VERTEX PHARMACEUTICALS INC / MA
Form S-3ASR
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As filed with the Securities and Exchange Commission on February 11, 2008

Registration No. 333-

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM S-3

REGISTRATION STATEMENT
UNDER
THE SECURITIES ACT OF 1933

VERTEX PHARMACEUTICALS INCORPORATED

(Exact name of registrant as specified in its charter)

Massachusetts	**04-3039129**
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification Number)

130 Waverly Street
Cambridge, Massachusetts 02139
(617) 444-6100
(Address, including zip code, and telephone number, including area code, of registrant's principal executive offices)

Joshua S. Boger
President and Chief Executive Officer
Vertex Pharmaceuticals Incorporated
130 Waverly Street
Cambridge, Massachusetts 02139
(617) 444-6100
(Name, address, including zip code, and telephone number, including area code, of agent for service)

With copies to:

Michael L. Fantozzi, Esq. **Daniel T. Kajunski, Esq.** **Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C.** **One Financial Center** **Boston, Massachusetts 02111** **(617) 542-6000**	**Kenneth S. Boger, Esq.** **Senior Vice President and General Counsel** **Vertex Pharmaceuticals Incorporated** **130 Waverly Street** **Cambridge, Massachusetts 02139** **(617) 444-6100**	**Leslie N. Silverman, Esq.** **Mark A. Adams, Esq.** **Cleary Gottlieb Steen & Hamilton LLP,** **One Liberty Plaza** **New York, New York 10006** **(212) 225-2000**

Approximate Date of Commencement of Proposed Sale to the Public: From time to time after the effective date of this registration statement.

If the only securities being registered on this Form are being offered pursuant to dividend or interest reinvestment plans, please check the following box: o

If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, check the following box: ý

If this Form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, please check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. o

If this Form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. o

If this Form is a registration statement pursuant to General Instruction I.D. or a post-effective amendment thereto that shall become effective upon filing with the Commission pursuant to Rule 462(e) under the Securities Act, check the following box: ý

If this Form is a post-effective amendment to a registration statement filed pursuant to General Instruction I.D. filed to register additional securities or additional classes of securities pursuant to Rule 413(b) under the Securities Act, check the following box: o

CALCULATION OF REGISTRATION FEE

Title of each class of securities to be registered	Amount to be registered	Proposed maximum offering price per security	Proposed maximum aggregate offering price	Amount of registration fee
Common Stock, $0.01 par value per share (1)	(2)	(2)	(2)	(2)

(1) Each share of common stock includes a right to purchase our series A junior participating preferred stock, which is initially attached to and trades with the shares of the common stock being registered hereby. No separate consideration will be received for these rights.

(2) An unspecified and indeterminate aggregate initial offering price and number or amount of common stock is being registered as may from time to time be sold at indeterminate prices. In accordance with Rule 456(b) and Rule 457(r), the Registrant is deferring payment of the entire registration fee.

The information in this prospectus is not complete and may be changed. This prospectus is not an offer to sell these securities and we are not soliciting an offer to buy these securities in any jurisdiction where the offer or sale is not permitted.

Subject to Completion
Preliminary Prospectus dated February 11, 2008

PROSPECTUS

6,000,000 Shares

VERTEX PHARMACEUTICALS INCORPORATED

Common Stock

We are offering 6,000,000 shares of our common stock.

Our common stock is listed on the Nasdaq Global Select Market under the symbol "VRTX." The last reported sale price of our common stock on the Nasdaq Global Select Market on February 8, 2008 was $18.10 per share.

Concurrently with this offering, we are offering $250,000,000 aggregate principal amount of % Convertible Senior Subordinated Notes due 2013 (or a total of $287,500,000 aggregate principal amount of notes if the underwriters exercise their overallotment option in full) pursuant to a separate registration statement and prospectus. Although this common stock offering is not contingent upon the note offering and the note offering is not contingent upon this common stock offering, we currently anticipate raising approximately $358,600,000 in aggregate gross proceeds from the two offerings based on the last reported sale price of our common stock. However, amounts sold in each offering may increase or decrease based on market conditions relating to that particular security. See "Concurrent Note Offering."

Investing in our common stock involves risks. See "Risk Factors" beginning on page 10 of this prospectus.

	Per Share	Total
Public offering price	$	$
Underwriting discount	$	$
Proceeds, before expenses, to Vertex	$	$

We have granted the underwriters an option to purchase up to an additional 900,000 shares of common stock to cover overallotments, if any.

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

The shares will be ready for delivery on or about , 2008.

Merrill Lynch & Co.

The date of this prospectus is , 2008.

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You should rely only on the information contained or incorporated by reference in this prospectus. We have not authorized anyone to provide you with information that is different. The information contained or incorporated by reference in this prospectus is accurate only as of the date hereof, regardless of the time of delivery or of any sale of common stock. It is important for you to read and consider all information contained in this prospectus, including the documents incorporated by reference herein, in making your investment decision. You should also read and consider the information in the documents to which we have referred you under the captions "Where You Can Find More Information" and "Incorporation by Reference" in this 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 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 must inform themselves about and observe any restrictions relating to the offering of the common stock and the distribution of this prospectus outside the United States. This prospectus does 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 by any person in any jurisdiction in which it is unlawful for such person to make such an offer or solicitation.

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

"Vertex" is a registered trademark of Vertex. "Lexiva," "Telzir" and "Agenerase" are registered trademarks of GlaxoSmithKline plc. Other brands, names and trademarks contained in this prospectus are the property of their respective owners.

SUMMARY

This summary highlights information contained elsewhere in or incorporated by reference in this 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 carefully, including the "Risk Factors" section contained in this prospectus and our consolidated financial statements and the related notes and the other documents incorporated by reference herein.

Business Overview

We are in the business of discovering, developing and commercializing small molecule drugs for the treatment of serious diseases. Telaprevir, our lead drug candidate, is an oral hepatitis C protease inhibitor and one of the most advanced of a new class of antiviral treatments in clinical development that target hepatitis C virus, or HCV, infection, a life-threatening disease. We expect to begin a Phase 3 clinical trial of telaprevir in March 2008 to evaluate 24-week telaprevir-based treatment regimens in treatment-naïve patients with genotype 1 HCV.

We have built a drug discovery capability that integrates biology, pharmacology, biophysics, chemistry, automation and information technologies in a coordinated manner, with the goal of more efficiently identifying promising drug candidates to address significant unmet medical needs. Using this drug discovery capability we have identified among other drug candidates: VX-770 and VX-809, two novel drug candidates targeting cystic fibrosis, or CF; VX-500 and VX-813, two second-generation HCV protease inhibitors; and VX-509, a novel janus kinase 3, or JAK3, inhibitor that targets immune- mediated inflammatory diseases, or IMID. We have a number of other drug candidates in clinical trials or preclinical studies being developed either by us or in collaboration with other pharmaceutical companies, including drug candidates targeting cancer, IMID, pain and other neurological diseases and disorders. We currently are building our drug development, supply chain management and commercialization organizations to prepare for the potential commercial launch of telaprevir and to support the development of the other drug candidates in our pipeline.

We are conducting a comprehensive global clinical development program for telaprevir in collaboration with Janssen Pharmaceutica, N.V., or Janssen, a Johnson & Johnson company, and Mitsubishi Tanabe Pharma Corporation. This program is designed to support potential registration of telaprevir by us in North America and our collaborators in international markets for treatment-naïve and treatment-experienced patients across a range of HCV genotypes. In March 2008, we expect to begin a global, 3-arm Phase 3 clinical trial of telaprevir designed to enroll approximately 1,050 treatment-naïve patients with genotype 1 HCV, the most prevalent form of HCV in the United States, European Union and Japan. Patients in the two 24-week telaprevir-based treatment arms will be dosed with telaprevir for 8 or 12 weeks in combination with pegylated interferon, or peg-IFN, and ribavirin, or RBV, and will continue to receive peg-IFN and RBV after the dosing of telaprevir is complete. The third arm is a control arm with peg-IFN and RBV treatment, alone, for 48 weeks. We expect to complete enrollment in this trial in the fourth quarter of 2008. We expect to receive sustained viral response, or SVR, data from all treatment arms in the first half of 2010.

We have additional clinical trials ongoing or planned that have the potential to fulfill the anticipated registration requirement of at least one additional adequate and well-controlled clinical trial. We expect to begin enrollment in a clinical trial designed to evaluate a 48-week telaprevir-based treatment regimen in the third quarter of 2008. We expect SVR data from all treatment arms of this clinical trial will be available in mid-2010. PROVE 3 is a Phase 2b clinical trial involving approximately 440 patients with genotype 1 HCV who did not achieve SVR with previous peg-IFN-based treatments, or treatment-experienced patients. We completed enrollment in this clinical trial in June 2007. We expect the first interim clinical trial data to be available in the second quarter of 2008 and the SVR data from all PROVE 3 treatment arms by the end of 2008.

We continue to evaluate interim data from our two Phase 2b clinical trials, PROVE 1 and PROVE 2, which enrolled an aggregate of approximately 580 treatment-naïve patients with genotype 1

HCV. On an intent-to-treat basis, in the 24-week telaprevir-based treatment arms of PROVE 1 and PROVE 2, 61% and 68%, respectively, of patients achieved SVR at 24 weeks post-treatment. In the control arm of PROVE 1, on an intent-to-treat basis, 37% of patients achieved undetectable HCV RNA levels at 12 weeks post-treatment. Post-treatment viral response data for the control arm of PROVE 2 are not yet available. Patients in our clinical trials who achieve SVR have undetectable HCV RNA levels less than 10 IU/mL as measured by the Roche TaqMan® assay 24 weeks after all treatment has ceased. The interim analyses of safety data from PROVE 1 and PROVE 2 indicated that the most common adverse events, regardless of treatment assignment, were fatigue, rash, headache and nausea. Gastrointestinal disorders, skin adverse events, including rash and pruritus, and anemia were more frequent, and the rash more frequently severe, in the telaprevir arms than in the control arms over the dosing period.

In addition to telaprevir, we are evaluating a number of other drug candidates, including:

VX-770, a cystic fibrosis transmembrane regulator, or CFTR, potentiator compound, which we are investigating for the treatment of CF. In the second quarter of 2007, we initiated a Phase 2a clinical trial of VX-770 in patients with CF.

VX-809, a CFTR corrector compound, which we are investigating for the treatment of CF. We have initiated a Phase 1a clinical trial of VX-809.

VX-500, a second generation oral HCV protease inhibitor, which we are investigating for the treatment of chronic HCV infection. We have initiated a Phase 1a clinical trial of VX-500. We expect VX-813, an additional investigational HCV protease inhibitor, to enter clinical development in 2008.

VX-509, a novel JAK3 inhibitor that we are investigating for the treatment of immune-mediated inflammatory diseases. We expect to initiate a Phase 1 clinical trial of VX-509 in mid-2008.

In 2006, we entered into a collaboration agreement with Janssen under which we have retained exclusive commercial rights to telaprevir in North America and are leading the clinical development program. Janssen will be responsible for the commercialization of telaprevir, including the manufacture of its own commercial supply of telaprevir, for the Janssen territories, which include the territories outside of North America and the Far East. Janssen has agreed to be responsible for 50% of drug development costs under the development program for North America and the Janssen territories and to make contingent milestone payments for the successful development, approval and launch of telaprevir. Mitsubishi Tanable is conducting clinical trials of telaprevir in Japan. Our pipeline also includes Aurora kinase inhibitors, which are being developed by Merck & Co., Inc., and AVN-944 (VX-944), which is being developed by Avalon Pharmaceuticals, Inc. A Vertex-discovered compound for the treatment of HIV infection, fosamprenavir calcium, is being marketed by our collaborator GlaxoSmithKline plc as Lexiva in the United States and Telzir in Europe.

Pipeline

Drug or Drug Candidate	Clinical Indication(s)	Phase	Marketing Rights (Region)
Infectious Diseases			
Lexiva/Telzir	HIV infection	Marketed	GlaxoSmithKline (Worldwide)
Telaprevir (VX-950)	Chronic HCV infection	Phase 3	Vertex (North America); Mitsubishi Tanabe (Far East); and Janssen (Rest of World)
VX-500	Chronic HCV infection	Phase 1a	Vertex (Worldwide)
VX-813	Chronic HCV infection	Preclinical	Vertex (Worldwide)
VX-883	Bacterial infection	Preclinical	Vertex (Worldwide)
Cystic Fibrosis			
VX-770	Cystic fibrosis	Phase 2a	Vertex (Worldwide)
VX-809	Cystic fibrosis	Phase 1a	Vertex (Worldwide)
Cancer			
MK-0457(VX-680)	Cancer	Phase 2	Merck (Worldwide)
AVN-944(VX-944)	Cancer	Phase 2	Avalon (Worldwide)
VX-689	Cancer	Preclinical	Merck (Worldwide)

Drug or Drug Candidate	Clinical Indication(s)	Phase	Marketing Rights (Region)
Immune-Mediated Inflammatory Diseases			
VX-702	Rheumatoid arthritis and other inflammatory diseases	Phase 2	Vertex (Worldwide)
VX-509	IMID	Preclinical	Vertex (Worldwide)

Strategy

Our goal is to become a fully integrated pharmaceutical company with industry-leading capabilities in research, development and commercialization of pharmaceutical products. The key elements of our strategy are:

Develop and commercialize telaprevir. We believe that telaprevir has advanced further along the clinical development pathway than any other new and potentially competing oral HCV therapy. In order to maintain the time-to-market advantage we believe that we have in relation to drug candidates being developed by our competitors, we have a comprehensive clinical development program for telaprevir consisting of multiple concurrent clinical trials, and we are investing significant resources in the Phase 3 clinical development and preparation for launch of telaprevir.

