VERTEX PHARMACEUTICALS INC / MA
Form 424B5
June 08, 2005

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Filed Pursuant to Rule 424(b)(5)
Registration No. 333-123731

PROSPECTUS SUPPLEMENT
(To prospectus dated April 25, 2005)

11,750,000 Shares

VERTEX PHARMACEUTICALS INCORPORATED

Common Stock

We are offering 11,750,000 shares of our Common Stock.

Our common stock is listed on the Nasdaq National Market under the symbol "VRTX." The last reported sale price of our common stock on the Nasdaq National Market on June 7, 2005 was $13.19 per share.

Investing in our common stock involves risks. See "Risk Factors" on page S-8 of this prospectus supplement.

	Per Share	Total
Public offering price	$13.00	$152,750,000
Underwriting discount	$.715	$8,401,250
Proceeds, before expenses, to Vertex	$12.285	$144,348,750

The underwriters may also purchase up to an additional 1,762,500 shares from us at the public offering price, less the underwriting discount, within 30 days from the date of this prospectus supplement to cover any overallotments. If the overallotment option is exercised in full, we will receive additional proceeds, before expenses, of $21,652,313.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus supplement or the prospectus to which it relates is truthful or complete. Any representation to the contrary is a criminal offense.

The shares will be ready for delivery on or about June 13, 2005.

Merrill Lynch & Co.

JPMorgan **UBS Investment Bank**

The date of this prospectus supplement is June 7, 2005.

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PROSPECTUS SUPPLEMENT

PROSPECTUS

You should rely only on the information contained in this prospectus supplement or contained in or incorporated by reference in the accompanying prospectus to which we have referred you. We have not authorized anyone to provide you with information that is different. The information contained in this prospectus supplement and contained, or incorporated by reference, in the accompanying prospectus is accurate only as of the respective dates thereof, regardless of the time of delivery of this prospectus supplement and the accompanying prospectus or of any sale of common stock. It is important for you to read and consider all information contained in this prospectus supplement and the accompanying prospectus, including the documents incorporated by reference therein, in making your investment decision. You should also read and consider the information in the documents to which we have referred you under the caption "Where You Can Find More Information" in the prospectus.

We are offering to sell, and are seeking offers to buy, the common stock only in jurisdictions where offers and sales are permitted. The distribution of this prospectus supplement and the accompanying prospectus and the offering of the common stock in certain jurisdictions may be restricted by law. Persons outside the United States who come into possession of this prospectus supplement and the accompanying prospectus must inform themselves about and observe any restrictions relating to the offering of the common stock and the distribution of this prospectus supplement and the accompanying prospectus outside the United States. This prospectus supplement and the accompanying prospectus do not constitute, and may not be used in connection with, an offer to sell, or a solicitation of an offer to buy, any securities offered by this prospectus supplement and the accompanying prospectus by any person in any jurisdiction in which it is unlawful for such person to make such an offer or solicitation.

ABOUT THIS PROSPECTUS SUPPLEMENT

This document is in two parts. The first part is this prospectus supplement, which describes the specific terms of this common stock offering and also adds to and updates information contained in the accompanying prospectus and the documents incorporated by reference into the prospectus. The second part, the accompanying prospectus, gives more general information, some of which does not apply to this offering.

If the description of the offering varies between this prospectus supplement and the accompanying prospectus, you should rely on the information contained in this prospectus supplement; provided that if any statement in one of these documents is inconsistent with a statement in another document having a later date for example, a document incorporated by reference in the accompanying prospectus the statement in the document having the later date modifies or supersedes the earlier statement.

We further note that the representations, warranties and covenants made by us in any agreement that is filed as exhibit to any document that is incorporated by reference in the accompanying prospectus were made solely for the benefit of the parties to such agreement, including, in some cases, for the purpose of allocating risk among the parties to such agreements, and should not be deemed to be a representation, warranty or covenant to you. Moreover, such representations, warranties or covenants were accurate only as of the date when made. Accordingly, such representations, warranties and covenants should not be relied on as accurately representing the current state of our affairs.

Unless we have indicated otherwise, or the context otherwise requires, references in this prospectus supplement and the accompanying prospectus to "Vertex," "Company," "we," "us" and "our" or similar terms are to Vertex Pharmaceuticals Incorporated and its subsidiaries.

PROSPECTUS SUPPLEMENT SUMMARY

This summary highlights information contained elsewhere in this prospectus supplement and the accompanying prospectus or incorporated by reference in the accompanying prospectus. This summary does not contain all of the information that you should consider before deciding to invest in our common stock. You should read this entire prospectus supplement and the accompanying prospectus carefully, including the "Risk Factors" section contained in this prospectus supplement and our consolidated financial statements and the related notes and the other documents incorporated by reference in the accompanying prospectus.

Business Overview

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

Our goal is to mature into a fully integrated pharmaceutical company with industry-leading capabilities in research, development and commercialization of products. We focus our efforts both on programs that we expect to control throughout the development and commercialization phases, and programs that we expect will be conducted principally by collaborators. We expect to continue to invest in our research and development capabilities as we advance our product candidates to market.

