VERTEX PHARMACEUTICALS INC / MA
Form 424B5
September 22, 2010

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Filed Pursuant to Rule 424(b)(5)
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The information in this prospectus supplement and the accompanying prospectus is not complete and may be changed. This prospectus supplement and the accompanying prospectus are not an offer to sell these securities and we are not soliciting an offer to buy these securities in any jurisdiction where the offer or sale is not permitted.

Subject to Completion
Preliminary Prospectus Supplement dated September 22, 2010

PROSPECTUS SUPPLEMENT
(To prospectus dated February 19, 2010)

$375,000,000

Vertex Pharmaceuticals Incorporated

% Convertible Senior Subordinated Notes due 2015

We are offering $375,000,000 of aggregate principal amount of % Convertible Senior Subordinated Notes due 2015. We will pay interest on the notes on April 1 and October 1 of each year beginning on April 1, 2011. The notes will mature on October 1, 2015, unless earlier redeemed or repurchased by us or converted. The notes will be our unsecured senior subordinated obligations and will rank junior in right of payment to our existing and future senior debt, equal in right of payment with our future senior subordinated debt, and senior in right of payment to our future subordinated debt. In addition, the notes will effectively rank junior in right of payment to all of our existing and future secured debt, to the extent of the value of the assets securing such debt, and to the debt and all other liabilities of our subsidiaries.

The notes are convertible, in integral multiples of $1,000 principal amount, by holders into shares of our common stock (which is equivalent to a conversion price of approximately $ per share), subject to adjustment upon certain events, at any time before the close of business on the second business day immediately preceding the stated maturity. If a holder elects to convert its notes in connection with certain changes in control, we will pay, to the extent described in this prospectus supplement, a make-whole premium by increasing the number of shares deliverable upon conversion of such notes. Our common stock is quoted on the Nasdaq Global Select Market under the symbol "VRTX." On September 21, 2010, the last reported sale price of our common stock on the

Nasdaq Global Select Market was $36.22 per share.

Holders may require us to repurchase all or any part of their notes upon the occurrence of a fundamental change, as defined in this prospectus supplement. Prior to October 1, 2013, we may redeem all or any portion of the notes, at once or over time, at a redemption price equal to 100% of the principal amount of the notes to be redeemed if the closing price of our common stock has exceeded 130% of the applicable conversion price for at least 20 trading days within a period of 30 consecutive trading days. If we elect to redeem your notes during this period, we will make an additional payment on the notes as described in this prospectus supplement. On and after October 1, 2013, we may redeem all or any portion of the notes, at once or over time, at redemption prices set out under "Description of the Notes Redemption at Our Option."

See "Risk Factors" beginning on page S-10 of this prospectus supplement to read about factors you should consider before buying the notes.

	Per Note	Total
Public offering price(1)	%	$
Underwriting discount	%	$
Proceeds, before expenses, to us	%	$

(1) Plus accrued interest from , 2010, if settlement occurs after that date

To the extent that the underwriter sells more than $375,000,000 in principal amount of the notes, the underwriter has the option to purchase up to an additional $25,000,000 in principal amount of the notes from us at the public offering price less the underwriting discount.

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.

The notes will be ready for delivery in book-entry form only through the facilities of The Depository Trust Company for the accounts of its participants on or about , 2010.

BofA Merrill Lynch

The date of this prospectus supplement is September , 2010.

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This document is in two parts. The first part is this prospectus supplement, which describes the specific terms of this note 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 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 the notes. 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 notes 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 notes 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 notes 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 the notes. 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. We have evaluated telaprevir, our lead drug candidate, in a registration program focused on treatment-naïve patients with hepatitis C virus, or HCV, infection and patients with HCV infection who have failed to achieve a sustained viral response, or SVR, with prior interferon-based treatment. We reported positive data from this registration program in the second and third quarters of 2010, and we intend to complete the submission of our new drug application, or NDA, for telaprevir in the United States in the fourth quarter of 2010. We are pursuing a number of other clinical development programs, including a registration program for VX-770, the lead drug candidate in our cystic fibrosis, or CF, program. We plan to continue investing in our research and development programs and to develop selected drug candidates that emerge from those programs, alone or with third-party collaborators.

Telaprevir

Our registration program for telaprevir, an HCV protease inhibitor, consists of two Phase 3 clinical trials, ADVANCE and ILLUMINATE, in treatment-naïve patients infected with genotype 1 HCV and a Phase 3 clinical trial, REALIZE, in patients infected with genotype 1 HCV who failed to achieve an SVR with prior interferon-based treatment. This clinical development program was designed to support registration by us of telaprevir in North America and by our collaborator, Janssen Pharmaceuticals, N.V., or Janssen, a Johnson & Johnson company, in the European Union and other international markets. An additional collaborator, Mitsubishi Tanabe Pharma Corporation, is responsible for the commercialization of telaprevir in Japan and specified other countries in the Far East.

As part of our rolling NDA submission with the United States Food and Drug Administration, or FDA, we have submitted our chemistry, manufacturing and controls (CMC) package and nonclinical package. We intend to complete the submission of the NDA for telaprevir in the fourth quarter of 2010. Janssen has indicated that it plans to submit its marketing authorization application, or MAA, for telaprevir to the European Medicines Evaluation Agency, or EMEA, in the fourth quarter of 2010.

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REALIZE

REALIZE was a pivotal three-arm double-blinded placebo-controlled clinical trial of telaprevir-based treatment regimens that enrolled 662 patients with genotype 1 HCV infection who failed to achieve an SVR after treatment with pegylated-interferon, or peg-IFN, and ribavirin, or RBV. Patients were randomized 2:2:1 to the two telaprevir-based treatment arms and the control arm, respectively. REALIZE included the following patient groups:

null responders those patients who experienced less than a 2 $\log_{10}$ reduction in HCV RNA levels at week 12 of prior therapy;

partial responders those patients who experienced at least a 2 $\log_{10}$ reduction in HCV RNA levels at week 12, but who failed to achieve undetectable HCV RNA levels by week 24 in their prior course of therapy; and

relapsers those patients who experienced undetectable HCV RNA levels at the completion of at least 42 weeks of prior treatment, but who relapsed after treatment ended.

REALIZE is the only Phase 3 clinical trial of an HCV protease inhibitor to enroll null responders. REALIZE's primary endpoint was SVR, defined as the percentage of patients who had undetectable HCV RNA levels both at the end of treatment and 24 weeks after the end of treatment, on an intent-to-treat basis in each of the two telaprevir-based treatment arms compared to the control arm, as well as across the three subgroups of patients in the trial arms. One of the two telaprevir-based treatment arms evaluated a delayed-start approach in which patients received four weeks of pre-treatment with peg-IFN and RBV prior to adding telaprevir. The secondary endpoint was the safety of telaprevir when dosed in combination with peg-IFN and RBV.

The following table sets forth the SVR rates on an intent-to-treat basis for patients in the control arm and the combined telaprevir-based treatment arms. In addition, the table includes a supplemental analysis of the SVR rates on an intent-to-treat basis of the combined relapsers and the partial responders in each of the control arm and the combined telaprevir-based treatment arms.

	Relapsers	Partial Responders	Null Responders	Overall
Telaprevir-based treatment arms	86% (245/286)	57% (55/97)	31% (46/147)	65% (346/530)
	Pooled Analysis 78% (300/383)			
Control arm	24% (16/68)	15% (4/27)	5% (2/37)	17% (22/132)
	Pooled Analysis: 21% (20/95)			

The table below sets forth the SVR rates on an intent-to-treat basis in each of the two telaprevir-based treatment arms and the control arm, as well as across the three subgroups of patients.

	Relapsers	Partial Responders	Null Responders	Overall
Telaprevir-based treatment arm (simultaneous start):				
telaprevir in combination with peg-IFN and RBV for 12 weeks, followed by peg-IFN combined with RBV for 36 weeks	83%	59%	29%	64%
Telaprevir-based treatment arm (delayed start):				
peg-IFN and RBV for 4 weeks, followed by telaprevir in combination with peg-IFN and RBV for 12 weeks, followed by peg-IFN combined with RBV for 32 weeks	88%	54%	33%	66%
Control arm:				
peg-IFN combined with RBV for 48 weeks	24%	15%	5%	17%

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ADVANCE

ADVANCE was a pivotal three-arm double-blinded placebo-controlled clinical trial that enrolled 1,095 treatment-naïve patients with genotype 1 HCV infection. ADVANCE had two telaprevir-based treatment arms, one in which patients received 12 weeks of telaprevir-based triple combination therapy and one in which patients received 8 weeks of telaprevir-based triple combination therapy, in each case taking peg-IFN and RBV for a period of time after completing telaprevir-dosing. Patients in both of the telaprevir-based treatment arms who met criteria for extended rapid viral response, or eRVR, completed all treatment after 24 weeks, while patients who responded to treatment but did not meet the eRVR criteria continued receiving peg-IFN and RBV for a total of 48 weeks of therapy. To satisfy our eRVR criteria, a patient must have undetectable HCV RNA levels at the end of week 4 and week 12 after the start of treatment.

The primary endpoint of ADVANCE was SVR in the telaprevir-based treatment arms compared to the control arm. The secondary endpoint was the safety of telaprevir when dosed in combination with peg-IFN and RBV. The SVR rates on an intent-to-treat basis for patients in ADVANCE are set forth in the table below.