Create a leadership position in the treatment of HCV infection. We believe that treatment of HCV infection will continue to require combination drug therapies in order to achieve high SVR rates. We intend to seek to create a leading multi-drug franchise in HCV. To complement telaprevir, VX-500 and/or VX-813, we are pursuing business development activities with complimentary therapies including polymerase inhibitors and novel interferons.

Expand the value of our portfolio of drug candidates. We have elected to diversify our research and development activities across a relatively broad array of investment opportunities. In 2008, we intend to progress VX-770 and VX-809, our drug candidates targeting CF, VX-509, our novel JAK3 inhibitor, which targets immune-mediated inflammatory diseases and other promising drug candidates in our pipeline.

Capitalize on the advances in our telaprevir clinical program to build our general drug development and commercialization capabilities. In 2008, we plan to continue our investment in key areas including clinical development, regulatory affairs, safety, quality control, pharmaceutical development, commercial operations and commercial supply chain management that will be necessary in order to complete development of telaprevir, to seek marketing approval for telaprevir and to commercialize telaprevir if we are successful in obtaining marketing approval. We expect that these capabilities also will support realization of additional drug candidates that may progress through our pipeline.

Invest in research and development and retain a greater proportion of rights to proprietary drug candidates. We intend to continue making significant investments in our research and development programs. We direct our research and development activities toward therapies designed to address serious diseases because these therapies have the potential to deliver the greatest value for patients, physicians and the healthcare system. In recent years, we have funded a greater proportion of our research programs using internal funds rather than collaborator funds. We adopted this strategy with the aim of retaining greater development control of, and commercial rights to, those proprietary drug candidates that may meet our strategic internal investment criteria as in effect from time to time.

Continue existing and establish new collaborations to develop and commercialize selected drug candidates. Collaborations provide us with financial support and other valuable resources for our development and research programs. We plan to continue to rely on collaborators to support, develop and commercialize a portion of our drug candidates either worldwide or in markets in which we are not concentrating our resources.

License and acquire technologies, resources, drugs or drug candidates. We also seek opportunistically to license and acquire technologies, resources and drugs or drug candidates that have the potential to strengthen our drug discovery platform, pipeline and commercial capabilities.

Telaprevir Clinical Development

Phase 3 Clinical Trial

In March 2008, we expect to begin a 1,050-patient Phase 3 clinical trial of telaprevir that will evaluate 24-week telaprevir-based treatment regimens compared to current standard treatment in treatment-naïve patients with genotype 1 HCV. The trial will be randomized equally across three treatment arms with approximately 350 patients per arm. The clinical trial will be conducted at approximately 100 centers primarily located in the United States and the European Union. The three planned treatment arms are:

- a 24-week telaprevir-based treatment arm, with telaprevir dosed for 12 weeks in combination with peg-IFN and RBV, followed by treatment with peg-IFN and RBV alone for 12 weeks;
- a 24-week telaprevir-based treatment arm, with telaprevir dosed for 8 weeks in combination with peg-IFN and RBV, followed by treatment with peg-IFN and RBV alone for 16 weeks; and
- a control arm with peg-IFN and RBV treatment, alone, for 48 weeks.

Patients in both telaprevir-based treatment arms who achieve extended rapid viral response, or eRVR, will receive 24 weeks of treatment. Our criteria for eRVR require that the patient have undetectable HCV RNA levels less than 10 IU/mL at 4 weeks and again at 12 weeks after the start of treatment. Patients in the telaprevir-based treatment arms who have undetectable HCV RNA levels at 24 weeks after the start of treatment but did not achieve eRVR will continue to receive treatment with peg-IFN and RBV for a total duration of 48 weeks. We expect to begin enrolling patients in the Phase 3 clinical trial in March 2008, and we expect to complete enrollment in this trial in the fourth quarter of 2008. We expect to have SVR data from all treatment arms of this clinical trial in the first half of 2010.

Well-Controlled Clinical Trials

We anticipate that we will need results from at least one additional adequate and well-controlled clinical trial of telaprevir in order to file a New Drug Application, or NDA, with the United States Food and Drug Administration, or FDA. We believe that the planned multi-arm clinical trial of a 48-week telaprevir-based treatment regimen and the PROVE 3 clinical trial each have the potential to fulfill this requirement. We expect that the 48-week telaprevir-based clinical trial will enroll approximately 400 treatment-naïve patients with genotype 1 HCV, beginning in the third quarter of 2008. We expect SVR data from all treatment arms of this clinical trial by mid-2010. The PROVE 3 clinical trial is a 440-patient trial that is being conducted in North America and the European Union in treatment-experienced patients. Patient enrollment in PROVE 3 was completed in June 2007, and SVR data from all PROVE 3 treatment arms are expected by the end of 2008.

PROVE 1 and PROVE 2

The PROVE 1 and PROVE 2 clinical trials are evaluating SVR rates in approximately 580 treatment-naïve patients infected with genotype 1 HCV, including patients who received telaprevir-based treatment, and also patients in standard treatment control arms. Patients achieve SVR if they have undetectable HCV RNA levels less than 10 IU/mL 24 weeks after all treatment has ceased.

On an intent-to-treat basis, in the 24-week telaprevir-based treatment arms of our Phase 2b clinical trials PROVE 1 and PROVE 2, 61% and 68%, respectively, of treatment-naïve patients achieved SVR. In the control arm of PROVE 1, on an intent-to-treat basis, 37% of patients achieved undetectable HCV RNA levels at 12 weeks post-treatment. Post-treatment viral response data for the control arm of PROVE 2 is not yet available. The interim analyses of telaprevir safety from PROVE 1 and PROVE 2, which are discussed below, showed that the most common adverse events, regardless of treatment assignment, were fatigue, rash, headache and nausea. Gastrointestinal disorders, skin adverse events, including rash and pruritus, and anemia were more frequent, and rash more frequently severe, in the telaprevir arms than in the control arms over the dosing period. Collection and analysis of data

from the PROVE 1 and PROVE 2 clinical trials is ongoing, and as such all of the interim data, including viral response, SVR, safety, RVR and viral breakthrough data, is subject to change as final data are confirmed.

Viral Response

Data in the tables below include patients who completed treatment, as well as those who discontinued treatment prior to completion of dosing but who had undetectable HCV RNA levels at the time of measurement. Patients in our Phase 2b clinical trials achieve SVR if they have undetectable HCV RNA levels 24 weeks after completion of treatment.

24-Week Telaprevir-Based Treatment Arms

SVR rates on an intent-to-treat basis for PROVE 1 and PROVE 2 for the 24-week telaprevir-based treatment arms are set forth in the table below.

	Number of Patients	SVR Rate (% with HCV RNA <10 IU/mL)
24-week telaprevir-based treatment arm (PROVE 1) telaprevir in combination with peg-IFN and RBV for 12 weeks, followed by peg-IFN and RBV alone for 12 weeks	79	61%
24-week telaprevir-based treatment arm (PROVE 2) telaprevir in combination with peg-IFN and RBV for 12 weeks, followed by peg-IFN and RBV alone for 12 weeks	81	68%

48-Week Treatment Arms

SVR data, which require undetectable HCV RNA levels measured 24 weeks after completion of treatment, are not yet available for the 48-week control arms in PROVE 1 and PROVE 2 or the 48-week telaprevir-based treatment arm in PROVE 1. The following table sets forth, on an intent-to-treat basis, the percentage of patients that had undetectable HCV RNA at end of treatment and 12 weeks post-treatment, where available.

	Number of Patients	End of Treatment (% with HCV RNA <10 IU/mL)	12 Weeks Post-Treatment (% with HCV RNA <10 IU/mL)
48-week control arm (PROVE 1) 48-weeks of therapy with peg-IFN and RBV	75	45%	37%
48-week control arm (PROVE 2) 48-weeks of therapy with peg-IFN and RBV	82	55%	Not Available
48-week telaprevir-based treatment arm (PROVE 1) telaprevir in combination with peg-IFN and RBV for 12 weeks, followed by peg-IFN and RBV alone for 36 weeks	79	65%	66%

Typically, following the completion of 48 weeks of treatment with peg-IFN and RBV alone, a portion of patients with undetectable HCV RNA at end of treatment relapse during the following 24 weeks.

Safety

The types of adverse events that have been commonly observed with peg-IFN and RBV treatment were seen across all treatment arms of PROVE 1 and PROVE 2. The most common adverse events, regardless of treatment assignment, were fatigue, rash, headache and nausea. Gastrointestinal

disorders, skin adverse events, including rash and pruritus, and anemia were more frequent, and rash more frequently severe, in the telaprevir arms than in the control arm over the dosing period.

In PROVE 1, the overall discontinuation rate through 12 weeks was 18% across all telaprevir treatment arms and 3% in the control arm. This includes discontinuations due to adverse events, withdrawal of consent and patients lost to follow-up. The incidence of treatment discontinuations through week 12 due to adverse events was 13% and 2% in the telaprevir and control arms, respectively. The most common reason for discontinuation was rash, with 7% of the patients discontinuing for this reason in the telaprevir arms during the first 12 weeks of treatment. After week 12, discontinuations due to adverse events were 8% in each of the telaprevir and control arms. Over the full course of the treatment period for all arms of the trial, the incidence of severe adverse events was 27% in the telaprevir arms and 24% in the control arm.

In PROVE 2, the overall discontinuation rate through 12 weeks of treatment was 14% across all telaprevir treatment arms and 6% in the control arm. This includes discontinuations due to adverse events, withdrawal of consent and patients lost to follow-up. The incidence of treatment discontinuations through week 12 due to adverse events was 10% and 3% in the telaprevir and control arms, respectively. As with PROVE 1, the most common reason for discontinuation was rash, with 7% of the patients in the telaprevir arms discontinuing due to rash, compared to less than 1% in the control arm during the first 12 weeks of treatment. Through to week 12, the incidence of severe adverse events was 17% in the telaprevir arms and 10% in the control arm.

The collection of adverse event and discontinuation data is ongoing in the PROVE clinical program.

Rapid Viral Response

A rapid viral response, or RVR, is one in which a patient has undetectable levels of HCV RNA less than 10 IU/mL at 4 weeks after commencement of treatment. Other third-party clinical trials suggest that patients undergoing standard-of-care treatment with peg-IFN and RBV therapy for 48 weeks who achieve RVR are substantially more likely to achieve SVR than patients on the same treatment who do not achieve RVR. In PROVE 1 and PROVE 2 combined, on an intent-to-treat basis, 77% of patients receiving telaprevir in combination with peg-IFN and RBV achieved RVR 79% in PROVE 1 and 75% in PROVE 2. In the control arms of PROVE 1 and PROVE 2, 12% of patients achieved RVR 11% in PROVE 1 and 13% in PROVE 2. The result of statistical testing is often defined in terms of a "p-value," with a level of 0.05 or less considered to be a statistically significant difference, which means the result is unlikely due to chance. The difference between the RVR rates in the telaprevir arms and the control arms was statistically significant, with a p-value of less than 0.001 in both the PROVE 1 and the PROVE 2 trials.

For those patients in the 24-week telaprevir treatment arms in PROVE 1 and PROVE 2 who achieved RVR, completed 24 weeks of telaprevir-based therapy and for whom data was available for analysis, 91% achieved SVR. We believe these data demonstrate a correlation between RVR and SVR in a 24-week telaprevir-based treatment regimen.

Viral Breakthrough

In PROVE 1 and PROVE 2, 90% of patients receiving telaprevir in combination with peg-IFN and RBV achieved undetectable HCV RNA on at least one occasion during treatment. The remaining 10% of patients either withdrew from treatment with detectable HCV RNA levels or did not achieve undetectable HCV RNA levels and had HCV RNA levels that increased at least 10-fold from their lowest levels while on treatment.

We consider a patient who first achieves undetectable viral levels less than 10 IU/mL and whose viral levels increase to more than 100 IU/mL during treatment to have experienced viral breakthrough. In addition, patients who do not achieve undetectable HCV RNA levels are considered to have experienced viral breakthrough if the patient's HCV RNA level increases by more than 10-fold

from its lowest level during therapy. Viral breakthrough is associated with selection of viral variants resistant to the drug regimen being evaluated. In PROVE 1 and PROVE 2 combined, 5% of patients in the telaprevir-based treatment arms experienced viral breakthrough, as described below, in the first 12 weeks of treatment 7% in PROVE 1 and 2% in PROVE 2. Most viral breakthroughs occurred in the first month of treatment, and generally were associated with low interferon blood levels. Less than 2% of patients in the telaprevir-based treatment arms who achieved undetectable HCV RNA levels experienced viral breakthrough while on treatment.

Viral Relapse

A patient who has undetectable HCV RNA at the end of treatment, but whose HCV RNA levels increase and are detectable during the post-treatment follow-up period, is said to have experienced viral relapse. Of the patients who experienced viral relapse in our trials to date, most relapsed during the first 12 weeks of follow-up. In PROVE 1 and PROVE 2, the relapse rate for patients who received 24 weeks of telaprevir-based treatment was 9% 2% in PROVE 1 and 14% in PROVE 2. However, the criteria for stopping all treatment after 24 weeks were different in PROVE 2 than in PROVE 1, and some patients who did not achieve an RVR at 4 weeks of treatment are included in the 24-week telaprevir-based treatment group of PROVE 2. If those patients who did not achieve RVR at 4 weeks of treatment are excluded from the calculation of the PROVE 2 viral relapse rate, the resulting relapse rate for patients who stopped all treatment after 24 weeks in that trial is 7%. The rate of viral relapse, measured at 12 weeks after completion of treatment, in the PROVE 1 48-week telaprevir-based treatment arm was 6%. The relapse rate in the PROVE 1 standard-of-care control arm, measured at 12 weeks after completion of treatment, was 23%.