Recent Developments

Vertex HCV Drug Candidates

We are developing two drug candidates targeting HCV infection through different mechanisms. Our most advanced compound is the IMPDH inhibitor merimepodib, which targets HCV indirectly and currently is in Phase IIb development. IMPDH inhibitors appear to work additively or synergistically with other treatments for HCV, including ribavirin. Vertex's second HCV drug candidate, VX-950, is one of the most advanced of a new class of antiviral treatments in development for HCV infection. We believe VX-950 has the potential to change the treatment paradigm for HCV infection.

VX-950 investigational oral viral protease inhibitor for Hepatitis C

Our investigational oral protease inhibitor, VX-950, targets HCV directly, by inhibiting hepatitis C NS3-4A protease, an enzyme necessary for HCV replication. On May 10, 2005, we announced interim results indicating that VX-950 was well-tolerated and demonstrated potent antiviral activity in a Phase Ib clinical trial. Anti-viral activity and preliminary safety data were further presented by one of the clinical investigators on May 17, 2005 at the Digestive Disease Week scientific conference ("DDW").

The data presented at DDW showed that significant reductions in HCV-RNA were observed in HCV-infected patients taking VX-950 over a period of 14 days across three dose groups 450 milligrams every 8 hours, 1,250 milligrams every 12 hours, or 750 milligrams every 8 hours. After three days of treatment, the median reduction in HCV-RNA was greater than 3 log10, a reduction of at least 1,000-fold, in all three dose groups. In the dose group receiving 750 milligrams of VX-950 every 8 hours, there was a further reduction in viral levels between days 3 and 14 of treatment, with a median HCV-RNA reduction of 4.4 log10, a 25,000-fold reduction, at day 14. At the end of 14 days of treatment, 4 of 8 patients in the 750 milligrams dose group tested HCV-RNA negative in the

quantitative Roche COBAS TaqMan assay (<30 IU/mL), and 2 of these 4 patients tested undetectable in the qualitative Roche COBAS TaqMan assay (limit of detection 10 IU/mL). Initial pharmacokinetic analyses indicate that trough blood plasma concentrations of VX-950 in the 750 milligrams dose group were approximately 42% higher than in the 450 milligrams dose group and approximately 46% higher than the 1250 milligrams dose group. Patients in all three dose groups were HCV genotype I and predominantly non-responders to interferon-based therapy.

Across the three dose groups, a total of five of the 28 patients given VX-950 in the Phase Ib study tested HCV-RNA negative in the quantitative Roche COBAS TaqMan assay (<30 IU/mL), reaching this level between day 11 and day 14. Following completion of the 14-day dosing period, a slow increase in HCV-RNA levels was observed in these five patients during a 28-day post-dosing period. Twenty-eight days after receiving their last dose of VX-950, two patients still had viral levels that were more than 1 log10 below their pre-treatment levels.

Preliminary data indicate that across the three dose groups, VX-950 was well-tolerated, with no serious adverse events or treatment discontinuations reported. In addition, no elevations of the liver enzymes ALT/AST or other adverse clinical chemistry findings were reported. Complete safety and pharmacokinetic analyses of the data from the Phase Ib study, along with viral sequencing and viral kinetic analyses, are ongoing.

Based on the results of the Phase Ib clinical study, we plan to explore the development of VX-950 both as a monotherapy and in combination with other therapies for HCV infection. We currently are planning to initiate a 14-day Phase Ib combination clinical study with a limited number of patients involving VX-950 and pegylated interferon (one of the two drugs currently used in the standard treatment for HCV infection) before the end of the year. We also plan to consult with the FDA and European regulatory authorities on additional specific development plans. Pending these discussions and those with clinical experts in the field, we currently are further planning to initiate a Phase II combination clinical study before the end of the year involving VX-950 and pegylated interferon in patients who have not previously been treated for HCV infection. In addition, we are currently planning to initiate a Phase II study of VX-950 administered as a monotherapy. Major objectives of the Phase II program will be to evaluate dose, dose regimen and treatment duration required to obtain sustained virologic responses in treated patients. We anticipate treatment durations of both one and three months in the initial Phase II VX-950 and pegylated interferon combination clinical study, and a three month treatment duration in the initial Phase II monotherapy clinical study.

We expect to file an investigational new drug ("IND") application in the second half of 2005 to support Phase II clinical development of VX-950 in the United States. In anticipation of that IND filing, we are continuing our ongoing formulation and toxicology activities. The VX-950 formulation used in the Phase Ib study allowed us to achieve good exposure following oral dosing, but we have been working to improve the formulation for purposes of pharmacokinetic performance and other characteristics. Our formulation development work to date has identified prototype formulations that achieve higher blood concentrations in animals and lower variability than the formulation used in the Phase Ib clinical study. We are in the process of further scale-up and expect to produce a solid dosage formulation in the second half of 2005 for use in the Phase II clinical program. In addition, prior to filing an IND, we expect to complete a number of non-clinical toxicology studies in support of the treatment durations in the Phase II clinical studies.

