979	Assignment	Filed 08-09-95
	#455902	Continuation	Filed 03-20-97
Oct. 02, 1992	#117565		SNET Credit, Inc. North Haven, CT 06473
	#175873	Assignment	Filed 07-26-93
	#330980	Assignment	Filed 08-09-95
	#460297	Continuation	Filed 04-10-97
Oct. 15, 1992	#119868		General Electric Capital Corporation Hunt Valley, MD
	#463703	Continuation	Filed 04-24-97
Jan. 20, 1993	#138847		General Electric Capital Corporation Hunt Valley, MD
	#485092	Continuation	Filed 07-23-97
Oct. 07, 1993	#190096		General Electric Capital Corporation Hunt Valley, MD 21031
	#542955	Continuation	Filed 04-15-98
Jan. 24, 1994	#211595		General Electric Capital Corporation Hunt Valley, MD 20131

PRECISION CORPORATE SERVICES, INC.

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File Date	File Number	Type	Description
	#567708	Continuation	Filed 07-29-98
Jan. 13, 1995	#286425		BayBank Boston, N.A. Boston, MA 01803
	#493006	Assignment	Filed 08-27-97
	#499617	Amendment	Filed 09-25-97
Apr. 24, 1995	#308152		BayBank Boston, N.A. Boston, MA 02110
	#499605	Assignment	Filed 09-25-97
	#499628	Amendment	Filed 09-25-97
May 15, 1995	#312413		Xerox Corporation Stamford, CT, 06907
Jun. 28, 1995	#322275		BayBank Boston, N.A. Boston, MA 02110
	#499606	Assignment	Filed 09-25-97
	#499627	Amendment	Filed 09-25-97
Sep. 29, 1995	#341260		BayBank Boston, N.A. Boston, MA 02110
	#499607	Assignment	Filed 09-25-97
	#499626	Amendment	Filed 09-25-97
Dec. 28, 1995	#360219		BayBank , N.A. Boston, MA 02110

PRECISION CORPORATE SERVICES, INC.

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File Date	File Number	Type	Description
	#499608	Assignment	Filed 09-25-97
	#499625	Amendment	Filed 09-25-97
Apr. 24, 1996	#384660		BayBank, N.A. Burlington, MA 01803
	#499624	Amendment	Filed 09-25-97
	#499909	Assignment	Filed 09-26-97
	#502436	Assignment	Filed 10-08-97
Jul. 01, 1996	#400581		BayBank, N.A. Burlington, MA 01803
	#499609	Assignment	Filed 09-25-97
	#499623	Amendment	Filed 09-25-97
	#502435	Assignment	Filed 10-08-97
Oct. 07, 1996	#421439		BayBank, N.A. Burlington, MA 01803
	#499610	Assignment	Filed 09-25-97
	#499622	Amendment	Filed 09-25-97
	#502434	Assignment	Filed 10-08-97
Jan. 10, 1997	#441294		BayBank, N.A. Burlington, Ma
	#499611	Assignment	Filed 09-25-97
	#499621	Amendment	Filed 09-25-97
Jan. 13, 1997	#442078		LINC Quantum Anayltics Inc. Foster City, CA 94404

File Date	File Number	Type	Description
Feb. 05, 1997	#446572		BayBank, N.A. Burlington, MA 01803
	#499612	Assignment	Filed 09-25-97
	#499620	Amendment	Filed 09-25-97
	#502432	Assignment	Filed 10-08-97
May 06, 1997	#466394		BayBank, N.A. Burlington, Ma
	#499613	Assignment	Filed 09-25-97
	#499619	Amendment	Filed 09-25-97
	#502433	Assignment	Filed 10-08-97
Aug. 14, 1997	#490197		BancBoston Leasing Inc. Burlington, MA 01803
	#499618	Amendment	Filed 09-25-97
Oct. 03, 1997	#501217		General Electric Capital Corporation Hunt Valley, MD
	#558209	Amendment	Filed 07-18-98
Nov. 13, 1997	#510374		Silicon Graphics Inc. Mountain View, CA
Jan. 05, 1998	#521048		General Electric Capital Corporation Hunt Valley, MD

PRECISION CORPORATE SERVICES, INC.

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SUBJECT: VERTEX PHARMACEUTICALS INCORPORATED

SEARCH REQUEST: UCC - MASSACHUSETTS SECRETARY OF STATE

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File Date	File Number	Type	Description
Jan. 09, 1998	#522144		Silicon Graphics, Inc. Mt. View, CA 94043
Apr. 08, 1998	#541304		General Electric Capital Corporation Hunt Valley, MD 20130
Jul. 09, 1998	#563183		General Electric Capital Corporation Hunt Valley, MD
Oct. 30, 1998	#587614		General Electric Capital Corporation Hunt Valley, MD 21030

SCHEDULE 5.5
INVESTMENT POLICIES

VERTEX PHARMACEUTICALS INCORPORATED
INVESTMENT POLICY GUIDELINES
FISHER, FRANCIS, TREES AND WATTS, INC.

I. PURPOSE

To establish policy and guidelines for investment of corporate surplus cash. "Surplus cash" is cash in corporate accounts not immediately required for debt repayment, working capital, capital investment, or other outstanding near-term financial obligations.

II. OBJECTIVES

The investment portfolio will be managed to:

A. Maximize returns versus the industry averages.

B. Diversify investments to minimize the risk and inappropriate concentrations of investments with any one entity.

Securities in the portfolio may be actively traded before maturation. Gains and losses may be realized on certain trades in order to more effectively reposition the portfolio for performance within specified parameters. Total net realized losses (realized losses net of realized gains) are not to exceed $175,000 per fiscal quarter.

III. INVESTMENT RESTRICTIONS

Investments shall be made in the context of the following investment guide lines:

The current benchmark for duration and performance of the portfolio:

25% in the Merrill 3 month treasury index 75% in the Merrill 1-3 year treasury index

Periodic liquidity in the portfolio will be required for use in funding the operations of the Company. Notification of a draw-down will be given with a reasonable amount of time as to avoid any unneccesary trading losses.

Eligible Investments:

1. Direct obligations of the U.S. Treasury including bills, notes, and bonds.

2. Obligations issued or guaranteed by agencies or instruments of the U.S. government.

3. Bank obligations, including certificates of deposit, bank notes and bankers acceptances. Investments in these securities is limited to banks whose long term debt is rated "A" or higher by Moody's or Standard & Poor's and short term obligations are rated "P-l " or higher by Moody's or "A-l " or higher by Standard & Poor's.

4. Corporateobligations, including intermediate term notes rated "A" or higher by Moody's or Standard & Poors and Commercial Paper rated "P-l" or higher by Moody's, or "A-l" or higher by Standard & Poor's.

5. At the discretion of the Treasurer, a maximum 20% of the portfolio, at the time of purchase, may be invested in corporate obligations with a short term rating of A2/P2 and long term ratings of Baa1/BBB+, with a maturity not to exceed six months.

6. Repurchase agreements collateralized at a minimum of 102% with U.S. Treasury securities or other securities rated "AAA/Aaa" or equivalent.

7. Internal money market funds may be utilized for excess cash in the portfolio. Outside money market funds over $1 billion in assets consisting of acceptable securities are appropriate for investing, as long as the fund's manager has been in business over five years, has name recognition, ant that performance that is easily tracked.

8. U.S. and dollar denominated International corporate debt of all types is acceptable as long as the issuer meets credit rating and marketability guidelines.

9. Asset backed and mortgage backed securities (including CMOs) with AAA/Aaa credit rating or equivalent are acceptable investments. Expected maturity should be no longer than four years.

10. Fannie Mae, Freddie Mac, and Ginnie Mae securities are acceptable investments.

11. Treasury futures, including Eurodollar futures, on allowable securities otherwise eligible for purchase into the portfolio may be used to manage the duration of the portfolio though their exercise dates must be within + (-) six months of the duration of the portfolio.

IV. MATURITIES, DURATION, VOLATILITY

The maximum maturity of individual securities or the maximum average life of a security in the portfolio may not exceed 4 years.

The effective duration of the portfolio may not exceed 2 years.

For securities which have put dates, reset dates, or are traded based on their average maturity, the put date, reset date, or average maturity will be used, instead of the final maturity date, for maturity guideline purposes.

The overall volatility of the entire portfolio will be 2% or less at all times.

V. CONCENTRATION LIMITS/RESTRICTIONS

There is no minimum or maximum limit to the percentage of the portfolio invested in securities issued by the U.S. Treasury or by its agencies and instrumentalities.

No one issuer or group of issuers from the same holding company, is to exceed 10% of the portfolio at time of purchase, with the exception of US Government securities.

Excess concentrations is any one sector or any one type of security (i.e. corporates, mortgage-backed, asset backed, repos) should be avoided and no one sector or class should represent more than 50% of the portfolio with the exception of US Government securities.