	SVR
12-week telaprevir-based treatment arm:	
telaprevir in combination with peg-IFN and RBV for 12 weeks, followed by peg-IFN combined with RBV for 12 weeks or 36 weeks	75%
8-week telaprevir-based treatment arm:	
telaprevir in combination with peg-IFN and RBV for 8 weeks, followed by peg-IFN combined with RBV for 16 weeks or 40 weeks	69%
48-week control arm:	
48 weeks of therapy with peg-IFN and RBV	44%

ILLUMINATE

ILLUMINATE was a supplemental two-arm Phase 3 clinical trial, which included evaluation of 24-week and 48-week total treatment durations in treatment-naïve patients infected with genotype 1 HCV who achieved an eRVR in response to telaprevir-based treatment regimens. This clinical trial was a randomized, open-label trial that enrolled 540 patients. ILLUMINATE was designed to supplement SVR data obtained from ADVANCE to evaluate the benefits and risks, for patients who achieve an eRVR, of extending total treatment duration from 24 to 48 weeks through a non-inferiority evaluation of the 24 week and 48 week regimens. The following table provides SVR rates for patients who achieved an eRVR at week 4 and week 12, and remained on treatment through week 20, which was the group of patients that ILLUMINATE was designed to evaluate and the group randomized to receive either 24- or 48-weeks of total treatment.

	SVR Rate (For Patients who Achieved eRVR)	Patients with SVR/Total Patients (who Achieved eRVR)
24-week telaprevir-based treatment regimen:		
telaprevir in combination with peg-IFN and RBV for 12 weeks, followed by peg-IFN combined with RBV for 12 weeks	92%	149/162
48-week telaprevir-based treatment regimen:		
telaprevir in combination with peg-IFN and RBV for 12 weeks, followed by peg-IFN combined with RBV for 36 weeks	88%	140/160

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These data met the pre-defined non-inferiority criteria that were established to compare the 24-week regimen and the 48-week regimen. The overall SVR for the patients enrolled in ILLUMINATE on an intent-to-treat basis was 72%.

For patients who achieved an eRVR at week 4 and week 12, remained on treatment through week 20 and whose HCV levels were undetectable at the end of treatment, the relapse rate for patients who received the 24-week telaprevir-based treatment regimen was 5.7% (9/159) and the relapse rate for patients who received the 48-week telaprevir-based treatment was 1.9% (3/154).

Safety and Tolerability

The safety and tolerability profile of the telaprevir-based regimens in our Phase 3 clinical trials was similar to results reported in earlier clinical trials of telaprevir. The most common adverse events reported in the telaprevir-based treatment arms were fatigue, rash, pruritus, nausea, flu-like symptoms, headache and anemia, of which anemia, rash, pruritus and nausea occurred more frequently in the telaprevir-based treatment arms than in the control arms. The majority of these adverse events were graded mild to moderate. In all of our Phase 3 clinical trials, telaprevir was dosed for no more than 12 weeks in the telaprevir-based treatment arms and the use of erythropoiesis-stimulating agents was not allowed.

In REALIZE, adverse events leading to discontinuation of all study drugs during the telaprevir-dosing period and up to week 16 (to account for the telaprevir delayed-start arm) occurred in 4% of people in the combined telaprevir-based treatment arms and 3% in the control arm during the same period. Discontinuation of all study drugs due to anemia and rash during the telaprevir-dosing period and up to week 16 occurred in 0.6% and 0.4% of patients, respectively, in the combined telaprevir arms, while discontinuation of all study drugs due to rash and anemia did not occur in the control arm during the same period.

In ADVANCE, adverse events leading to discontinuation of all study drugs occurred in 6.9%, 7.7% and 3.6% of patients in the 12-week telaprevir-based treatment arm, the 8-week telaprevir-based treatment arm and the control arm, respectively. Discontinuation of all treatment due to rash was 1.4%, 0.5% and 0.0% in the 12-week telaprevir-based treatment arm, the 8-week telaprevir-based treatment arm and the control arm, respectively, while discontinuation due to anemia was 0.8%, 3.3% and 0.6% in the 12-week telaprevir-based treatment arm, the 8-week telaprevir-based treatment arm and the control arm, respectively.

In ILLUMINATE, adverse events leading to discontinuation of all study drugs during the 12-week telaprevir-dosing period occurred in 6.9% of people in the clinical trial. Treatment discontinuation of all study drugs due to anemia and rash occurred in 1.1% and 0.6% of people in the clinical trial, respectively, during the telaprevir-dosing period.

VX-770

We are conducting a registration program for VX-770, which is focused on patients with CF who have the G551D mutation in the gene responsible for CF. CF is an inherited disorder that results in progressive decline in lung function and a significant decrease in the life expectancy of patients with CF. The G551D mutation is present in approximately 4% of the CF population in the United States. The three clinical trials in this registration program are the Phase 3 STRIVE clinical trial in patients 12 years of age and older with the G551D mutation, the Phase 3 ENVISION clinical trial in patients between 6 to 11 years of age with the G551D mutation and the Phase 2 DISCOVER trial in patients 12 years of age and older with only the F508del mutation. We completed enrollment in STRIVE in the first quarter of 2010 and completed enrollment in ENVISION in the second quarter of 2010. In STRIVE and ENVISION, patients in VX-770 treatment arms will receive 48-weeks of treatment with VX-770. In DISCOVER, all patients have completed dosing in their 16-week treatment regimens. We

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expect that we will receive final data from the registration program in the first half of 2011, and if we believe the data from the registration program supports approval, we could submit an NDA for VX-770 to the FDA in the second half of 2011.

Earlier-stage Programs

In addition to our two registration programs, we are engaged in a number of other clinical development programs and intend to continue to invest in our research programs, with the goal of adding promising new compounds to our drug development pipeline. We are conducting a Phase 2a clinical trial to evaluate telaprevir in combination with VX-222, an investigational HCV polymerase inhibitor. We also are planning to initiate a Phase 2a clinical trial in 2010 to evaluate VX-770 in combination with VX-809 in patients with the F508del mutation, the most common mutation in the gene responsible for CF. In addition, we are conducting a Phase 2a clinical trial of VX-509 in patients with moderate-to-severe rheumatoid arthritis and a fully-enrolled Phase 2a clinical trial of VX-765 in patients with treatment-resistant epilepsy. We expect interim data from the VX-765 clinical trial in the fourth quarter of 2010 and the VX-509 clinical trial in 2011.

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.

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The Offering

Unless otherwise indicated, all information in this prospectus supplement assumes that the underwriter does not exercise its option to purchase additional notes.

Issuer	Vertex Pharmaceuticals Incorporated
Notes to be offered	$375 million aggregate principal amount, or $400 million if the underwriter exercises its option to purchase additional notes in full, of convertible senior subordinated notes due 2015.
Maturity date	October 1, 2015.
Interest and payment dates	% per year on the outstanding principal amount, payable semiannually in arrears in cash on April 1 and October 1 of each year, beginning on April 1, 2011.
Conversion rights	The notes are convertible, at the option of the holder, at any time on or prior to the close of business on the second business day immediately preceding the stated maturity date, into shares of our common stock at a conversion rate of shares per $1,000 principal amount of notes, which is equal to a conversion price of approximately $ per share. The conversion rate is subject to adjustment in certain circumstances.
Provisional redemption	Prior to October 1, 2013, we may redeem all or any portion of the notes, at once or over time, at a redemption price equal to 100% of the principal amount of the notes to be redeemed if the closing price of our common stock has exceeded 130% of the applicable conversion price (as determined based on the applicable conversion rate) for at least 20 trading days within a period of 30 consecutive trading days. We refer to redemption pursuant to this provision as provisional redemption. Upon any provisional redemption, we will make an additional payment (the "additional payment upon provisional redemption") with respect to the notes called for redemption to holders of record on the notice date in an amount equal to $ per $1,000 principal amount of notes (three years of interest on the notes), less the amount of any interest paid on the notes from their issuance, so that the interest paid by us on such notes, together with the additional payment upon provisional redemption, shall equal an amount corresponding to three years of interest on the applicable notes. We will be obligated to make the additional payment upon provisional redemption on all notes called for provisional redemption, including any notes converted after the notice date and before the provisional redemption date.

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We may, at our option, pay the additional payment upon provisional redemption in our common stock instead of cash, as long as our common stock is then listed on a national securities exchange and we register our delivery of common stock as payment under the Securities Act of 1933, as amended, or the Securities Act, and applicable state securities laws, in each case to the extent required in order to deliver unrestricted common stock. The number of shares we will be required to deliver to a holder if we pay the additional payment upon provisional redemption in our common stock would be equal to the cash amount otherwise payable divided by 98% of the 5-day volume-weighted average price (as defined under "Description of the Notes Redemption at Our Option") of a share of our common stock on the date on which we give notice of a provisional redemption.

Optional redemption

On and after October 1, 2013, we may redeem all or any portion of the notes, at once or over time, without regard to the closing price of our common stock. The notes may be redeemed for cash at the redemption prices set forth below, plus accrued and unpaid interest, if any, to, but excluding, the redemption date. The following prices are for notes redeemed during the 12-month period commencing on October 1 of the years set forth below, and are expressed as percentages of principal amount:

Year	Redemption Price
2013	%
2014	%

Make-whole premium upon a fundamental change

Upon a fundamental change described under clauses (1) or (2) of the definition of a change in control described below under "Description of the Notes Repurchase at Option of Holders Upon a Fundamental Change," we will pay a make-whole premium on notes converted in connection with a fundamental change by increasing the conversion rate on such notes.

The amount of the make-whole premium, if any, will be based on our common stock price and the effective date of the fundamental change. A description of how the make-whole premium will be determined and a table showing the make-whole premium that would apply at various common stock prices and fundamental change effective dates is set forth under "Description of the Notes Make-Whole Premium Upon a Fundamental Change."

