VERTEX PHARMACEUTICALS INC / MA
Form 424B2
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Filed Pursuant to Rule 424(b)(2)
Registration No. 333-149161

CALCULATION OF REGISTRATION FEE

Title of each class of securities to be registered	Amount to be registered(1)	Proposed maximum offering price per security	Proposed maximum aggregate offering price(1)	Amount of registration fee(2)
Convertible Senior Subordinated Notes due 2013	$287,500,000	100%	$287,500,000	$11,299.00
Common Stock, $0.01 par value per share(3)	(4)	(4)	(4)	(5)

(1) Includes notes that may be purchased by the underwriters pursuant to their option to purchase additional notes to cover overallotments.

(2) This filing fee is calculated in accordance with Rule 457(r) and relates to the Registration Statement on Form S-3 (File No. 333-149161) filed by the Registrant on February 11, 2008.

(3) Each share of common stock includes a right to purchase 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.

(4) An indeterminate number of shares of common stock may be issued from time to time upon conversion of the convertible senior subordinated notes due 2013.

(5) No additional consideration will be received for the common stock issuable upon conversion of the convertible senior subordinated notes due 2013. No additional registration fee is required pursuant to Rule 457(i) under the Securities Act.

PROSPECTUS

$250,000,000

VERTEX PHARMACEUTICALS INCORPORATED

4.75% Convertible Senior Subordinated Notes due 2013

We are offering $250,000,000 of convertible notes. The notes will bear interest at the rate of 4.75% per year, payable in cash semiannually in arrears on February 15 and August 15 of each year, beginning on August 15, 2008. The notes will mature on February 15, 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 43.2171 shares per $1,000 principal amount of notes, which is equal to a conversion price of approximately $23.14 per share, subject to adjustment.

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 amount thereof, together with accrued and unpaid interest, if any, to, but excluding, the repurchase date. 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.

On or after February 15, 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.

Our common stock is listed on the Nasdaq Global Select Market under the symbol "VRTX." On February 12, 2008, the last sale price for our common stock as reported on the Nasdaq Global Select Market was $17.14 per share.

Concurrently with this offering, we are offering 6,000,000 shares of our common stock (or a total of 6,900,000 shares if the underwriters exercise their overallotment option in full) pursuant to a separate registration statement and prospectus. Although this note offering is not contingent upon the common stock offering and the common stock offering is not contingent upon this note offering, we expect to raise approximately $352,840,000 in aggregate gross proceeds from the two offerings. See "Concurrent Common Stock Offering."

Investing in the notes involves risks. See "Risk Factors" beginning on page 11 of this prospectus.

	Per Note	Total
Public offering price	100%	$250,000,000
Underwriting discount	3%	$7,500,000
Proceeds, before expenses, to Vertex	97%	$242,500,000

We have granted the underwriters an option to purchase up to an additional $37,500,000 principal amount of the notes 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 notes will be ready for delivery in book entry form only through the facilities of the Depository Trust Company on or about February 19, 2008.

Merrill Lynch & Co.

Goldman, Sachs & Co.

Morgan Stanley

JPMorgan

The date of this prospectus is February 12, 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 the notes. 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 notes only in jurisdictions where offers and sales are permitted. The distribution of this prospectus and the offering of the notes 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 notes 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 the notes. 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 complementary 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, will receive 24 weeks 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 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 levels of 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 that, 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

The following is a brief summary of the terms of this offering. For a complete description of the terms of the notes, see "Description of the Notes" in this prospectus.

Issuer	Vertex Pharmaceuticals Incorporated
Notes to be offered	$250.0 million aggregate principal amount, or $287.5 million if the underwriters exercise their option to purchase additional notes in full, of convertible senior subordinated notes due 2013.
Maturity date	February 15, 2013.
Interest and payment dates	4.75% per year on the outstanding principal amount, payable semiannually in arrears in cash on February 15 and August 15 of each year, beginning August 15, 2008.
Conversion rights	The notes are convertible, at the option of the holder, at any time on or prior to the close of business on the second business day immediately preceding the stated maturity date, into shares of our common stock at a conversion rate of 43.2171 shares per $1,000 principal amount of notes, which is equal to a conversion price of approximately $23.14 per share. The conversion rate is subject to adjustment in certain circumstances.
Redemption at our option	On or after February 15, 2010, we may redeem the notes, in whole or in part, at our option at any time or from time to time at the redemption prices set forth herein, plus accrued and unpaid interest thereon (if any) to, but excluding, the redemption date.
Make-whole premium upon a fundamental change	If a fundamental change (as described in this prospectus) described under clauses (1) or (2) of the definition of a change in control described below under "Description of the Notes Repurchase at Option of Holders Upon a Fundamental Change," we will pay a make-whole premium on notes converted in connection with a fundamental change by increasing the conversion rate on such notes. The amount of the make-whole premium, if any, will be based on our common stock price and the effective date of the fundamental change. A description of how the make-whole premium will be determined and a table showing the make-whole premium that would apply at various common stock prices and fundamental change effective dates is set forth under "Description of the Notes Make-Whole Premium Upon a Fundamental Change."
Repurchase of notes by us at the option of the holders upon a fundamental change	If we undergo a fundamental change, except in certain circumstances, each holder will have the option to require us to repurchase all or any portion of such holder's notes. The fundamental change repurchase price will be 100% of the principal amount of the notes to be repurchased plus accrued and unpaid interest, if any, to, but excluding, the repurchase date.

Ranking	The notes will be unsecured and rank subordinated to future senior debt, equally with any future senior subordinated debt, and senior to any future subordinated debt. Because the notes will be subordinated to any future senior debt, in the event of bankruptcy, liquidation, dissolution or acceleration of payment on the senior debt, holders of the notes will not receive any payment until holders of the senior debt have been paid in full. The indenture under which the notes will be issued will not prevent us or our subsidiaries from incurring additional senior debt or other obligations.
Use of Proceeds	We intend to use the net proceeds from this offering, together with the net proceeds from the concurrent common stock 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."
Denomination	The notes will be issued in minimum denominations of $1,000 and any integral multiple of $1,000.
Trading	The notes will not be listed on any securities exchange or included in any automated quotation system. The notes will be new securities for which there is currently no public market.
Nasdaq symbol for common stock	Our common stock is listed on the Nasdaq Global Select Market under the symbol "VRTX."
Risk Factors	See "Risk Factors" and other information included in this prospectus and the documents incorporated by reference in this prospectus for a discussion of factors you should carefully consider before deciding to invest in our notes.
Concurrent common stock offering	Concurrently with this offering, we are offering 6,000,000 shares of our common stock (or a total of 6,900,000 shares if the underwriters exercise their overallotment option in full) pursuant to a separate registration statement and prospectus. This note offering is not contingent upon the common stock offering and the common stock offering is not contingent upon this 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	$ 786,761
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

	December 31, 2007	
Total assets	$ 601,477	$ 928,817
Deferred revenues	$ 126,745	$ 126,745
Accrued restructuring expense	35,292	35,292
Other liabilities	148,148	148,148
Convertible Subordinated Notes (due 2013)		250,000
Collaborator development loan (due 2008)	19,997	
Stockholders' equity	271,295	368,632
Total liabilities and stockholders' equity	$ 601,477	$ 928,817

(1) Reflects the sale of $250.0 million in aggregate principal amount of notes offered hereby, after deducting the underwriting discount and estimated offering expenses, the concurrent sale of 6,000,000 shares of common stock at a public offering price of $17.14 per share, after deducting the 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 the notes 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 the notes. 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 value of the notes 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 regula