VI. INVESTMENT PERFORMANCE

The company shall review the performance of it's investment managers on at least an annual basis. A quarterly meeting will be held in person or by telephone with the Treasurer to review performance figures and any updated liquidity needs and to discuss portfolio strategy.

VII. CREDIT QUALITY

Should any investment held in Vertex's portfolio be down-graded below the minimum prescribed rating, immediate notification must be made to Vertex.

VIII. MARKETABILITY

All securities are to be purchased through investment banking and brokerage firms of high quality and reputation, with a history of making markets for the securities in which we invest. All holdings will be of sufficient size and held in issues traded actively enough to facilitate minimum transaction costs and accurate market valuations.

IX. TRADING GUIDELINES

Normal investing practice is to actively manage the account and reinvest funds to take advantage of changing market conditions or reinvest on the day a security matures to maximize interest. A daily transaction log is to be maintained and available for review at

any time. All trading firms must generate a hard copy document for each transaction which is mailed to Vertex on a timely basis, and then matched to the transaction log.

X. SAFEKEEPING

Assets are to be held in a segregated bank custody account at State Street Bank with separate fiduciary account documents executed by and between State Street and Vertex. Assets shall not be held by any investment manager or securities dealer.

Xl. FIDUCIARY DISCRETION

The manager has full discretion to invest capital subject with strict adherence to these guidelines. These guidelines are to be reviewed periodically by the Treasurer and revisions made consistent with objectives set forth herein.

APPROVED BY: DATE: 11/17/97
Thomas G. Auchincloss, Treasurer

VERTEX PHARMACEUTICALS INCORPORATED
INVESTMENT POLICY GUIDELINES
MERRILL LYNCH

I. PURPOSE

To establish policy and guidelines for investment of corporate surplus cash. "Surplus cash" is cash in corporate accounts not immediately required for debt repayment, working capital, capital investment, or other outstanding near-term financial obligations.

II. OBJECTIVES

The investment portfolio will be managed to:

A. Maximize returns versus the industry averages.

B. Diversify investments to minimize the risk and inappropriate concentrations of investments with any one entity.

Securities in the portfolio may be actively traded before maturation. Gains and losses may be realized on certain trades in order to more effectively reposition the portfolio for performance within specified parameters. Total net realized losses (realized losses net of realized gains) are not to exceed $175,000 per fiscal quarter.

III. INVESTMENT RESTRICTIONS

Investments shall be made in the context of the following investment guide lines:

The current BENCHMARK for duration and performance of the portfolio:

25% in the Merrill 3 month treasury index 75% in the Merrill 1-3 year treasury index

Periodic liquidity in the portfolio will be required for use in funding the operations of the Company. Notification of a draw-down will be given with a reasonable amount of time as to avoid any unnecessary trading losses.

Eligible Investments:

1. Direct obligations of the U.S. Treasury including bills, notes, and bonds.

2. Obligations issued or guaranteed by agencies or instruments of the U.S. government.

3. Bank obligations, including certificates of deposit, bank notes and bankers

acceptances. Investments in these securities is limited to banks whose long term debt is rated "A" or higher by Moody's or Standard & Poor's and short term obligations are rated "P-l " or higher by Moody's or "A-l " or higher by Standard & Poor's.

4. Corporate obligations, including intermediate term notes rated "A" or higher by Moody's or Standard & Poors and Commercial Paper rated "P-l" or higher by Moody's, or "A-l" or higher by Standard & Poor's.

5. At the discretion of the Treasurer, a maximum 20% of the portfolio, at the time of purchase, may be invested in corporate obligations with a short term rating of A2/P2 and long term ratings of Baa1/BBB+, with a maturity not to exceed six months.

6. Repurchase agreements collateralized at a minimum of 102% with U.S.. Treasury securities or other securities rated "AAA/Aaa" or equivalent.

7. Internal money market funds may be utilized for excess cash in the portfolio. Outside money market funds over $1 billion in assets consisting of acceptable securities are appropriate for investing, as long as the fund's manager has been in business over five years, has name recognition, ant that performance that is easily tracked.

8. U.S. and dollar denominated International corporate debt of all types is acceptable as long as the issuer meets credit rating and marketability guidelines.

9. Asset backed and mortgage backed securities (including CMOs) with AAA/Aaa credit rating or equivalent are acceptable investments. Expected maturity should be no longer than four years.

10. Fannie Mae, Freddie Mac, and Ginnie Mae securities are acceptable investments.

IV. MATURITIES, DURATION, VOLATILITY

The maximum maturity of individual securities or the maximum average life of a security in the portfolio may not exceed 4 years.

The effective duration of the portfolio may not exceed 2 years.

For securities which have put dates, reset dates, or are traded based on their average maturity, the put date, reset date, or average maturity will be used, instead of the final maturity date, for maturity guideline purposes.

The overall volatility of the entire portfolio will be 2% or less at all times.

V. CONCENTRATION LIMITS/RESTRICTIONS

There is no minimum or maximum limit to the percentage of the portfolio invested in securities issued by the U.S. Treasury or by its agencies and instrumentalities.

No one issuer or group of issuers from the same holding company, is to exceed 10% of the portfolio at time of purchase, with the exception of US Government securities.

Excess concentrations is any one sector or any one type of security (i.e. corporates, mortgage-backed, asset backed, repos) should be avoided and no one sector or class should represent more than 50% of the portfolio with the exception of US Government securities.

VI. INVESTMENT PERFORMANCE

The company shall review the performance of it's investment managers on at least an annual basis. A quarterly meeting will be held in person or by telephone with the Treasurer to review performance figures and any updated liquidity needs and to discuss portfolio strategy.

VII. CREDIT QUALITY

Should any investment held in Vertex's portfolio be down-graded below the minimum prescribed rating, immediate notification must be made to Vertex.

VIII. MARKETABILITY

All securities are to be purchased through investment banking and brokerage firms of high quality and reputation, with a history of making markets for the securities in which we invest. All holdings will be of sufficient size and held in issues traded actively enough to facilitate minimum transaction costs and accurate market valuations.

IX. TRADING GUIDELINES

Normal investing practice is to actively manage the account and reinvest funds to take advantage of changing market conditions or reinvest on the day a security matures to maximize interest. A daily transaction log is to be maintained and available for review at any time. All trading firms must generate a hard copy document for each transaction which is mailed to Vertex on a timely basis, and then matched to the transaction log.

X. SAFEKEEPING

Assets are to be held in a segregated bank custody account at State Street Bank with separate fiduciary account documents executed by and between State Street and Vertex. Assets shall not be held by any investment manager or securities dealer.

Xl. FIDUCIARY DISCRETION

The manager has full discretion to invest capital subject to strict adherence to these guidelines. These guidelines are to be reviewed periodically by the Treasurer and revisions made consistent with objectives set forth herein.

APPROVED BY: DATE: 11/17/97
Thomas G. Auchincloss, Treasurer

VERTEX PHARMACEUTICALS INC.
INVESTMENT POLICY GUIDELINES FOR:
CAPITAL ADVISORS

I. PURPOSE

To establish policy and guidelines for investment of corporate surplus cash. "Surplus cash" is cash in corporate accounts not immediately required for debt repayment, working capital, capital investment, or other outstanding near-term financial obligation-.

OBJECTIVES

Conservation of capital and maintenance of liquidity until funds can be used in business operations.

A Preserve capital.

B. Anticipate liquidity requirements.

C. Maximize returns versus the industry averages.

D. Diversify investments to minimize the risk and inappropriate concentrations of investments with any one entity.

E. Provide fiduciary control of cash and investments by individuals approved by the Board.

II. LIQUIDITY GUIDELINES

Excess cash is invested with liquidity in mind, and without any loss of principal. Daily liquidity is essential, restriction on liquidity are:

At least $1,000,000 must be available each business day until 2:30 p.m. Eastern time with no loss of principal.

At least $2,500,000 must be available within 30 days with no loss of principal.

The remainder of the funds are to be invested, consistent with anticipated cash needs, in securities with maturities no longer than 4 years. Repositioning of these securities before their maturity, generating small gains or losses, is permitted for managing liquidity requirements only. Any repositioning of securities causing a gain or loss must be pre-approved by the V.P. Finance and Treasurer for fiduciary control

purposes.

III. INVESTMENT RESTRICTIONS

Investments shall be made in the context of the following investment guide lines:

ELIGIBLE INVESTMENTS

1. Direct obligations of the U.S. Treasury including bills, notes, and bonds.

2. Obligations issued or guaranteed by agencies or instruments of the U.S. government.

3. Bank obligations, including certificates of deposit, bank notes and bankers acceptances. Investments in these securities is limited to banks whose long term debt is rated "A" or higher by Moody's or Standard & Poor's and short term obligations are rated "P-l " or higher by Moody's or "A-l " or higher by Standard & Poor's.

4. Corporate obligations, including intermediate term notes rated "A" or higher by Moody's or Standard & Poors and Commercial Paper rated "P-l" or higher by Moody's, or "A-l" or higher by Standard & Poor's.