Hepatitis C Virus Infection

HCV infection causes chronic inflammation in the liver. In a majority of patients, HCV infection can persist for decades and eventually lead to cirrhosis, liver failure and liver cancer. HCV infection represents a significant medical problem worldwide. Sources at the Centers for Disease Control have estimated that approximately 2.7 million Americans are chronically infected with HCV, and the World

Health Organization estimates that there are as many as 185 million chronic carriers of the virus worldwide.

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

Rheumatoid Arthritis

VX-702- Investigational Oral p38 MAP Kinase Inhibitor for Rheumatoid Arthritis

On May 31, 2005, we began screening patients in our Phase II clinical study with VX-702. The study will help define the safety, tolerability and clinical activity of VX-702 in approximately 300 patients with moderate to severe rheumatoid arthritis treated for three months. The double-blind, randomized, placebo-controlled Phase II study will assess two doses of VX-702 compared to placebo. VX-702 will be dosed once-daily as monotherapy.

Commercial Products and Clinical Development Programs

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

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

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

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

Our Strategy

Our goal is to mature into a fully integrated pharmaceutical company with industry-leading capabilities in research, development and commercialization. As we continue building these capabilities, we have elected to diversify our research and development activities across a relatively broad array of investment opportunities in order to increase the likelihood that one or more of our product candidates will succeed.

The key elements of our strategy are:

Broadly advance our HCV portfolio. We are developing two drug candidates targeting HCV infection through different mechanisms. We plan to explore the development of VX-950 both as a

monotherapy and in combination with other therapies for HCV infection. We also are exploring the development of merimepodib as an additive anti-viral agent for use with both the current standard of care, and with other evolving therapies, to treat HCV infection. We believe that these drug candidates could form the basis of an exclusively oral therapy alternative for the treatment of HCV infection.

Maximize commercial opportunity for our products. We seek to develop and market breakthrough products and to advance the products ourselves in therapeutic areas where we believe commercialization can be effective with comparatively fewer resources, through the use of a specialist-focused sales force. We expect to retain control of the development of our HCV product candidates and certain of our other product candidates that are in areas where we currently believe we can compete effectively. We continually assess our portfolio of drug candidates in order to make judgments about the role of pharmaceutical company collaborators in the commercial path forward for each compound. We expect to focus our Vertex-controlled commercialization efforts in North America, and to concentrate on identifying collaborative relationships for development of our HCV infection and inflammation product candidates outside of North America.

Continue existing and new collaborations to research, develop and commercialize products. We will continue to pursue strategic transactions with collaborators to accelerate research, development and commercialization of our novel drug candidates where we believe collaborators have the development and commercial infrastructure to access therapeutic areas that would be more difficult for us to pursue. We are currently seeking alliances for VX-409 and VX-692 under collaborative arrangements that would reinforce this strategy.

Collaborations with pharmaceutical companies have played an important role in helping us advance our drug discovery as well as to grow and advance our product pipeline. Collaborations provide us with financial support and other valuable resources for our research programs, development resources for our clinical drug candidates and marketing and sales support for our products and product candidates. We currently are collaborating with Novartis Pharma AG, GlaxoSmithKline plc, Merck & Co., Inc., Mitsubishi Pharma Corp., Kissei Pharmaceutical Co., Ltd., Cystic Fibrosis Foundation Therapeutics Incorporated and other companies.

Continue to introduce multiple product candidates into development each year. We plan to continue to add promising potential products to our development pipeline through our continuing commitment to discovery research. We believe our drug design approach integrates biology, chemistry, biophysics, automation and information technologies to make the drug discovery process more efficient and productive. In addition to our efforts to research and develop kinase inhibitors, we currently are conducting research programs in other areas, including the area of ion channel modulation.

License and acquire technologies, resources and products. In addition to forging new collaborations, we also seek to opportunistically license and acquire technologies, resources and products that have the potential to strengthen our drug discovery platform, product pipeline and commercial capabilities.

Corporate Information

We were incorporated in Massachusetts in 1989. Our principal executive offices are located at 130 Waverly Street, Cambridge, Massachusetts 02139, and our telephone number is (617) 444-6100. Our internet address is *www.vrtx.com*. The information found on our website and on websites linked from it are not incorporated into or a part of this prospectus supplement or the prospectus.

The Offering

Unless otherwise indicated, all information in this prospectus supplement assumes that the underwriters do not exercise their overallotment option.

Common stock offered by Vertex	11,750,000 shares
Common stock to be outstanding after the offering	92,953,170 shares
Overallotment option	1,762,500 shares
Use of proceeds	For general corporate purposes, which may include working capital, capital expenditures, research and development expenditures, clinical trial expenditures, acquisitions of new technologies, and investments. See "Use of Proceeds" on page S-20.
Nasdaq National Market symbol	VRTX

The information above is based on 81,203,170 shares of common stock outstanding as of March 31, 2005. It does not include:

- 16,538,000 shares of common stock issuable upon the exercise of stock options outstanding as of March 31, 2005 at a weighted average exercise price of $21.93 per share;
- 128,075 shares of common stock issuable upon the exercise of stock options granted to employees after March 31, 2005 at a weighted exercise price of $12.90 per share;
- 22,070 restricted shares of common stock issued to employees after March 31, 2005, at a purchase price of $0.01 per share; and
- 16,454,000 shares of common stock reserved for issuance upon conversion of our outstanding convertible notes.