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Repurchase of notes by us at the option of the holders upon a fundamental change	If we undergo a fundamental change, except in certain circumstances, each holder will have the option to require us to repurchase all or any portion of such holder's notes. The fundamental change repurchase price will be 100% of the principal amount of the notes to be repurchased plus accrued and unpaid interest, if any, to, but excluding, the repurchase date.
Ranking	The notes will be unsecured and rank subordinated to our existing and any future senior debt, equally with any future senior subordinated debt, and senior to any future subordinated debt. Because the notes will be subordinated to our existing and any future senior debt, in the event of bankruptcy, liquidation, dissolution or acceleration of payment on the senior debt, holders of the notes will not receive any payment until holders of the senior debt have been paid in full. The indenture under which the notes will be issued will not prevent us or our subsidiaries from incurring additional senior debt or other obligations. As of September 21, 2010, we had $155 million of outstanding debt that would be senior to the notes. In addition, the notes will effectively rank junior in right of payment to all of our existing and future secured debt to the extent of the value of the assets securing such debt, and to the debt and all other liabilities of our subsidiaries.
Use of proceeds	We intend to use the net proceeds from this offering for general corporate purposes, which we expect will 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. See "Use of Proceeds" on page S-34.
Denomination	The notes will be issued in minimum denominations of $1,000 and any integral multiple of $1,000.
Trading	The notes will not be listed on any securities exchange or included in any automated quotation system. The notes will be new securities for which there is currently no public market.
Nasdaq symbol for common stock	Our common stock is listed on the Nasdaq Global Select Market under the symbol "VRTX."
Risk factors	See "Risk Factors" beginning on page S-10 and other information included in this prospectus supplement and the documents incorporated by reference in this prospectus supplement for a discussion of factors you should carefully consider before deciding to invest in our 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, 2009 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 six months in the periods ended June 30, 2010 and 2009 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, 2009, as filed with the Securities and Exchange Commission, or SEC, on February 19, 2010 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 June 30, 2010, as filed with the SEC on August 3, 2010.

	Year Ended December 31,			Six Months Ended June 30,	
	2009	2008	2007	2010	2009
	(in thousands, except per share amounts)				
Consolidated Statements of Operations Data:					
Revenues:					
Royalty revenues	$ 28,320	$ 37,483	$ 47,973	$ 13,669	$ 12,057
Collaborative revenues	73,569	138,021	151,039	40,382	30,986
Total revenues	101,889	175,504	199,012	54,051	43,043
Costs and expenses:					
Royalty expenses	14,202	15,686	13,904	6,453	6,843
Research and development expenses	550,274	516,912	519,227	298,094	282,912
Sales, general and administrative expenses	130,192	101,290	78,554	76,467	61,046
Restructuring expense	6,240	4,324	7,119	2,892	3,509
Intangible asset impairment charges	7,200				
Acquisition-related expenses	7,793				7,793
Total costs and expenses	715,901	638,212	618,804	383,906	362,103
Loss from operations	(614,012)	(462,708)	(419,792)	(329,855)	(319,060)
Other income (loss)	(28,166)	2,857	28,513	(35,422)	(14,909)
Net loss	$ (642,178)	$ (459,851)	$ (391,279)	$ (365,277)	$ (333,969)
Basic and diluted net loss per common share	$ (3.71)	$ (3.27)	$ (3.03)	$ (1.83)	$ (2.03)
Basic and diluted weighted-average number of common shares outstanding	173,259	140,556	128,986	199,670	164,258

	June 30, 2010	
	Actual	As Adjusted(1)
	(in thousands)	

Consolidated Balance Sheet Data:		
Cash, cash equivalents and marketable securities	$ 979,145	$ 1,349,995
Intangible assets	518,700	518,700
Total assets	$ 1,654,202	$ 2,029,202
Total current liabilities	$ 292,376	$ 292,376
Deferred tax liability	160,278	160,278
Convertible senior subordinated notes (due October 2015)		375,000
Secured notes (due October 2012), excluding current portion	86,407	86,407
Liability related to sale of potential future milestone payments	63,082	63,082
Other liabilities, net of current portion	224,924	224,924
Stockholders' equity	827,135	827,135
Total liabilities and stockholders' equity	$ 1,654,202	$ 2,029,202

(1) Reflects the sale of $375 million in aggregate principal amount of notes offered hereby, after deducting estimated underwriting discount and offering expenses.

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RISK FACTORS

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

Risks Related to Our Business

We depend heavily on the success of our lead drug candidate, telaprevir, which has not yet been approved by the FDA. If we experience material delays in obtaining or are unable to obtain marketing approval for telaprevir our business will be materially harmed.

We believe that a significant portion of the value attributed to our company by investors relates to the commercial potential of telaprevir, which has not yet been approved by the FDA. While we and Janssen have completed the Phase 3 clinical trials for telaprevir, we need to obtain approval from the FDA to market telaprevir in the United States. Submitting an NDA for approval of a drug candidate, such as telaprevir, is a complex and resource intensive process. In addition, the FDA will have substantial discretion in deciding whether or not telaprevir should be granted approval based on the benefits and risks of telaprevir-based therapies in the treatment of genotype 1 HCV infection.

Obtaining approval to market telaprevir in a timely manner will depend on many factors, including the following:

- successful completion and submission of our NDA, which will require, among other things, compiling, analyzing and synthesizing data from the clinical trials of telaprevir; developing proposed labeling; and providing plans for post-marketing studies, safety monitoring and risk evaluation and mitigation;

- whether or not the FDA determines that the evidence gathered in well-controlled clinical trials, other clinical trials and nonclinical studies of telaprevir demonstrates that telaprevir is safe and effective as a treatment for genotype 1 HCV infection;

- whether or not the FDA is satisfied that the manufacturing facilities, processes and controls for telaprevir are adequate, that labeling is satisfactory and plans for post-marketing studies, safety monitoring and risk evaluation and mitigation are sufficient; and

- the timing and nature of the FDA's comments and questions regarding the NDA for telaprevir, the scheduling and recommendations of any advisory committee meeting to consider telaprevir, the time required to respond to the FDA's comments and questions and to obtain the final labeling for telaprevir and any delays that may be associated with the NDA review process.

If we experience material delays or are unable to obtain marketing approval for telaprevir in the United States, our business will be materially harmed.

In addition, Janssen will need to seek approval from the EMEA to market telaprevir in the European Union. The regulatory process in the European Union is similar to the process in the United States, but typically takes longer to complete. If Janssen experiences material delays or is unable to obtain marketing approval for telaprevir in its territories, our business may be materially harmed.

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In order to execute our business plan and achieve profitability, we need to effectively commercialize telaprevir.

We can not be sure that telaprevir will be commercially successful in the pharmaceutical market even if we and Janssen gain marketing approval for telaprevir in a timely manner. In addition to the other challenges related to a company launching its first commercial drug, we may face competition from Merck & Co., Inc., which is developing boceprevir, a potentially competitive HCV protease inhibitor. In August 2010, Merck announced that the primary endpoints in the Phase 3 clinical trials of boceprevir had been achieved and that Merck expected to complete the regulatory submissions for boceprevir in the United States and European Union in 2010.

We expect that the initial commercial success of telaprevir will depend on many factors, including the following:

- the efficacy, cost, breadth of approved use, side-effect profile and cost of co-therapies of telaprevir-based treatment regimens relative to competitive treatment regimens, including boceprevir if it is approved;
- the relative timing of marketing approvals from the FDA and comparable foreign regulatory authorities for telaprevir and boceprevir;
- the effectiveness of our commercial strategy for the launch and marketing of telaprevir;
- the number of patients with genotype 1 HCV infection, including treatment-naïve patients and patients who did not achieve an SVR with prior treatment, who seek treatment based on the SVR rates of telaprevir-based treatment regimens compared to the current standard of care or to other competitive treatment regimens, including boceprevir if it is approved;
- maintaining and successfully monitoring commercial manufacturing arrangements for telaprevir with third-party manufacturers to ensure they meet our standards and those of regulatory authorities, including the FDA, which extensively regulate and monitor pharmaceutical manufacturing facilities;
- our ability to increase awareness of the benefits of early treatment of HCV infection and to increase the rates of diagnosis of currently undiagnosed patients with genotype 1 HCV infection;
- the acceptance of telaprevir by patients, the medical community and third-party payors; and
- the effect of new health care legislation currently being implemented in the United States.

If we do not effectively commercialize telaprevir, we will not be able to execute our business plan or may not be able to achieve profitability. If our revenues, market share and/or other indicators of market acceptance of telaprevir do not meet the expectations of investors or public market analysts, the market price of our common stock would likely decline.

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 $642.2 million, $459.9 million and $391.3 million during the years ended December 31, 2009, 2008 and 2007, respectively, and $365.3 million in the six months ended June 30, 2010. We expect to continue to incur operating losses at least until we are able to obtain approval in the United States for and successfully commercialize telaprevir, because we are continuing to invest significant amounts in telaprevir and VX-770, in expanding our commercial capabilities and 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

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other things, our stockholders' equity, total assets and working capital. We expect that our results of operations will fluctuate from quarter to quarter and year to year, and that such fluctuations may be substantial. We can not provide assurance that we will ever become profitable.

If any of our drug candidates receive regulatory approval, the approved drug will be subject to ongoing regulatory review. If we or our collaborators fail to comply with continuing United States and applicable foreign regulations, the drug candidate could lose its approval or sales could be suspended, and our business would be seriously harmed.

If we or our collaborators receive regulatory approval of any of our drug candidates in development, we and our collaborators will be subject to continuing regulatory review, including the review of clinical results that are reported after our drug candidates become commercially available. Drugs are more widely used by patients once approval has been obtained and therefore side-effects and other problems may be observed after approval that were not seen or anticipated during pre-approval clinical trials or nonclinical studies. In addition, the manufacturers and the manufacturing facilities we engage to make any of our approved drugs will also be subject to periodic review and inspection by the FDA and applicable foreign regulatory authorities. 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, inability to use the facilities to make our drug or a determination that drug inventories are not safe for commercial sale. If we or our collaborators fail to comply with applicable continuing regulatory requirements, we or our collaborators may be subject to fines, suspension or withdrawal of regulatory approval, product recalls and seizures, operating restrictions and/or criminal prosecutions.

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, particularly 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 are developing marketing capabilities and will need to develop an independent sales force in order to market telaprevir in North America and have entered into collaborations in order to market telaprevir in the rest of the world if it is approved. We will need to expand these capabilities and/or enter into additional arrangements with third parties to sell and market our other drug candidates, if they are approved for sale by regulatory authorities.