5. At the discretion of the Senior Director of Finance, a maximum 20% of the portfolio, at the time of purchase, may be invested in corporate obligations with a short term rating of A2/P2 and long term ratings of Baa1/BBB+, with a maturity not to exceed six months.

6. Repurchase agreements collateralized at a minimum of 102% with U.S.. Treasury securities or other securities rated "AAA/Aaa" or equivalent.

7. Money market funds over $1 billion in assets consisting of acceptable securities are appropriate for investing, as long as the fund's manager has been in business over five years, has name recognition, ant that performance that is easily tracked.

8. U.S. and dollar denominated International corporate debt of all types is acceptable as long as the issuer meets credit rating and

marketability guidelines. Pre-approval of Senior Director of Finance shall be obtained.

9. Floating rate note securities are acceptable with maturities greater than 18 months only if they have a readjustment period of 6 months or less, are government issued (AAA Credit Rating) and are to reset off a common short term index (3 month treasury index). Terms of reset mechanisms including caps, floors and spreads shall be reviewed and approved by the

Senior Director of Finance.

IV. MATURITIES

The maximum maturity of individual securities in the portfolio may not exceed 4 years.

The average maturity of the portfolio may not exceed 2 years.

For securities which have put dates, reset dates, or are traded based on their average maturity, the put date, reset date, or average maturity will be used, instead of the final maturity date, for maturity guideline purposes. Notification to the Treasurer is needed prior to purchase of any maturity greater than 1 year.

V. CONCENTRATION LIMITS/RESTRICTIONS

There is no limit to be percentages of the portfolio which may be maintained in securities issued by the U.S. Treasury or by its agencies and instrumentalities.

No one issuer or group of issuers from the same holding company, is to exceed 15% of the portfolio at time of purchase, with the exception of Government securities.

U.S. bank and insurance company securities (CDs, commercial paper, BAs, etc..), must not in total exceed 60% of the portfolio. Holdings of one issuer cannot exceed 10% of the total portfolio at the time of purchase.

VI. INVESTMENT PERFORMANCE

The company shall review the performance of it's investment managers on at least an annual basis. A quarterly meeting will be held with the individual appointed by the board for fiduciary controls, to review performance figures and any updated liquidity needs and to discuss portfolio strategy.

VII. CREDIT QUALITY

Trends for a given company or industry must be reviewed periodically by the Treasurer and adjustments in percentage positions made accordingly. Should any investment held in Vertex's portfolio fall short of prescribed guidelines, immediate notification must be made to the individual appointed by the board to oversee fiduciary controls.

VIII. MARKETABILITY

All securities are to be purchased through investment banking and brokerage firms of high quality and reputation, with a history of making markets for the securities in which we invest. In the unlikely event that securities must be sold before their maturity, the securities must be easily remarketed. To accomplish this, the securities must be conventional "products" with strong name recognition.

IX. TRADING GUIDELINES

Normal investing practice is to reinvest the funds on the day a security matures, to maximize interest. A daily transaction log is to be maintained and available for review at any time. All trading firms must generate a hard copy document for each transaction which is mailed to us on a timely basis, and then matched to the transaction log. Quarterly summaries of our investment holdings and cash usage are to be made available for board review.

X. SAFEKEEPING

Assets are to be held in a segregated bank custody account with separate fiduciary account documents executed by the bank. Assets

shall not be held by any investment manager or securities dealer.

Xl. FIDUCIARY DISCRETION

The Treasurer and his/her authorized employees are responsible for securing and managing investments and cash for operations. These individuals have full discretion to invest any excess capital subject to strict adherence to these guidelines. These guidelines are to be reviewed periodically with the Chief Business Officer and revisions made consistent with objectives set forth herein.

EXHIBIT A TO CREDIT AGREEMENT

TERM NOTE

$20,000,000.00 Boston, Massachusetts December 21, 1999

1. PROMISE TO PAY.

FOR VALUE RECEIVED, VERTEX PHARMACEUTICALS INCORPORATED, a Massachusetts corporation, having an address at 130 Waverly Street, Cambridge, Massachusetts 02139, ("Borrower") promises to pay to the order of FLEET NATIONAL BANK, a national banking association, having an address at One Federal Street, Boston, Massachusetts 02110 ("Lender"), the principal sum of TWENTY MILLION DOLLARS ($20,000,000.00), or so much thereof as may be advanced as Term Loans from time to time under the Credit Agreement, defined below, with interest thereon, or on the amount thereof from time to time outstanding, to be computed, as hereinafter provided, on each advance from the date of its disbursement until such principal sum shall be fully paid. Interest and principal shall be payable as set forth in
Section 4 below. The total principal sum, or the amount thereof outstanding, together with any accrued but unpaid interest, shall be due and payable in full on December 30, 2005 ("Maturity Date"), or earlier, as provided under Section 7 hereof. All payments shall be in lawful money of the United States in immediately available funds.

2. CREDIT AGREEMENT.

This Note is issued pursuant to the terms, provisions and conditions of a certain Credit Agreement between Borrower and Lender dated as of the date hereof (the "Credit Agreement"), as amended from time to time, and evidences the Term Loans made pursuant thereto. Capitalized terms used herein which are specifically defined herein shall have the meanings assigned to such terms herein, and Capitalized Terms which are not otherwise specifically defined shall have the same meaning herein as in the Credit Agreement.

3. INTEREST RATES.

3.1 BORROWER'S OPTIONS. Principal amounts outstanding hereunder shall bear interest at the following rates, at Borrower's selection, subject to the conditions and limitations provided for in this Note: (i) Variable Rate or (ii) Libo Rate.

3.1.1. SELECTION TO BE MADE. Borrower shall select, and thereafter may change the selection of, the applicable interest rate, from the alternatives otherwise provided for in this Note, by giving Lender a Notice of Rate Selection: (i) prior to the end of each Interest Period applicable to a Libor Advance, or (iii) on any Business Day on which Borrower desires to convert an outstanding Variable Rate Advance to a Libor Advance.

3.1.2. NOTICE OF RATE SELECTION. A "Notice of Rate Selection" shall be a written notice, given by cable, tested telex, telecopier (with authorized signature), or by telephone if immediately confirmed by such a written notice, from an Authorized Representative of Borrower which: (i) is irrevocable with respect to the interest rate, amount, and Interest Period selected; (ii) is received by Lender not later than 10:00 o'clock A.M. Eastern Time: (a) if a Libo Rate is selected, at least three (3) Business Days prior to the first day of the Interest Period to which such selection is to apply, (b) if a Variable Rate is selected, on the first day to which it applies; and (iii) as to each selected interest rate option, sets forth the aggregate principal amount(s) to which such interest rate option(s) shall apply and the Interest Period(s) applicable to each Libor Advance.

3.1.3. IF NO NOTICE. If Borrower submits a borrowing request without a Notice of Rate Selection, the Borrower authorizes the Lender in its discretion to (a) refuse to make the requested Term Loans, or (b) make such Term Loans as Variable Rate Advances. At the end of each applicable Interest Period, the applicable Libor Advance shall be converted to a Variable Rate Advance unless Borrower selects another option in accordance with the provisions of this Note.

3.2. TELEPHONIC NOTICE. Without in any way limiting Borrower's obligation to confirm in writing any telephonic notice, Lender may act without liability upon the basis of telephonic notice believed by Lender in good faith to be from Borrower prior to receipt of written confirmation. In each case Borrower hereby waives the right to dispute Lender's record of the terms of such telephonic Notice of Rate Selection in the absence of manifest error.

3.3 LIMITS ON OPTIONS. Each Libor Advance shall be in a minimum amount of $1,000,000 or an integral multiple of $100,000 in excess thereof. At no time shall there be outstanding a total of more than six (6) Libor Advances.

4. PAYMENT OF INTEREST AND PRINCIPAL.

4.1 PAYMENT AND CALCULATION OF INTEREST. All interest shall be payable in arrears (i) on the last Business Day of each month (with respect to Variable Rate Advances) or (ii) on the last day of each Interest Period and, if such Interest Period is longer than three months, at three-month intervals following the first day of such Interest Period (with respect to Libor Advances) until the principal together with all interest and other charges payable with respect to the Loan Advances shall be fully paid. All computations of interest under this Note shall be made on the basis of a three hundred sixty (360) day year and the actual number of days elapsed. Each change in the Prime Rate shall simultaneously change the Variable Rate payable under this Note, without notice or demand. Interest at the Libo Rate shall be computed from and including the first day of the applicable Interest Period to, but excluding, the last day thereof.

4.2 PRINCIPAL. Term Loans shall be paid in twenty (20) quarterly installments, as follows: (x) the first nineteen (19) of which shall be payable on the last Business Day of each calendar quarter commencing on March 31, 2001 and in an amount equal to the quotient of (i) the aggregate principal amount of such Term Loans at the close of business on December 31,

2000 divided by (ii) the Amortization Number (as defined below); and (y) the twentieth (20th) installment shall be payable on December 30, 2005 and shall be in the then outstanding amount of such Term Loans. The "Amortization Number" shall be equal to: (a) forty (40), with respect to the first installment that is payable after a Qualifying Participation Event and with respect to all subsequent quarterly installments; and (b) twenty-eight (28), at all other times.