Additional Clinical Trials for Telaprevir

In addition to the telaprevir clinical trials that we are conducting, Tibotec is conducting:

- a Phase 2 clinical trial in Europe to evaluate twice-daily, or BID, dosing of telaprevir in combination with peg-IFN and RBV;
- a Phase 2 viral kinetics clinical trial in Europe to evaluate telaprevir in patients infected with genotype 2 and genotype 3 HCV; and
- a Phase 2 viral kinetics clinical trial in Europe to evaluate telaprevir in patients infected with genotype 4 HCV.

Mitsubishi Tanabe is also conducting a Phase 1 clinical trial in Japan to assess the safety and pharmacokinetics of telaprevir administered as a monotherapy in patients with genotype 1 HCV.

Corporate Information

We were incorporated in Massachusetts in 1989. Our principal executive offices are located at 130 Waverly Street, Cambridge, Massachusetts 02139, and we have research sites located in San Diego, California, Iowa City, Iowa and Milton Park, U.K. Our telephone number is (617) 444-6100, and 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.

The Offering

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

Common stock offered by us	6,000,000 shares
Common stock to be outstanding after this offering	138,875,540 shares
Overallotment option	900,000 shares
Use of proceeds	We intend to use the net proceeds from this offering, together with the net proceeds from the concurrent note offering, for general corporate purposes, which we expect to include investment in the development and commercialization of telaprevir and the development of our other drug candidates, research expenditures, manufacture and supply of drug substances, repayment of a development loan from a collaborator, and which may include capital expenditures, investments and potentially acquisitions. See "Use of Proceeds" on page 29.
Risk factors	See "Risk Factors" beginning on page 10 and other information included in this prospectus for a discussion of factors you should carefully consider before deciding to invest in shares of our common stock.
Nasdaq Global Select Market symbol	VRTX

The information above is based on 132,875,540 shares of common stock outstanding as of December 31, 2007. It does not include:

- 15,357,591 shares of common stock issuable upon the exercise of stock options outstanding as of December 31, 2007 at a weighted average exercise price of $28.70 per share;
- 1,782,775 shares of common stock issuable upon the exercise of stock options granted to employees after December 31, 2007 and on or before February 8, 2008 at a weighted exercise price of $18.97 per share, including 537,000 shares of common stock issuable upon the exercise of stock options that are contingent upon receiving shareholder approval;
- 425,403 restricted shares of common stock issued to employees after December 31, 2007 and on or before February 8, 2008; and
- shares of common stock that will be issuable upon the conversion of the % Convertible Senior Subordinated Notes due 2013 that we are offering in the concurrent note offering.

Concurrent Note Offering

Concurrently with this offering, we are offering $250.0 million aggregate principal amount of % Convertible Senior Subordinated Notes due 2013 (or a total of $287.5 million aggregate principal amount of notes if the underwriters exercise their overallotment option in full) pursuant to a separate registration statement and prospectus. Although this common stock offering is not contingent upon the note offering and the note offering is not contingent upon this common stock offering, we currently anticipate raising approximately $358.6 million in aggregate gross proceeds from the two offerings (up to $412.4 million if the underwriters' exercise their overallotment option for each offering in full). However, amounts sold in each offering may increase or decrease based on market conditions relating to that particular security. For additional details about the note offering, see "Concurrent Note Offering."

Summary Consolidated Financial Data

The following unaudited summary consolidated financial data for each of the three years in the period ended December 31, 2007 are derived from our audited consolidated financial statements. These data should be read in conjunction with our audited consolidated financial statements and related notes and "Management's Discussion and Analysis of Financial Condition and Results of Operations" that are incorporated by reference into this prospectus from our Annual Report on Form 10-K for the year ended December 31, 2007, as filed with the SEC on February 11, 2008.

	Year Ended December 31,		
	2007	2006	2005
	(In thousands, except per share amounts)		
Consolidated Statements of Operations Data:			
Revenues:			
Royalties	$ 47,973	$ 41,208	$ 32,829
Collaborative and other research and development revenues	151,039	175,148	128,061
Total revenues	199,012	216,356	160,890
Costs and expenses:			
Royalty payments	13,904	12,170	10,098
Research and development expenses	513,054	371,713	248,540
Sales, general and administrative expenses	84,727	57,860	43,990
Restructuring expense	7,119	3,651	8,134
Total costs and expenses	618,804	445,394	310,762
Loss from operations	(419,792)	(229,038)	(149,872)
Other income/(expense)	28,513	21,101	(53,545)
Cumulative effect of a change in accounting principle SFAS 123(R)		1,046	
Net loss	$ (391,279)	$ (206,891)	$ (203,417)
Basic and diluted net loss per common share	$ (3.03)	$ (1.83)	$ (2.28)
Basic and diluted weighted average number of common shares outstanding	128,986	113,221	89,241

	December 31, 2007	
	Actual	As Adjusted(1)
	(In thousands)	
Consolidated Balance Sheet Data:		
Cash, cash equivalents and marketable securities	$ 467,796	$ 792,262
Other current assets	35,980	37,655
Restricted cash	30,258	30,258
Property and equipment, net	66,509	66,509
Other non-current assets	934	7,634
Total assets	$ 601,477	$ 934,318

	December 31, 2007	
Deferred revenues	$ 126,745	$ 126,745
Accrued restructuring	35,292	35,292
Other liabilities	148,148	148,148
Convertible Senior Subordinated Notes due 2013		250,000
Collaborator development loan (due 2008)	19,997	
Stockholders' equity	271,295	374,133
Total liabilities and stockholders' equity	$ 601,477	$ 934,318

(1) Reflects the sale of our common stock offered hereby at an assumed offering price of $18.10 per share, after deducting underwriting discount and estimated offering expenses, the concurrent sale of $250.0 million aggregate principal amount of notes, after deducting underwriting discount and estimated offering expenses and the use of a portion of the net proceeds to repay a $20.0 million collaborator development loan.

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 and incorporated by reference into this 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, including net losses of $391.3 million, $206.9 million and $203.4 million during 2007, 2006 and 2005, respectively, and expect to incur a significant operating loss in 2008. We believe that operating losses will continue beyond 2008, because we are planning to make significant investments in research and development and in building commercial supply of telaprevir to prepare for the potential launch of telaprevir, and because we will incur significant selling, general and administrative expenses in the course of researching, developing and commercializing our drug candidates, particularly telaprevir. We are investing significant research and development resources across a relatively broad array of therapeutic areas, due in part to the high risks associated with the biotechnology and pharmaceutical business and the relatively high potential for failure of any specific effort. This diversification strategy requires more significant financial resources than would be required if we pursued a more limited approach or focused exclusively on telaprevir. In particular, in 2008 we expect to invest significant resources in order to advance the development of VX-770, VX-809, VX-500, VX-813 and VX-509, and to start clinical trials of one or more additional compounds that are currently emerging from our research activities. Our net losses have had and will continue to have an adverse effect on, among other things, our stockholders' equity, total assets and working capital. 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 DEPEND HEAVILY ON THE SUCCESS OF OUR LEAD DRUG CANDIDATE, TELAPREVIR, WHICH IS STILL UNDER DEVELOPMENT. IF WE ARE UNABLE TO COMMERCIALIZE TELAPREVIR, OR EXPERIENCE DELAYS IN DOING SO, WE COULD BE REQUIRED TO SEEK ADDITIONAL FINANCING AND OUR BUSINESS WILL BE MATERIALLY HARMED.

We are investing a significant portion of our time, personnel and financial resources in the development of telaprevir, and we expect to commence a Phase 3 clinical trial of telaprevir in March 2008. The clinical development and commercial success of telaprevir will depend on several factors, including the following:

- successful completion and favorable outcomes of clinical trials;
- ongoing discussions with the FDA and comparable foreign authorities regarding the scope and design of our clinical trials, the quality of our manufacturing process for telaprevir and our clinical trial results;
- receipt and timing of marketing approvals for telaprevir from the FDA and similar foreign regulatory authorities;
- receipt and timing of marketing approvals from the FDA and similar foreign regulatory authorities for products being developed for the treatment of HCV by our competitors;

our ability to conduct clinical trials with respect to telaprevir in a timely manner to support a potential application for marketing approval;

establishing and maintaining commercial manufacturing arrangements for telaprevir with third-party manufacturers that are subject to extensive regulation by the FDA;

launching commercial sales of telaprevir by us and our collaborators;

the efficacy and other characteristics of telaprevir relative to existing and future treatments for HCV; and

our ability to increase awareness of the benefits of early treatment for HCV if telaprevir is approved;

acceptance of telaprevir, if approved, in the medical community and with third-party payors.

If the data from our ongoing clinical trials or non-clinical studies regarding the safety or efficacy of telaprevir are not favorable, we may be forced to delay or terminate the clinical development of telaprevir, which would materially harm our business. Further, even if we gain marketing approvals from the FDA and comparable foreign regulatory authorities in a timely manner, we cannot be sure that telaprevir will be commercially successful in the pharmaceutical market. Even if we obtain marketing approval and successfully commercialized telaprevir, we are investing significant amounts of cash in the development and commercialization process, and any significant delay in realizing a return on the investment would require us to engage in additional financing activities to recoup that investment, which may not be available on satisfactory terms, if at all. If the results of clinical trials of telaprevir, the anticipated or actual timing of marketing approvals for telaprevir, or the market acceptance of telaprevir, if approved, do not meet the expectations of investors or public market analysts, the market price of our common stock would likely decline.

WE 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, undertake clinical trials of drug candidates resulting from such compounds, and build our drug supply, regulatory, development and commercial capabilities. We also expect to incur substantial administrative and commercialization expenses in the future. In particular, we expect the continuing development and commercialization of telaprevir to require additional capital beyond our current resources including the net proceeds of this offering and the concurrent note offering. We are making significant capital investments in building our drug product supply chain and creating pre-launch inventory and may need to make additional significant capital investments for one or more of our other drug candidates. We anticipate that we will finance these substantial cash needs with:

public offerings or private placements of our debt or equity securities or other methods of financing;

cash received from our existing collaborative agreements;

cash received from new collaborative agreements or from the sale of existing assets, such as royalty streams from drugs and drug candidates being developed and commercialized by third parties;

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

future product sales to the extent that we market drugs directly.

While we believe that our current cash, cash equivalents and marketable securities, together with amounts we expect to receive from our collaborators under existing contractual agreements, would

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be sufficient to fund our operations beyond 2008, we will need to raise additional capital in addition to this offering and the concurrent note offering through public offerings or private placements of our debt or equity securities, agreements with third-parties with respect to certain of our assets or through other methods of financing. Any such capital transactions may or may not be similar to transactions in which we have engaged in the past. Any equity financings could result in dilution to our then-existing security holders. Any debt financing may be on terms that, among other things, restrict our ability to pay interest and dividends although we do not intend to pay dividends for the foreseeable future. If adequate funds are not available on acceptable terms, or at all, we may be required to curtail significantly or discontinue one or more of our research, drug discovery or development programs, including clinical trials, incur significant cash exit costs, or attempt to obtain funds through arrangements with collaborators or others that may require us to relinquish rights to certain of our technologies, drugs or drug candidates. Additional financing may not be available on acceptable terms, if at all.

MANY OF OUR DRUG CANDIDATES ARE STILL IN THE EARLY STAGES OF DEVELOPMENT, AND ALL OF OUR DRUG CANDIDATES REMAIN SUBJECT TO CLINICAL TESTING AND REGULATORY APPROVAL. IF WE ARE UNABLE TO SUCCESSFULLY DEVELOP AND TEST OUR DRUG CANDIDATES, WE WILL NOT BE SUCCESSFUL.

The success of our business depends primarily upon our ability, and our collaborators' ability, to develop and commercialize our drug candidates, including telaprevir, successfully. Due to the development efforts of our competitors, in order to develop a successful franchise in a therapeutic area it is often necessary to develop follow-on compounds and/or develop new combination therapies. Our drug candidates are in various stages of development and must satisfy rigorous standards of safety and efficacy before they can be approved by the FDA or other regulatory authorities for sale. To satisfy these standards, we and/or our collaborators must allocate our resources among our various development programs and must engage in expensive and lengthy testing of our drug candidates. These discovery and development efforts for a new pharmaceutical product, including follow-on compounds, are lengthly and resource-intensive, and may take 10 to 15 years or more. Despite our efforts, our drug candidates may not:

offer therapeutic or other improvement over existing competitive drugs;

be proven safe and effective in clinical trials;

meet applicable regulatory standards;

be capable of being produced in commercial quantities at acceptable costs; or

if approved for commercial sale, be successfully commercialized.

Positive results in preclinical studies of a drug candidate may not be predictive of similar results in humans during clinical trials, and promising results from earlier clinical trials of a drug candidate may not be replicated in later clinical trials. Findings, including toxicology findings, in nonclinical studies conducted concurrently with clinical trials could result in abrupt changes in our development activities, including the possible cessation of development activities associated with a drug candidate. Furthermore, results from our clinical trials may not meet the level of statistical significance required by the FDA or other regulatory authorities for approval of a drug candidate.

We and many other companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late-stage clinical trials even after achieving promising results in early-stage development. Accordingly, the results from the completed preclinical studies and clinical trials and ongoing clinical trials for our drug candidates may not be predictive of the results we may obtain in later stage trials, and may not be predictive of the likelihood of approval of a drug candidate for commercial sale. In addition, from time to time, we report interim data from our clinical trials,

including the PROVE 1 and PROVE 2 clinical trials of telaprevir. Interim data is subject to change as final data are confirmed, and there can be no assurances that interim data will be confirmed upon the analysis of final data.