RISK FACTORS

Investing in our common stock involves a high degree of risk. You should carefully consider the following risk factors and all other information contained in this prospectus supplement and the accompanying prospectus and incorporated by reference into the accompanying prospectus before purchasing our common stock. The risks and uncertainties described below are not the only ones facing us. Additional risks and uncertainties that we are unaware of, or that we currently deem immaterial, also may become important factors that affect us. If any of such risks or the risks described below occur, our business, financial condition or results of operations could be materially and adversely affected. In that case, the trading price of our common stock could decline, and you may lose some or all of your investment.

Risks Related to Our Business

We expect to incur future losses and we may never become profitable.

We have incurred significant operating losses each year since our inception and expect to incur a significant operating loss in 2005. We believe that operating losses will continue beyond 2005, even if we receive significant future payments under our existing and future collaborative agreements, because we are planning to make significant investments in research and development, and because we will incur significant selling, general and administrative expenses in the course of researching and developing our potential products. We expect that losses will fluctuate from quarter to quarter and year to year, and that such fluctuations may be substantial. We cannot predict when we will become profitable, if at all.

We do not know whether Lexiva/Telzir will continue to be competitive in the market for HIV protease inhibitors.

We currently receive royalties from sales of Lexiva/Telzir and Agenerase, two HIV protease inhibitors discovered in our collaboration with GlaxoSmithKline. Agenerase sales have decreased, which we attribute to the availability and acceptance of Lexiva/Telzir, and we anticipate that this trend will continue until Agenerase is largely replaced by Lexiva/Telzir in the market. Lexiva/Telzir's share of the worldwide protease inhibitor market may decrease due to competitive forces and market dynamics. Other HIV protease inhibitors and a number of other products, including Gilead Science's Viread, Bristol-Myers Squibb's Sustiva and GlaxoSmithKline's Ziagen, are on the market for the treatment of HIV infection and AIDS. Other drugs are still in development by our competitors, including Bristol-Myers Squibb and Boehringer Ingelheim, which may have better efficacy, fewer side effects, easier administration and/or lower costs than Lexiva/Telzir. Moreover, the growth in the worldwide market for HIV protease inhibitors has, to a certain extent, occurred as a result of early and aggressive treatment of HIV infection with a protease inhibitor-based regimen. Changes in treatment strategy, in which treatment is initiated later in the course of infection, or in which treatment is more often initiated with a regimen that does not include a protease inhibitor, may result in reduced use of HIV protease inhibitors. In addition, the clinical benefit of strategies used by clinicians to boost drug levels of Lexiva/Telzir by co-administering other antiretroviral agents may not prove to be effective, or may not result in increased revenues. As a result, the total market for protease inhibitors may decline, decreasing the sales potential of Lexiva/Telzir. Further, although we co-promote Lexiva/Telzir in the U.S. and key markets in Europe, GlaxoSmithKline directs the majority of the marketing and sales efforts and the positioning of Lexiva/Telzir in the overall market, and we have little control over the direction or success of those efforts. GlaxoSmithKline has the right to terminate its agreement with us without cause upon twelve months' notice, and would have no obligation to pay further royalties upon any such termination. In such event, we may not be positioned to take over sales of Lexiva/Telzir or to license rights to Lexiva/Telzir to another company.

We may not successfully develop our drug pipeline.

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

The failure to demonstrate adequately the safety and efficacy of a therapeutic drug under development, for the disease indication being targeted, could delay or prevent regulatory approval of the product and could have a material adverse effect on us. In addition, the FDA or regulatory authorities in other jurisdictions may require additional clinical or nonclinical studies, which could result in increased costs and significant delays in obtaining required marketing approvals and commercialization of a product. While all or a portion of these additional costs may be covered by payments under our collaborative agreements, we bear all of the costs for our development candidates for which we have no financial support from a collaborator.

Our drug development efforts are data-driven and therefore potentially subject to abrupt changes in expected outcomes.

Small molecule drug discovery and development involve, initially, the identification of chemical compounds that may have promise as treatments for specific diseases. Once identified as drug candidates, compounds are subjected to years of testing in a laboratory setting, in animals and in people. Our ultimate objective is to determine whether or not the compounds have physical characteristics, both intrinsically and in animal and human systems and including a toxicological profile, that are compatible with clinical and commercial success in treatment of the disease being targeted. Throughout this process experiments are conducted and data are gathered that could reinforce a decision to move to the next step in the evaluation process for a particular drug candidate, could result in uncertainty over the proper course to pursue, or could result in the termination of further drug development efforts with respect to the compound being evaluated.

