VERTEX PHARMACEUTICALS INC / MA
Form 424B5
December 02, 2009

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Filed Pursuant to Rule 424(b)(5)
Registration No. 333-153543

The information in this preliminary prospectus supplement and the accompanying prospectus is not complete and may be changed. This preliminary prospectus supplement and the accompanying prospectus are not an offer to sell nor do they seek an offer to buy these securities in any jurisdiction where such offer or sale would not be permitted.

Subject to Completion. Dated December 2, 2009.

PROSPECTUS SUPPLEMENT
(To prospectus dated September 17, 2008)

10,000,000 Shares

VERTEX PHARMACEUTICALS INCORPORATED

Common Stock

Vertex Pharmaceuticals Incorporated is offering 10,000,000 shares of its common stock to be sold in the offering.

The common stock is quoted on the Nasdaq Global Select Market under the symbol "VRTX." The last reported sale price of the common stock on December 1, 2009 was $39.86 per share.

See "Risk Factors" beginning on page S-8 of this prospectus supplement to read about factors you should consider before buying shares of the common stock.

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

	Per Share	Total
Initial price to public	$	$
Underwriting discount	$	$
Proceeds, before expenses, to Vertex	$	$

To the extent that the underwriters sell more than 10,000,000 shares of common stock, the underwriters have the option to purchase up to an additional 1,500,000 shares from us at the initial price to public less the underwriting discount.

The underwriters expect to deliver the shares against payment in New York, New York on , 2009.

Goldman, Sachs & Co.

Prospectus supplement dated , 2009.

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Prospectus Supplement

Prospectus

This document is in two parts. The first part is this prospectus supplement, which describes the specific terms of this common stock offering and also adds to and updates information contained in the accompanying prospectus and the documents incorporated by reference into the prospectus. The second part, the accompanying prospectus, gives more general information, some of which does not apply to this offering. If the description of the offering varies between this prospectus supplement and the accompanying prospectus, you should rely on the information contained in this prospectus supplement. However, if any statement in one of these documents is inconsistent with a statement in another document having a later date for example, a document incorporated by reference in this prospectus supplement or the accompanying prospectus the statement in the document having the later date modifies or supersedes the earlier statement. You should rely only on the information contained in or incorporated by reference into this prospectus supplement or contained in or incorporated by reference into the accompanying prospectus to which we have referred you. We have not authorized anyone to provide you with information that is different. The information contained in, or incorporated by reference into, this prospectus supplement and contained in, or incorporated by reference into, the accompanying prospectus is accurate only

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as of the respective dates thereof, regardless of the time of delivery of this prospectus supplement and the accompanying prospectus or of any sale of common stock. It is important for you to read and consider all information contained in this prospectus supplement and the accompanying prospectus, including the documents incorporated by reference herein and therein, in making your investment decision. You should also read and consider the information in the documents to which we have referred you under the captions "Incorporation by Reference" in this prospectus supplement and "Where You Can Find More Information" and "Incorporation by Reference" in the accompanying prospectus.

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

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PROSPECTUS SUPPLEMENT SUMMARY

This summary highlights information contained elsewhere in this prospectus supplement and the accompanying prospectus or incorporated by reference in this prospectus supplement and the accompanying prospectus. This summary does not contain all of the information that you should consider before deciding to invest in our common stock. You should read this entire prospectus supplement and the accompanying prospectus carefully, including the "Risk Factors" section contained in this prospectus supplement and our consolidated financial statements, our condensed consolidated financial statements and the respective related notes and the other documents incorporated by reference in this prospectus supplement and the accompanying prospectus. Unless we have indicated otherwise, or the context otherwise requires, references in this prospectus supplement, the accompanying prospectus or the documents incorporated by reference herein and therein to "we," "us," "our," "Vertex," and the "Company," or similar terms are to Vertex Pharmaceuticals Incorporated, a Massachusetts corporation, and its subsidiaries.

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 targets hepatitis C virus, or HCV, infection. Telaprevir is being evaluated in a fully-enrolled registration program focused on treatment-naïve and treatment-failure patients infected with genotype 1 HCV. We currently intend to submit a new drug application, or NDA, for telaprevir in the United States in the second half of 2010, assuming the successful completion of the registration program. We also are developing, among other compounds, VX-770 and VX-809, drug candidates for the treatment of patients with cystic fibrosis, or CF, and VX-509, a Janus kinase 3, or JAK3, inhibitor designed for the treatment of immune-mediated inflammatory diseases including rheumatoid arthritis. In the second quarter of 2009, we began a registration program for VX-770 that focuses on patients with CF who have the G551D mutation in the gene responsible for CF. We intend to continue investing in our research programs with the goal of adding to our pipeline drug candidates designed to address significant unmet medical needs and provide substantial benefits to patients.

HCV

HCV infection is a life-threatening disease suffered by approximately 3.2 million people in the United States that causes inflammation of the liver, significantly increasing the risk that a patient will develop liver failure or liver cancer. Genotype 1 HCV is the most prevalent HCV genotype in North America, the European Union and Japan.

Telaprevir

Telaprevir, our oral HCV protease inhibitor, is being investigated in a registration program focused on patients with genotype 1 HCV infection that includes ADVANCE and ILLUMINATE, which are Phase 3 clinical trials in treatment-naïve patients infected with genotype 1 HCV, and REALIZE, which is a Phase 3 clinical trial in patients infected with genotype 1 HCV who failed prior treatment with pegylated-interferon, or peg-IFN, and ribavirin, or RBV. Enrollment in ADVANCE, ILLUMINATE and REALIZE was completed in October 2008, January 2009 and February 2009, respectively. Telaprevir dosing is complete in all three of these Phase 3 clinical trials. We expect to have sustained viral response, or SVR, data from the ADVANCE and ILLUMINATE clinical trials in the first half of 2010 and SVR data from the REALIZE clinical trial in mid-2010. We currently intend to submit an NDA for telaprevir in the second half of 2010, assuming the successful completion of our ongoing registration program.