4.3 BUSINESS DAYS; LATE FEE. If the entire amount of any required principal and/or interest is not paid in full within ten (10) days after the same is due, Borrower shall pay the Lender a late fee equal to five percent (5%) of the required payment.

4.4 PREPAYMENT. The Loan Advances or any portion thereof may be prepaid in full or in part at any time without premium or penalty with respect to Variable Rate Advances and, with respect to Libor Advances subject to a make-whole provision, as set forth in Section 4.7, and upon payment of the yield maintenance fee (as defined herein). Any partial prepayment of principal shall first be applied to any installment of principal then due and then be applied to the principal due in the reverse order of maturity, and no such partial prepayment shall relieve Borrower of the obligation to pay each subsequent installment of principal when due.

4.5 MATURITY. At maturity all accrued interest, principal and other charges due with respect to the Loan Advances shall be due and payable in full and the principal balance and such other charges, but not unpaid interest, shall continue to bear interest at the Default Rate until so paid.

4.6 DEFAULT RATE. Upon and during the continuance of an Event of Default or after judgment has been rendered on this Note, the unpaid principal of all Loan Advances shall, at the option of the Lender, bear interest at a rate which is four (4) percentage points per annum greater than that which would otherwise be applicable (the "Default Rate").

4.7 MAKE WHOLE PROVISION. Borrower may prepay a Libor Advance only upon at least three (3) Business Days prior written notice to Lender (which notice shall be irrevocable), and any such prepayment shall occur only on the last day of the Interest Period for such Libor Advance. Borrower shall pay Lender, upon request of Lender, such amount or amounts as shall be sufficient (in the reasonable opinion of Lender) to compensate it for any loss, cost, or expense incurred as a result of: (i) any payment of a Libor Advance on a date other than the last day of the Interest Period for such Libor Advance; (ii) any failure by Borrower to borrow a Libor Advance on the date specified by Borrower's written notice; (iii) any failure by Borrower to pay a Libor Advance on the date for payment specified in Borrower's written notice. Upon the occurrence of any of the events set forth in items (i), (ii), or (iii) of the foregoing sentence, and without limiting the foregoing, Borrower shall pay to Lender a "yield maintenance fee" in an amount computed as follows: The current rate for United States Treasury securities (bills on a discounted basis shall be converted to a bond equivalent) (the "United States Treasury Security Rate") with a maturity date closest to the maturity date of the term chosen pursuant to the Libor Election (as defined below) as to which the prepayment is made, shall be subtracted from the Libo Rate in effect at the time of prepayment. If the result is zero or a negative number, there shall be no yield maintenance fee. If the result is a positive number, then the resulting percentage shall be

multiplied by the amount of the principal balance being prepaid. The resulting amount shall be divided by 360 and multiplied by the number of days remaining in the term chosen pursuant to the Libor Election as to which the prepayment is made. Said amount shall be reduced to present value calculated by using the number of days remaining in the designated term and using the above-referenced United States Treasury Security Rate and the number of days remaining in the term chosen pursuant to the Libor Election as to which the prepayment is made. The resulting amount shall be the yield maintenance fee due to Lender upon prepayment of any Libor Advance. Each reference in this paragraph to "Libor Election" shall mean the election by the Borrower to apply the Libo Rate to the Loan, pursuant to a Notice of Rate Selection. If by reason of an Event of Default, Lender elects to declare the Obligations to be immediately due and payable, then any yield maintenance fee with respect to the Loan shall become due and payable in the same manner as though Borrower had exercised such right of prepayment.

5. CERTAIN DEFINITIONS AND PROVISIONS RELATING TO INTEREST RATE.

5.1 ADJUSTED LIBO RATE. The term "Adjusted Libo Rate" means for each Interest Period the rate per annum obtained by dividing (i) the Applicable Libo Rate for such Interest Period, by (ii) a percentage equal to one hundred percent (100%) minus the maximum reserve percentage applicable during such Interest Period under regulations issued from time to time by the Board of Governors of the Federal Reserve System for determining the maximum reserve requirements (including, without limitation, any basic, supplemental, marginal and emergency reserve requirements) for Lender (or of any subsequent holder of this Note which is subject to such reserve requirements) in respect of liabilities or assets consisting of or including Eurocurrency liabilities (as such term is defined in Regulation D of the Board of Governors of the Federal Reserve System) having a term equal to the Interest Period.

5.2 APPLICABLE LIBO RATE. "Applicable Libo Rate" shall mean, as applicable to any Libor Advance, the rate per annum (rounded upward, if necessary, to the nearest 1/32 of one percent) as determined on the basis of the offered rates for deposits in U.S. dollars, for a period of time comparable to such Libor Advance which appears on the Telerate page 3750 as of 11:00 a.m. London time on the day that is two London Banking days preceding the first day of such Libor Advance; provided, however, if the rate described above does not appear on the Telerate system on any applicable interest determination date, the Applicable Libo Rate shall be the rate (rounded upwards as described above, if necessary) for deposits in dollars for a period of time substantially equal to the interest period on the Reuters Page "LIBO" (or such other page as may replace the LIBO Page on that service for the purpose of displaying such rates), as of 11:00 a.m. (London Time), on the day that is two (2) London Banking Days prior to the beginning of such interest period.

If both the Telerate and Reuters system are unavailable, then the rate for that date will be determined on the basis of the offered rates for deposits in U.S. dollars for a period of time comparable to such Libor Advance which are offered by four major banks in the London interbank market at approximately 11:00 a.m. London time, on the day that is two
(2) London Banking Days preceding the first day of such Libor Advance as selected by the Lender. The principal London office of

each of the four major London banks will be requested to provide a quotation of its U.S. dollar deposit offered rate. If at least two such quotations are provided, the rate for that date will be the arithmetic mean of the quotations. If fewer than two quotations are provided as requested, the rate for that date will be determined on the basis of the rates quoted for loans in U.S. dollars to leading European banks for a period of time comparable to such Libor Advance offered by major banks in New York City at approximately 11:00 a.m. New York City time, on the date that is two London Banking Days preceding the first day of such Libor Advance. In the event that Lender is unable to obtain any such quotation as provided above, it will be deemed that the Applicable Libo Rate pursuant to a Libor Advance cannot be determined. In the event that the Board of Governors of the Federal Reserve System shall impose a Reserve Percentage with respect to Lender then for any period during which such Reserve Percentage shall apply, the Applicable Libo Rate shall be equal to the amount determined above divided by an amount equal to 1 minus the Reserve Percentage. "Reserve Percentage" means the maximum aggregate reserve requirement (including all basic, supplemental, marginal and other reserves) which is imposed on member banks of the Federal Reserve System against "Euro-currency Liabilities" as defined in Regulation D.

5.3 APPLICABLE MARGIN. The "Applicable Margin" shall be determined based upon the financial position and results of the Borrower based upon the financial statements and Compliance Certificates furnished by the Borrower pursuant to the Credit Agreement. The term "Applicable Margin" means, for any period set forth below the percentage set forth below opposite such period:

PERIOD	APPLICABLE MARGIN
Level I Period	[****]
Level II Period	[****]

5.4 BUSINESS DAY; SAME CALENDAR MONTH. If any day on which a payment is due is not a Business Day, then the payment shall be due on the next day following which is a Business Day, unless, with respect to Libor Advances, the effect would be to make the payment due in the next calendar month, in which event such payment shall be due on the next preceding day which is a Business Day. Further, if there is no corresponding day for a payment in the given calendar month (i.e., there is no "February 30th"), the payment shall be due on the last Business Day of the calendar month.

5.5 DOLLARS. The term "Dollars" or "$" means lawful money of the United States.

5.6 INTEREST PERIOD.

5.6.1. The term "Interest Period" means with respect to each Libor Advance: a period of an integral multiple of one month, but no Interest Period shall be greater than three (3) months, subject to availability, as selected, or deemed selected, by Borrower at least three (3)

Business Days prior to the end of the current Interest Period or the commencement of the next Interest Period. Each such Interest Period shall commence on the Business Day so selected, or deemed selected, by Borrower and shall end on the numerically corresponding day in the month in which the Interest Period ends; PROVIDED, HOWEVER: (i) if there is no such numerically corresponding day, such Interest Period shall end on the last Business Day of the applicable month, (ii) if the last day of such an Interest Period would otherwise occur on a day which is not a Business Day, such Interest Period shall be extended to the next succeeding Business Day; but (iii) if such extension would otherwise cause such last day to occur in a new calendar month, then such last day shall occur on the next preceding Business Day.