In order to market telaprevir in North America if it is approved, we are building a marketing organization and will need to build a specialized sales force, which requires substantial efforts and significant management and financial resources. In addition, if VX-770 is approved, we will also need to establish a sales force in North America and Europe for VX-770. In order to support an effective launch of telaprevir, we currently are making significant financial commitments to our marketing organization. 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, difficulties in successfully developing our own marketing capabilities or independent sales force for telaprevir in North America may adversely affect an effective launch of telaprevir if it is approved for sale.

We have granted commercialization rights to other pharmaceutical companies with respect to telaprevir in specific geographic locations. To the extent that our collaborators have commercial rights to our drugs, any revenues we receive from sales of any approved drugs in those locations will depend

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primarily on the sales and marketing efforts of others, which we do not control and may not be able to effectively influence.

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 the ability of our collaborators, if any, to develop and commercialize our drug candidates, including telaprevir and VX-770, successfully. 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 resources among our various development programs and must engage in expensive and lengthy testing of our drug candidates. These discovery and development efforts for new pharmaceutical products, including follow-on compounds and/or new combination therapies, 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.

In addition to our registration programs for telaprevir and VX-770, we have ongoing and planned Phase 2a clinical trials for a number of our earlier-stage drug candidates, including an ongoing clinical trial of telaprevir in combination with VX-222 in patients infected with HCV, a planned clinical trial of VX-809 in combination with VX-770 in patients with the most common CF mutation, a clinical trial of VX-509 in patients with moderate-to-severe rheumatoid arthritis and a clinical trial of VX-765 in patients with epilepsy. While we are heavily dependent on the success of our registration programs, the strength of our company's pipeline of drug candidates, including drug candidates that could potentially be complementary to telaprevir and/or VX-770, will depend in large part upon the outcomes of these ongoing and planned Phase 2a clinical trials. Findings, including toxicology findings, in nonclinical studies conducted concurrently with clinical trials as well as results of our clinical trials could lead to abrupt changes in our development activities, including the possible cessation of development activities associated with a particular drug candidate or program. 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 later-stage clinical trials even after achieving promising results in earlier-stage clinical trials. Accordingly, the results from the completed preclinical studies and 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 or 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 our HCV drug candidates, data regarding patients' HCV RNA levels during treatment, at the completion 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.

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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 evaluation, manufacturing and commercialization. Rigorous nonclinical 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 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 and NDA process 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 nonclinical 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. Additionally, approval by foreign regulatory authority does not ensure approval by the FDA.

We depend on third-party manufacturers, including sole source suppliers, to manufacture 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 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 rely on third parties for the foreseeable future to meet our commercial supply needs for any of our drug candidates that 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. Third-party contract manufacturers, including some in Asia, supply us with raw materials, and contract manufacturers in the European Union and the United States convert these raw materials into drug substance and convert the drug substance into final dosage form. Establishing and managing this global supply chain requires a significant financial commitment and the creation and maintenance of numerous third-party contractual relationships. Although we attempt to effectively manage the business relationships with companies in our supply chain, we do not have control over their operations. There can be no assurance that we will be able to establish and maintain commercial supply chains on

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commercially reasonable terms, or at all, in order to support a timely launch of telaprevir or any of our other drug candidates.

We will require a supply of telaprevir for sale in North America if we are successful in obtaining marketing approval. We are currently exercising our contractual rights from our third-party manufacturers to provide a supply to Janssen and Mitsubishi Tanabe of telaprevir and/or materials required to manufacture telaprevir. We have completed the transfer of 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. 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. We also believe that supply of materials that can not be second-sourced can be managed with inventory planning. However, 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 require a supply of VX-770 for clinical trials in North America and Europe, and we will require a supply of VX-770 for sale in North America and Europe if we obtain marketing approval. We obtain VX-770 to meet our clinical supply needs through a third-party manufacturer network and are focused on completing the technical development work to produce VX-770 at a commercial scale. We are in the process of expanding our existing relationships with our third-party manufacturers and establishing new relationships with third-party manufacturers, in order to establish the supply chain for VX-770 that would be required to support the potential commercial launch 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 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. If any of our drug candidates are approved for sale, we similarly may be at risk of supply chain disruption for our commercial drug supply.

In the course of providing 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.

If clinical trials for a drug candidate are prolonged or delayed, our development timelines for the affected drug candidate could be extended, our costs to develop the drug candidate could increase and the competitive position of the drug candidate could be adversely affected.

We can not predict whether or not we will encounter problems with any of our completed, ongoing or planned clinical trials that will cause us or regulatory authorities to delay or suspend clinical

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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 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, unforeseen complications in testing or clinical investigator error;
- inadequate supply or deficient quality of drug candidate materials or other materials necessary for the conduct of our clinical trials;
- unfavorable FDA or foreign regulatory authority 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 scientific results from clinical trials of our drug candidates;
- serious and unexpected drug-related side-effects experienced by participants in our clinical trials;
- favorable results in testing of our competitors' drug candidates, or FDA or foreign regulatory authority approval of our competitors' products; or
- action by the FDA or a foreign regulatory authority to place 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 ongoing and 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.

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 or other applicable regulatory authority 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.

Government and other third-party payors seek to contain costs of health care through legislative and other means and if they fail to provide coverage and adequate payment rates for our future drugs, our revenues 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. Third-party payors include government health programs such as Medicare and Medicaid, managed care providers, private health insurers and other

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organizations. Governments and other third-party payors generally seek to contain or reduce the costs of health care through various means. For example, in certain foreign markets, pricing or profitability of therapeutic and other pharmaceutical products is subject to governmental control. In the United States, there have been, and we expect that there will continue to be, a number of federal and state proposals to implement similar governmental control. Additional and broad health care proposals currently are being implemented in the United States. The adoption and implementation of such proposals could have a material adverse effect on our business, financial condition and potential profitability.

In addition, 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 our investment in product development.

Reimbursement rates may vary according to the use of the drug and the clinical setting in which it is used, may be based on payments allowed for lower-cost products that are already reimbursed, may be incorporated into existing payments for other products or services, and may reflect budgetary constraints and/or imperfections in Medicare or Medicaid data used to calculate these rates. Net prices for drugs may be reduced by mandatory discounts or rebates required by government health care programs. 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.

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.

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. 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 competitors' 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 more than one year, the information that we, our collaborators and our competitors disclose may be based on interim rather than final data that may involve interpretation difficulties and may in any event not accurately reflect final results.

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. There are many other companies developing drugs for the same indications that we are pursuing. In order to compete

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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 nonclinical testing and human clinical trials of drug candidates, scaling up manufacturing operations and obtaining regulatory approvals of drugs and manufacturing facilities. Accordingly, our competitors may succeed in obtaining regulatory approval for drugs more rapidly than we do. If we obtain regulatory approval and launch commercial sales of our drug candidates, we also will compete with respect to manufacturing efficiency and sales and marketing capabilities, areas in which we currently have limited experience.

In particular, a significant number of companies are focused on developing treatments for genotype 1 HCV infection. In addition to the initial competition that we may face from Merck's boceprevir, we are aware of a number of companies that are developing new treatments for HCV infection including additional HCV protease inhibitors, HCV polymerase inhibitors, HCV NS5A inhibitors and advanced interferons. Although drug development is a lengthy process and involves a high degree of risk, at some point during the next several years one or more of these earlier-stage drug candidates may be approved by the FDA. As a result, the longer-term commercial prospects for telaprevir will depend on, among other factors:

- the efficacy, safety and other characteristics of telaprevir relative to future treatments for HCV infection;
- our ability to establish telaprevir as a significant component of any oral combination therapies that may be approved as a treatment for HCV infection; and
- the timing of marketing approvals for products being developed by our competitors, including in particular any future protease inhibitors and any oral combination therapies.

As a result, even if we are initially successful in commercializing telaprevir, it is possible that one or more of these competing therapies could be approved with a better safety and efficacy profile, which we believe could negatively impact telaprevir sales.

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 have completed enrollment in the registration program for VX-770 focused on CF patients with the G551D mutation. 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. This is a relatively small database from which to project the final outcomes of a drug development program. 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 portion of the CF population is under age 18, VX-770's potential commercial success will be dependent not only on marketing approval for adult patients, but also on approval for pediatric patients. If we are unable to show the safety and efficacy of VX-770 in the relevant patient populations, or experience delays in doing so, our business could be materially harmed.

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If physicians, patients and third-party payors do not accept our future drugs, we may be unable to generate significant revenues, if any.

Even if we obtain regulatory approval for our drug candidates, our approved drugs may not gain market acceptance among physicians and patients. 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 prescribe our drugs, and patients may elect not to request or take them, for a variety of reasons including:

- lower demonstrated clinical safety and efficacy compared to other drugs;
- prevalence and severity of adverse side-effects;
- lack of cost-effectiveness;
- lack of reimbursement availability from third-party payors;
- a decision to wait for the approval of other therapies that have significant perceived advantages over our drug candidates;
- convenience and ease of administration;
- 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 revenues.

If our processes and systems are not compliant with regulatory requirements, we could be subject to delays in submitting 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 have been 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 subject to later restrictions on manufacturing or sale, or may even risk withdrawal, which could have a material adverse effect on our business.

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We depend on our collaborators to work with us to develop, manufacture and commercialize some of our drug candidates.

We have granted development and commercialization rights for telaprevir to Janssen (worldwide other than North America and Far East) and to Mitsubishi Tanabe (Far East). We expect to receive meaningful regulatory, technical and manufacturing contributions to the telaprevir program from Janssen. The success of our telaprevir program is dependent upon the continued support that Janssen has agreed to provide, and Janssen has significant discretion in determining the efforts and resources that it will apply to the collaboration.

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 agreement with Janssen, termination without cause. Any such termination by Janssen could have a material adverse effect on our financial condition and/or delay the development and commercial sale of telaprevir in Janssen's territories.

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.

Any future 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 their collaborations with us.

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.