IF WE ARE UNABLE TO OBTAIN UNITED STATES AND/OR FOREIGN REGULATORY APPROVAL, WE WILL BE UNABLE TO COMMERCIALIZE OUR DRUG CANDIDATES.

Our drug candidates are subject to extensive governmental regulations relating to their development, clinical trials, manufacturing and commercialization. Rigorous preclinical testing and clinical trials and an extensive regulatory approval process are required in the United States and in most other countries prior to the commercial sale of our drug candidates. Satisfaction of these and other regulatory requirements is costly, time consuming, uncertain and subject to unanticipated delays. It is possible that none of the drug candidates we are developing independently, or in collaboration with others, will be approved for marketing.

We have limited experience in conducting and managing the late-stage clinical trials necessary to obtain regulatory approvals, including approval by the FDA. The time required to complete clinical trials and to satisfy the FDA and other countries' regulatory review processes is uncertain and typically takes many years. Our analysis of data obtained from preclinical and clinical activities is subject to confirmation and interpretation by regulatory authorities, which could delay, limit or prevent regulatory approval. We may also encounter unanticipated delays or increased costs due to government regulation from future legislation or administrative action or changes in FDA policy during the period of drug development, clinical trials and FDA regulatory review.

Any delay in obtaining or failure to obtain required approvals could materially adversely affect our ability to successfully commercialize any drug candidate. Furthermore, any regulatory approval to market a drug may be subject to unexpected limitations on the indicated uses for which we may market the drug. These limitations may limit the size of the market for the drug.

We are also subject to numerous foreign regulatory requirements governing the conduct of clinical trials, manufacturing and marketing authorization, pricing and third-party reimbursement. The foreign regulatory approval process includes all of the risks associated with the FDA approval process described above, as well as risks attributable to the satisfaction of foreign requirements. Approval by the FDA does not ensure approval by regulatory authorities outside the United States. Foreign jurisdictions may have different approval procedures than those required by the FDA and may impose additional testing requirements for our drug candidates.

IF CLINICAL TRIALS FOR OUR DRUG CANDIDATES ARE PROLONGED OR DELAYED, WE MAY BE UNABLE TO COMMERCIALIZE OUR DRUG CANDIDATES ON A TIMELY BASIS, WHICH WOULD REQUIRE US TO INCUR ADDITIONAL COSTS, WOULD DELAY OUR RECEIPT OF ANY PRODUCT REVENUE AND COULD HARM OUR COMPETITIVE POSITION.

We cannot predict whether or not we will encounter problems with any of our completed, ongoing or planned clinical trials that will cause us or regulatory authorities to delay or suspend clinical trials, or delay the analysis of data from our completed or ongoing clinical trials. Any of the following could delay the clinical development of our drug candidates:

- ongoing discussions with the FDA or comparable foreign authorities regarding the scope or design of our clinical trials and the number of clinical trials we must conduct;
- delays in receiving or the inability to obtain required approvals from IRBs at one or more of the institutions at which a clinical trial is conducted or other reviewing entities at clinical sites selected for participation in our clinical trials;
- delays in enrolling volunteers or patients into clinical trials;

a lower than anticipated retention rate of volunteers or patients in clinical trials;

the need to repeat clinical trials as a result of inconclusive results or unforeseen complications in testing;

inadequate supply or deficient quality of drug candidate materials or other materials necessary for the conduct of our clinical trials;

unfavorable FDA inspection and review of a manufacturing facility for a drug candidate or its relevant manufacturing records or a clinical trial site or records of any clinical or preclinical investigation;

serious and unexpected drug-related side effects experienced by participants in our clinical trials; or

the placement by the FDA of a clinical hold on a trial.

Our ability to enroll patients in our clinical trials in sufficient numbers and on a timely basis will be subject to a number of factors, including the size of the patient population, the nature of the protocol, the proximity of patients to clinical sites, the availability of effective treatments for the relevant disease, the number of other clinical trials competing for patients in the same indication and the eligibility criteria for the clinical trial. In addition, subjects may drop out of our clinical trials or may be lost to follow-up medical evaluation after treatment ends, and this could possibly impair the validity or statistical significance of the trials. Delays in patient enrollment or unforeseen drop-out rates may result in increased costs and longer development times. 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.

We, our collaborators, the FDA or other applicable regulatory authorities may suspend clinical trials of a drug candidate at any time if we or they believe the subjects or patients participating in such clinical trials are being exposed to unacceptable health risks or for other reasons. In November 2007, Merck suspended enrollment in clinical trials of MK-0457 (VX-680), pending a full analysis of all efficacy and safety data of MK-0457 (VX-680). Any such suspension could materially adversely impact the development of a particular drug candidate and our business.

In addition, it is impossible to predict whether legislative changes will be enacted, or whether FDA regulations, guidance or interpretations will be changed, or what the impact of such changes, if any, may be. If we experience any such problems, we may not have the financial resources to continue development of the drug candidate that is affected or the development of any of our other drug candidates.

IF OUR COMPETITORS BRING SUPERIOR DRUGS TO MARKET OR BRING THEIR DRUGS TO MARKET BEFORE WE DO, WE MAY BE UNABLE TO FIND A MARKET FOR OUR DRUG CANDIDATES.

Our drug candidates in development may not be able to compete effectively with drugs that are currently on the market or new drugs that may be developed by others. No assurance can be given that telaprevir will be approved for marketing prior to competing therapies, or at all. There are many other companies developing drugs for the same indications that we are pursuing in development in particular for the treatment of HCV infection. In order to compete successfully in these areas, we must demonstrate improved safety, efficacy and ease of manufacturing and gain market acceptance over competing drugs that may receive regulatory approval before or after our drug candidates, and over those that currently are marketed. Many of our competitors, including major pharmaceutical companies such as GlaxoSmithKline, Wyeth, Pfizer, Roche, Amgen, Novartis, Johnson & Johnson and Schering-Plough 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 drug candidates, scaling up manufacturing operations and obtaining regulatory approvals of drugs and manufacturing facilities. Accordingly, our competitors may succeed in obtaining regulatory approval for drugs more rapidly than we do. If we obtain regulatory approval and launch commercial sales of our drug candidates, we also will compete with respect to manufacturing efficiency and sales and marketing capabilities, areas in which we currently have limited experience.

We believe that the first company that is able to successfully develop and obtain marketing approval for a new treatment for chronic HCV infection with significant advantages over the current standard of care may have a significant competitive advantage over later-approved therapies for HCV infection. We are aware of a number of companies that are developing new treatments for HCV infection including protease inhibitor compounds like telaprevir, polymerase inhibitor compounds and advanced interferons. Even if we are able to obtain marketing approval for telaprevir, it is possible that one or more of these therapies could be approved prior to or shortly after we obtain such approval for telaprevir, which we believe could negatively impact telaprevir sales.

IF OUR PROCESSES AND SYSTEMS ARE NOT COMPLIANT WITH REGULATORY REQUIREMENTS, WE COULD BE SUBJECT TO DELAYS IN FILING NDAs OR RESTRICTIONS ON MARKETING OF DRUGS AFTER THEY HAVE BEEN APPROVED.

We currently are developing drug candidates 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 drug 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 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, or if compliance issues are identified at any point in the development and approval process, we may experience delays in filing for regulatory approval for our drug candidates, or delays in obtaining regulatory approval after filing. In addition, any later discovery of previously unknown problems or safety issues with approved drugs or manufacturing processes, or failure to comply with regulatory requirements, may result in restrictions on such drugs or manufacturing processes, withdrawal of drugs 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 agreements that transfer responsibility for complying with specified regulatory requirements, such as filing and maintenance of marketing authorizations and safety reporting or compliance with manufacturing requirements, to our collaborators and third-party manufacturers. If our collaborators or third-party manufacturers do not fulfill these regulatory obligations, any drugs 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 OBTAIN REGULATORY APPROVALS, OUR DRUG CANDIDATES WILL BE SUBJECT TO ONGOING REGULATORY REVIEW. IF WE FAIL TO COMPLY WITH CONTINUING UNITED STATES AND APPLICABLE FOREIGN REGULATIONS, WE COULD LOSE THOSE APPROVALS, AND OUR BUSINESS WOULD BE SERIOUSLY HARMED.

If we receive regulatory approval of any drug candidates that we are developing, we will be subject to continuing regulatory review, including the review of clinical results that are reported after our drug candidates become commercially available, approved drugs. Since drugs are more widely used by patients once approval has been obtained, side effects and other problems may be observed after approval that were not seen or anticipated during pre-approval clinical trials. In addition, the

manufacturers and the manufacturing facilities we engage to make any of our drug candidates will also be subject to periodic review and inspection by the FDA. The subsequent discovery of previously unknown problems with the drug, manufacturers or manufacturing facilities may result in restrictions on the drug, manufacturers or facilities, including withdrawal of the drug from the market or our inability to use the facilities to make our drug. If we fail to comply with applicable continuing regulatory requirements, we may be subject to fines, suspension or withdrawal of regulatory approval, product recalls and seizures, operating restrictions and criminal prosecutions.

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 humans. Our ultimate objective is to determine whether the drug candidates have physical characteristics, both intrinsically and in animal and human systems, and 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 investigation 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 monitor the results of our discovery research and our nonclinical studies 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.

WE DEPEND ON OUR COLLABORATORS TO WORK WITH US TO DEVELOP, MANUFACTURE AND COMMERCIALIZE MANY OF OUR DRUG CANDIDATES.

We have granted development and commercialization rights to telaprevir to Janssen (worldwide other than North America and Far East) and to Mitsubishi Tanabe (Far East). We expect to receive significant financial support under our Janssen collaboration agreement, as well as meaningful technical and manufacturing contributions to the telaprevir program. The success of some of our key in-house programs, such as for telaprevir, is dependent upon the continued financial and other support that our collaborators have agreed to provide.

For some drug candidates on which we are not currently focusing our development efforts, we have granted worldwide rights to a collaborator, as in our collaborations with Merck and Avalon.

The success of our collaborations depends on the efforts and activities of our collaborators. Each of our collaborators has significant discretion in determining the efforts and resources that it will apply to the collaboration. Our existing collaborations may not be scientifically or commercially successful, and we may fail in our attempts to establish further collaborations to develop our drug candidates on acceptable terms.

The risks that we face in connection with these existing and any future collaborations include the following:

Our collaboration agreements are subject to termination under various circumstances, including, as in the case of our agreements with Janssen and Merck, termination without cause. Any such termination could have an adverse material effect on our financial condition and/or delay the development and commercial sale of our drug candidates, including telaprevir.

Our collaborators may change the focus of their development and commercialization efforts. Pharmaceutical and biotechnology companies historically have re-evaluated their development and commercialization priorities following mergers and consolidations, which have been common in recent years in these industries. The ability of some of our drug candidates to reach their potential could be limited if our collaborators decrease or fail to increase development or commercialization efforts related to those drug candidates.

Our collaboration agreements may have the effect of limiting the areas of research and development that we may pursue, either alone or in collaboration with third parties.

Our collaborators may develop and commercialize, either alone or with others, drugs that are similar to or competitive with the drugs or drug candidates that are the subject of the collaboration with us.

IF WE ARE UNABLE TO ATTRACT AND RETAIN COLLABORATORS FOR THE DEVELOPMENT AND COMMERCIALIZATION OF OUR DRUGS AND DRUG CANDIDATES, WE MAY NOT BE ABLE TO FUND OUR DEVELOPMENT AND COMMERCIALIZATION ACTIVITIES.

Our collaborators have agreed to fund portions of our pharmaceutical development programs and/or to conduct the development and commercialization of specified drug candidates and, if they are approved, drugs. In exchange, we have given them technology, sales and marketing rights relating to those drugs and drug candidates. Some of our corporate collaborators have rights to control the planning and execution of drug development and clinical programs including for our aurora kinase inhibitor drug candidates, including MK-0457 (VX-680) and VX-689, and AVN-944 (VX-944). 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 our collaborators were to terminate its relationship with us, or fail to meet its contractual obligations, that action could have a material adverse effect on our ability to develop, manufacture and market any drug candidates being developed under the collaboration. We expect to seek additional collaborative arrangements, which may not be available to us on favorable terms, or at all, to develop and commercialize our drug candidates in the future. We plan to seek a collaborator for our oral MAP kinase inhibitor VX-702 for the treatment of rheumatoid arthritis and other inflammatory diseases. No assurance can be given that these efforts will be successful. Even if we are able to establish acceptable collaborative arrangements in the future, these collaborations may not be successful.

OUR INVESTMENT IN THE CLINICAL DEVELOPMENT AND MANUFACTURE OF A COMMERCIAL SUPPLY OF TELAPREVIR MAY NOT RESULT IN ANY BENEFIT TO US IF TELAPREVIR IS NOT APPROVED FOR COMMERCIAL SALE.

We are investing significant resources in the clinical development of telaprevir. In 2006 and 2007, we increased our investment in telaprevir to support our Phase 2b clinical development program and in 2008 we will be investing in our global registration program, including our Phase 3 clinical trial. Telaprevir is the first drug candidate for which we expect to perform all activities related to late stage development, drug supply, registration and commercialization in a major market. We are planning for and investing significant resources now in preparation for application for marketing approval, commercial supply and sales and marketing. We also expect to incur significant costs in 2008 to manufacture registration batches and invest in telaprevir commercial supply. Our engagement in these resource-intensive activities could make it more difficult for us to maintain our portfolio focus, and puts significant investment at risk if we do not obtain regulatory approval and successfully commercialize telaprevir in North America. There is no assurance that our development of telaprevir will lead successfully to regulatory approval, or that obtaining regulatory approval will lead to commercial success. If telaprevir is not approved for commercial sale or if its development is delayed for any

reason, our full investment in telaprevir may be at risk, we may face significant costs to dispose of unusable inventory, and our business and financial condition could be materially adversely affected.