We constantly monitor the results of our discovery research and our nonclinical and clinical trials and regularly evaluate and re-evaluate our portfolio investments with the objective of balancing risk and potential return in view of new data and scientific, business and commercial insights. This process can result in relatively abrupt changes in focus and priority as new information comes to light and we gain additional insights into ongoing programs and potential new programs.

If delays in patient enrollment slow our development progress, we may lose competitive advantage or be unable to bring our drugs to market.

The rate of completion of clinical trials of our products is dependent upon, among other factors, the rate of patient accrual. Patient accrual is a function of many factors, including the size of the patient population, the proximity of patients to clinical sites, the eligibility criteria for the trial, the level of compliance by the clinical sites to clinical trial protocols, and the availability of clinical trial material. Delays in patient enrollment in clinical trials may result in increased costs, program delays, or both, which could have a material adverse effect on us. While all or a portion of these additional costs may

be covered by payments under our collaborative agreements, we bear all of the costs for our development candidates that are not licensed to a collaborator. If our clinical trials are not completed, we may not be able to submit a new drug application. If we are able to file a new drug application, such application may not be reviewed and approved in a timely manner, if at all.

If our processes and systems are not compliant with regulatory requirements, we could be subject to delays in filing new drug applications or restrictions on marketing of products after they have been approved.

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

If we do not obtain regulatory approval for our products on a timely basis, or at all, our revenues will be negatively impacted.

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

If we are unable to attract and retain collaborators for research support and the development and commercialization of our products, we may not be able to fund our research and development activities.

Our research, development and commercialization collaborators have agreed to fund portions of our research and development programs and/or to conduct the development and commercialization of specified products. In exchange, we have given them technology, product and marketing rights relating to those products. Some of our corporate collaborators, including GlaxoSmithKline, Merck and

Novartis, have rights to control the planning and execution of product development and clinical programs. Our collaborators may exercise their control rights in ways that may negatively affect the timing and success of those programs. Our collaborations are subject to termination rights by the collaborators. If any of GlaxoSmithKline, Merck or Novartis were to terminate its relationship with us, or fail to meet its contractual obligations, it could have a material adverse effect on our ability to undertake research, to fund related and other programs and to develop, manufacture and market any products that may have resulted from the collaboration. We expect to seek additional collaborative arrangements, which may not be available to us, to provide research support and to develop and commercialize our products in the future. For example, a significant portion of our overall research effort is conducted under our research collaborations with Novartis, Merck and CFFT, all of which are scheduled to conclude in the period between December 2005 and June 2006. If we are unable to enter into collaborative arrangements that would extend or replace these research collaborations, or to find other means of financing the effort currently devoted to these research programs, our ability to conduct our research, development and commercial activities could be adversely affected to a material degree. Even if we are able to establish acceptable collaborative arrangements in the future, they may not be successful.

If we lose our technological advantages, we may not be able to compete in the marketplace.

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

If our competitors bring superior products to market or bring their products to market before we do, we may be unable to find a market for our products.

Our products in development may not be able to compete effectively with products that are currently on the market or new products that may be developed by others. There are many other companies developing products for the same indications that we are pursuing in development. In order to compete successfully in these areas, we must demonstrate improved safety, efficacy and ease of manufacturing and gain market acceptance over competing products that have received regulatory approval and currently are marketed. Many of our competitors, including major pharmaceutical companies such as Abbott Laboratories, GlaxoSmithKline, Merck, and Novartis, possess substantially greater financial, technical and human resources than we possess. In addition, many of our competitors have significantly greater experience than we have in conducting preclinical and nonclinical testing and human clinical trials of new pharmaceutical products, scaling up manufacturing operations and obtaining regulatory approvals of products and manufacturing facilities. Accordingly, our competitors may succeed in obtaining regulatory approval for products more rapidly than we do. If we obtain

regulatory approval and launch commercial sales of our products, we also will compete with respect to manufacturing efficiency and sales and marketing capabilities, areas in which we currently have limited experience.

The loss of the services of key employees or the failure to hire qualified employees would negatively impact our business and future growth.

Because our products are highly technical in nature, we require the services of highly qualified and trained scientists who have the skills necessary to develop our products. Our future success will depend in large part on the continued services of our key scientific and management personnel. We have entered into employment agreements with some individuals and provide compensation-related benefits to all of our key employees that vest over time and therefore induce them to remain with the Company. However, the employment agreements can be terminated by the employee on relatively short notice. The value to employees of stock-related benefits that vest over time such as options and restricted stock will be significantly affected by movement in our stock price that we cannot control, and may at any point in time be insufficient to counteract more lucrative offers from other companies.

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

If we fail to manage our growth effectively, our business may suffer.

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

We depend on third-party manufacturers, and if we are unable to obtain contract manufacturing on reasonable terms, we may not be able to develop or commercialize our products.

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

have yet to be developed for our drug candidates other than Agenerase and Lexiva/Telzir. As a result, we or our collaborators may encounter difficulties developing commercial formulations and manufacturing processes for our drug candidates, which could result in delays in clinical trials, regulatory submissions, regulatory approvals and commercialization of our products.