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We designed our registration program based on data from our Phase 2b clinical trials, including data from our PROVE 1 and PROVE 2 clinical trials in treatment-naïve patients, in which the SVR rates in the 24-week telaprevir-based treatment arms were 61% and 69% compared to 41% and 46% in the control arms, respectively. Our registration program also is based on promising interim data from our Phase 2b clinical trial in treatment-failure patients. In addition to the clinical trials in our registration program, we and our collaborators are conducting several additional clinical trials. Our clinical development program is designed to support registration by us of telaprevir in North America and by our collaborators, Janssen Pharmaceuticals, N.V., a Johnson & Johnson company, and Mitsubishi Tanabe Pharma Corporation, in international markets.

The adverse event profile of telaprevir generally has been consistent across our Phase 2 clinical trials, which have principally involved clinical trial sites in North America and Europe. Safety data from our Phase 2 clinical trials indicated that the most common adverse events, regardless of treatment assignment, were fatigue, rash, headache and nausea. The most common adverse events reported more frequently in patients receiving telaprevir than in the control arms were gastrointestinal events, skin events rash and pruritis and anemia. There have been reports of severe rashes in clinical trials involving telaprevir-based treatments, including several reports from the clinical trials being conducted by Mitsubishi Tanabe in Japan, where telaprevir has advanced into Phase 3 clinical trials in combination with peg-IFN and RBV. Rash resulted in treatment discontinuations in the telaprevir-based treatment arms in approximately 7% of patients in PROVE 1 and PROVE 2 and 5% of patients in PROVE 3. Other adverse events reported in our Phase 2 clinical trials generally were similar in type and frequency to those seen with peg-IFN and RBV treatment.

VX-222

We are conducting a multi-dose viral kinetics clinical trial to evaluate the antiviral activity, safety, tolerability and pharmacokinetics of VX-222 in patients infected with genotype 1 HCV. VX-222 is an HCV polymerase inhibitor, which is a class of direct-acting antivirals that inhibit the ability of HCV to replicate, through a mechanism distinct from HCV protease inhibitors such as telaprevir. We acquired VX-222 in our March 2009 acquisition of ViroChem Pharma Inc. This ongoing multi-dose clinical trial of VX-222 will evaluate the antiviral activity of VX-222 dosed as monotherapy for three days in approximately 32 treatment-naïve patients infected with genotype 1 HCV. We also are conducting a drug-drug interaction clinical trial of VX-222 and telaprevir in healthy volunteers. We expect data from these clinical trials in the fourth quarter of 2009, which we expect to enable the initiation of a combination trial of telaprevir and VX-222 in patients infected with genotype 1 HCV in the first quarter of 2010, depending on the results of the ongoing trials involving VX-222.

Cystic Fibrosis

Cystic fibrosis is an inherited disorder that results in a progressive decline in lung function and a significant decrease in the life expectancy of patients with CF. The drug candidates that we are developing for CF are designed to address the underlying cause of CF by partially restoring the function of defective cystic fibrosis transmembrane conductance regulator, or CFTR, proteins in patients.

VX-770

In May 2009, we initiated a registration program, referred to as ENDEAVOR, for VX-770. The VX-770 registration program focuses on patients with the G551D mutation, which is present in approximately 4% of the CF population in the United States. ENDEAVOR consists of three clinical trials that have opened to enrollment. The primary clinical trial, which is referred to as STRIVE, is a

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Phase 3 clinical trial of VX-770 in patients 12 years of age and older with the G551D mutation on at least one of the patient's two *CFTR* genes, or alleles. The second clinical trial, which is referred to as ENVISION, is a Phase 3 clinical trial of VX-770 in patients between 6 to 11 years of age with the G551D mutation on at least one allele. The third clinical trial, which is referred to as DISCOVER, is a Phase 2 exploratory clinical trial of VX-770 in patients with CF who are 12 years of age and older and homozygous for the F508del mutation in the *CFTR* gene, which is present in approximately 85% of the patients with CF in the United States and is the most common mutation in patients with CF.

VX-809

In the first quarter of 2009, we initiated a Phase 2a clinical trial primarily designed to evaluate the safety and tolerability of multiple doses of VX-809, another drug candidate for the treatment of patients with CF. This clinical trial enrolled approximately 90 patients with CF homozygous for the F508del mutation in the *CFTR* gene. In addition to assessing safety, this Phase 2a trial will evaluate the effect of VX-809 on biomarkers of CFTR function and whether VX-809 has an effect on FEV_1, the lung function test most commonly used to monitor CF disease progression. Enrollment in this trial is complete, and we expect to obtain data from this clinical trial in early 2010.

We have initiated a drug-drug interaction clinical trial of VX-809 and VX-770. Based on *in vitro* data, we believe that there is a rationale to explore the clinical potential for combining VX-809 and VX-770 and may seek to commence a combination clinical trial in patients with CF in the second half of 2010.

Immune-mediated Inflammatory Diseases

VX-509 is a novel oral JAK3 inhibitor that we believe has the potential to be used in multiple immune-mediated inflammatory disease indications. We have completed the Phase 1 clinical trials of VX-509, including a Phase 1 single and multiple, 14-day, dose-ranging clinical trial of VX-509 in healthy volunteers. We expect to initiate a Phase 2a clinical trial of VX-509 in patients with moderate to severe rheumatoid arthritis in the first quarter of 2010. This double-blind, randomized, placebo-controlled 12-week trial is expected to enroll approximately 200 patients, and we expect that initial clinical data from this trial, including measurements of safety, tolerability and clinical activity, will be available in the second half of 2010.