WE DEPEND ON THIRD-PARTY MANUFACTURERS, INCLUDING SOLE SOURCE SUPPLIERS, TO MANUFACTURE CLINICAL TRIAL MATERIALS FOR CLINICAL TRIALS AND EXPECT TO CONTINUE TO RELY ON THEM TO MEET OUR COMMERCIAL SUPPLY NEEDS FOR ANY DRUG CANDIDATE THAT IS APPROVED FOR SALE. WE MAY NOT BE ABLE TO ESTABLISH OR MAINTAIN THESE RELATIONSHIPS AND COULD EXPERIENCE DISRUPTIONS OUTSIDE OF OUR CONTROL.

We currently are relying on a worldwide network of third-party manufacturers to manufacture and distribute our drug candidates for clinical trials, and we expect that we will continue to do so to meet our commercial supply needs for these drugs, including telaprevir, if they are approved for sale. As a result of our reliance on these third-party manufacturers and suppliers, including sole source suppliers of certain components of our drug candidates and drugs, we may be subject to significant supply disruptions outside of our control.

We will be responsible for supplying telaprevir for sale in North America if we are successful in obtaining marketing approval. Establishing the commercial supply chain for telaprevir is a multi-step international endeavor involving the purchase of several raw materials, the application of certain manufacturing processes requiring significant lead times, the conversion of active pharmaceutical ingredient to tablet form and the packaging of tablets for distribution. We expect to source raw materials, drug substance and drug product, including finished packaging, from third parties located in China, the European Union, Japan and the United States, and we currently are establishing and expanding those third-party relationships. Establishing and providing quality assurance for this global supply chain requires a significant financial commitment, experienced personnel and the creation or expansion of numerous third-party contractual relationships. While we believe that there are multiple third parties that are capable of providing the materials and services that we need in order to manufacture and distribute telaprevir, if it is approved for sale, some of these services are in high demand and capacity is constrained. Because of the significant lead times involved in the manufacture and supply of telaprevir, we may have less flexibility to adjust our supply in response to changes in demand than if we had shorter lead times. There can be no assurance that we will be able to establish and maintain this commercial supply chain on commercially reasonable terms in order to support a timely launch of telaprevir or at all.

We plan to identify and enter into commercial relationships with multiple third-party manufacturers in order to reduce the risk of supply chain disruption by limiting our reliance on any one manufacturer. In addition, we are in the process of transferring technical information regarding the manufacture of telaprevir to Janssen so that Janssen will be able to manufacture telaprevir, if approved, for sale in Janssen's territories and as a secondary source for us. There is no assurance, however, that we will be able to establish second sources for each stage of manufacturing of telaprevir, or any other drug or drug candidate, or that any second source will be able to produce sufficient quantities in the required timeframe to avoid a supply chain disruption if there is a problem with one of our suppliers.

Even if we successfully establish arrangements with third-party manufacturers, supply disruptions may result from a number of factors including shortages in product raw materials, labor or technical difficulties, regulatory inspections or restrictions, shipping or customs delays or any other performance failure by any third-party manufacturer on which we rely.

Any supply disruptions could impact the timing of our clinical trials and the commercial launch of any approved pharmaceutical drugs. Furthermore, we may be required to modify our production methods to permit us to economically manufacture our drugs for commercial launch and sale. These modifications may require us to reevaluate our resources and the resources of our third-party

manufacturers, which could result in abrupt changes in our production methods and supplies. Upon approval of a pharmaceutical drug for sale, if any, we similarly may be at risk of supply chain disruption for our commercial drug supply. In the course of its services, a contract manufacturer may develop process technology related to the manufacture of our drug candidates that the manufacturer owns, either independently or jointly with us. This would increase our reliance on that manufacturer or require us to obtain a license from that manufacturer in order to have our products manufactured by other suppliers utilizing the same process.

WE RELY ON THIRD PARTIES TO CONDUCT OUR CLINICAL TRIALS, AND THOSE THIRD PARTIES MAY NOT PERFORM SATISFACTORILY, INCLUDING FAILING TO MEET ESTABLISHED DEADLINES FOR THE COMPLETION OF SUCH TRIALS.

We do not have the ability to independently conduct clinical trials for our drug candidates, and we rely on third parties such as contract research organizations, medical institutions and clinical investigators to enroll qualified patients and conduct our clinical trials. Our reliance on these third parties for clinical development activities reduces our control over these activities. Accordingly, these third-party contractors may not complete activities on schedule, or may not conduct our clinical trials in accordance with regulatory requirements or our trial design. If these third parties do not successfully carry out their contractual duties or meet expected deadlines, we may be required to replace them. Although we believe that there are a number of other third-party contractors we could engage to continue these activities, it may result in a delay of the affected trial. Accordingly, our efforts to obtain regulatory approvals for and commercialize our drug candidates could be delayed.

IF WE ARE UNABLE TO DEVELOP INDEPENDENT SALES AND MARKETING CAPABILITIES OR ESTABLISH THIRD-PARTY RELATIONSHIPS FOR THE COMMERCIALIZATION OF OUR DRUG CANDIDATES, WE WILL NOT BE ABLE TO SUCCESSFULLY COMMERCIALIZE OUR DRUG CANDIDATES EVEN IF WE ARE ABLE TO OBTAIN REGULATORY APPROVAL.

We currently have limited experience as a company in sales and marketing or with respect to pricing and obtaining adequate third-party reimbursement for drugs. GlaxoSmithKline currently markets Lexiva/Telzir. We will need to either develop marketing capabilities and an independent sales force or enter into arrangements with third parties to sell and market any of our drug candidates if they are approved for sale by regulatory authorities.

In order to market telaprevir in North America if it is approved, we intend to build a marketing organization and a direct sales force, which will require substantial efforts and significant management and financial resources. During 2008, we intend to commit significant personnel and financial resources to this effort, staging our commitments to the extent possible in consideration of the ongoing telaprevir development timeline. We will need to devote significant effort, in particular, to recruiting individuals with experience in the sales and marketing of pharmaceutical products. Competition for personnel with these skills is intense and may be particularly difficult for us since telaprevir is still an investigational drug candidate and we will be competing with companies that are currently marketing successful drugs. As a result, we may not be able to successfully develop our own marketing capabilities or independent sales force for telaprevir in North America in order to support an effective launch of telaprevir if it is approved for sale.

We have granted commercialization rights to other pharmaceutical companies with respect to certain of our drug candidates in specific geographic locations, including telaprevir (Janssen worldwide except for North America and the Far East, and Mitsubishi Tanabe in the Far East), Aurora kinase inhibitors (Merck worldwide) and AVN-944 (VX-944) (Avalon worldwide). To the extent that our collaborators have commercial rights to our drugs, any revenues we receive from any approved drugs will depend primarily on the sales and marketing efforts of others. We do not know whether we will be able to enter into additional third-party sales and marketing arrangements with respect to any of our other drug candidates on acceptable terms, if at all, or whether we will be able to leverage the sales and marketing capabilities we intend to build for telaprevir in order to market and sell any other drug candidate if it is approved for sale.

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

We currently receive royalties from net sales of Lexiva/Telzir under our collaboration with GlaxoSmithKline. Lexiva/Telzir's share of the worldwide protease inhibitor market may decrease due to competitive forces and market dynamics. Other HIV protease inhibitors including Bristol-Myers Squibbs' Reyataz® and Abbott Laboratories' Kaletra®, and a number of other products 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, Boehringer Ingelheim Merck, and Johnson & Johnson, 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. As a result, the total market for HIV protease inhibitors may decline, decreasing the sales potential of Lexiva/Telzir. Further, GlaxoSmithKline directs 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 to us upon any such termination.

RISKS ASSOCIATED WITH OUR INTERNATIONAL BUSINESS RELATIONSHIPS COULD MATERIALLY ADVERSELY AFFECT OUR BUSINESS.

We have manufacturing, collaborative and clinical trial relationships, and we and our collaborators are seeking approval for our drug candidates, outside the United States. In addition, we expect that if telaprevir is approved for commercial sale, a significant portion of our commercial supply chain, including sourcing of raw materials and manufacturing, will be located in China, Japan and European Union. Consequently, we are, and will continue to be, subject to risks related to operating in foreign countries. Risks associated with conducting operations in foreign countries include:

- differing regulatory requirements for drug approvals in foreign countries;
- unexpected changes in tariffs, trade barriers and regulatory requirements;
- economic weakness, including inflation, or political instability in particular foreign economies and markets;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;
- foreign taxes, including withholding of payroll taxes;
- foreign currency fluctuations, which could result in increased operating expenses or reduced revenues, and other obligations incident to doing business or operating a subsidiary in another country;
- workforce uncertainty in countries where labor unrest is more common than in the United States;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad; and
- business interruptions resulting from geo-political actions, including war and terrorism.

These and other risks associated with our international operations could materially adversely affect our business.

IF WE ARE UNABLE TO REALIZE THE EXPECTED BENEFITS OF OUR DRUG DISCOVERY CAPABILITIES AND OTHER TECHNOLOGIES, WE MAY NOT BE ABLE TO COMPETE IN THE MARKETPLACE.

The pharmaceutical research field is characterized by rapid technological progress and intense competition. As a result, we may not realize the expected benefits from our integrated drug discovery capabilities and 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 WE FAIL TO EXPAND OUR HUMAN RESOURCES AND MANAGE OUR GROWTH EFFECTIVELY, OUR BUSINESS MAY SUFFER.

We expect that if our clinical drug 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. For example, the number of our full-time employees increased by 20% in 2007, and we expect to experience significant growth in 2008. Our ability to commercialize our drug candidates, 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.

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 drug discovery and development activities are highly technical in nature, we require the services of highly qualified and trained scientists who have the skills necessary to conduct these activities. In addition, as we attempt to grow our capabilities with respect to clinical development, regulatory affairs, quality control and sales and marketing, we will need to attract and retain employees with experience in these fields. 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 us. 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 movements 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 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 have 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 to these areas. A failure to retain, as well as hire, train and effectively integrate into our organization a sufficient number of qualified scientists, professionals and sales personnel would negatively affect our business and our ability to grow our business.

IF OUR PATENTS DO NOT PROTECT OUR DRUGS, OR OUR DRUGS 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 drugs, 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 similar drugs 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, regardless of whether or not 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 drugs, any of which outcomes could have a material adverse effect on our business.

IF PHYSICIANS, PATIENTS AND THIRD-PARTY PAYORS DO NOT ACCEPT OUR FUTURE DRUGS, WE MAY BE UNABLE TO GENERATE SIGNIFICANT REVENUE, IF ANY.

Even if our drug candidates obtain regulatory approval, they may not gain market acceptance among physicians, patients and health care payors. Physicians may elect not to recommend our drugs for a variety of reasons including:

- the timing of the market introduction of competitive drugs;
- lower demonstrated clinical safety and efficacy compared to other drugs;
- lack of cost-effectiveness;
- lack of availability of reimbursement from third-party payors;
- convenience and ease of administration;
- prevalence and severity of adverse side effects;
- other potential advantages of alternative treatment methods; and
- ineffective marketing and distribution support.

If our approved drugs fail to achieve market acceptance, we will not be able to generate significant revenue.

IF THE GOVERNMENT AND OTHER THIRD-PARTY PAYORS FAIL TO PROVIDE COVERAGE AND ADEQUATE PAYMENT RATES FOR OUR FUTURE DRUGS, OUR REVENUE AND PROSPECTS FOR PROFITABILITY WILL BE HARMED.

In both domestic and foreign markets, our sales of any future drugs will depend in part upon the availability of reimbursement from third-party payors. Such third-party payors include government health programs such as Medicare, managed care providers, private health insurers and other organizations. These third-party payors are increasingly attempting to contain health care costs by demanding price discounts or rebates and limiting both the types and variety of drugs that they will cover and the amounts that they will pay for these drugs. As a result, they may not cover or provide adequate payment for our future drugs. We might need to conduct post-marketing studies in order to demonstrate the cost-effectiveness of any future drugs to such payors' satisfaction. Such studies might require us to commit a significant amount of management time and financial and other resources. Our future drugs might not ultimately be considered cost-effective. Adequate third-party reimbursement might not be available to enable us to maintain price levels sufficient to realize an appropriate return on investment in product development.

Reimbursement rates may vary according to the use of the drug and the clinical setting in which it is used, may be based on payments allowed for lower-cost products that are already reimbursed, may be incorporated into existing payments for other products or services, and may reflect budgetary constraints and/or imperfections in Medicare or Medicaid data used to calculate these rates. Net prices for drugs may be reduced by mandatory discounts or rebates required by government health care programs. In addition, legislation has been introduced in Congress that, if enacted, would permit more widespread importation of drugs from foreign countries into the United States, which may include importation from countries where the drugs are sold at lower prices than in the United States. Such legislation, or similar regulatory changes or relaxation of laws that restrict imports of drugs from other countries, could reduce the net price we receive for our marketed drugs.

OUR BUSINESS HAS A SUBSTANTIAL RISK OF PRODUCT LIABILITY CLAIMS. IF WE ARE UNABLE TO OBTAIN APPROPRIATE LEVELS OF INSURANCE, A PRODUCT LIABILITY CLAIM COULD ADVERSELY AFFECT OUR BUSINESS.