5.6.2. No Interest Period may be selected which would end beyond the Maturity Date.

5.7 LEVEL I PERIOD. The term "Level I Period" means any period (a) from and including the Business Day immediately following the Business Day on which a senior financial officer of the Borrower shall have delivered to the Lender a Compliance Certificate, together with the related financial statements referred to in Section 4.1 of the Credit Agreement, demonstrating in reasonable detail that the Debt Service Coverage Ratio, as of the last day of the fiscal quarter of the Borrower most recently ended, is greater than or equal to 1.5 to 1.0, to, but excluding, the next succeeding Reporting Date; and (b) during which no Event of Default shall have occurred and be continuing.

5.8 LEVEL II PERIOD. The term "Level II Period" means any period, other than a Level I Period.

5.9 LIBOR ADVANCE. The term "Libor Advance" means any principal outstanding under this Note which pursuant to this Note bears interest at the Libo Rate.

5.10 LIBO RATE. The term "Libo Rate" means the per annum rate equal to the Adjusted Libo Rate plus the Applicable Margin.

5.11 LOAN ADVANCE. The term "Loan Advance" means any portion of principal outstanding under this Note.

5.12 LONDON BANKING DAY. The term "London Banking Day" means a day on which commercial banks settle payments in London.

5.13 MATURITY. The term "Maturity" means the Termination Date.

5.14 PRIME RATE. The term "Prime Rate" means the variable per annum rate of interest so designated from time to time by Lender as its prime rate. The Prime Rate is a reference rate and does not necessarily represent the lowest or best rate being charged to any customer. Changes in the rate of interest resulting from changes in the Prime Rate shall take place immediately without notice or demand of any kind.

5.15 REPORTING DATE. The term "Reporting Date" means the first to occur of (i) the Business Day following the Business Day that the Lender receives a Compliance Certificate providing the information required to determine whether a period is a Level I Period or a Level II Period and (ii) the first Business Day after (a) with respect to the first three quarterly fiscal periods of the Borrower's fiscal year, the date on which the quarterly financial statement and Compliance Certificate is required to be delivered to the Lender pursuant to
Section 4.1(c) of the Credit Agreement; and (b) with respect to the fourth quarterly fiscal period of the Borrower's fiscal year, 45 days after the end of such fiscal period.

5.16 TREASURY RATE. The term "Treasury Rate" means, as of the date of any calculation or determination, the latest published rate for United States Treasury Notes or Bills (but the rate on Bills issued on a discounted basis shall be converted to a bond equivalent) as published weekly in the Federal Reserve Statistical Release H.15(519) of Selected Interest Rates in an amount which approximates (as reasonably determined by Lender) the amount (i) approximately comparable to the portion of the Loan Advance to which the Treasury Rate applies for the Interest Period, or (ii) in the case of a prepayment, the amount prepaid and with a maturity closest to the original maturity of the installment which is prepaid in whole or in part.

5.17 VARIABLE RATE. The term "Variable Rate" means a per annum rate equal at all times to the Prime Rate, with changes therein to be effective simultaneously with any change in the Prime Rate, without notice or demand.

5.18 VARIABLE RATE ADVANCE. The term "Variable Rate Advance" means any principal amount outstanding under this Note which pursuant to this Note bears interest at the Variable Rate.

6. ADDITIONAL PROVISIONS RELATED TO INTEREST RATE SELECTION.

6.1 INCREASED COSTS. If, due to any one or more of: (i) the introduction of any applicable law or regulation or any change (other than any change by way of imposition or increase of reserve requirements already referred to in the definition of Libo Rate) in the interpretation or application by any authority charged with the interpretation or application thereof of any law or regulation; or (ii) the compliance with any guideline or request from any governmental central bank or other governmental authority (whether or not having the force of law), there shall be an increase in the cost to Lender of agreeing to make or making, funding or maintaining Libor Advances, including without limitation changes which affect or would affect the amount of capital or reserves required or expected to be maintained by Lender, with respect to all or any portion of the Loan Advances, or any corporation controlling Lender, on account thereof, then Borrower from time to time shall, upon written demand by Lender made within ninety (90) days of such increase in cost, pay Lender additional amounts sufficient to indemnify Lender against the increased cost. A certificate as to the amount of the increased cost and the reason therefor submitted to Borrower by Lender, in the absence of manifest error, shall be conclusive and binding for all purposes.

6.2 ILLEGALITY. Notwithstanding any other provision of this Note, if the introduction of

or change in or in the interpretation of any law, treaty, statute, regulation or interpretation thereof shall make it unlawful, or any central bank or government authority shall assert by directive, guideline or otherwise, that it is unlawful, for Lender to make or maintain Libor Advances or to continue to fund or maintain Libor Advances then, on written notice thereof and demand by Lender to Borrower, (a) the obligation of Lender to make Libor Advances and to convert or continue any Loan Advances as Libor Advances shall terminate and (b) Borrower shall convert all principal outstanding under this Note into Variable Rate Advances.

6.3 ADDITIONAL LIBOR CONDITIONS. The selection by Borrower of a Libo Rate and the maintenance of Loan Advances at such rate shall be subject to the following additional terms and conditions:

6.3.1. AVAILABILITY. If, before or after Borrower has selected to take or maintain a Libor Advance, Lender notifies Borrower that:

6.3.1.1. dollar deposits in the amount and for the maturity requested are not available to Lender in the London interbank market at the rate specified in the definition of Libo Rate set forth above, or

6.3.1.2. reasonable means do not exist for Lender to determine the Libo Rate for the amounts and maturity requested,

then the principal which would have been a Libor Advance shall be a Variable Rate Advance.

6.3.2. PAYMENTS NET OF TAXES. All payments and prepayments of principal and interest under this Note shall be made net of

any taxes and costs resulting from having principal outstanding at or computed with reference to a Libo Rate. Without limiting the generality of the preceding obligation, illustrations of such taxes and costs are taxes, or the withholding of amounts for taxes, of any nature whatsoever including income, excise, interest equalization taxes (other than United States or state income taxes) as well as all levies, imposts, duties or fees whether now in existence or as the result of a change in or promulgation of any treaty, statute, regulation, or interpretation thereof or any directive guideline or otherwise by a central bank or fiscal authority (whether or not having the force of law) or a change in the basis of, or the time of payment of, such taxes and other amounts resulting therefrom.

6.4. VARIABLE RATE ADVANCES. Each Variable Rate Advance shall continue as a Variable Rate Advance until the Maturity Date, unless sooner converted or prepaid, in whole or in part, to a Libor Rate Advance, subject to the limitations and conditions set forth in this Note.

7. ACCELERATION; EVENT OF DEFAULT.

Upon the occurrence of any Event of Default, Lender may, at Lender's option,

immediately exercise one or more of the following rights: (a) declare all obligations of Lender to Borrower, including, without limitation, the Commitments to be terminated, whereupon such obligations shall immediately terminate; and (b) declare all obligations of Borrower to Lender, including, without limitation, the Loans and all other amounts owing under the Credit Agreement and this Note to be immediately due and payable, whereupon they shall immediately become due and payable without presentment, demand, protest or notice of any kind, all of which are hereby expressly waived; PROVIDED, however, that upon the occurrence of any such Event of Default specified in Sections
7.1(h) or 7.1(i) of the Credit Agreement, the Commitments shall immediately terminate and all obligations of Borrower to Lender, including, without limitation, Loans and all other amounts owing under the Credit Agreement and this Note shall immediately become due and payable without presentment, further demand, protest or notice of any kind, all of which are hereby expressly waived.

8. CERTAIN WAIVERS, CONSENTS AND AGREEMENTS.

Each and every party liable hereon or for the indebtedness evidenced hereby whether as maker, endorser, guarantor, surety or otherwise hereby: (a) waives presentment, demand, protest, suretyship defenses and defenses in the nature thereof; (b) waives any defenses based upon and specifically assents to any and all extensions and postponements of the time for payment, changes in terms and conditions and all other indulgences and forbearances which may be granted by the holder to any party now or hereafter liable hereunder or for the indebtedness evidenced hereby; (c) agrees to any substitution, exchange, release, surrender or other delivery of any security or collateral now or hereafter held hereunder or in connection with the Credit Agreement, or any of the other Loan Documents, and to the addition or release of any other party or person primarily or secondarily liable; (d) agrees that if any security or collateral given to secure this Note or the indebtedness evidenced hereby or to secure any of the obligations set forth or referred to in the Credit Agreement, or any of the other Loan Documents, shall be found to be unenforceable in full or to any extent, or if Lender or any other party shall fail to duly perfect or protect such collateral, the same shall not relieve or release any party liable hereon or thereon nor vitiate any other security or collateral given for any obligations evidenced hereby or thereby; (e) subject to the terms of the Credit Agreement, agrees to pay all costs and expenses incurred by Lender or any other holder of this Note in connection with the indebtedness evidenced hereby, including, without limitation, all reasonable attorneys' fees and costs, for the implementation of the Term Loans evidenced hereby, the collection of the indebtedness evidenced hereby and the enforcement of rights and remedies hereunder or under the other Loan Documents, whether or not suit is instituted; and (f) consents to all of the terms and conditions contained in this Note, the Credit Agreement, and all other instruments now or hereafter executed evidencing or governing all or any portion of the security or collateral for this Note and for such Credit Agreement, or any one or more of the other Loan Documents.