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 in order to submit an application for marketing approval, to build our commercial supply inventories of drug product, and to complete our scale-up of sales and marketing capacity. Our costs to obtain a commercial supply of telaprevir have included approximately $20 million, $17 million and $75 million in 2009, 2008 and 2007, respectively, and approximately $33 million for the six months ended June 30, 2010. We expect these costs to increase as 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 of telaprevir. 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 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, and build our drug supply, regulatory, development and commercial capabilities. We also expect to incur substantial administrative and commercialization

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expenses. As a result, we may raise additional capital beyond our current resources, including the net proceeds of this offering. 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 will be sufficient to fund our operations for the next twelve months, we may raise additional capital beyond the net proceeds of this offering through public offerings or private placements of our debt or equity securities. Any such capital transactions may or may not be similar to the transactions that we have completed in the past. 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 foreseeable future. Any equity financings would result in dilution to our then-existing security holders. 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.

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 and/or our earlier-stage drug candidates. VX-222 and VX-759 were still in Phase 1 clinical development at the time of the acquisition and have only been evaluated in nonclinical 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 therapy involving either VX-222 or VX-759, including:

- data from trials involving drug candidates evaluated separately may not predict possible outcomes, such as unforeseen drug interactions, from drug candidates dosed in combination, which could negatively impact the efficacy and safety profile of the combination product candidate;
- positive results in small clinical trials and nonclinical studies may not be predictive of results in clinical trials involving large numbers of patients; and
- favorable results of testing or earlier FDA or foreign regulatory approval of competitors' products.

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, and if we are not successful in developing VX-222 or VX-759, we may not realize any benefits from our March 2009 acquisition of ViroChem.

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At the time of acquisition, we allocated $525.9 million to intangible assets related to the in-process research and development associated with the ViroChem drug candidates. In the fourth quarter of 2009, we recorded expense of $7.2 million in connection with an impairment of the intangible assets related to VCH-286, a drug candidate for the treatment of HIV infection that we acquired from ViroChem. At June 30, 2010, our consolidated balance sheet included $518.7 million of intangible assets related to in-process research and development, approximately 80% of which related to VX-222 and approximately 20% of which related to VX-759. If the value of these drug candidates, and in particular VX-222, becomes impaired, we may incur significant impairment charges, including potentially the entire amount of the intangible assets reflected on our consolidated balance sheet 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 nonclinical studies or competitive factors affecting the potential market for the drug candidate. VX-759, which is considered a backup compound to VX-222, could be impaired by data pertaining to the potential successful development of VX-222, which could result in a significant impairment charge in the period in which that determination is made. 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.

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 or in specific circumstances might result in a requirement that a trial be redone. Accordingly, our efforts to obtain regulatory approvals for and commercialize our drug candidates could be delayed.

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

As of June 30, 2010, we had 202.5 million shares of common stock issued and outstanding. As of June 30, 2010, we also had outstanding options to purchase 21.0 million shares of common stock with a weighted-average exercise price of $32.07 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 stockholders. 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 options would be dilutive, and may cause the market price for a share of our common stock to decline.

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

We are obligated to repay an aggregate of $155.0 million no later than October 31, 2012 as a result of our issuance of our secured notes due 2012, or the 2012 Notes, and if we complete this offering we will have significant amounts of convertible debt outstanding. We may issue additional convertible debt or incur other types of indebtedness in the future. 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 any outstanding debt, including periodic interest payments, thereby reducing the amount of cash available for other purposes.

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. Even if we complete a license or other transaction, we might never realize the anticipated benefits of the transaction or we may incur impairment charges related to assets acquired in any such transaction. Future licenses or acquisitions could result in potentially dilutive issuances of equity securities, the incurrence of debt, the creation of contingent liabilities, impairment expenses related to goodwill, and impairment or amortization expenses related to other intangible assets, which could harm our financial condition.

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 the 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.

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We may not have the resources to develop and commercialize all the drug candidates for which we have rights and we may not be able to attract collaborators for the development and commercialization of these drug candidates.

As part of our ongoing strategy, we may seek additional collaborative arrangements. We have a number of research programs and early-stage and mid-stage clinical development programs. Depending on how these programs progress, we may not have the funding and/or the personnel to continue the development and commercialization of all of these programs internally. At any time, we may make the determination that in order to continue development of a drug candidate or program we need to identify a collaborator. Potentially, and depending on the circumstances, we may desire that a collaborator either agree to fund portions of a drug development program led by us, or agree to provide all the funding and directly lead the development and commercialization of a program. No assurance can be given that any efforts we make to seek additional collaborative arrangements will be successfully completed on a timely basis or at all. If we are unable to enter into acceptable collaborative relationships, one or more of our development programs could be delayed or terminated, and the possibility of our receiving a return on our investment in the program could be impaired.

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;
- 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 fail to expand our human resources, and in particular our commercial organization, and manage our growth effectively, our business may suffer.

We expect that if our clinical drug candidates continue to progress in development and our drug discovery efforts continue to generate drug candidates, we will require significant additional investment in personnel, management systems and resources, particularly in the build out of our

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commercial capabilities. In advance of the potential approval of telaprevir we will need to build the commercial organization that will be responsible for the commercial launch of telaprevir, if it receives marketing approval, in the United States. The number of our full-time employees increased by 6% in 2009 and 18% in 2008, and we expect to experience additional growth in 2010. 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 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 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 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 can not 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 companies in our segment of the pharmaceutical industry that focus 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 can not be certain that any patents will issue from 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.

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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.

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 can not 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.

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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 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 ours are highly volatile. From January 1, 2008 to September 21, 2010, our common stock traded between $13.84 and $44.24 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.

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Risks Related to This Offering

The notes will be unsecured and subordinated to our existing and future senior debt.

The notes will be unsecured and subordinated in right of payment to our existing and future senior debt. In the event of bankruptcy, liquidation or reorganization or upon acceleration of the notes due to an event of default and in specific other events, our assets will be available to pay obligations on the notes only after all senior debt and any secured debt has been paid in full in cash or other payment satisfactory to the holders of such indebtedness has been made. There may not be sufficient assets remaining to pay amounts due on any or all of the notes then outstanding. As a result of these payments, our general creditors may recover less, ratably, than the holders of our senior or secured debt and such general creditors may recover more, ratably, than the holders of our notes or our other subordinated debt. The indenture will not limit the creation of additional senior debt, secured debt or any other indebtedness. Any significant additional senior or secured debt incurred may also materially adversely impact our ability to service our debt, including the notes. In addition, the holders of our senior debt may, under certain circumstances, restrict or prohibit us from making payments on the notes. As of September 21, 2010, we had $155 million of outstanding debt that would be senior to the notes.

The indenture contains no financial covenants and, therefore, the note holders will not have protection against adverse changes in our business.

The indenture does not contain any financial covenants, restrict our ability to repurchase our securities, pay dividends or make restricted payments or contain covenants or other provisions to afford holders protection in the event of a transaction that substantially increases the level of our indebtedness. Furthermore, the indenture contains only limited protections in the event of a fundamental change. We could engage in many types of transactions, such as acquisitions, refinancings or recapitalizations, that could substantially affect our capital structure and the value of the notes and our common stock but would not constitute a "fundamental change" permitting holders to require us to repurchase their notes under the indenture.

The notes are effectively subordinated to the liabilities of our subsidiaries, which may reduce our ability to use the assets of our subsidiaries to make payments on the notes.

The notes are not guaranteed by our subsidiaries and therefore the notes will be effectively subordinated to all existing and future indebtedness and other liabilities of our subsidiaries. In the event of a bankruptcy, liquidation or dissolution of a subsidiary, following payment by the subsidiary of its liabilities, the subsidiary may not have sufficient assets to make payments to us. As of June 30, 2010, our subsidiaries had no indebtedness outstanding (excluding intercompany debt and liabilities and accounts payable incurred in the ordinary course of business).

We may not have the ability to repurchase notes for cash pursuant to their terms.

In certain circumstances, you may require us to repurchase all or a portion of your notes in cash. If you were to require us to repurchase your notes, including following certain fundamental changes, we can not assure you that we will be able to pay the amount required in cash. Our ability to repurchase the notes is subject to our liquidity position at the time, and may be limited by law, by the indenture, and by indebtedness and agreements that we may enter into in the future that may replace, supplement or amend our existing or future debt. In addition, if we did not have sufficient cash to meet our obligations, while we could seek to obtain third-party financing to pay for any amounts due in cash upon such events, we can not be sure that such third-party financing will be available on commercially reasonable terms, if at all. Our failure to repurchase the notes would constitute an event

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of default under the indenture under which we issued the notes, which might constitute an event of default under the terms of our other indebtedness at that time.

The make-whole premium that may be payable upon conversion in connection with a fundamental change may not adequately compensate you for the lost option time value of your notes as a result of such change of control.

If you convert notes in connection with a fundamental change, we may be required to pay a make-whole premium by increasing the conversion rate. The make-whole payment is described under "Description of the Notes Make-Whole Premium Upon a Fundamental Change." While the make-whole premium is designed to compensate you for the lost option time value of your notes as a result of a fundamental change, the make-whole amount is only an approximation of such lost value and may not adequately compensate you for such loss. In addition, in some other cases described below under "Description of the Notes Make-Whole Premium Upon a Fundamental Change," there will be no such make-whole premium.

Because your right to require us to repurchase the notes is limited, the market price of the notes may decline if we enter into a transaction that is not a fundamental change under the indenture.

The term "fundamental change" is limited and may not include every event that might cause the market price of the notes to decline. The term "fundamental change" does not apply to transactions in which all of the consideration paid for our common stock, excluding cash payments for fractional shares and cash payments made in respect of dissenters' appraisal rights, in a merger or similar transaction is publicly traded common stock. Our obligation to repurchase the notes upon a fundamental change may not preserve the value of the notes in the event of a highly leveraged transaction, reorganization, merger or similar transaction. See "Description of the Notes Repurchase at Option of Holders Upon a Fundamental Change."