If our patents do not protect our products, or our products infringe third-party patents, we could be subject to litigation and substantial liabilities.

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

If we are not able to sublet our Kendall Square Facility on acceptable terms, or at all, we could be obligated to pay as much as the full amount due under the lease, as and when due under the lease agreement.

We have decided not to occupy a facility located in Kendall Square, Cambridge, Massachusetts that we lease under a 15-year agreement expiring in 2018. We have estimated our net ongoing obligations under this lease to be $52,305,000 as of March 31, 2005. This estimate is based on underlying estimates of the timing for executing subleases of the remaining space, the sublease rental terms we might expect to receive, and other assumptions and estimates we consider appropriate given current market conditions and other factors. To date, we have subleased 45,000 square feet of the 290,000 square foot facility. If we are unable to find a tenant or tenants willing to sublease the balance of the facility on the terms we have incorporated into our estimate, including the rental rate, timing and term of any such sublease(s), or if the market for specialized laboratory space in Cambridge, Massachusetts or other real estate fundamentals should change before we are able to sublease the remaining unoccupied space, or if any of our other assumptions or estimates are inaccurate or circumstances bearing upon the potential restructuring should change before we are able to sublease the facility, our estimated obligations could increase to as much as the full amount due under the lease. As of December 31, 2004, our future obligations under the lease could be as much as $312 million.

We may need to raise additional capital that may not be available.

We expect to incur substantial research and development and related supporting expenses as we design and develop existing and future compounds and undertake clinical trials of potential drugs resulting from such compounds. We also expect to incur substantial administrative and commercialization expenditures in the future and substantial expenses related to the filing, prosecution, defense and enforcement of patent and other intellectual property claims. We anticipate that we will finance these substantial cash needs with:

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

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

Our sales and marketing experience is limited.

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

If we incur product liability expenses, our earnings could be negatively impacted.

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

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

Our outstanding indebtedness may make it more difficult to obtain additional financing or reduce our flexibility to act in our best interests.

As of March 31, 2005, we had approximately $82.6 million in aggregate principal amount of 5% Convertible Subordinated Notes due in September 2007 and approximately $232.4 million in aggregate principal amount of 5.75% Convertible Senior Subordinated Notes due in February 2011 outstanding. The high level of our indebtedness will affect us by:

- exposing us to fixed rates of interest, which may be in excess of prevailing market rates;
- making it more difficult to obtain additional financing for working capital, capital expenditures, debt service requirements or other purposes;
- constraining our ability to react quickly in an unfavorable economic climate or to changes in our business, or the pharmaceutical industry; and
- requiring the dedication of a substantial portion of our expected cash flow to service of our indebtedness, thereby reducing the amount of expected cash flow available for other purposes.

Our revenue depends, and will likely continue to depend, on a limited number of products.

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

Market acceptance of our products will be limited if users of our products are unable to obtain adequate reimbursement from third-party payors.

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

which may stop selling Lexiva/Telzir, thus terminating the royalties we receive on sales of these products.

The recent Medicare prescription drug coverage legislation and future legislative or regulatory reform of the healthcare system may affect our collaborator's ability to sell Agenerase or Lexiva profitably.

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

Government investigations or litigation against our collaborators could impact our business.

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

Risks Related to Our Common Stock and This Offering

Our stock price may fluctuate based on factors beyond our control.

Market prices for securities of companies such as Vertex are highly volatile. Within the twelve months ended March 31, 2005, our common stock traded between $8.00 and $12.05. The market for our stock, like that of other companies in the biotechnology field, has from time to time experienced significant price and volume fluctuations that are unrelated to our operating performance. The future market price of our securities could be significantly and adversely affected by factors such as:

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

developments in domestic and international governmental policy or regulation, for example relating to intellectual property rights.

Management will have broad discretion as to the use of the proceeds from this offering, and we may not use the proceeds effectively.

We have not designated the amount of net proceeds we will use for any particular purpose. Accordingly, our management will have broad discretion as to the application of the net proceeds and could use them for purposes other than those contemplated at the time of this offering. Our stockholders may not agree with the manner in which our management chooses to allocate and spend the net proceeds. Moreover, our management may use the net proceeds for corporate purposes that may not yield profitable results or increase our market value.

Sales of additional shares of our common stock could cause the price of our common stock to decline.

Sales of substantial amounts of our common stock in the open market, or the availability of such shares for sale, could adversely affect the price of our common stock. In addition, the issuance of common stock upon exercise of any outstanding option or the conversion of any of our outstanding convertible debt could be dilutive, and may cause the market price for a share of our common stock to decline. As of March 31, 2005, we had approximately 81,203,170 shares of common stock issued and outstanding, together with outstanding options to purchase approximately 16,538,000 shares of common stock with a weighted average exercise price of $21.93 per share, and notes convertible into approximately 16,454,000 shares of common stock with conversion prices of $14.94 and $92.26 per share and a weighted average conversion price of $19.15 per share. Outstanding options and convertible notes may be exercised or converted, as the case may be, if the market price of our common stock exceeds the applicable exercise or conversion price.