Our business exposes us to significant potential product liability risks that are inherent in the development, manufacturing and sales and marketing of human therapeutic products. We currently have clinical trial insurance and will seek to obtain product liability insurance prior to the sales and marketing of any of our drug candidates. However, our insurance may not provide adequate coverage against potential liabilities. Furthermore, clinical trial and product liability insurance is becoming increasingly expensive. As a result, we may be unable to maintain current amounts of insurance coverage or obtain additional or sufficient insurance at a reasonable cost to protect against losses that could have a material adverse effect on us. If a claim is brought against us, we might be required to pay legal and other expenses to defend the claim, as well as uncovered damages awards resulting from a claim brought successfully against us. Furthermore, whether or not we are ultimately successful in defending any such claims, we might be required to direct significant financial and managerial resources to such defense, and adverse publicity is likely to result.

IF WE DO NOT COMPLY WITH LAWS REGULATING THE PROTECTION OF THE ENVIRONMENT AND HEALTH AND HUMAN SAFETY, OUR BUSINESS COULD BE ADVERSELY AFFECTED.

Our research and development efforts involve the controlled use of hazardous materials, chemicals and various radioactive compounds. Although we believe that our safety procedures for handling and disposing of these materials comply with the standards prescribed by state and federal regulations, the risk of accidental contamination or injury from these materials cannot be eliminated. If

an accident occurs, we could be held liable for resulting damages, which could be substantial. We are also subject to numerous environmental, health and workplace safety laws and regulations, including those governing laboratory procedures, exposure to blood-borne pathogens and the handling of biohazardous materials. Although we maintain workers' compensation insurance to cover us for costs we may incur due to injuries to our employees resulting from the use of these materials, this insurance may not provide adequate coverage against potential liabilities. Due to the small amount of hazardous materials that we generate, we have determined that the cost to secure insurance coverage for environmental liability and toxic tort claims far exceeds the benefits. Accordingly, we do not maintain any insurance to cover pollution conditions or other extraordinary or unanticipated events relating to our use and disposal of hazardous materials. Additional federal, state and local laws and regulations affecting our operations may be adopted in the future. We may incur substantial costs to comply with, and substantial fines or penalties if we violate, any of these laws or regulations.

WE HAVE ADOPTED ANTI-TAKEOVER PROVISIONS AND ARE SUBJECT TO MASSACHUSETTS CORPORATE LAWS THAT MAY FRUSTRATE ANY ATTEMPT TO REMOVE OR REPLACE OUR CURRENT MANAGEMENT.

Our corporate charter and by-law provisions, Massachusetts state laws, 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 us or our 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. Massachusetts state law prohibits us from engaging in specified business combinations, unless the combination is approved or consummated in a prescribed manner, and prohibits voting by any stockholder who acquires 20% or more of our voting stock without stockholder approval. As a result, stockholders or other parties may find it more difficult to remove or replace our current management.

OUR STOCK PRICE MAY FLUCTUATE BASED ON FACTORS BEYOND OUR CONTROL.

Market prices for securities of companies such as Vertex are highly volatile. From January 1, 2007 to February 8, 2008, our common stock traded between $17.59 and $41.42 per share. 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 trials or nonclinical studies relating to our drug candidates or those of our competitors;
- announcements of financial results and other operating performance measures, or capital structuring or financing activities;
- technological innovations or the introduction of new drugs by our competitors;
- government regulatory action;

public concern as to the safety of drugs developed by others;

developments in patent or other intellectual property rights or announcements relating to these matters;

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

developments relating specifically to other companies and market conditions for pharmaceutical and biotechnology stocks or stocks in general.

OUR ESTIMATES OF OUR LIABILITY UNDER OUR KENDALL SQUARE LEASE MAY BE INACCURATE.

We leased a 290,000 square foot facility in Kendall Square, Cambridge, Massachusetts in January 2003 for a 15-year term. We currently are occupying approximately 120,000 square feet of the facility. We have sublease arrangements in place for the remaining rentable square footage of the facility. In determining our obligations under the lease for the portion of the facility that we are not occupying, we have made certain assumptions relating to the time necessary to sublease the space after the expiration of the initial subleases, projected future sublease rental rates and the anticipated durations of future subleases. Our estimates have changed in the past, and may change in the future, resulting in additional adjustments to the estimate of liability, and the effect of any such adjustments could be material.

GOVERNMENT INVESTIGATIONS OR LITIGATION AGAINST OUR COLLABORATORS COULD ADVERSLY AFFECT 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 addition, recent government litigation against pharmaceutical companies has focused on allegations of off-label promotion in connection with the filing of false claims for government reimbursement. In any AWP cases or other cases brought by the government where our collaborators or licensees are named as defendants with respect to any products licensed from us, the outcome of the case could have a material adverse effect on our financial results.

SALES OF ADDITIONAL SHARES OF OUR COMMON STOCK COULD CAUSE THE PRICE OF OUR COMMON STOCK TO DECLINE.

Sales of substantial amounts of our common stock in the open market, or the availability of such shares for sale, could adversely affect the price of our common stock. In addition, the issuance of restricted common stock or common stock upon exercise of any outstanding option would be dilutive, and may cause the market price for a share of our common stock to decline. As of December 31, 2007, we had approximately 132.9 million shares of common stock issued and outstanding. We also had outstanding options to purchase approximately 15.4 million shares of common stock with a weighted-average exercise price of $28.70 per share. Outstanding options may be exercised if the market price of our common stock exceeds the applicable exercise price. We may issue additional common stock or restricted securities in the future as part of our financing activities and any such issuances may have a dilutive effect on existing shareholders. Although we and our officers and directors have agreed to

lock-up restrictions for a 90-day period following the offering, these restrictions are subject to waiver by the underwriters.

Risks Related to Our Common Stock and This Offering

WE WILL HAVE BROAD DISCRETION AS TO THE USE OF THE PROCEEDS FROM THIS OFFERING AND THE CONCURRENT NOTE OFFERING, AND WE MAY NOT USE THE PROCEEDS EFFECTIVELY.

We have not designated the amount of net proceeds from this offering or the concurrent note offering we will use for any particular purpose other than the repayment of a $20 million development loan. 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 management may use the net proceeds for corporate purposes that may not yield profitable results or increase our market value.

CONVERSION OF ANY NOTES SOLD PURSUANT TO THE CONCURRENT NOTE OFFERING WILL REDUCE THE PERCENTAGE OWNERSHIP INTERESTS OF EXISTING STOCKHOLDERS.

Concurrently with this offering, we are offering $250.0 million aggregate principal amount of % Convertible Senior Subordinated Notes due 2013 (or a total of $287.5 million aggregate principal amount of notes if the underwriters exercise their overallotment option in full) pursuant to a separate registration statement and prospectus. Upon conversion of any notes sold pursuant to the concurrent note offering, the percentage ownership interests of existing stockholders will be reduced. Any sales in the public market of our common stock issuable upon such conversion could adversely affect prevailing market prices of our common stock. In addition, the existence of such equity-related securities may encourage short selling by market participants because the conversion of such securities could depress the price of our common stock.

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 an assumed public offering price of $18.10 per share, if you purchase shares of common stock in this offering, you will suffer immediate and substantial dilution of $15.41 per share in the net tangible book value of the common stock. If the underwriters exercise their overallotment option, you will experience additional dilution. See "Dilution" on page 30 for a more detailed discussion of the dilution you will incur in this offering.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus and the documents incorporated by reference herein 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:

- our expectations regarding clinical trials, development timelines and regulatory authority filings for telaprevir and other drug candidates under development by us and our collaborators;

- our expectations regarding the number of patients that will be evaluated, the trial design that will be utilized, the anticipated date by which enrollment will commence and/or be completed and the expected date by which SVR data and/or interim data will be available for our Phase 3 clinical trial of telaprevir, the planned clinical trial to evaluate 48-week telaprevir-based treatment regimens in approximately 400 patients, the PROVE 1, PROVE 2 and PROVE 3 clinical trials, the Phase 2b clinical trials of telaprevir being conducted by Tibotec, the Phase 2a and planned Phase 2b clinical trial of VX-770, the Phase 1a and planned Phase 1b clinical trial of VX-809, the Phase 1a clinical trial of VX-500, the planned clinical trial of VX-813, and the clinical trials being conducted by our collaborators of drug candidates for the treatment of cancer;

- the data that will be generated by ongoing and planned clinical trials, and the ability to use that data for the design and initiation of further clinical trials and to support regulatory filings, including potentially an NDA for telaprevir;

- our expectations regarding the potential of our ongoing and planned clinical trials of telaprevir to meet the anticipated registration requirements with respect to the number and design of the clinical trials and the number of patients that will be part of the safety database of patients that have received 12 weeks of telaprevir;

- the design of our global clinical program for telaprevir and our ability to potentially register telaprevir across a range of HCV genotypes and patient populations;

- our expectations regarding the future market demand and medical need for telaprevir and our other drug candidates;

- our ability to retain greater development control of, and commercial rights to, drug candidates by funding a greater portion of our research programs;

- our beliefs regarding the support provided by clinical trials and preclinical and nonclinical studies of our drug candidates for further investigation, clinical trials or potential use as an effective treatment;

- our ability to capitalize on the advances in our telaprevir clinical program by building our drug development, supply chain management and commercialization organizations in order to prepare for the potential commercial launch of telaprevir and to support the development of our other drug candidates;

- our business strategy, including: our plan to invest in our development of telaprevir in order to maintain the time-to-market advantage we believe we have in relation to drug candidates being developed by our competitors; our ability to establish a leadership position with respect to treatment of HCV infection; and our ability to expand the value of our portfolio of drug candidates;

- the focus of our drug development efforts;

the expected uses of the proceeds of this offering and the concurrent note offering;

the establishment, development and maintenance of collaborative relationships;

our ability to use our research programs to identify and develop new drug candidates to address series diseases and significant unmet medical needs;

our ability to increase our headcount and scale up our drug development and commercialization capabilities;

our estimates regarding obligations associated with a lease of a facility in Kendall Square, Cambridge, Massachusetts;

the potential for the acquisition of new and complementary technologies, resources and drugs or drug candidates; and

our liquidity.

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 and in the documents incorporated by reference herein. 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, assuming a public offering price of $18.10 per share, will be approximately $102.8 million (or $118.4 million if the underwriters exercise their overallotment option in full), after deducting the estimated underwriting discount and offering expenses. In addition, we estimate that the net proceeds from the concurrent note offering will be approximately $241.6 million (or $278.0 million if the underwriters exercise their overallotment option in full), after deducting the estimated underwriting discount and offering expenses. It is possible that, based on market conditions, we may increase or decrease the number of shares offered hereby and increase or decrease the aggregate principal amount of the notes offered in our concurrent notes offering or complete one offering without the other.

We intend to use the net proceeds from this offering, together with the net proceeds from the concurrent note offering, for general corporate purposes, which we expect to include investment in the development and commercialization of telaprevir, clinical trial expenditures and other development expenses for telaprevir and our other drug candidates, investment in our research programs and manufacture and supply of drug substances, and repayment of the $20.0 million interest free development loan from Novartis Pharma AG due May 2008, and which may include capital expenditures, investments and potentially acquisitions. 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 and the concurrent note offering. We have no current 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 December 31, 2007.

Our net tangible book value at December 31, 2007 was $271.3 million, or $2.04 per share, based on 132.9 million shares of our common stock outstanding. After giving effect to the sale of 6,000,000 shares of common stock by us at an assumed public offering price of $18.10 per share, less the estimated underwriting discount and offering expenses, our net tangible book value at December 31, 2007 would be $374.0 million, or $2.69 per share. This represents an immediate increase in net tangible book value of $102.8 per share to existing stockholders and an immediate dilution of $0.65 per share to investors in this offering. The following table illustrates this per share dilution:

Assumed public offering price per share		$ 18.10
Net tangible book value per share as of December 31, 2007	$ 2.04	
Increase per share attributable to new investors purchasing shares in this offering	$ 0.65	
Net tangible book value per share after this offering		2.69
Dilution per share to new investors		$ 15.41

A $1.00 increase in the assumed public offering price of $18.10 per share would increase our net tangible book value per share after this offering to $2.73 per share, representing an immediate increase in net tangible book value of $0.69 per share to existing stockholders and an immediate dilution of $16.37 per share to investors in this offering, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting the estimated underwriting discount and offering expenses. A $1.00 decrease in the assumed public offering price of $18.10 per share would decrease our net tangible book value per share after this offering to $2.65 per share, representing an immediate increase in net tangible book value of $0.61 per share to existing stockholders, and an immediate dilution of $14.45 per share to investors in this offering, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting the estimated underwriting discount and offering expenses. The information discussed above is illustrative only and will adjust based on the actual offering price and other terms of this offering determined at pricing.

If the underwriters exercise their overallotment option in full, the net tangible book value per share after this offering would be $2.79 per share, representing an increase to existing stockholders of $0.75 per share, and there would be an immediate dilution of $15.31 per share to new investors.

The foregoing information does not take into account the concurrent note offering.

PRICE RANGE OF COMMON STOCK

Our common stock is listed on the Nasdaq Global Select Market under the symbol "VRTX." The last reported sale price for our common stock on February 8, 2008 was $18.10 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, 2006		
First quarter	$ 44.71	$ 26.50
Second quarter	40.00	29.00
Third quarter	37.10	29.75
Fourth quarter	45.38	32.50
Fiscal Year ended December 31, 2007		
First quarter	$ 38.95	$ 26.98
Second quarter	32.51	25.61
Third quarter	41.42	27.55
Fourth quarter	39.48	22.80

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 cash position and capitalization as of December 31, 2007:

- on an actual basis;
- on an as adjusted basis to give effect to the issuance and sale of 6,000,000 shares of our common stock in this offering at an assumed public offering price of $18.10 per share, after deducting the estimated underwriting discount and offering expenses; and
- on a pro forma as adjusted basis to give further effect to the issuance and sale of $250.0 million aggregate principal amount of % Convertible Senior Subordinated Notes due 2013 in the concurrent note offering, after deducting the estimated underwriting discount and offering expenses and the use of a portion of the net proceeds to repay a $20.0 million development loan.