Sales of the common stock issuable upon conversion of the notes could adversely affect our stock price.

Any sales in the public market of the common stock issuable upon conversion of the notes could adversely affect prevailing market prices of our common stock. In addition, the existence of the notes may encourage short selling by market participants because the conversion of the notes could depress the price of our common stock. If you convert your notes into shares of common stock, you will be subject to the same dilution as other holders of shares of common stock, including from subsequent conversions by other note holders.

The conversion rate of the notes may not be adjusted for all dilutive events.

The conversion rate of the notes is subject to adjustment for certain events, including, among others, the issuance of stock dividends on our common stock, the issuance of certain rights or warrants to acquire shares of our common stock or securities convertible into or exchangeable for shares of our common stock, subdivisions and combinations of our common stock, dividends of our capital stock, certain cash dividends and certain tender or exchange offers. The conversion rate will not be adjusted for other events, such as an issuance of shares of common stock for cash, that may adversely affect the trading price of the notes or our common stock. We can not assure you that an event that adversely affects the value of the notes, but does not result in an adjustment to the conversion rate, will not occur.

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If you hold notes, you are not entitled to any rights with respect to our common stock, but you may be subject to all changes made with respect to our common stock.

If you hold notes, you are not entitled to any rights with respect to our common stock, including, without limitation, voting rights and rights to receive any dividends or other distributions on our common stock, but you may be subject to all changes affecting the common stock. You will only be entitled to rights on the common stock if and when we deliver shares of common stock to you in exchange for your notes or in limited cases under the anti-dilution adjustments of the notes. For example, in the event that an amendment is proposed to our restated certificate of incorporation or bylaws requiring stockholder approval and the record date for determining the stockholders of record entitled to vote on the amendment occurs prior to delivery of the common stock, you will not be entitled to vote on the amendment, although you will nevertheless be subject to any changes in the powers or rights of our common stock.

We may have to pay taxes with respect to distributions on our common stock that you do not receive.

The conversion rate of the notes is subject to adjustment for certain events arising from stock splits and combinations, stock dividends and other actions by us that modify our capital structure. See "Description of the Notes Conversion Rights." If the conversion rate is adjusted, under certain circumstances you may be deemed to have received a constructive dividend from us, resulting in ordinary income to you for U.S. federal income tax purposes, even though you would not receive any cash related to that adjustment and even though you might not exercise your conversion right. Any constructive dividend deemed paid would not be eligible for preferential rates of U.S. federal income tax applicable to certain dividends and corporate holders would not be entitled to claim the dividends received deduction with respect to any such constructive dividends. Because this deemed income would not give rise to any cash from which any applicable withholding tax could be satisfied, we may offset any such withholding tax applicable to non-U.S. holders against cash payments of interest or other distributions payable on the notes. See "Material U.S. Federal Income Tax Considerations."

An active trading market for the notes may not develop, and you may not be able to sell your notes at attractive prices or at all.

The notes are a new issue of securities for which there is currently no public market, and no active trading market might ever develop. If the notes are traded after their initial issuance, they may trade at a discount from their initial offering price, depending on prevailing interest rates, the market for similar securities, the price, and volatility in the price, of shares of our common stock, our performance and other factors. In addition, we do not know whether an active trading market will develop for the notes. To the extent that an active trading market does not develop, the liquidity and trading prices for the notes may be harmed.

We have no plans to list the notes on a securities exchange. We have been advised by the underwriter that it presently intends to make a market in the notes. However, the underwriter is not obligated to do so. Any market-making activity, if initiated, may be discontinued at any time, for any reason or for no reason, without notice. If the underwriter ceases to act as the market makers for the notes, we can not assure you another firm or person will make a market in the notes.

The liquidity of any market for the notes will depend upon the number of holders of the notes, our results of operations and financial condition, the market for similar securities, the interest of securities dealers in making a market in the notes and other factors.

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We expect that the trading price of the notes will be significantly affected by the trading price of our common stock.

Because the notes are convertible into shares of our common stock, volatility or depressed prices of our common stock could have a similar effect on the trading price of the notes. This may result in greater volatility in the trading price of the notes than would be expected for any non-convertible debt securities we may issue. Holders who receive our common stock upon conversion of the notes will also be subject to the risk of volatility and depressed prices of our common stock.

An adverse rating of the notes may cause their trading prices to fall.

If a rating agency rates the notes, it may assign a rating that is lower than investors' expectations. Rating agencies also may lower ratings on the notes in the future. If rating agencies assign a lower-than-expected rating or reduce, or indicate that they may reduce, their ratings in the future, the trading price of the notes could decline significantly.

We may issue additional shares of common stock and/or securities convertible into or exchangeable or exercisable for our common stock and such issuances may materially and adversely affect the price of our notes.

We are not restricted from issuing additional shares of common stock and/or securities convertible into or exchangeable or exercisable for common stock during the term of the notes. When we issue additional such securities, the price of our common stock may be adversely affected, and in turn, the price of the notes may decline.

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 from this offering we will use for any particular purpose. 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.

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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 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 and submissions for telaprevir, VX-770, VX-222, VX-809, VX-509, VX-765, including our intention to complete the NDA submission for telaprevir in the United States in the fourth quarter of 2010, Janssen's plans to submit its MAA for telaprevir to the EMEA in the fourth quarter of 2010, and the possibility that we could submit an NDA for VX-770 in the second half of 2011;

- our belief that if we are able to successfully commercialize telaprevir in accordance with current development timelines, we will begin generating revenues and cash flows from sales of telaprevir in 2011;

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

- our expectations regarding the timing and structure of clinical trials of our other drug candidates, including VX-770, VX-222, VX-509 and VX-765 and combinations of telaprevir with VX-222 and VX-770 with VX-809 and the timing of our receipt of interim data from our VX-765 and VX-509 clinical trials;

- expectations regarding the amount of, timing of and trends with respect to our revenues, 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 September 2009 financial transactions;

- the data that will be generated by ongoing and planned clinical trials and the ability to use that data to support regulatory filings, including potential applications for marketing approval for telaprevir and VX-770;

- our plan to initiate a Phase 3b clinical trial of telaprevir to evaluate twice-daily dosing in the fourth quarter of 2010 and a Phase 2a clinical trial to evaluate combination regimens of VX-770 and VX-809 in patients with CF in 2010;

- 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;

- the focus of our drug development efforts and our financial and management resources and our plan to continue investing in our research and development programs and to develop selected drug candidates that emerge from those programs, alone or with third-party collaborators;

- the establishment, development and maintenance of collaborative relationships;

- potential business development activities;

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;

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our liquidity and our expectations regarding the possibility of raising 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 can not 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 will be approximately $370.9 million (or $395.6 million if the underwriter exercises its option to purchase additional notes 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 aggregate principal amount of the notes 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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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 September 21, 2010 was $36.22 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, 2008		
First quarter	$ 24.67	$ 13.84
Second quarter	34.97	23.40
Third quarter	35.00	24.62
Fourth quarter	33.19	18.43
Fiscal Year ended December 31, 2009		
First quarter	$ 35.97	$ 26.67
Second quarter	36.30	25.94
Third quarter	38.50	31.85
Fourth quarter	44.04	31.83
Fiscal Year ending December 31, 2010		
First quarter	$ 44.24	$ 36.15
Second quarter	41.62	32.41
Third quarter (through September 21, 2010)	37.95	31.25

DIVIDEND POLICY

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

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CAPITALIZATION

The following table sets forth our cash position and capitalization as of June 30, 2010:

- on an actual basis; and
- on an as adjusted basis to give effect to the issuance and sale of $375 million aggregate principal amount of % Convertible Senior Subordinated Notes due 2015 in this offering, after deducting the estimated underwriting discount and offering expenses.

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

	June 30, 2010	
	Actual	As adjusted
	(in thousands, except share and per share amounts)	
Cash, cash equivalents and marketable securities	$ 979,145	$ 1,349,995
Convertible Senior Subordinated Notes due 2015	$	$ 375,000
Secured notes (due October 2012)	132,183	132,183
Stockholders' equity:		
Preferred stock, $0.01 par value; 1,000,000 shares authorized; none issued and outstanding at June 30, 2010		
Common stock, $0.01 par value; 300,000,000 shares authorized at June 30, 2010; 202,532,925 shares issued and outstanding actual and as adjusted at June 30, 2010	2,007	2,007
Additional paid-in capital	3,880,746	3,880,746
Accumulated other comprehensive loss	(558)	(558)
Accumulated deficit	(3,055,060)	(3,055,060)
Total stockholders' equity	827,135	827,135
Total capitalization	$ 959,318	$ 1,334,318

The table above excludes the following shares:

- 20,993,012 shares of common stock issuable upon the exercise of stock options outstanding as of June 30, 2010 at a weighted-average exercise price of $32.07 per share;
- 1,762,320 shares of common stock issuable upon the exercise of stock options granted to employees after June 30, 2010 and on or before September 13, 2010 at a weighted-average exercise price of $33.92 per share; and
- 248,829 restricted shares of common stock issued to employees after June 30, 2010 and on or before September 13, 2010.

We are obligated to pay an aggregate of $155.0 million to retire the secured notes (due October 2012). The liability for the secured notes is reflected on the capitalization table at its book value of $132.2 million as of June 30, 2010.

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RATIO OF EARNINGS TO FIXED CHARGES

We present below the ratio of our earnings to our fixed charges, which is computed by dividing earnings before taxes adjusted for fixed charges, minority interest and capitalized interest net of amortization by fixed charges. Fixed charges include interest expense and capitalized interest incurred, plus the portion of interest expense under operating leases deemed by us to be representative of the interest factor, plus amortization of the debt issuance costs.

	Year Ended December 31,					Six Months Ended June 30,
	2009	2008	2007	2006	2005	2010
Ratio of earnings to fixed charges	(1)	(1)	(1)	(1)	(1)	(1)

(1) Due to our loss from continuing operations before cumulative effect of a change in accounting principle for the years ended December 31, 2009, 2008, 2007, 2006 and 2005, earnings were insufficient to cover fixed charges by $642.2 million, $459.9 million, $391.3 million, $207.9 million and $203.4 million, respectively and for the six months ended June 30, 2010 were insufficient to cover fixed charges by $365.3 million.