You will experience immediate dilution in the book value per share of the common stock you purchase.

Because the price per share of our common stock being offered is substantially higher than the net tangible book value per share of our common stock, you will suffer substantial dilution in the net tangible book value of the common stock you purchase in this offering. Based on the public offering price of $13.00 per share, if you purchase shares of common stock in this offering, you will suffer immediate and substantial dilution of $11.60 per share in the net tangible book value of the common stock. If the underwriters exercise their over-allotment option, you will experience additional dilution. See "Dilution" on page S-20 for a more detailed discussion of the dilution you will incur in this offering.

Anti-takeover provisions of Massachusetts law, provisions in our charter and bylaws and our stockholders' rights plan, or poison pill, could make a third-party acquisition of us difficult and may frustrate any attempt to remove or replace our current management.

Because we are a Massachusetts corporation, the anti-takeover provisions of Massachusetts law could make it more difficult for a third-party to acquire control of us, even if the change in control would be beneficial to stockholders. We are subject to the provisions of Chapter 110F of the Massachusetts General Laws, which prohibits us from engaging in certain business combinations, unless the business combination is approved or consummated in a prescribed manner. We are subject to the provisions of Chapter 110D of the Massachusetts General Laws which prohibits voting by any stockholder who acquires 20% or more of our voting stock without stockholder approval.

Our corporate charter and by-law provisions and stockholder rights plan may discourage certain types of transactions involving an actual or potential change of control of Vertex that might be beneficial to the Company or its security holders. Our charter provides for staggered terms for the

members of the Board of Directors. Our by-laws grant the directors a right to adjourn annual meetings of stockholders, and certain provisions of the by-laws may be amended only with an 80% stockholder vote. Pursuant to our stockholder rights plan, each share of common stock has an associated preferred share purchase right. The rights will not trade separately from the common stock until, and are exercisable only upon, the acquisition or the potential acquisition through tender offer by a person or group of 15% or more of the outstanding common stock. We may issue shares of any class or series of preferred stock in the future without stockholder approval and upon such terms as our Board of Directors may determine. The rights of the holders of common stock will be subject to, and may be adversely affected by, the rights of the holders of any class or series of preferred stock that may be issued in the future. As a result, stockholders or other parties may find it more difficult to remove or replace our current management.

These provisions may discourage certain types of transactions in which our stockholders might otherwise receive a premium for their shares over then current market price, and may limit the ability of our stockholders to approve transactions that they think may be in their best interests.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus supplement, the accompanying prospectus and the documents incorporated by reference in the accompanying prospectus contain forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended and Section 21E of the Securities Exchange Act of 1934, as amended. These statements relate to future events and our future financial performance. These statements include but are not limited to statements:

that VX-950 has the potential to change the treatment paradigm for HCV infection and become a powerful option in future HCV therapy;

that the Company expects to explore development of VX-950 as a monotherapy and as part of a combination therapy;

that we plan to file an IND and initiate Phase Ib and Phase II combination clinical studies involving VX-950 before the end of the year;

that we plan to initiate a Phase II study of VX-950 as a monotherapy;

relating to the proposed objectives and treatment durations of our clinical studies;

that we expect to produce a solid dosage formulation of VX-950 in the second half of 2005;

that we expect to complete a number of non-clinical toxicology studies in support of the treatment durations in the Phase II clinical studies prior to filing the IND;

that VX-950 and merimepodib could form the basis of an exclusively oral therapy alternative for the treatment of HCV;

that we expect to retain control of the development of our HCV product candidates and certain other product candidates that are in areas where we currently believe we can compete effectively;

that we expect to focus our Vertex-controlled commercialization efforts in North America and concentrate on identifying collaborative relationships to develop our HCV infection and inflammation product candidates outside of North America;

that we intend to continue to pursue strategic transactions with collaborators to accelerate research, development and commercialization of our novel drug candidates, including VX-409 and VX-692, where we believe collaborators have the development and commercialization infrastructure to access therapeutic areas that would be more difficult for us to pursue;

that we plan to continue to add promising potential products to our development pipeline through discovery research;

that we believe our drug design approach makes the drug discovery process more efficient and productive; and

that we intend to opportunistically license and acquire technologies, resources and products that have the potential to strengthen our drug discovery platform, product pipeline and commercial capabilities.

In some cases, you can identify forward-looking statements by terminology such as "may," "will," "should," "expects," "anticipates," "believes," "estimates," "predicts," "potential," or "continue" or the negative of such terms or other comparable terminology. These statements are only predictions and involve known and unknown risks, uncertainties and other factors, including the risks outlined above under "Risk Factors," that may cause our or our industry's actual results to differ materially from the results, levels of activity, performance or achievements expressed or implied by such forward-looking statements. Before deciding to purchase our securities you should carefully consider the risks described

in the "Risk Factors" section, in addition to the information set forth in this prospectus supplement and in the prospectus and the documents incorporated by reference therein. Although we believe that the expectations reflected in the forward-looking statements are reasonable, we cannot guarantee future results, levels of activity, performance or achievements.