9. DELAY NOT A BAR.

No delay or omission on the part of the holder in exercising any right hereunder or any right under any instrument or agreement now or hereafter executed in connection herewith, or any

agreement or instrument which is given or may be given to secure the indebtedness evidenced hereby or by the Credit Agreement, or any other agreement now or hereafter executed in connection herewith or therewith shall operate as a waiver of any such right or of any other right of such holder, nor shall any delay, omission or waiver on any one occasion be deemed to be a bar to or waiver of the same or of any other right on any future occasion.

10. PARTIAL INVALIDITY.

The invalidity or unenforceability of any provision hereof, of the Credit Agreement, of the other Loan Documents, or of any other instrument, agreement or document now or hereafter executed in connection with the Credit Agreement made pursuant hereto and thereto shall not impair or vitiate any other provision of any of such instruments, agreements and documents, all of which provisions shall be enforceable to the fullest extent now or hereafter permitted by law.

11. COMPLIANCE WITH USURY LAWS.

All agreements between Borrower and Lender are hereby expressly limited so that in no contingency or event whatsoever, whether by reason of acceleration of maturity of the indebtedness evidenced hereby or otherwise, shall the amount paid or agreed to be paid to Lender for the use or the forbearance of the indebtedness evidenced hereby exceed the maximum permissible under applicable law. As used herein, the term "applicable law" shall mean the law in effect as of the date hereof, PROVIDED, HOWEVER, that in the event there is a change in the law which results in a higher permissible rate of interest, then this Note shall be governed by such new law as of its effective date. In this regard, it is expressly agreed that it is the intent of Borrower and Lender in the execution, delivery and acceptance of this Note to contract in strict compliance with the laws of the Commonwealth of Massachusetts from time to time in effect. If, under or from any circumstances whatsoever, fulfillment of any provision hereof or of any of the Loan Documents at the time performance of such provision shall be due, shall involve transcending the limit of validity prescribed by applicable law, then the obligation to be fulfilled shall automatically be reduced to the limit of such validity, and if under or from any circumstances whatsoever Lender should ever receive as interest an amount which would exceed the highest lawful rate, such amount which would be excessive interest shall be applied to the reduction of the principal balance evidenced hereby and not to the payment of interest. This provision shall control every other provision of all agreements between Borrower and Lender.

12. WAIVER OF JURY TRIAL.

BORROWER AND LENDER MUTUALLY HEREBY KNOWINGLY, VOLUNTARILY AND INTENTIONALLY WAIVE THE RIGHT TO A TRIAL BY JURY IN RESPECT OF ANY LITIGATION BASED HEREON, ARISING OUT OF, UNDER OR IN CONNECTION WITH THIS NOTE OR ANY OTHER LOAN DOCUMENTS CONTEMPLATED TO BE EXECUTED IN CONNECTION HEREWITH, OR ANY COURSE OF CONDUCT, COURSE OF DEALINGS, STATEMENTS (WHETHER VERBAL OR WRITTEN) OR ACTIONS OF ANY PARTY. THIS WAIVER CONSTITUTES A MATERIAL INDUCEMENT FOR LENDER TO ACCEPT THIS NOTE AND MAKE THE LOANS.

13. NO ORAL CHANGE.

This Note and the other Loan Documents may only be amended, terminated, extended or otherwise modified by a writing signed by the party against which enforcement is sought. In no event shall any oral agreements, promises, actions, inactions, knowledge, course of conduct, course of dealing, or the like be effective to amend, terminate, extend or otherwise modify this Note or any of the other Loan Documents.

14. RIGHTS OF THE HOLDER.

This Note and the rights and remedies provided for herein may be enforced by Lender or any subsequent holder hereof. Wherever the context permits each reference to the term "holder" herein shall mean and refer to Lender or the then subsequent holder of this Note.

15. SETOFF.

Borrower hereby grants to Lender a lien, security interest and right of set off as security for all liabilities and obligations to Lender, whether now existing or hereafter arising, upon and against all deposits, credits, collateral and property, now or hereafter in the possession, custody, safekeeping or control of Lender or any entity under the control of Fleet Financial Group, Inc., or in transit to any of them. At any time, without demand or notice, Lender may set off the same or any part thereof and apply the same to any liability or obligation of Borrower even though unmatured and regardless of the adequacy of any other collateral securing the Loans. ANY AND ALL RIGHTS TO REQUIRE LENDER TO EXERCISE ITS RIGHTS OR REMEDIES WITH RESPECT TO ANY OTHER COLLATERAL WHICH SECURES THE LOANS, PRIOR TO EXERCISING ITS RIGHT OF SETOFF WITH RESPECT TO SUCH DEPOSITS, CREDIT OR OTHER PROPERTY OF THE BORROWER ARE HEREBY KNOWINGLY, VOLUNTARILY AND IRREVOCABLY WAIVED.

IN WITNESS WHEREOF, Borrower has caused this Note to be duly executed as of the date set forth above as a sealed instrument.

Witness:

VERTEX PHARMACEUTICALS INCORPORATED

By:

Name: Thomas G. Auchincloss, Jr.
Title: Vice President of Finance

EXHIBIT B TO CREDIT AGREEMENT

COMPLIANCE CERTIFICATE

To be delivered by the Bank

EXHIBIT C TO CREDIT AGREEMENT

PLEDGE AGREEMENT

PLEDGE AGREEMENT (this "AGREEMENT"), dated as of December 21, 1999, by VERTEX PHARMACEUTICALS INCORPORATED ("BORROWER"), a Massachusetts corporation, to FLEET NATIONAL BANK, a national banking association ("LENDER").

W I T N E S S E T H:

WHEREAS, the Borrower and the Lender are parties to a Credit Agreement of even date (as amended, supplemented or otherwise modified from time to time, the "CREDIT AGREEMENT"; capitalized terms used but not otherwise defined shall have the meanings ascribed to such terms in the Credit Agreement), pursuant to which the Lender has agreed to make up to $20,000,000 in Term Loans to the Borrower on the terms and subject to the conditions set forth therein;

WHEREAS, to induce to the Lender to enter into the Credit Agreement and make the Term Loans thereunder, the Borrower has agreed to enter into this Pledge Agreement and pledge all of the capital stock of Vertex Securities Corp. (the "Subsidiary") a Massachusetts corporation, to the Lender;

NOW, THEREFORE, in consideration of the foregoing and for other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, the Borrower and the the Lender hereby agree as follows:

1. PLEDGE. The Borrower hereby grants, assigns and pledges to the Lender, a valid lien on and security interest in, all of the Borrower's right, title and interest in and to the following, whether now owned or at any time hereafter acquired (collectively, the "Collateral"):

(a) All of the issued and outstanding capital stock of the Borrower in the Subsidiary as set forth on SCHEDULE 1 (the "Pledged Shares") and the certificates representing the Pledged Shares, and all dividends, distributions, cash, instruments, investment property and other property from time to time received, receivable or otherwise distributed in respect of or in exchange for any or all of the Pledged Shares, and all additional capital stock in Subsidiary from time to time acquired in any manner by the Borrower, and the certificates representing such additional capital stock, and all dividends, distributions, cash, instruments, investment property and other property from time to time received, receivable or otherwise distributed in respect of or in exchange for any or all of such capital stock; and

(b) all proceeds of any of the foregoing (including, without limitation, proceeds constituting any property of the types described above).

2. ALL OBLIGATIONS SECURED. This Agreement secures the prompt and complete payment and

performance when due (whether at the stated maturity, by acceleration or otherwise) of all of the Obligations.

3. REPRESENTATIONS AND WARRANTIES. Borrower represents and warrants as follows:

(a) Borrower has the requisite corporate power and authority to execute, deliver and perform this Agreement and all corporate action necessary for the execution, delivery and performance of this Agreement has been taken.

(b) The execution, delivery and performance of this Agreement by Borrower does not, and will not, contravene (i) the Articles of Organization and By-Laws of Borrower, (ii) any legal requirement or (iii) any franchise, license, permit, indenture, contract, lease, agreement, instrument or other commitment to which it is a party or by which it or any of its properties are bound, and will not, except as contemplated herein, result in the imposition of any liens or security interests upon any of its properties.

(c) This Agreement is the legal, valid and binding obligation of Borrower, enforceable in accordance with its terms.

(d) Borrower is the legal and beneficial owner of record of the Pledged Shares set forth in SCHEDULE 1, free and clear of any lien other than liens created pursuant to this Agreement. On the date hereof, no effective financing statement or other instrument similar in effect covering all or any part of the Collateral will be on file in any recording office.

(e) The pledge of the Collateral and granting of the liens hereunder, together with the delivery of the stock certificates pledged hereunder and appropriate filings of Uniform Commercial Code financing statements, create a valid and perfected first priority lien on the Collateral, securing the payment and performance of the Obligations, and all filings and other actions necessary or desirable to perfect and protect such lien have been duly made or taken.