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DESCRIPTION OF THE NOTES

This description highlights some information concerning the notes to be sold in this offering. We have included in this description what we believe is the most important information concerning the notes. However, this description may not contain all of the information that is important to you. Important information is incorporated by reference into this prospectus. To understand the notes fully, you should read carefully the entire prospectus supplement and the accompanying prospectus, including "Risk Factors," the consolidated financial statements and related notes and the other information incorporated by reference. This description supplements, and should be read together with, the description of the general terms and provisions of the debt securities set forth in the accompanying prospectus under the caption "Description of Debt Securities." This Description of Notes, however, supersedes the information set forth in the accompanying prospectus under the caption "Description of Debt Securities" to the extent inconsistent with that information. The notes will not be subject to the provisions described in the accompanying prospectus under the heading "Description of Debt Securities Discharge."

We will issue the notes under the subordinated indenture described in the accompanying prospectus, to be entered into upon the closing of this offering and dated as of the closing date (which we refer to, as supplemented, as the "indenture") between us, as issuer, and U.S. Bank National Association, as trustee (which we refer to as the "trustee"), as supplemented by a supplemental indenture thereto, between the same parties, which is also to be entered into upon the closing of this offering and dated as of the closing date. Copies of the form of indenture and the notes will be made available to prospective investors upon request to us as described under "Incorporation by Reference."

We have summarized portions of the indenture and the notes below. This summary is not complete and is subject to, and qualified by references to, all of the provisions of the indenture and the notes. We urge you to read the indenture and the notes because they define your rights as a holder of the notes. Capitalized terms not defined in this description have the meanings given them in the indenture. In this section, "Vertex," "we," "our" and "us" each refers only to Vertex Pharmaceuticals Incorporated and not to any existing or future subsidiary.

General

The notes are our unsecured, senior subordinated obligations and are convertible into our common stock as described under " Conversion Rights" below. The notes are limited to an aggregate principal amount of $375 million (or $400 million if the underwriter exercises its option to purchase additional notes in full) and will mature on October 1, 2015, unless earlier converted, repurchased or redeemed.

The notes bear interest at the rate of % per year from the date of issuance of the notes, or from the most recent date to which interest had been paid or provided for. Interest is payable semi-annually in arrears on April 1 and October 1 of each year, commencing April 1, 2011 to holders of record at the close of business on the preceding March 15 and September 15, respectively. Interest is computed on the basis of a 360-day year comprised of twelve 30-day months. In the event of the maturity, conversion, redemption or purchase by us at the option of the holder of a note, interest ceases to accrue on the note under the terms of, and subject to the conditions of, the indenture.

Principal is payable, and notes may be presented for conversion, registration of transfer and exchange, without service charge, at our office or agency in New York, New York, which is initially the office or agency of the trustee in New York, New York.

The indenture does not contain any financial covenants or any restrictions on the payment of dividends, the incurrence of senior debt (as defined below) or other indebtedness, or the issuance or repurchase of securities by us. The indenture does not contain any covenants or other provisions to protect holders of the notes in the event of a highly leveraged transaction or a change of control,

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except to the extent described under " Make-Whole Premium Upon a Fundamental Change" and " Repurchase at Option of Holders Upon a Fundamental Change" below.

Ranking

The notes will be unsecured obligations and will be:

- subordinated in right of payment, as provided in the indenture, to the prior payment in full of our existing and any future senior debt,
- equal in right of payment with any future senior subordinated debt, and
- senior in right of payment to any future subordinated debt.

The notes will effectively rank junior in right of payment to all of our existing and future secured debt, to the extent of the value of the assets securing such debt, and to the debt and all other liabilities of our subsidiaries.

The indenture does not restrict the incurrence by us or our existing or future subsidiaries of indebtedness or other obligations, including additional senior debt or additional senior subordinated debt.

At June 30, 2010, we had senior debt outstanding of $155 million. The term "senior debt" means all the:

- principal of,
- premium, if any, on,
- interest, including all interest accruing subsequent to the commencement of any bankruptcy or similar proceeding, whether or not a claim for post-petition interest is allowable as a claim in any such proceeding, on,
- rent payable on,
- termination payments with respect to or in connection with, and
- fees, costs, expenses and other amounts accrued or due on or in connection with,

our Indebtedness (as defined below), whether outstanding on the date of the indenture or subsequently created, incurred, assumed, guaranteed or in effect guaranteed by us, including all deferrals, renewals, extensions or refundings of, or amendments, modifications or supplements to, the preceding, except for:

- any Indebtedness that by its terms expressly provides that such Indebtedness shall not be senior in right of payment to the notes or expressly provides that such Indebtedness is equal with or junior in right of payment to the notes, and

any Indebtedness between or among us or any of our subsidiaries, a majority of the voting stock of which we directly or indirectly own.

At June 30, 2010, we had no senior subordinated debt outstanding. The term "senior subordinated debt" means, with respect to us, the notes and any other Indebtedness of ours that specifically provides that such Indebtedness is to have the same rank as the notes in right of payment and is not subordinated by its terms in right of payment to any Indebtedness or other obligations of ours that is not senior Indebtedness.

The term "Indebtedness" means, with respect to any person:

all indebtedness, obligations and other liabilities, contingent or otherwise, of that person:

1. for borrowed money, including obligations in respect of overdrafts and any loans or advances from banks, whether or not evidenced by notes or similar instruments, or

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2. evidenced by bonds, notes or other instruments for the payment of money, or

3. incurred in connection with the acquisition of any property, services or assets, whether or not the recourse of the lender is to the whole of the assets of such person or to only a portion thereof, other than any account payable or other accrued current liability or obligation to trade creditors incurred in the ordinary course of business in connection with the obtaining of materials or services;

all reimbursement obligations and other liabilities, contingent or otherwise, of that person with respect to letters of credit, bank guarantees, bankers' acceptances, surety bonds, performance bonds or other guaranty of contractual performance;

all obligations and liabilities, contingent or otherwise, in respect of:

1. leases of such person required, in conformity with generally accepted accounting principles, to be accounted for as capitalized lease obligations on the balance sheet of such person, and

2. any lease or related documents, including a purchase agreement, in connection with the lease of real property which provides that such person is contractually obligated to purchase or cause a third party to purchase the leased property and thereby guarantee a minimum residual value of the leased property to the landlord and the obligations of such person under such lease or related document to purchase or to cause a third party to purchase the leased property;

all obligations of such person, contingent or otherwise, with respect to an interest rate or other swap, cap or collar agreement or other similar instrument or agreement or foreign currency hedge, exchange, purchase or similar instrument or agreement;

all direct or indirect guaranties or similar agreements by that person in respect of, and obligations or liabilities, contingent or otherwise, of that person to purchase or otherwise acquire or otherwise assure a creditor against loss in respect of, indebtedness, obligations or liabilities of another person of the kind described in the first four bullet points above;

any indebtedness or other obligations described in the first four bullet points above secured by any mortgage, pledge, lien or other encumbrance existing on property which is owned or held by such person, regardless of whether the indebtedness or other obligation secured thereby shall have been assumed by such person; and

any and all deferrals, renewals, extensions, refinancings, replacements, restatements and refundings of, or amendments, modifications or supplements to, any indebtedness, obligation or liability of the kind described in any of the six bullet points above.

Any senior debt will continue to be senior debt and will be entitled to the benefits of the subordination provisions irrespective of any amendment, modification or waiver of any of its terms, unless such amendment, modification or waiver expressly provides that such debt shall not be senior in right of payment to the notes.

The indenture will provide that in the event of any payment or distribution of our assets upon our dissolution, winding up, liquidation or reorganization, the holders of our senior debt shall first be paid in respect of all senior debt in full in cash or other payment satisfactory to the holders of senior debt before we make any payments of principal of, or premium, if any, and interest on the notes. In addition, if the notes are accelerated because of an event of default, the holders of any senior debt would be entitled to payment in full in cash or other payment satisfactory to the holders of senior debt of all obligations in respect of senior debt before the holders of the notes are entitled to receive any

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payment or distribution. Under the indenture, we must promptly notify holders of senior debt if payment of the notes is accelerated because of an event of default.

The indenture will further provide that if any default by us has occurred and is continuing in the payment of principal of, premium, if any, or interest on, rent or other payment obligations in respect of, any senior debt, then no payment shall be made on account of principal of, premium, if any, or interest on the notes until all such payments due in respect of that senior debt have been paid in full in cash or other payment satisfactory to the holders of that senior debt.

Because of these subordination provisions, if we become insolvent, funds which we would otherwise use to pay the holders of notes will be used to pay the holders of senior debt. As a result of these payments, holders of the notes in certain circumstances may receive less, ratably, than our general creditors whose claims are not contractually subordinated to senior debt.

The notes are effectively subordinated to all existing and future liabilities of our subsidiaries. Any right we have to receive assets of our existing subsidiaries or any future subsidiaries upon their liquidation or reorganization (and the consequent right of the holders of the notes to participate in those assets) will be effectively subordinated to the claims of that subsidiary's creditors, except to the extent that we are ourselves recognized as a creditor of that subsidiary, in which case our claims would still be subordinate to any security interests in the assets of that subsidiary and any indebtedness of that subsidiary senior to that held by us. There are no restrictions in the indenture on the ability of our existing subsidiaries or any future subsidiaries to incur indebtedness or other liabilities. As of June 30, 2010, our existing subsidiaries had no indebtedness outstanding (excluding intercompany debt and liabilities and accounts payable in the ordinary course of business).

We will be obligated to pay reasonable compensation to the trustee and to indemnify the trustee on terms reasonably satisfactory to it against any losses, liabilities or expenses it incurs in connection with its duties relating to the notes. The trustee's claims for such payments will be senior to those of holders of the notes in respect of all funds collected or held by the trustee.