Recent Developments

In October 2009, we announced data from an exploratory open-label clinical trial of telaprevir that enrolled 161 treatment-naïve patients infected with genotype 1 HCV, which we refer to as the C208 trial. The purpose of the C208 trial was to compare twice-daily dosing regimens of telaprevir 1,125 mg every 12 hours in combination with peg-IFN and RBV, with three-times daily dosing regimens 750 mg every 8 hours in combination with peg-IFN and RBV. A three-times daily dosing regimen is being used in the ongoing registration program for telaprevir and also has been used in the other clinical trials for telaprevir.

Patients received telaprevir, peg-IFN and RBV for 12 weeks followed by an additional 12 or 36 weeks of peg-IFN and RBV alone in a response-guided trial design. Patients who achieved undetectable HCV RNA <25 IU/mL, undetectable per Roche COBAS TaqMan HCV test at week 4, which is referred to as a rapid viral response, or RVR, and who maintained undetectable HCV RNA through week 20, were able to stop all treatment after 24 weeks. Patients who did not meet the response-guided criteria received a total of 48 weeks of peg-IFN and RBV therapy. 18% of patients across the treatment arms were required to continue treatment for 48 weeks.

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The following table summarizes the RVR and SVR data on an intent-to-treat basis from the C208 trial.

Telaprevir Dosing	Combination Therapy	Total Number of Patients	RVR (undetectable at week 4 on treatment)	SVR (undetectable 24 weeks after end-of-treatment)
1,125 mg every 12 hours	alfa-2a (PEGASYS)/RBV	40	83% (n=33)	83% (n=33)
1,125 mg every 12 hours	alfa-2b (PEGINTRON)/RBV	39	67% (n=26)	82% (n=32)
750 mg every 8 hours	alfa-2a (PEGASYS)/RBV	40	80% (n=32)	85% (n=34)
750 mg every 8 hours	alfa-2b (PEGINTRON)/RBV	42	69% (n=29)	81% (n=34)

The frequency and severity of adverse events and the rate of treatment discontinuations were similar to those reported in prior telaprevir trials. The most common adverse events reported in patients in this clinical trial were pruritis, nausea, rash, anemia, flu-like illness, fatigue and headache, and the adverse events were similar overall between the patient groups receiving three-times daily dosing and those receiving twice-daily dosing. Serious adverse events leading to permanent treatment discontinuation of all drugs occurred in 5% of patients and were mainly related to rash, which resulted in discontinuation of 4 out of 161, or 3%, of patients and anemia, which resulted in discontinuation of 3 out of 161, or 2%, of patients.

Corporate Information

We were incorporated in Massachusetts in 1989. Our principal executive offices are located at 130 Waverly Street, Cambridge, Massachusetts 02139. 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 is not incorporated into or a part of this prospectus supplement, the accompanying prospectus or the documents incorporated by reference herein and therein.

"Vertex" and the Vertex logo in the form appearing on the cover page of this prospectus supplement are registered trademarks of Vertex. "Lexiva" and "Telzir" are registered trademarks of GlaxoSmithKline plc. Other brands, names and trademarks contained in this prospectus supplement, the accompanying prospectus or the documents incorporated by reference herein and therein are the property of their respective owners.

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The Offering

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

Common stock offered by us	10,000,000 shares
Common stock to be outstanding after this offering	190,898,858 shares
Option to purchase additional shares	1,500,000 shares
Use of proceeds	We intend to use the net proceeds from this offering for general corporate purposes, which we expect to include investment in the development and commercialization of telaprevir and VX-770 and our other drug candidates, research expenditures, manufacture and supply of drug substances, and which may include capital expenditures, investments and potentially acquisitions. See "Use of Proceeds" on page S-28.
Risk factors	See "Risk Factors" beginning on page S-8 and other information included in this prospectus supplement 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 180,898,858 shares of common stock outstanding as of September 30, 2009. It does not include:

- 19,087,107 shares of common stock issuable upon the exercise of stock options outstanding as of September 30, 2009 at a weighted-average exercise price of $30.59 per share;
- 1,096,000 shares of common stock issuable upon the exercise of stock options granted to employees after September 30, 2009 and on or before November 20, 2009 at a weighted-average exercise price of $33.17 per share;
- 25,550 restricted shares of common stock issued to employees after September 30, 2009 and on or before November 20, 2009;
- 4,980,838 shares of common stock that were issued in November 2009 upon the exchange of $111.9 million in aggregate principal amount of our 4.75% convertible senior subordinated notes due 2013, or the 2013 Notes; and
- 1,386,015 shares of common stock that are issuable upon the conversion of the remaining $32.1 million in aggregate principal amount of the 2013 Notes.

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Summary Consolidated Financial Data

The following unaudited summary consolidated financial data for each of the three years in the period ended December 31, 2008 are derived from our audited consolidated financial statements incorporated by reference into this prospectus supplement and the accompanying prospectus. The following unaudited summary consolidated financial data for each of the nine months in the periods ended September 30, 2009 and 2008 are derived from our unaudited condensed consolidated financial statements incorporated by reference into this prospectus supplement and the accompanying prospectus. The 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 supplement from our Annual Report on Form 10-K for the year ended December 31, 2008, as filed with the Securities and Exchange Commission, or SEC, on February 17, 2009 and our unaudited condensed 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 supplement from our Quarterly Report on Form 10-Q for the period ended September 30, 2009, as filed with the SEC on November 9, 2009.