(f) No authorization, approval, or other action by, and no notice to or filing with, any Person or governmental authority is required for (i) the pledge by Borrower of the Collateral pursuant to this Agreement, the grant by Borrower of the liens granted hereby or the execution, delivery or performance of this Agreement by Borrower, (ii) the perfection of the liens granted pursuant to this Agreement, except for the delivery to the Lender of the stock certificates representing the Pledged Shares in Subsidiary and appropriate filings of Uniform Commercial Code financing statements, or (iii) the exercise by the Lender of the rights or remedies provided for in this Agreement.

(g) The Pledged Shares represented by the certificates identified in SCHEDULE 1 are, and all other Pledged Shares in which Borrower shall hereafter obtain an interest will be duly authorized, fully paid and nonassessable and none of such Pledged Shares is or will be subject to any contractual restriction upon the transfer of such Pledged Shares.

(h) The Pledged Shares represented by the certificates identified in SCHEDULE 1 constitute all of the issued and outstanding shares of capital stock or other equity securities of any class in the Subsidiary, and SCHEDULE 1 correctly identifies, as at the date hereof, the respective class of the shares comprising such Pledged Shares and the respective number of shares represented by each such certificate.

4. FURTHER ASSURANCES; COVENANTS; REPLACEMENT COLLATERAL.

(a) Borrower covenants and agrees that at any time and from time to time, at the expense of Borrower, Borrower will promptly execute and deliver all further instruments and

documents, and take all further action, that may be necessary or desirable, or that the Lender may request, to perfect and protect any security interest granted or purported to be granted hereby or to enable the Lender to exercise and enforce its rights and remedies hereunder with respect to any Collateral. Without limiting the generality of the foregoing, Borrower will execute and file such financing or continuation statements, or amendments thereto, and such other instruments or notices, as may be necessary or desirable, or as the Lender may request, to perfect and preserve the liens granted or purported to be granted hereby, and cause third parties to acknowledge and to register the pledge of securities hereunder on their books and to deliver statements of account upon the Lender's request therefor.

(b) Borrower covenants and agrees that, without the prior written consent of the Lender, Borrower will not (i) sell, assign (by operation of law or otherwise) or otherwise dispose of, or grant any option with respect to, any of the Collateral, (ii) create or suffer to exist any lien upon or with respect to any of the Collateral, except for the liens under this Agreement, (iii) vote to enable, or take any other action to permit, Subsidiary to issue any capital stock or other equity securities of any nature or to issue any other securities convertible into, exchangeable for or granting the right to purchase any capital stock or other equity securities of any nature of Subsidiary or to convey, exchange, lease, assign, transfer, sell or otherwise dispose of any material assets of the Subsidiary, (iv) enter

into any agreement or undertaking restricting the right or ability of the Lender to sell, assign or transfer any of the Collateral or (v) permit Subsidiary to issue any shares of capital stock or other equity securities of any nature or to issue any securities convertible into or granting the right to purchase or otherwise acquire any shares of capital stock or equity securities of Subsidiary or to convey, exchange, lease, assign, transfer, sell or otherwise dispose of any material assets of the Subsidiary.

(c) If Borrower acquires any additional capital stock in Subsidiary, Borrower shall hold the same in trust for the Lender and promptly deliver to the Lender the stock certificates evidencing such capital stock, together with undated stock powers related thereto duly executed in blank by Borrower.

5. RIGHTS OF THE BORROWER; VOTING; ETC.

(a) So long as no Event of Default shall have occurred and be continuing, Borrower shall be entitled to exercise any and all voting and other consensual rights pertaining to the Collateral or any part thereof for any purpose not inconsistent with the terms of this Agreement and the other Loan Documents and in a manner which does not impair any of the Collateral and to receive and retain any and all cash dividends and distributions paid in respect of the Pledged Shares.

(b) Upon the occurrence and during the continuance of an Event of Default:

(i) All rights of Borrower to receive the cash dividends and distributions that Borrower would otherwise be authorized to receive and retain pursuant to Section 5(a) hereof shall cease, and all such rights shall thereupon become vested in the Lender who shall thereupon have the sole right to receive and hold as Collateral such dividends, distributions and payments.

(ii) Any and all other dividends and distributions payable to Borrower in respect of the Collateral shall be received by Borrower in trust for the benefit of the Lender, shall be

segregated from other funds of Borrower and shall be forthwith paid over to the Lender as Collateral in the same form as so received (with any necessary endorsement).

6. PRINCIPAL PLACE OF BUSINESS; RECORDS. Borrower shall keep its principal place of business and the place where it keeps its records concerning the Collateral at the address of the Borrower specified in the Credit Agreement. The Borrower will hold and preserve such records and, upon reasonable notice from the Lender, will permit representatives of the Lender at any time during normal business hours to inspect and make abstracts from such records.

7. TRANSFER OR LIENS. Borrower agrees that it will not sell, transfer or convey any interest in, grant any option with respect to, or suffer or permit any lien to be created upon or with respect to, any of the Pledged Shares during the term of this Agreement, except to or in favor of the Lender.

8. LENDER APPOINTED ATTORNEY-IN-FACT; IRREVOCABLE AUTHORIZATION AND INSTRUCTION TO THE SUBSIDIARIES. Borrower hereby appoints the Lender as Borrower's attorney-in-fact, with full authority in the place and stead of the Borrower and in the name of the Borrower or otherwise, from time to time in the Lender's discretion, to, upon the occurrence and during the continuance of an Event of Default, take any action and to execute any instrument which the Lender may deem necessary or advisable to accomplish the purposes of this Agreement, including, without limitation, to exercise the voting and other consensual rights which Borrower would otherwise be entitled to exercise pursuant to Section 5(a) (and all right of Borrower to exercise such rights shall cease) and to receive, endorse and collect all instruments made payable to the Borrower representing any distribution in respect of the Collateral or any part thereof and to give full discharge for the same. Borrower hereby authorizes and instructs Subsidiary to comply with any instruction received by it from the Lender in writing that (i) states that an Event of Default has occurred and is continuing and (ii) is otherwise in accordance with the terms of this Agreement, without any other or further instructions from Borrower, and Borrower agrees that Subsidiary shall be fully protected in so complying. Borrower hereby ratifies all that such attorney shall lawfully do or cause to be done by virtue hereof. This power of attorney is coupled with an interest and is irrevocable.

9. REASONABLE CARE; RETURN OF COLLATERAL.

(a) Prior to the exercise of its remedies hereunder, the Lender shall be deemed to have exercised reasonable care in the custody and preservation of the Collateral in its possession if the Collateral is accorded treatment substantially equal to that which the Lender accords its own similar property, it being understood that the Lender shall not have the responsibility under this Agreement for taking any necessary steps to preserve rights against any parties with respect to any Collateral except as set forth in subsection (b) below.

(b) Upon the indefeasible payment in full in cash of all the Obligations and the termination of the Credit Agreement, Borrower shall be entitled to the return of all of the Collateral pledged by Borrower hereunder.

10. LENDER MAY PERFORM. If Borrower fails to perform any agreement contained herein, the Lender may itself perform, or cause performance of, such agreement, and the expenses of

the Lender incurred in connection therewith shall be payable by Borrower.

11. REMEDIES UPON DEFAULT. If any Event of Default shall have occurred and be continuing, the Lender may exercise in respect of the Collateral, in addition to other rights and remedies provided for herein or otherwise available to it, all the rights and remedies of a secured party under the Uniform Commercial Code (the "CODE") and the Lender may also, without notice except as specified below, transfer the Collateral into its name or that of its nominee, sell the Collateral or any part thereof in one or more parcels at public or private sale, at any exchange, broker's board or at any of the Lender's offices or elsewhere, for cash, on credit or for future delivery, and upon such other terms as the Lender may deem commercially reasonable. Borrower agrees that, to the extent notice of sale shall be required by law, at least ten days' notice to Borrower of the time and place of any public sale or the time after which any private sale is to be made shall constitute reasonable notification. The Lender shall not be obligated to make any sale of Collateral regardless of notice of sale having been given. The Lender may adjourn any public or private sale from time to time by announcement at the time and place fixed therefor, and such sale may, without further notice, be made at the time and place to which it was so adjourned.

12. INDEMNITY AND EXPENSES.

(a) Borrower agrees to and hereby indemnifies the Lender from and against any and all claims, damages, losses, liabilities and expenses arising out of, or in connection with, or resulting from, this Agreement (including, without limitation, enforcement of this Agreement) other than such as arise from the Lender's gross negligence or willful misconduct.

(b) Borrower will, upon demand, pay to the Lender the amount of any and all expenses, including the reasonable fees and expenses of its counsel and of any experts and agents, that the Lender may incur in connection with
(i) the administration of this Agreement, (ii) the custody or preservation of, or the sale of, collection from, or other realization upon, any of the Collateral, (iii) the exercise or enforcement of any of the rights of the Lender hereunder, (iv) the failure of Borrower to perform or observe any of the provisions hereof, or (v) any action taken by the Lender pursuant to this Agreement.