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

	December 31, 2007		
	(Unaudited) (In thousands, except share data)		
	Actual	As adjusted	Pro forma as adjusted
Cash, cash equivalents and marketable securities	$ 467,796	$ 570,634	$ 792,262
Collaborator development loan	$ 19,997	$ 19,997	
Convertible Senior Subordinated Notes due 2013			250,000
Stockholders' equity (deficit):			
Preferred stock, $0.01 par value, 1,000,000 shares authorized; none issued and outstanding at December 31, 2007			
Common stock $0.01 par value; 200,000,000 shares authorized; 132,875,540 shares actual, 138,875,540 shares as adjusted and pro forma as adjusted, issued and outstanding at December 31, 2007	1,312	1,372	1,372
Additional paid-in capital	1,856,856	1,959,634	1,959,634
Accumulated other comprehensive income	881	881	881
Accumulated deficit	(1,587,754)	(1,587,754)	(1,587,754)
Total stockholders' equity	271,295	374,133	374,133
Total capitalization	$ 291,292	$ 394,130	$ 624,133

The table above excludes the following shares:

- 15,357,591 shares of common stock issuable upon the exercise of stock options outstanding as of December 31, 2007 at a weighted average exercise price of $28.70 per share;

1,782,775 shares of common stock issuable upon the exercise of stock options granted to employees after December 31, 2007 and on or before February 8, 2008 at a weighted exercise price of $18.97 per share, including 537,000 shares of common stock issuable upon the exercise of stock options that are contingent upon receiving shareholder approval; and

425,403 restricted shares of common stock issued to employees after December 31, 2007 and on or before February 8, 2008.

We will evaluate the Convertible Senior Subordinated Notes due 2013 under SFAS No. 133 and other related literature to determine whether any provisions in the notes will be separately accounted for as an embedded derivative financial instrument. If we determine that there is an embedded derivative instrument: it would be reflected separately on the balance sheet as a liability at fair value; and the liability associated with the Convertible Senior Subordinated Notes due 2013 would be reduced by the initial fair value of the embedded derivative and acreted to face value as additional interest expense. The value of the embedded derivative, if any, would be adjusted quarterly for changes in fair values.

CONCURRENT NOTE OFFERING

Concurrently with this offering, we are offering $250.0 million aggregate principal amount of % Convertible Senior Subordinated Notes due 2013 (or a total of $287.5 million aggregate principal amount of notes if the underwriters exercise their over-allotment option in full) pursuant to a separate registration statement and prospectus. Although this common stock offering is not contingent upon the note offering and the note offering is not contingent upon this common stock offering, we currently anticipate raising approximately $358.6 million in aggregate gross proceeds from the two offerings (up to $412.4 million if the underwriters' exercise their overallotment option in full). However, amounts sold in each offering may increase or decrease based on market conditions relating to that particular security. We cannot assure you that we will complete the concurrent note offering.

The following description is a summary of the material provisions of the notes we are offering in the concurrent note offering and the indenture that governs the notes. It does not purport to be complete. This summary is subject to and is qualified by reference to all the provisions of the indenture, including the definitions of some terms used in the indenture.

The notes will bear interest at the rate of % per year, payable in cash semiannually in arrears on February and August of each year, beginning on August , 2008. The notes will mature on February , 2013. The notes will be our unsecured senior subordinated obligations and will rank junior in right of payment to our existing and future senior debt, equal in right of payment with our existing and future senior subordinated debt, and senior in right of payment to our existing and future subordinated debt. In addition, the notes will effectively rank junior in right of payment to all of our existing and future secured debt, to the extent of the value of the assets securing such debt, and to the debt and all other liabilities of our subsidiaries.

Holders may convert, at any time prior to maturity, any outstanding notes into shares of our common stock. The notes are convertible at a conversion rate of shares per $1,000 principal amount of notes, which is equal to a conversion price of approximately $ per share, subject to adjustment. If a holder elects to convert notes in connection with certain fundamental change events, such holder may also be entitled to receive a make- whole premium upon conversion.

Upon a fundamental change relating to our company, each holder may require us to purchase all or a portion of such holder's notes at a price equal to the principal and accrued and unpaid interest, if any.

After February , 2010, we may redeem all or a portion of the notes at the redemption prices specified in this prospectus, plus accrued and unpaid interest to, but excluding, the redemption date.

UNDERWRITING

We intend to offer the shares of common stock through the underwriters named below. Merrill Lynch, Pierce, Fenner & Smith Incorporated is acting as representative of the underwriters named below. Subject to the terms and conditions described in an underwriting agreement among us and the underwriters, we have agreed to sell to the underwriters, and the underwriters severally have agreed to purchase from us, the number of shares listed opposite their names below.

Underwriter	Number of Shares
Merrill Lynch, Pierce, Fenner & Smith Incorporated	
Total	

The underwriters have agreed to purchase all of the shares sold under the underwriting agreement if any of these shares are purchased. If an underwriter defaults, the underwriting agreement provides that the purchase commitments of the non-defaulting underwriters may be increased or the underwriting agreement may be terminated.

We have agreed to indemnify the underwriters against certain liabilities, including liabilities under the Securities Act of 1933, as amended, or to contribute to payments the underwriters may be required to make in respect of those liabilities.

The underwriters are offering the shares, subject to prior sale, when, as and if issued to and accepted by them, subject to approval of legal matters by their counsel, including the validity of the shares, and other conditions contained in the underwriting agreement, such as the receipt by the underwriters of officers' certificates and legal opinions. The underwriters reserve the right to withdraw, cancel or modify offers to the public and to reject orders in whole or in part.

Commissions and Discounts

The representative has advised us that the underwriters propose initially to offer the shares to the public at the public offering price on the cover page of this prospectus, and to dealers at that price less a concession not in excess of $ per share. The underwriters may allow, and the dealers may reallow, a discount not in excess of $ per share to other dealers. After the offering, the public offering price, concession and discount may be changed.

The following table shows the public offering price, underwriting discount and proceeds before expenses to us. The information assumes either no exercise or full exercise by the underwriters of their overallotment option.

	Per Share	Without Option	With Option
Public offering price	$	$	$
Underwriting discount	$	$	$
Proceeds, before expenses, to Vertex	$	$	$

The expenses of the offering, not including the underwriting discount (and assuming no exercise of the overallotment option), are estimated at $875,000 and are payable by us.

Overallotment Option

We have granted an option to the underwriters to purchase up to 900,000 additional shares at the public offering price listed on the cover page of this prospectus, less the underwriting discount. The underwriters may exercise this option for 30 days from the date of this prospectus solely to cover any overallotments. If the underwriters exercise this option, each will be obligated, subject to conditions contained in the underwriting agreement, to purchase a number of additional shares proportionate to that underwriter's initial amount reflected in the above table.

No Sale of Similar Securities

We, our directors and our executive officers have agreed, with certain exceptions, not to sell or transfer any common stock for 90 days after the date of the underwriting agreement (the "lock-up period") without first obtaining the written consent of the representative. Specifically, we and these directors and officers have agreed, subject to such exceptions, not to directly or indirectly:

- offer, pledge, sell or contract to sell any common stock or any securities convertible into or exchangeable or exercisable for our common stock (the "lock-up securities");
- sell any option or contract to purchase any lock-up securities;
- purchase any option or contract to sell any lock-up securities;
- grant any option, right or warrant for the sale of any lock-up securities;
- otherwise dispose of or transfer any lock-up securities;
- file, or cause to be filed, any registration statement under the Securities Act of 1933, as amended, with respect to any lock-up securities; or
- enter into any swap or any other agreement or any transaction that transfers, in whole or in part, directly or indirectly, the economic consequence of ownership of any lock-up securities, whether any such swap or transaction is to be settled by delivery of common stock or other securities, in cash or otherwise.

Listing on the Nasdaq Global Select Market

Our shares of common stock are traded on the Nasdaq Global Select Market under the symbol "VRTX."

Price Stabilization, Short Positions and Penalty Bids

Until the distribution of our shares is completed, SEC rules may limit underwriters from bidding for and purchasing our common stock. However, the representative may engage in transactions that stabilize the price of the common stock, such as bids or purchases to peg, fix or maintain that price.

If the underwriters create a short position in the common stock in connection with the offering, i.e., if they sell more shares than are listed on the cover page of this prospectus, the representative may reduce that short position by purchasing shares in the open market. The representative may also elect to reduce any short position by exercising all or part of the overallotment option described above. Purchases of the common stock to stabilize its price or to reduce a short position may cause the price of the common stock to be higher than it might be in the absence of such purchases.

"Covered" short sales are sales made in an amount not greater than the underwriters' option to purchase additional shares from us in the offering. The underwriters may close out any covered short position by either exercising their option to purchase additional shares or purchasing

shares in the

open market. In determining the source of shares to close out the covered short position, the underwriters will consider, among other things, the price of shares available for purchase in the open market as compared to the price at which they may purchase shares through the overallotment option. "Naked" short sales are any sales in excess of such option. The underwriters must close out any naked short position by purchasing stock in the open market. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of our common stock in the open market after pricing that could adversely affect investors who purchase in the offering. Stabilizing transactions consist of various bids for or purchases of common stock made by the underwriters in the open market prior to the completion of the offering.

The underwriters may also impose a penalty bid. This occurs when a particular underwriter repays to the underwriters a portion of the underwriting discount received by it because the representative has repurchased shares sold by or for the account of such underwriter in stabilizing or short covering transactions.

Similar to other purchase transactions, the underwriters' purchases to cover the syndicate short sales may have the effect of raising or maintaining the market price of our common stock or preventing or retarding a decline in the market price of our common stock. As a result, the price of our common stock may be higher than the price that might otherwise exist in the open market. Neither we nor any of the underwriters make any representation or prediction as to the direction or magnitude of any effect that the transactions described above may have on the price of the common stock. In addition, neither we nor the underwriters make any representation that the underwriters will engage in these transactions or that these transactions, once commenced, will not be discontinued without notice.

Passive Market Making

In connection with this offering, underwriters and selling group members may engage in passive market making transactions in our common stock on the Nasdaq Global Select Market in accordance with Rule 103 of Regulation M under the Exchange Act during a period before the commencement of offers or sales of our common stock and extending through completion of the distribution. A passive market maker must display its bid at a price not in excess of the highest independent bid of that security. However, if all independent bids are lowered below the passive market maker's bid, that bid must then be lowered when specified purchase limits are exceeded.

Electronic Distribution

A prospectus in electronic format may be made available on the website maintained by the representative. Other than the electronic prospectus, the information on the website of the representative is not part of this prospectus. The representative may agree to allocate a number of shares to itself for sale to its online brokerage account holders.

Other Relationships

The underwriters and their affiliates have provided investment and commercial banking and financial advisory services from time to time to us in the ordinary course of business, for which they have received customary fees. Any of the underwriters or their respective affiliates may in the future engage in investment banking or other transactions of a financial nature with us or our affiliates, including the provision of advisory services and the making of loans to us or our affiliates, for which they would receive customary fees or other payments.

LEGAL MATTERS

The validity of the shares of common stock offered hereby will be passed upon for us by Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C., Boston, Massachusetts. Certain legal matters will be passed upon for the underwriters by Cleary Gottlieb Steen & Hamilton LLP, New York, New York.

EXPERTS

The consolidated financial statements of Vertex Pharmaceuticals Incorporated appearing in Vertex Pharmaceuticals Incorporated's Annual Report (Form 10-K) for the year ended December 31, 2007, have been audited by Ernst & Young LLP, independent registered public accounting firm, as set forth in their report thereon, included therein, and incorporated herein by reference. Such consolidated financial statements are incorporated herein by reference in reliance upon such report given on the authority of such firm as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

We are a public company and are required to file annual, quarterly and current reports, proxy statements and other information with the SEC pursuant to the Securities Exchange Act of 1934, as amended (hereinafter referred to as the "Exchange Act"). You may read and copy any document we file at the SEC's Public Reference Room at 100 F Street, N.E., Washington, D.C. 20549. You can request copies of these documents by writing to the SEC and paying a fee for the copying cost. Please call the SEC at 1-800-SEC-0330 for more information about the operation of the public reference room. Our SEC filings are also available to the public at the SEC's web site at "http://www.sec.gov."

We filed a registration statement on Form S-3 under the Securities Act of 1933, as amended (hereinafter referred to as the "Securities Act"), with the SEC with respect to the securities being offered pursuant to this prospectus. This prospectus is only part of the registration statement and omits certain information contained in the registration statement, as permitted by the SEC. You should refer to the registration statement, including the exhibits, for further information about us and the securities being offered pursuant to this prospectus. Statements in this prospectus regarding the provisions of certain documents filed with, or incorporated by reference in, the registration statement are not necessarily complete and each statement is qualified in all respects by that reference. You may:

- inspect a copy of the registration statement, including the exhibits and schedules, without charge at the public reference room;
- obtain a copy from the SEC upon payment of the fees prescribed by the SEC; or
- obtain a copy from the SEC web site.