	Year Ended December 31,			Nine Months Ended September 30,	
	2008	2007	2006	2009	2008
	(In thousands, except per share amounts)				
Consolidated Statements of Operations Data:					
Revenues:					
Royalty revenues	$ 37,483	$ 47,973	$ 41,208	$ 19,891	$ 28,355
Collaborative and other research and development revenues	138,021	151,039	175,148	48,109	114,338
Total revenues	175,504	199,012	216,356	68,000	142,693
Costs and expenses:					
Royalty expenses	15,686	13,904	12,170	10,555	11,471
Research and development expenses	516,292	518,677	379,228	415,044	377,574
Sales, general and administrative expenses	101,910	79,104	50,345	97,618	71,810
Restructuring expense	4,324	7,119	3,651	4,283	2,683
Acquisition-related expenses				7,793	
Total costs and expenses	638,212	618,804	445,394	535,293	463,538
Loss from operations	(462,708)	(419,792)	(229,038)	(467,293)	(320,845)
Other income (loss)	2,857	28,513	21,101	(16,241)	3,326
Cumulative effect of a change in accounting principle			1,046		
Net loss	$ (459,851)	$ (391,279)	$ (206,891)	$ (483,534)	$ (317,519)
Basic and diluted net loss per common share	$ (3.27)	$ (3.03)	$ (1.83)	$ (2.86)	$ (2.30)
Basic and diluted weighted-average number of common shares outstanding	140,556	128,986	113,221	169,137	137,788

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	September 30, 2009		
	Actual	Pro Forma(1)	As Adjusted(2)
	(In thousands)		
Consolidated Balance Sheet Data:			
Cash, cash equivalents and marketable securities	$ 856,610	$ 856,610	$ 1,246,888
Receivable related to sale of potential future milestone payments	32,783	32,783	32,783
Other current assets	24,673	24,673	24,673
Restricted cash	30,313	30,313	30,313
Property and equipment, net	62,444	62,444	62,444
Intangible assets	525,900	525,900	525,900
Goodwill	26,102	26,102	26,102
Other non-current assets	14,666	12,168	12,168
Total assets	$ 1,573,491	$ 1,570,993	$ 1,961,271
Other liabilities	$ 150,350	$ 149,685	$ 149,685
Accrued restructuring expense	33,358	33,358	33,358
Deferred tax liability	162,503	162,503	162,503
Deferred revenues	319,536	319,536	319,536
Convertible senior subordinated notes (due February 2013)	144,000	32,071	32,071
Secured notes (due October 2012)	118,840	118,840	118,840
Liability related to sale of potential future milestone payments	36,160	36,160	36,160
Stockholders' equity	608,744	718,840	1,109,118
Total liabilities and stockholders' equity	$ 1,573,491	$ 1,570,993	$ 1,961,271

(1) Reflects the exchange of $111.9 million in aggregate principal amount of the 2013 Notes for 4,980,838 shares of our common stock in November 2009.

(2) Reflects the sale of 10,000,000 shares of our common stock offered hereby at an assumed initial price to the public of $39.86 per share, after deducting the estimated underwriting discount and offering expenses.

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RISK FACTORS

Investing in our common stock involves a high degree of risk. You should carefully consider the following risk factors and all other information contained in this prospectus supplement and the accompanying prospectus and incorporated by reference herein and therein 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 $459.9 million during the year ended December 31, 2008 and $483.5 million during the nine months ended September 30, 2009, and expect to incur significant operating losses for the remainder of 2009 and in 2010. We expect to continue to incur operating losses until we are able to obtain approval for and successfully commercialize telaprevir, because we are continuing to incur significant operating expenses as we continue the late-stage development of telaprevir and VX-770, and continue to invest in clinical development of our earlier-stage drug candidates and research activities. As a result, we believe that it is likely that our expenses will exceed our revenues at least until we begin receiving substantial product revenues. There can be no assurance that any of our drug candidates will be approved or, if approved, will be commercially successful. 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 ever.

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, our business will be materially harmed.

We are investing a substantial portion of our personnel and financial resources in the development of telaprevir, and we believe that a significant portion of the value attributed to our company by investors relates to the commercial potential of telaprevir. We expect that we will be making numerous additional investments in telaprevir in order to be prepared for the potential commercial launch of telaprevir in the United States in 2011, including the establishment of a sales force and additional investments in commercial inventory. The clinical development and commercial success of telaprevir will depend on several factors, including the following:

- successful completion of clinical trials with favorable outcomes relative to current standards of care and future competitive therapies;
- receipt and timing of marketing approvals for telaprevir from the United States Food and Drug Administration, or 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 infection by our competitors, including Merck & Co., Inc.'s (formerly Schering-Plough Corp.'s) boceprevir;

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additional discussions with the FDA and similar foreign authorities regarding the quality of our manufacturing process for telaprevir and our clinical trial results, including the results we expect to obtain by mid-2010 from our Phase 3 clinical trials of telaprevir;

establishing and maintaining commercial manufacturing arrangements for telaprevir with third-party manufacturers that are subject to extensive regulation by the FDA, and successfully monitoring those manufacturing operations to ensure they meet our standards and those of regulatory authorities, including the FDA, that extensively monitor pharmaceutical manufacturing facilities;

our ability to establish telaprevir if approved, as a significant component of any oral combination therapies that may be approved as a treatment for HCV infection;

the ability to launch commercial sales of telaprevir by us and our collaborators;

the efficacy and other characteristics, including the side-effect profile, of telaprevir relative to existing and future treatments for HCV infection;

our ability to increase awareness of the benefits of early treatment for HCV infection if telaprevir is approved, and to increase the rates of diagnosis of currently undiagnosed patients with HCV infection; and

the acceptance of telaprevir by patients, and 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. 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, including treatment reimbursement levels agreed to by third-party payors, do not meet the expectations of investors or public market analysts, the market price of our common stock would likely decline.