13. SECURITY INTEREST ABSOLUTE. All rights of the Lender and security interests hereunder, and all obligations of Borrower hereunder, shall be absolute and unconditional irrespective of:

(a) any lack of validity or enforceability of the Credit Agreement, the Note or any other Loan Document;

(b) any change in the time, manner or place of payment of, or in any other term of, all or any of the Obligations, or any other amendment or waiver of or any consent to departure from any of the Loan Documents;

(c) any taking and holding of collateral or any guaranty for all or any of the Obligations, or any amendment, alteration, exchange, substitution, transfer, enforcement, waiver, subordination, termination or release of any collateral or such guaranty, or any non-perfection of any collateral, or any consent to departure from any such guaranty;

(d) any manner of application of collateral, or proceeds thereof, to all or any of the Obligations, or the manner of sale of any collateral;

(e) any consent by Lender to the restructure of the Obligations, or any other restructure or

refinancing of the Obligations or any portion thereof;

(f) any modification, compromise, settlement or release by Lender, by operation of law or otherwise, collection or other liquidation of the Obligations or the liability of any guarantor, or of any collateral, in whole or in part, and any refusal of payment by the Lender, in whole or in part, from any obligor or guarantor in connection with any of the Obligations, whether or not with notice to, or further assent by, or any reservation of rights against, any Borrower; or

(g) any other circumstance (including, without limitation, any statute of limitations) which might otherwise constitute a defense available to, or a discharge of, any third party pledgor or guarantor.

14. AMENDMENTS; WAIVERS; PARTIAL EXERCISE. No amendment or waiver of any provision of this Agreement or consent to any departure by the Borrower here from shall be effective unless in writing and signed by Borrower and the Lender, and any such amendment, waiver or consent shall be effective only to the extent set forth therein. No failure to exercise or any delay in exercising on the part of the Lender any right, power or privilege under this Agreement shall operate as a waiver thereof. No single or partial exercise of any right, power or privilege under this Agreement shall preclude any other or further exercise thereof or the exercise of any other right, power or privilege.

15. ADDRESSES FOR NOTICES. All notices and correspondence hereunder shall be provided in the manner, to the Persons and to the addresses set forth in the Credit Agreement.

16. CONTINUING SECURITY INTEREST; ASSIGNMENTS OF SECURED DEBT. This Agreement shall create a continuing security interest in and lien on the Collateral and shall (i) remain in full force and effect until released in accordance with the terms hereof, (ii) be binding upon Borrower, its successors and assigns, and (iii) inure, together with the rights and remedies of the Lender hereunder, to the benefit of their respective successors and assigns. Without limiting the generality of the foregoing clause (iii), the Lender, in accordance with the terms of the Credit Agreement, may assign or otherwise transfer all or any portion of their rights and obligations under this Agreement to any other Person, and such other Person shall thereupon become vested with all the benefits in respect hereof granted herein.

17. GOVERNING LAW; DEFINED TERMS. This Agreement shall be governed by and construed in accordance with the laws of the Commonwealth of Massachusetts without giving effect to principles of conflicts of law. Unless otherwise defined herein or in the Credit Agreement, terms used in Articles 8 and 9 of the Code are used herein as therein defined. This Agreement shall be deemed for all purposes to be a Loan Document under the Credit Agreement.

18. MARSHALLING. Borrower hereby waives any right to require the Lender to marshal any security or Collateral or otherwise compel the Lender recourse against or satisfaction of the Obligations from one source before seeking recourse or satisfaction from another source.

19. EXECUTION IN COUNTERPARTS; TELECOPIED SIGNATURES. This Agreement may be executed in counterparts, each of which shall constitute an original, but all of which taken together shall constitute one and the same instrument. This Agreement, and any notices to be given pursuant to this Agreement, may be executed and delivered by telecopier or other facsimile transmission all with the same force and effect as if the same was a fully executed and delivered original counterpart.

20. SUBMISSION TO JURISDICTION. ALL DISPUTES AMONG THE BORROWER AND THE LENDER, WHETHER SOUNDING IN CONTRACT, TORT, EQUITY OR OTHERWISE, SHALL BE RESOLVED ONLY BY STATE AND FEDERAL COURTS LOCATED IN BOSTON, MASSACHUSETTS, AND THE COURTS TO WHICH AN APPEAL THEREFROM MAY BE TAKEN; PROVIDED, HOWEVER, THAT THE LENDER SHALL HAVE THE RIGHT, TO THE EXTENT PERMITTED BY APPLICABLE LAW, TO PROCEED AGAINST THE BORROWER OR ITS PROPERTY IN ANY LOCATION REASONABLY SELECTED BY THE LENDER IN GOOD FAITH TO ENABLE THE LENDER TO REALIZE ON SUCH PROPERTY, OR TO ENFORCE A JUDGMENT OR

OTHER COURT ORDER IN FAVOR OF THE LENDER. THE BORROWER AGREES THAT IT WILL NOT ASSERT ANY PERMISSIVE COUNTERCLAIMS, SETOFFS OR CROSS-CLAIMS IN ANY PROCEEDING BROUGHT BY THE LENDER. THE BORROWER WAIVES ANY OBJECTION THAT IT MAY HAVE TO THE LOCATION OF THE COURT IN WHICH THE LENDER HAS COMMENCED A PROCEEDING, INCLUDING, WITHOUT LIMITATION, ANY OBJECTION TO THE LAYING OF VENUE OR BASED ON FORUM NON CONVENIENS.

21. JURY TRIAL. THE BORROWER AND, BY ITS ACCEPTANCE HEREOF, THE LENDER EACH HEREBY WAIVE ANY RIGHT TO A TRIAL BY JURY.

IN WITNESS WHEREOF, the Borrower has caused this Agreement to be executed by its proper and duly authorized officer as of the day and year first above written.

VERTEX PHARMACEUTICALS INCORPORATED

By:

Name:

Title:

Accepted:

FLEET NATIONAL BANK

By:
Name:
Title:

Schedule 1

Pledge Agreement between
Vertex Pharmaceuticals Incorporated and Fleet National Bank

Pledged Shares

Issuer: Vertex Securities Corp.

Class of Shares: Common

Number of Pledged Shares: one hundred (100)

Date of Issuance: December 22, 1993

Date of Pledge: December 21, 1999

EXHIBIT 21

SUBSIDIARIES OF THE REGISTRANT

Vertex Securities Corp. (incorporated in Massachusetts)

Vertex Pharmaceuticals (Europe) Limited (incorporated in England)

Exhibit 23

CONSENT OF INDEPENDENT ACCOUNTANTS

We hereby consent to the incorporation by reference in the Registration Statements on Form S-8 (File Nos. 33-48030, 33-48348, 33-65742, 33-93224, 33-12325, 333-27011, 333-56179 and 333-79549) of Vertex Pharmaceuticals Incorporated of our report dated February 16, 2000, except as to the information in Note R for which the date is February 28, 2000, relating to the financial statements, which appears in this Form 10-K.

PricewaterhouseCoopers LLP

Boston, Massachusetts
March 3, 2000

ARTICLE 5
THIS SCHEDULE CONTAINS SUMMARY FINANCIAL INFORMATION EXTRACTED FROM THE COMPANY'S YEAR END REPORT ON FORM 10-K, FOR THE TWELVE MONTHS ENDED DECEMBER 31, 1999 AND IS QUALIFIED IN ITS ENTIRETY BY REFERENCE TO SUCH FINANCIAL STATEMENTS.
CIK: 0000875320
NAME: VERTEX PHARMACEUTICALS, INCORPORATED
MULTIPLIER: 1,000

PERIOD TYPE	YEAR
FISCAL YEAR END	DEC 31 1999
PERIOD START	JAN 01 1999
PERIOD END	DEC 31 1999
CASH	31,548
SECURITIES	156,254
RECEIVABLES	5,956
ALLOWANCES	0
INVENTORY	0
CURRENT ASSETS	195,197
PP&E	58,831
DEPRECIATION	34,351
TOTAL ASSETS	232,445
CURRENT LIABILITIES	18,518
BONDS	0
PREFERRED MANDATORY	0
PREFERRED	0
COMMON	257
OTHER SE	208,977
TOTAL LIABILITY AND EQUITY	232,445
SALES	8,053
TOTAL REVENUES	61,648
CGS	2,925
TOTAL COSTS	102,614
OTHER EXPENSES	0
LOSS PROVISION	0
INTEREST EXPENSE	654
INCOME PRETAX	(40,966)
INCOME TAX	0
INCOME CONTINUING	(40,966)
DISCONTINUED	0
EXTRAORDINARY	0
CHANGES	0
NET INCOME	(40,966)
EPS BASIC	(1.61)
EPS DILUTED	(1.61)

End of Filing