INCORPORATION BY REFERENCE

The SEC allows us to "incorporate by reference" information that we file with them. Incorporation by reference allows us to disclose important information to you by referring you to those other documents. The information incorporated by reference is an important part of this prospectus, and any information incorporated by reference is considered part of this prospectus. Any reports filed by us with the SEC after the date of this prospectus and before the date that offering of securities by means of this prospectus is terminated will automatically update and, where applicable, supersede any information contained in this prospectus or incorporated by reference in this prospectus. We incorporate by reference into this prospectus the following documents or information filed with the SEC (other than, in each case, documents or information therein deemed to have been furnished and not filed in accordance with SEC rules):

(a) Our Annual Report on Form 10-K for the fiscal year ended December 31, 2007 (filing date February 11, 2008: Commission File No. 000-19319);

(b) The portions of our definitive proxy statement on Schedule 14A that are deemed "filed" with the SEC under the Exchange Act (filing date April 12, 2007: Commission File No. 000-19319); and

(c) The description of our common stock and the outstanding series A junior participating preferred stock purchase rights contained in our Registration Statement on Form 8-A, including any amendment or report filed for the purpose of updating such description (filing date May 30, 1991: Commission File No. 000-19319).

In addition, all documents filed by us pursuant to Section 13(a), 13(c), 14 or 15(d) of the Exchange Act on or after the date of this prospectus and before the termination of offering under this prospectus are deemed to be incorporated by reference into, and to be a part of, this prospectus.

Our SEC filings are available to the public at the SEC's website at *http://www.sec.gov*. You also may request, orally or in writing, a copy of these documents, which will be provided to you at no cost, by contacting us at:

Vertex Pharmaceuticals Incorporated
130 Waverly Street
Cambridge, Massachusetts 02139
Attn: Investor Relations
(617) 444-6100

6,000,000 Shares

VERTEX PHARMACEUTICALS INCORPORATED

Common Stock

PROSPECTUS

Merrill Lynch & Co.

, 2008

PART II

INFORMATION NOT REQUIRED IN PROSPECTUS

Item 14. Other Expenses of Issuance and Distribution

The following table sets forth the Company's estimates of the expenses in connection with the issuance and distribution of the securities being registered, other than underwriting discounts and commissions.

SEC registration fee	$	*
Legal fees and expenses		250,000
Accounting fees and expenses		75,000
Printing Fees		200,000
Miscellaneous fees and expenses		350,000
Total	$	875,000*

* Omitted because the registration fee is being deferred pursuant to Rule 456(b).

Item 15. Indemnification of Directors and Officers.

Part D of Article 6 of the Articles of Organization of the Registrant provides that no director of the Registrant shall be personally liable to the Registrant or its stockholders for monetary damages for any breach of fiduciary duty as a director. Such paragraph provides further, however, that to the extent provided by applicable law it will not eliminate or limit the liability of a director "(i) for any breach of the director's duty of loyalty to the Registrant or its stockholders, (ii) for acts or omissions not in good faith or which involve intentional misconduct or a knowing violation of law, (iii) under Section 61 or 62 of the Massachusetts Business Corporation Law, or (iv) for any transactions from which the director derived an improper personal benefit."

Article V of the Registrant's By-laws provides that the Registrant shall indemnify each of its directors and officers (including persons who serve at the Registrant's request as a director, officer, or trustee of another organization in which the Registrant has any interest, direct or indirect, as a stockholder, creditor, or otherwise or who serve at the Registrant's request in any capacity with respect to any employee benefit plan) against all liabilities and expenses, including amounts paid in satisfaction of judgments, in compromise, or as fines and penalties, and counsel fees reasonably incurred by such director or officer in connection with the defense or disposition of any action, suit, or other proceeding, whether civil or criminal, in which such director or officer may be involved or with which such person may be threatened, while in office or thereafter, by reason of such person's being or having been such a director, officer, or trustee, except with respect to any matter as to which such director or officer shall have been adjudicated in any proceeding not to have acted in good faith in the reasonable belief that such director's or officer's action was in the best interest of the Registrant or, to the extent that such matter relates to service with respect to an employee benefit plan, in the best interest of the participants or beneficiaries of such employee benefit plan.

As to any matter disposed of by a compromise payment by any such person, pursuant to a consent decree or otherwise, Article V of the Registrant's By-laws provides that no indemnification shall be provided to such person for such payment or for any other expenses unless such compromise has been approved as in the best interests of the Registrant, after notice that it involves such indemnification (i) by a disinterested majority of the directors then in office or (ii) by a majority of the disinterested directors then in office provided there has been obtained an opinion in writing of independent legal counsel to the effect that such director or officer appeared to have acted in good

faith in the reasonable belief that such person's action as in the best interest of the Registrant, or (iii) by the holders of a majority of the outstanding stock at the time entitled to vote for directors, voting as a single class, exclusive of any stock owned by any interested director or officer.

Article V of the Registrant's By-laws provides that expenses, including counsel fees, reasonably incurred by any director or officer in connection with the defense or disposition of any such action, suit or other proceeding may be paid from time to time by the Registrant at the discretion of a majority of the disinterested directors then in office, in advance of the final disposition thereof, upon receipt of an undertaking by such director or officer to repay the Registrant the amounts so paid if it is ultimately determined that indemnification for such expenses is not authorized under Article V of the By-laws, which undertaking may be accepted by the Registrant without reference to the financial ability of such director or officer to make repayment.

Article V of the Registrant's By-laws gives the Board of Directors of the Registrant the power to authorize the purchase and maintenance of insurance, in such amounts as the Board of Directors may from time to time deem appropriate, on behalf of any person who is or was a director, officer, or agent of the Registrant, or who is or was serving at the request of the Registrant as a director, officer or agent of another organization in which the Registrant has any interest, direct or indirect, as a shareholder, creditor or otherwise, or with respect to any employee benefit plan, against any liability incurred by such person in any such capacity, or arising out of such person's status as such agent, whether or not such person is entitled to indemnification by the Registrant pursuant to Article V of otherwise and whether or not the Registrant would have the power to indemnify the person against such liability.

Subdivision E of Part 8 of the Massachusetts Business Corporation Act (the "MBCA") authorizes the provisions, described above, contained in Part D Article 6 of the Articles of Organization of the Registrant.

Sections 8.30 and 8.92 of the MBCA provide that if an officer or director discharges his duties in good faith and with the care that a person in a like position would reasonably exercise under similar circumstances and in a manner the officer or director reasonably believes to be in the best interests of the corporation, he or she will not be liable for such actions.

Item 16. Exhibits

(a) Exhibits.

Exhibit Number	Description of Document
1.1	Form of Underwriting Agreement.*
5.1	Opinion of Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C.
23.1	Consent of Ernst & Young LLP.
23.2	Consent of Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C. (included in the opinion filed as Exhibit 5.1).
24.1	Power of Attorney (included on signature page).

*

To be filed as an exhibit to a Current Report on Form 8-K.

Item 17. Undertakings

The undersigned Registrant hereby undertakes:

(1) To file, during any period in which offers or sales are being made, a post-effective amendment to this registration statement:

(i) To include any prospectus required by Section 10(a)(3) of the Securities Act of 1933;

(ii) To reflect in the prospectus any facts or events arising after the effective date of the registration statement (or the most recent post-effective amendment thereof) which, individually or in the aggregate, represent a fundamental change in the information set forth in the registration statement. Notwithstanding the foregoing, any increase or any decrease in volume of securities offered (if the total dollar value of securities offered would not exceed that which was registered) and any deviation from the low or high end of the estimated maximum offering range may be reflected in the form of prospectus filed with the Commission pursuant to Rule 424(b) if, in the aggregate, the changes in volume and price represent no more than a 20% change in the maximum aggregate offering price set forth in the "Calculation of Registration Fee" table in the effective registration statement; and

(iii) To include any material information with respect to the plan of distribution not previously disclosed in the registration statement or any material change to such information in the registration statement;

provided, however, that paragraphs (1)(i), (1)(ii) and (1)(iii) do not apply if the information required to be included in a post-effective amendment by those paragraphs is contained in reports filed with or furnished to the Commission by the Registrant pursuant to Section 13 or Section 15(d) of the Securities Exchange Act of 1934 that are incorporated by reference in the registration statement, or is contained in a form of prospectus filed pursuant to Rule 424(b) that is part of the registration statement.

(2) That, for the purpose of determining any liability under the Securities Act of 1933, each such post-effective amendment shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial *bona fide* offering thereof.

(3) To remove from registration by means of a post-effective amendment any of the securities being registered which remain unsold at the termination of the offering.

(4) That, for the purpose of determining liability under the Securities Act of 1933 to any purchaser:

(i) Each prospectus filed by the Registrant pursuant to Rule 424(b)(3) shall be deemed to be part of the registration statement as of the date the filed prospectus was deemed part of and included in the registration statement; and

(ii) Each prospectus required to be filed pursuant to Rule 424(b)(2), (b)(5) or (b)(7) as part of a registration statement in reliance on Rule 430B relating to an offering made pursuant to Rule 415(a)(l)(i), (vii) or (x) for the purpose of providing the information required by Section 10(a) of the Securities Act of 1933 shall be deemed to be part of and included in the registration statement as of the earlier of the date such form of prospectus is first used after

effectiveness or the date of the first contract of sale of securities in the offering described in the prospectus. As provided in Rule 430B, for liability purposes of the issuer and any person that is at that date an underwriter, such date shall be deemed to be a new effective date of the registration statement relating to the securities in the registration statement to which the prospectus relates, and the offering of such securities at that time shall be deemed to be the initial *bona fide* offering thereof. *Provided, however*, that no statement made in a registration statement or prospectus that is part of the registration statement or made in a document incorporated or deemed incorporated by reference into the registration statement or prospectus that is part of the registration statement will, as to a purchaser with a time of contract of sale prior to such effective date, supersede or modify any statement that was made in the registration statement or prospectus that was part of the registration statement or made in any such document immediately prior to such effective date.

(5)

That, for the purpose of determining liability of a Registrant under the Securities Act of 1933 to any purchaser in the initial distribution of the securities, the undersigned Registrant undertakes that in a primary offering of securities of an undersigned Registrant pursuant to this registration statement, regardless of the underwriting method used to sell the securities to the purchaser, if the securities are offered or sold to such purchaser by means of any of the following communications, the undersigned Registrant will be a seller to the purchaser and will be considered to offer or sell such securities to such purchaser:

(i)

Any preliminary prospectus or prospectus of an undersigned Registrant relating to the offering required to be filed pursuant to Rule 424;

(ii)

Any free writing prospectus relating to the offering prepared by or on behalf of an undersigned Registrant or used or referred to by an undersigned Registrant;

(iii)

The portion of any other free writing prospectus relating to the offering containing material information about an undersigned Registrant or its securities provided by or on behalf of an undersigned Registrant; and

(iv)

Any other communication that is an offer in the offering made by an undersigned Registrant to the purchaser.

(6)

That, for purposes of determining any liability under the Securities Act of 1933, each filing of the Registrant's annual report pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934 (and, where applicable, each filing of an employee benefit plan's annual report pursuant to Section 15(d) of the Securities Exchange Act of 1934) that is incorporated by reference in the registration statement shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial *bona fide* offering thereof.

(7)

Insofar as indemnification for liabilities arising under the Securities Act of 1933 may be permitted to directors, officers and controlling persons of the Registrant pursuant to the foregoing provisions, or otherwise, the Registrant has been advised that in the opinion of the Securities and Exchange Commission such indemnification is against public policy as expressed in the Securities Act of 1933 and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities

(other than the payment by a Registrant of expenses incurred or paid by a director, officer or controlling person of a Registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, that Registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it against public policy as expressed in the Securities Act of 1933 and will be governed by the final adjudication of such issue.

SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, the Registrant certifies that it has reasonable grounds to believe that it meets all of the requirements for filing on Form S-3 and has duly caused this registration statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of Cambridge, The Commonwealth of Massachusetts, on February 11, 2008.

VERTEX PHARMACEUTICALS INCORPORATED

By: /s/ JOSHUA S. BOGER

Joshua S. Boger

President and Chief Executive Officer

We, the undersigned officers and directors of Vertex Pharmaceuticals Incorporated, hereby severally constitute and appoint Joshua S. Boger, Ian F. Smith and Valerie L. Andrews, and each of them singly (with full power to each of them to act alone), our true and lawful attorneys-in-fact and agents, with full power of substitution and resubstitution in each of them for him and in his name, place and stead, and in any and all capacities, to sign any and all amendments (including post-effective amendments) to this registration statement, and to file the same, with all exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing requisite or necessary to be done in and about the premises, as full to all intents and purposes as he might or could do in person, hereby ratifying and confirming all that said attorneys-in-fact and agents or any of them or their or his substitute or substitutes may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Act of 1933, this registration statement on Form S-3 has been signed below by the following persons in the capacities and on the dates indicated.

Signature	Title	Date
By: /s/ JOSHUA S. BOGER **Joshua S. Boger**	Director, President and Chief Executive Officer (principal executive officer)	February 11, 2008
By: /s/ IAN F. SMITH **Ian F. Smith**	Executive Vice President and Chief Financial Officer (principal financial officer)	February 11, 2008
By: /s/ JOHANNA MESSINA POWER **Johanna Messina Power**	Vice President and Corporate Controller (principal accounting officer)	February 11, 2008
By: /s/ ERIC K. BRANDT **Eric K. Brandt**	Director	February 11, 2008

By:	/s/ ROGER W. BRIMBLECOMBE **Roger W. Brimblecombe**	Director	February 11, 2008
By:	/s/ STUART J.M. COLLINSON **Stuart J.M. Collinson**	Director	February 11, 2008
By:	/s/ EUGENE H. CORDES **Eugene H. Cordes**	Director	February 11, 2008
By:	/s/ MATTHEW W. EMMENS **Matthew W. Emmens**	Director	February 11, 2008
By:	/s/ BRUCE I. SACHS **Bruce I. Sachs**	Director	February 11, 2008
By:	/s/ CHARLES A. SANDERS **Charles A. Sanders**	Director, Chairman	February 11, 2008
By:	/s/ ELAINE S. ULLIAN **Elaine S. Ullian**	Director	February 11, 2008

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