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 and VX-770, successfully. Due to the development efforts of our competitors, in order to be successful 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 comparable foreign 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 resource-intensive and may take 10 to 15 years or longer for each drug candidate. 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 marketed as pharmaceutical products.

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In addition to our ongoing registration programs for telaprevir and VX-770, we have ongoing and planned Phase 2 clinical trials for a number of our earlier-stage drug candidates, including a planned combination clinical trial in patients infected with HCV of telaprevir with VX-222, ongoing and planned Phase 2 clinical trials of VX-809 alone and in combination with VX-770 in patients with the most common CF mutation, and a planned Phase 2 clinical trial of VX-509 in patients with moderate to severe rheumatoid arthritis. While we are heavily dependent on the successful development of telaprevir and VX-770, the strength of our company's pipeline of drug candidates and potential drug candidates beyond telaprevir and VX-770 will depend in large part upon the outcomes of these Phase 2 clinical trials. Findings, including toxicology findings, in nonclinical studies conducted concurrently with clinical trials as well as results of our clinical trials could result in abrupt changes in our development activities, including the possible cessation of development activities associated with a particular drug candidate or program, including telaprevir and VX-770. 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 earlier-stage clinical trials. Accordingly, the results from the completed preclinical studies and clinical trials, positive results in preclinical studies and early clinical trials may not be replicated in later 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 with respect to telaprevir data regarding patients' HCV RNA levels during treatment, at the end-of-treatment or 12 weeks after completion of treatment. Interim data are subject to change, and there can be no assurances that interim data will be confirmed upon the analysis of final data. In addition, interim data with respect to patients' HCV RNA levels may not be predictive of the final SVR rates that will be achieved in the clinical trial.

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

We expect to incur substantial 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. As a result, we may raise additional capital in order to maintain adequate working capital and cash reserves to continue our diversified research, discovery and development efforts. We anticipate that we would finance any additional cash needs with some combination of:

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

cash received from existing and future collaborative agreements; and

future product sales.

While we believe that our current cash, cash equivalents and marketable securities, together with the proceeds of the offering contemplated by this prospectus supplement, would be sufficient to fund our operations for the next twelve months, we may need to raise additional capital through public offerings or private placements of our debt or equity securities. Any such capital transactions may or may not be similar to the offering contemplated by this prospectus supplement or transactions that we have completed in the past. Any equity financings would result in dilution to our then-existing security holders. Any debt financing may be on terms that, among other things, include conversion features that could result in dilution to our then-existing security holders and restrict our ability to pay interest and dividends although we do not intend to pay dividends for the

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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. Based on many factors, including general economic conditions, additional financing may not be available on acceptable terms, if at all.

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 limitations that we do not currently expect on the indicated uses for which we may market the drug. Any such limitations could 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.

We are investing significant resources in our development program for VX-770, based primarily on data from a relatively small clinical trial in which patients received VX-770 over a short duration. If we are unable to show the safety and efficacy of VX-770, or experience delays in doing so, our business could be materially harmed.

We are increasing the resources that we are investing in the development of VX-770 and began a registration program for VX-770 focused on CF patients with the G551D mutation in the first half of 2009. We initiated this registration program based primarily on data from a Phase 2a clinical trial of VX-770 in 39 patients with CF, in which patients received VX-770 over 14-day and 28-day periods. In order to receive approval for VX-770, we will need to show that VX-770 is safe and effective in a larger number of patients than were involved in the Phase 2a clinical trial over significantly longer dosing periods. In addition, our registration program for VX-770 includes pediatric patient populations in which VX-770 has not previously been studied. Since a substantial

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portion of the CF population is under age 18, VX-770's potential commercial success will be dependent on not only being able to obtain approval for adult patients, but also for pediatric patients. If we are unable to show the safety and efficacy of VX-770, or experience delays in doing so, our business could be materially harmed.

Issuances 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 September 30, 2009, we had 180.9 million shares of common stock issued and outstanding and in November 2009 we issued an additional 5.0 million shares upon the exchange of $111.9 million in aggregate principal amount of the 2013 Notes. As of September 30, 2009, we also had outstanding options to purchase approximately 19.1 million shares of common stock with a weighted-average exercise price of $30.59 per share. Outstanding vested options are likely to be exercised if the market price of our common stock exceeds the applicable exercise price. In addition, we may issue additional common stock or restricted securities in the future as part of our financing activities or business development activities and any such issuances may have a dilutive effect on existing shareholders. Although we have agreed to lock-up restrictions for a 90-day period following the offering and our officers and directors have agreed to lock-up restrictions for a 60-day period following the offering, these restrictions are subject to certain exceptions and waiver by the underwriters.

We may not be successful in developing any of the drug candidates we acquired in our March 2009 acquisition of ViroChem and, as a result, we may not realize any benefits from this acquisition and could be subject to significant impairment charges in future periods.

In March 2009, we acquired ViroChem for $100.0 million in cash and 10.7 million shares of our common stock. We acquired ViroChem primarily in order to secure rights to two HCV polymerase inhibitors, VX-222 and VX-759, as part of our strategy to pursue drug candidates that could potentially be developed in combination with telaprevir or our earlier-stage protease inhibitors. VX-222 and VX-759 were still in Phase 1 clinical development at the time of the acquisition and have only been evaluated in preclinical studies and in a limited number of patients infected with HCV. While we believe the data from the clinical trials to date, together with studies in animal models and *in vitro* data, support the development of combination therapies, there are numerous reasons why we may not be able to successfully develop a combination involving either VX-222 or VX-759, including:

- data from trials involving drug candidates separately may not be predictive of results involving drug candidates dosed in combination, including as a result of unforeseen drug interactions, which could negatively impact the efficacy and safety profile of the combination product candidate;
- positive results in small clinical trials and preclinical studies may not be predictive of results in clinical trials involving large numbers of patients; and
- favorable results of testing of or FDA approval of products of our competitors.