USE OF PROCEEDS

We estimate that the net proceeds we will receive from this offering, at a public offering price of $13.00 per share, will be approximately $143.3 million, after deducting the underwriting discounts and our estimated offering expenses. If the underwriters exercise their overallotment option, we estimate that our net proceeds will be approximately $165.0 million. We intend to use the net proceeds from this offering for general corporate purposes, which may include working capital, capital expenditures, research and development expenditures, clinical trial expenditures, acquisitions of new technologies, and investments.

We have not determined the amounts we plan to spend on any of the areas listed above or the timing of these expenditures. As a result, our management will have broad discretion to allocate the net proceeds from this offering. We have no current plans, commitments or agreements with respect to any acquisitions and may not make any acquisitions. Pending application of the net proceeds as described above, we intend to invest the net proceeds of the offering in short-term, investment-grade, interest-bearing securities.

DILUTION

If you purchase our common stock in this offering, your interest will be diluted to the extent of the difference between the public offering price per share and the net tangible book value per share of our common stock after this offering. We calculate net tangible book value (deficit) per share by subtracting our total liabilities from our total tangible assets and dividing the difference by the number of outstanding shares of our common stock. Total tangible assets excludes deferred debt costs included in other assets on our condensed consolidated balance sheet at March 31, 2005.

Our net tangible book value (deficit) at March 31, 2005 was $(13.6) million, or $(0.17) per share, based on 81.2 million shares of our common stock outstanding. After giving effect to the sale of 11,750,000 shares of common stock by us at a public offering price of $13.00 per share, less the underwriting discounts and commissions and our estimated offering expenses, our net tangible book value at March 31, 2005 would be $129.8 million, or $1.40 per share. This represents an immediate increase in net tangible book value of $1.57 per share to existing stockholders and an immediate dilution of $11.60 per share to investors in this offering. The following table illustrates this per share dilution:

Public offering price per share		$ 13.00
Net tangible book value (deficit) per share as of March 31, 2005	$ (0.17)	
Increase per share attributable to new investors purchasing shares in this offering	$ 1.57	
Net tangible book value per share after this offering		$ 1.40
Dilution per share to new investors		$ 11.60

PRICE RANGE OF COMMON STOCK

Our common stock is listed on the Nasdaq National Market under the symbol "VRTX." The last reported sale price for our common stock on June 7, 2005 was $13.19 per share. The table below sets forth closing information on the range of high and low closing prices for our common stock during the periods indicated.

	Price Range of Common Stock	
	High	Low
Fiscal Year ended December 31, 2003:		
Quarter Ended:		
March 31, 2003	$ 16.36	$ 9.72
June 30, 2003	16.40	10.28
September 30, 2003	16.28	12.18
December 31, 2003	13.80	8.00
Fiscal Year ended December 31, 2004:		
Quarter Ended:		
March 31, 2004	$ 11.37	$ 8.90
June 30, 2004	10.84	8.17
September 30, 2004	10.88	8.17
December 31, 2004	11.91	10.01
Fiscal Year ended December 31, 2005:		
Quarter Ended:		
March 31, 2005	$ 11.99	$ 9.23
June 30, 2005 (through June 7, 2005)	14.55	8.83

DIVIDEND POLICY

We have never declared or paid any cash dividends on our common stock, and we currently expect that future earnings, if any, will be retained for use in our business. Accordingly, we do not expect to pay cash dividends on our common stock in the foreseeable future.

CAPITALIZATION

The following table sets forth our capitalization:

- as of March 31, 2005; and
- as adjusted to give effect to the issuance and sale of the common stock (assuming no exercise of the underwriters' overallotment option) in this offering, at a public offering price of $13.00 per share, and after deducting the underwriting discounts and commissions and estimated offering expenses payable by us.

The table excludes the following shares:

- 16,538,000 shares of common stock issuable upon the exercise of stock options outstanding as of March 31, 2005 at a weighted average exercise price of $21.93 per share;
- 128,075 shares of common stock issuable upon the exercise of stock options granted to employees after March 31, 2005 at a weighted exercise price of $12.90 per share;
- 22,070 restricted shares of common stock issued to employees after March 31, 2005, at a purchase price of $0.01 per share; and
- 16,454,000 shares of common stock reserved for issuance upon conversion of our outstanding convertible notes.

You should read this table with the financial statements and the notes thereto incorporated by reference into the accompanying prospectus.

	March 31, 2005 (Unaudited) (In thousands, except share data)	
	Actual	As Adjusted
Collaborator development loan	$ 19,997	$ 19,997
Convertible subordinated notes (due September 2007)	82,552	82,552
Convertible senior subordinated notes (due February 2011)	232,448	232,448
Stockholders' equity (deficit):		
Preferred stock, $0.01 par value; 1,000,000 shares authorized; none issued and outstanding at March 31, 2005		
Common stock, $0.01 par value; 200,000,000 shares authorized; 81,203,170 shares actual, 92,953,170 shares as adjusted, issued and outstanding at March 31, 2005	$ 812	$ 930
Additional paid-in capital	838,531	981,762