There can be no assurance that we will be able to successfully develop either VX-222 or VX-759 alone or in combination with telaprevir or our other HCV protease inhibitors, or at all, and if we are not successful in developing VX-222 or VX-759, we may not realize any benefits from our March 2009 acquisition.

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We allocated $525.9 million to intangible assets related to the in-process research and development associated with the ViroChem drug candidates. If the value of these drug candidates becomes impaired, we may incur significant impairment charges, including potentially the entire amount of the intangible assets reflected on our consolidated balance sheets associated with the drug candidate, in the period in which the impairment becomes known. An impairment could result from, among other things, unfavorable safety or efficacy results from clinical trials or non-clinical studies or competitive factors affecting the potential market for the drug candidate. If we incur a significant impairment charge in a future period related to the intangible assets acquired in the ViroChem transaction, the value of our common stock could decrease.

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

As of November 30, 2009, we had outstanding $32.1 million in aggregate principal amount of 2013 Notes and are obligated to repay an aggregate of $155.0 million as a result of our issuance of our secured notes due 2012. The level of our indebtedness could affect us by:

- making it more difficult to obtain additional financing for working capital, capital expenditures, debt service requirements or other purposes;
- constraining our ability to react quickly in an unfavorable economic climate or to changes in our business or the pharmaceutical industry; or
- requiring the dedication of substantial cash to service the repayment of our outstanding debt, including the semi-annual interest payments on our outstanding debt, thereby reducing the amount of cash available for other purposes.

The results from our and our collaborators' clinical development activities and the clinical development activities of our competitors are released periodically, and have often resulted in significant volatility in the price of our common stock.

We, our collaborators and our competitors periodically provide updates regarding drug development programs typically through press releases, conference calls and presentations at medical conferences. These periodic updates often include interim or final results from clinical trials conducted by us, our collaborators or our competitors and/or information about our or our competitor's expectations regarding future clinical development of our drug candidates or potentially competitive drugs or drug candidates. The timing of the release of information by us regarding our drug development programs is often beyond our control and is influenced by when we receive data from our clinical trials and by the general preference among pharmaceutical companies to disclose clinical data during medical conferences. In addition, because clinical trials of drug candidates for the treatment of HCV infection often occur over two years, the information that we, our collaborators and our competitors disclose is often based on interim data and subject to significant interpretation by investors. Any new information regarding our drug candidates or potentially competitive drugs or drug candidates, and in particular any new information regarding telaprevir and potentially competitive HCV drug candidates, can substantially affect investors' perceptions regarding our future prospects.

If clinical trials for our drug candidates are prolonged or delayed, we may be unable to commercialize our drug candidates on a timely basis or at all, 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

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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 Institutional Review Boards 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, including as a result of low numbers of patients that meet the eligibility criteria for the trial;
- 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;
- unfavorable results of clinical trials of our product candidates;
- serious and unexpected drug-related side-effects experienced by participants in our clinical trials;
- favorable results of testing of or FDA approval of products of our competitors; 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. Any such suspension could materially adversely affect 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. Any delay in the approval of any of our drug candidates, including telaprevir, could have a material adverse impact on our ability to effectively commercialize the drug candidate after approval if one or more of our competitors are able to bring competing therapies to market before or in closer proximity to our drug candidates.

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If we are unable to develop effective 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, and in particular telaprevir, 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. We will need to either develop marketing capabilities and an independent sales force or enter into arrangements with third parties to sell and market 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 specialized sales force, which will require substantial efforts and significant management and financial resources. In addition, if VX-770 is approved, we would also need to establish a small sales force in North America and Europe for VX-770. While we intend to stage our commitments to the extent possible in consideration of the development timelines, in order to support an effective launch of telaprevir, we will need to make significant financial commitments to our marketing organization prior to receiving regulatory approval. 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 very high 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 and Aurora kinase inhibitors. 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.

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 assurances can be given that telaprevir will be approved for marketing prior to competing therapies, including Merck's boceprevir, 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 Merck, Bristol-Myers Squibb, GlaxoSmithKline, Pfizer, Roche, Amgen, Novartis and Johnson & Johnson 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

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compete with respect to manufacturing efficiency and sales and marketing capabilities, areas in which we currently have limited experience.

We are aware of a number of companies that are developing new treatments for HCV infection including protease inhibitor compounds like telaprevir, such as Merck's boceprevir, polymerase inhibitor compounds, NS5A 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 competing therapies could be approved prior to or shortly after we obtain such approval for telaprevir, which we believe may negatively impact telaprevir sales.

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. We believe that effectively marketing telaprevir, if it is approved, and our other drug candidates, if any of them are approved, will require substantial efforts, both prior to launch and after approval. Physicians may elect not to recommend our drugs for a variety of reasons including:

- the anticipated 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

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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.

If we acquire or license technologies, resources or drug candidates, we will incur a variety of costs and may never realize benefits from the transaction.

If appropriate opportunities become available, we might attempt to license or acquire technologies, resources and drugs or drug candidates, including potentially complimentary HCV therapies. The process of negotiating the license or acquisition might result in operating difficulties and expenditures and, whether or not any such transaction is ever consummated, might require significant management attention that would otherwise be available for ongoing development of our business. Moreover, even if we complete a license or other transaction, we might never realize the anticipated benefits of the transaction. Future licenses or acquisitions could result in potentially dilutive issuances of equity securities, the incurrence of debt, contingent liabilities, or impairment expenses related to goodwill, and impairment or amortization expenses related to other intangible assets, which could harm our financial condition.

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

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our drug candidates become commercially available. Drugs are more widely used by patients once approval has been obtained, therefore, 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 manufacturing 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/or 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 collaboration with Merck for Aurora kinase inhibitors for the treatment of cancer.

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.

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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 or may have insufficient resources to effectively develop our drug candidates. 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 fully 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. 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 and could adversely affect our revenues and net loss. As part of our ongoing strategy, 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 may seek a collaborator for our JAK3 inhibitors, including VX-509. 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. 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 are incurring significant costs to obtain a commercial supply of telaprevir, including $17.4 million in the year ended December 31, 2008 and $14.3 million in the nine months ended September 30, 2009, and expect these costs to increase as

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we near the potential launch of telaprevir. Our engagement in these resource-intensive activities 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 supply disruptions outside of our control.

We currently rely 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, we may be subject to significant supply disruptions outside of our control. Our supply chain for sourcing raw materials and manufacturing drug product ready for distribution is a multi-step international endeavor in which we rely on third-party contract manufacturers in Asia for the supply of raw materials, and in the European Union and the United States for the application of specific manufacturing processes for the conversion of raw materials into drug substance and drug substance into final dosage form. Establishing and managing this global supply chain requires significant financial commitments, experienced personnel and the creation or expansion of numerous third-party contractual relationships. There can be no assurance that we will be able to establish and maintain commercial supply chains on commercially reasonable terms, or at all, in order to support a timely launch of telaprevir or any of our other drug candidates.

We currently require for our own use, and are responsible to Janssen and Mitsubishi Tanabe for, a supply of telaprevir for clinical trials in North America, the European Union and the Far East, respectively. We will require a supply of telaprevir for sale in North America if we are successful in obtaining marketing approval. We have transferred 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 supply source of drug substance for us. While we believe there are multiple third parties capable of providing most of the materials and services we need in order to manufacture and distribute telaprevir, and supply of materials which cannot be second-sourced can be managed with inventory planning, there is a risk that we may underestimate or overestimate demand, and the manufacturing capacity, for which we planned and contracted with third-party manufacturers, may not be sufficient or may result in more inventory than is necessary. In addition, because of the significant lead times involved in our supply chain for telaprevir, we may have less flexibility to adjust our supply in response to changes in demand than if we had shorter lead times.

We currently require a supply of VX-770 for clinical trials in North America and Europe, and will require a supply of VX-770 for sale in North America and Europe, if we are successful in obtaining marketing approval of this drug candidate. We are manufacturing VX-770 through our third-party manufacturer network to meet our clinical supply needs. Over the next several years, we will need to expand our relationships with the third-party manufacturers that comprise our supply chain for telaprevir or establish new relationships with third-party manufacturers in order to establish a supply

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chain for VX-770 and support the potential commercial launch and subsequent commercial supply of VX-770.

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 re-evaluate 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, to help manage our clinical trial process and on 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. If clinical trials are not conducted in accordance with our contractual expectations or regulatory requirements, action by regulatory authorities might significantly and adversely affect the conduct or progress of these trials. Accordingly, our efforts to obtain regulatory approvals for and commercialize our drug candidates could be delayed.

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 Asia and the 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;

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- 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, or at all, 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 16% in 2008, and we are experiencing additional growth in 2009. 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 need to attract and retain employees with experience in these fields. 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

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parts of the country to these areas. 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 to hire qualified personnel or 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 effectively integrate key employees could negatively impact our business and future growth.

Our future success will depend in large part on our ability to retain the services of our key scientific and management personnel and to integrate new scientific and management personnel into our business. As we expand our capabilities in anticipation of the possible launch of commercial products, a loss of key personnel or a failure to properly integrate new personnel could be disruptive. 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. A failure to retain, as well as hire, train and effectively integrate into our organization a sufficient number of qualified scientists, professionals, sales personnel and senior management 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 issued patents and 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. In particular, we believe that composition-of-matter claims are generally the most significant patent claims for that segment of the pharmaceutical industry that focuses on small molecule drug candidates that are new chemical compounds. While we currently have patents or patent applications with composition-of-matter claims for each of our more advanced clinical drug candidates only a portion of these patents have been granted at this time. 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.

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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, clinical testing, 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 or effectuate a business combination involving Vertex.

Our corporate charter and by-law provisions, Massachusetts state laws and our 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 our 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

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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 December 1, 2009, our common stock traded between $13.84 and $41.75 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;

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

general worldwide or national economic, political and capital market conditions.

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 not occupying the entire 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 part 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.

Risks Related to This Offering

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

We expect to use the net proceeds from this offering for general corporate purposes and have not designated any portion of the net proceeds for any particular purpose. See "Use of Proceeds"

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on page S-28. Accordingly, our management will have broad discretion as to the application of the net proceeds from this offering and could use them for purposes other than those contemplated at the time of this offering. Our management may use the net proceeds from this offering for corporate purposes that may not yield profitable results or increase our market value.

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 initial price to the public of $39.86 per share, if you purchase shares of common stock in this offering, you will suffer immediate and substantial dilution of $37.59 per share in the net tangible book value of the common stock. If the underwriters exercise their option to purchase additional shares, you will experience additional dilution. See "Dilution" on page S-29 for a more detailed discussion of the dilution you will incur in this offering.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus supplement, the accompanying prospectus and the documents incorporated by reference herein and therein 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 regarding:

- our expectations regarding clinical trials, development timelines and regulatory authority filings for telaprevir, VX-770, VX-809, VX-509, VX-222 and other drug candidates under development by us and our collaborators including our intention to submit an NDA for telaprevir in the United States in the second half of 2010 and regarding the potential commercial launch of telaprevir in the United States;

- our expectations regarding the expected date by which SVR data will be available and/or publicly announced for our ADVANCE, REALIZE and ILLUMINATE trials, and 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 be completed and the expected date interim data and/or final data will be available and/or publicly announced for our ongoing clinical trials in the ENDEAVOR registration program for VX-770, including the STRIVE, ENVISION and DISCOVER trials and for the planned and ongoing clinical trials of VX-809, VX-222 and VX-509 and our other drug candidates under development by us and our collaborators;

- expectations regarding the amount of, timing of and trends with respect to our revenues, our costs and expenses and other gains and losses, including those related to the intangible assets associated with the ViroChem acquisition and to the liabilities we recorded in connection with the financial transactions that we entered into in September 2009;

- our belief that if we are able to successfully commercialize telaprevir in accordance with current development timelines, we will begin receiving cash flows from the sale of telaprevir in 2011;

- 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 applications for marketing approval for telaprevir and VX-770;

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our plan to begin clinical evaluation of novel combination regimens of telaprevir with VX-222 and the timing thereof and the possibility that we will begin evaluation of combination regimens of VX-770 and VX-809 in patients with CF in the second half of 2010;

our expectation that we will conduct several significant clinical trials that we believe will provide meaningful information regarding a number of our earlier-stage drug candidates;

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

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 a treatment of those drug candidates;

our ability to successfully market telaprevir and VX-770 or any of our other drug candidates if we are able to obtain regulatory approval;

the focus of our drug development efforts and our financial and management resources and our plan to invest significant resources in telaprevir and our other drug candidates;

the establishment, development and maintenance of collaborative relationships;

potential business development activities, including with respect to our JAK3 program;

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

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

our liquidity and our expectations regarding our needs for and ability to raise additional capital; and

the amount, and our expected uses, of the net proceeds of this offering.

In some cases, you can identify forward-looking statements by terminology such as "may," "will," "should," "expects," "anticipates," "believes," "estimates," "predicts," "potential," "intends," 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. In addition, the forward-looking statements contained herein represent our estimate only as of the date of this prospectus supplement and should not be relied upon as representing our estimate as of any subsequent date. While we may elect to update these forward-looking statements at some point in the future, we specifically disclaim any obligation to do so to reflect actual results, changes in assumptions or changes in other factors affecting such forward-looking statements. Before deciding to purchase our securities you should carefully consider the risks described in the "Risk Factors" section, in addition to the information set forth in this prospectus supplement, the accompanying prospectus and in the documents incorporated by reference herein and therein. Although we believe that the expectations reflected in the forward-looking statements are reasonable, we cannot guarantee future results, levels of activity, performance or achievements.

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USE OF PROCEEDS

We estimate that the net proceeds we will receive from this offering, assuming an initial price to the public of $39.86 per share, will be approximately $390.3 million (or $448.9 million if the underwriters exercise their option to purchase additional shares 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.

We intend to use the net proceeds from this offering for general corporate purposes, which we expect to include investment in the development and commercialization of telaprevir and VX-770, clinical trial expenditures and other development expenses for telaprevir and VX-770 and our other drug candidates, research expenditures, manufacture and supply of drug substances, 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 and the expected corporate purposes listed above may change at any time. As a result, our management will have broad discretion to allocate the net proceeds from this offering. 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.

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DILUTION

If you purchase our common stock in this offering, your interest will be diluted to the extent of the difference between the initial price to the public per share and the net tangible book value per share of our common stock after this offering. We calculate net tangible book value 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 intangible assets, goodwill and deferred debt issuance costs and royalty and milestone sale transaction expenses included in other assets on our condensed consolidated balance sheet at September 30, 2009. In addition, these calculations do not reflect our issuance of 4,980,838 shares of common stock in November 2009 upon the exchange of $111.9 million in aggregate principal amount of the 2013 Notes.

Our net tangible book value at September 30, 2009 was $43.6 million, or $0.24 per share, based on 180.9 million shares of our common stock outstanding. After giving effect to the sale of 10,000,000 shares of common stock by us at an assumed initial price to the public of $39.86 per share, less the estimated underwriting discount and offering expenses, our net tangible book value at September 30, 2009 would be $433.9 million, or $2.27 per share. This represents an immediate increase in net tangible book value of $2.03 per share to existing stockholders and an immediate dilution of $37.59 per share to investors in this offering. The following table illustrates this per share dilution:

Assumed initial price to the public per share		$ 39.86
Net tangible book value per share as of September 30, 2009	$ 0.24	
Increase per share attributable to new investors purchasing shares in this offering	$ 2.03	
Net tangible book value per share after this offering		2.27
Dilution per share to new investors		$ 37.59

A $1.00 increase in the assumed initial price to the public of $39.86 per share would increase our net tangible book value per share after this offering to $2.32 per share, representing an immediate increase in net tangible book value of $2.08 per share to existing stockholders and an immediate dilution of $38.54 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 supplement, remains the same and after deducting the estimated underwriting discount and offering expenses. A $1.00 decrease in the assumed initial price to the public of $39.86 per share would increase our net tangible book value per share after this offering to $2.22 per share, representing an immediate increase in net tangible book value of $1.98 per share to existing stockholders, and an immediate dilution of $36.64 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 supplement, 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 initial price to the public, the actual number of shares offered and other terms of this offering determined at pricing.

If the underwriters exercise their option to purchase additional shares in full, the net tangible book value per share after this offering based on an assumed initial price to the public of $39.86 per share, less the estimated underwriting discount and offering expenses, would be $2.56 per share, representing an increase to existing stockholders of $2.32 per share, and an immediate dilution of $37.30 per share to new investors.

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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 December 1, 2009 was $39.86 per share. The table below sets forth information on the range of high and low prices for our common stock during the periods indicated.

	Price Range of Common Stock	
	High	Low
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