Conversion Rights

Holders may convert their notes into shares of our common stock at any time prior to the close of business on the second business day immediately preceding the stated maturity date, unless the notes have been previously repurchased or redeemed. A holder may convert any outstanding notes into our common stock at an initial conversion rate of shares of our common stock for each $1,000 principal amount of notes, equal to an initial conversion price of approximately $, subject to adjustments as described below. Upon conversion in connection with a fundamental change, described under clause (1) or (2) of the definition of a change in control described below under " Repurchase at Option of Holders Upon a Fundamental Change," we will pay a make-whole premium to holders of notes upon the conversion of their notes.

The conversion rate and the equivalent conversion price in effect at any given time are referred to as the "applicable conversion rate" and the "applicable conversion price," respectively, and will be subject to adjustment as described below. A holder may convert fewer than all of such holder's notes so long as the amount of notes converted is an integral multiple of $1,000 principal amount.

Upon conversion of a note, a holder will not receive any cash payment of interest (unless in certain circumstances such conversion occurs between a regular record date and the interest payment date to which it relates) and we will not adjust the applicable conversion rate to account for accrued and unpaid interest. Our delivery to the holder of the full number of shares of our common stock into which the note is convertible, together with any cash payment for such holder's fractional shares, will be deemed to satisfy our obligation to pay the principal amount of the note and our obligation to pay accrued and unpaid interest. As a result, any accrued but unpaid interest to the conversion date is deemed to be cancelled, extinguished and forfeited upon conversion. For a discussion of the tax

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treatment to you of receiving our common stock upon conversion, see "Material U.S. Federal Income Tax Considerations."

If a holder converts notes, we will pay any documentary, stamp or similar issue or transfer tax due on the issuance of shares of our common stock upon the conversion, unless the tax is due because the holder requests the shares to be issued or delivered to a person other than the holder, in which case the holder will pay that tax.

If a holder wishes to exercise its conversion right, such holder must deliver an irrevocable duly completed conversion notice (which, if applicable, must comply with the applicable procedures of The Depository Trust Company, or DTC), together, if the notes are in certificated form, with the certificated security, to the conversion agent along with appropriate endorsements and transfer documents, if required, and pay any transfer or similar tax, if required. The conversion agent will, on the holder's behalf, convert the notes into shares of our common stock. Holders may obtain copies of the required form of the conversion notice from the conversion agent. A certificate, or a book-entry transfer through DTC, for the number of full shares of our common stock into which any notes are converted, together with a cash payment for any fractional shares, will be delivered through the conversion agent as soon as practicable, but no later than the third business day, following the conversion date. The trustee will initially act as the conversion agent.

If a holder has already delivered a purchase notice as described under " Repurchase at Option of Holders Upon a Fundamental Change" with respect to a note, however, the holder may not surrender that note for conversion until the holder has withdrawn the purchase notice in accordance with the indenture.

Holders may surrender their notes for conversion into shares of our common stock at the applicable conversion rate at any time prior to the close of business on the second business day immediately preceding the stated maturity date.

Holders of notes at the close of business on a regular record date will receive payment of interest payable on the corresponding interest payment date notwithstanding the conversion of such notes at any time after the close of business on the applicable regular record date. Notes surrendered for conversion by a holder during the period from the close of business on any regular record date to the opening of business on the next interest payment date must be accompanied by payment of an amount equal to the interest that the holder is to receive on the notes; *provided*, *however*, that no such payment need be made (1) if we have specified a purchase date following a fundamental change or specified a redemption date, in either case, that is after a regular record date and on or prior to the next interest payment date, (2) only to the extent of overdue interest, if any overdue interest exists at the time of conversion with respect to such note, or (3) if conversion occurs after the last regular record date prior to the maturity date.

Adjustment of Conversion Rate

The initial conversion rate will be adjusted for certain events, including:

- the issuance of our common stock as a dividend or distribution on our common stock; certain subdivisions and combinations of our common stock;

- the issuance to all or substantially all holders of our common stock of certain rights or warrants to purchase our common stock (or securities convertible into our common stock) at less than (or having a conversion price per share less than) the current market price of our common stock;

- the dividend or other distribution to all or substantially all holders of our common stock of shares of our capital stock (other than common stock) or evidences of our indebtedness or our assets (including securities, but excluding those rights and warrants referred to above and

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dividends and distributions in connection with a reclassification, consolidation, merger, combination, sale or conveyance resulting in a change in the conversion consideration pursuant to the fifth succeeding paragraph below or dividends or distributions paid exclusively in cash);

dividends or other distributions consisting exclusively of cash to all or substantially all holders of our common stock; and

payments to holders of our common stock above the then-prevailing market price pursuant to a tender or exchange offer made by us or any of our subsidiaries.

In the event that we pay a dividend or make a distribution on shares of our common stock consisting of capital stock of, or similar equity interests in, as described in the third bullet point above, a subsidiary or other business unit of ours, the applicable conversion rate will be adjusted based on the market value of the securities so distributed relative to the market value of our common stock, in each case based on the average sale prices of those securities for the 10 trading days commencing on and including the fifth trading day after the date on which "ex-dividend trading" commences for such dividend or distribution on the Nasdaq Global Select Market or such other national or regional exchange or market on which the securities are then listed or quoted.

If any adjustment of the conversion rate would be less than 1% of the then effective rate, such adjustment shall be carried forward and adjustment with respect thereto made at the time of and together with any subsequent adjustment which, together with the original adjustment shall aggregate at least 1% of the then effective conversion rate; *provided*, *however*, that any carry forward amount shall be paid to the holder upon conversion regardless of the 1% threshold.

Under the provisions of our stockholder rights plan, holders will receive, and if we implement a new stockholder rights plan, this new rights plan must provide that upon conversion of the existing notes the holders will receive, in addition to the common stock issuable upon such conversion, the rights under such rights plan unless the rights have separated from the common stock before the time of conversion, in which case the applicable conversion rate will be adjusted as if we distributed to all holders of our common stock, shares of our capital stock, evidences of indebtedness or assets as described above, subject to readjustment in the event of the expiration, termination or redemption of such rights.

Except as stated above, the conversion rate will not be adjusted for the issuance of our common stock or any securities convertible into or exchangeable for our common stock or carrying the right to purchase any of the foregoing.

In the case of:

any recapitalization, reclassification or change of our common stock, other than changes resulting from a subdivision or combination,

a consolidation, merger or combination involving us,

a sale, conveyance or lease to another corporation of all or substantially all of our property and assets, or

any statutory share exchange,

in each case as a result of which holders of our common stock are entitled to receive stock, other securities, other property or assets (including cash or any combination thereof) with respect to or in exchange for our common stock, the holders of the notes then outstanding will be entitled thereafter to convert those notes into the kind and amount of shares of stock, other securities or other property or assets (including cash or any combination thereof) which they would have owned or been entitled to receive upon such business combination had such notes been converted into our common stock immediately prior to such business combination. We may not become a party to any such transaction

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unless its terms are consistent with the preceding. None of the foregoing provisions shall affect the right of a holder of notes to convert its notes into shares of our common stock prior to the effective date of such transaction.

In the event holders of our common stock have the opportunity to elect the form of consideration to be received in such business combination, the notes will be convertible into the weighted average of the kind and amount of consideration received by the holders of our common stock that affirmatively make such an election. We may not become a party to any such transaction unless its terms are consistent with the preceding. None of the foregoing provisions shall affect the right of a holder of notes to convert its notes into shares of our common stock prior to the effective date of the business combination.

Holders of the notes may, in certain circumstances, be deemed to have received a taxable distribution if the conversion rate is adjusted with the effect of increasing the holder's proportionate interest in our assets and earnings (including on a taxable distribution to holders of our common stock or other transaction which results in an adjustment of the conversion rate), other than adjustments to the conversion price made pursuant to a bona fide reasonable adjustment formula which has the effect of preventing the dilution of the interest of the holders of the notes. In certain circumstances, the failure to provide for such an adjustment may also result in a deemed distribution. As a result of a deemed distribution, U.S. holders (as defined in "Material U.S. Federal Income Tax Considerations") of the notes would generally realize taxable income and the deemed distribution would generally result in withholding taxes for non-U.S. holders (as defined in "Material U.S. Federal Income Tax Considerations"). Any constructive dividend deemed paid would not be eligible for preferential rates of U.S. federal income tax applicable to certain dividends and corporate holders would not be entitled to claim the dividends received deduction with respect to any constructive dividends. Because this deemed income would not give rise to any cash from which any applicable withholding tax could be satisfied, we may offset any such withholding tax applicable to non-U.S. holders against cash payments of interest payable on the notes. See "Material U.S. Federal Income Tax Considerations Consequences to U.S. Holders Constructive Dividends" and " Consequences to Non-U.S. Holders Dividends."

We may from time to time, to the extent permitted by law, increase the applicable conversion rate of the notes by any amount for any period of at least 20 business days. In that case we will give at least 15 days' notice of such increase. We may make such increase in the applicable conversion rate, in addition to those set forth above, as our board of directors deems advisable to avoid or diminish any income tax to holders of our common stock resulting from any dividend or distribution of stock (or rights to acquire stock) or from any event treated as such for income tax purposes.

Redemption at Our Option

Provisional Redemption. Prior to October 1, 2013, we may redeem all or any portion of the notes, at once or over time, at a redemption price equal to 100% of the principal amount of the notes to be redeemed if the closing price of our common stock has exceeded 130% of the applicable conversion price (as determined based on the applicable conversion rate) for at least 20 trading days within a period of 30 consecutive trading days ending on the trading day prior to the date of mailing of the provisional redemption notice (which date shall be at least 30 but not more than 60 days prior to the provisional redemption date). The redemption price for provisional redemption does not include accrued and unpaid interest because unpaid interest is taken into account in calculating the additional payment upon provisional redemption described below. If the provisional redemption date occurs after a regular record date and on or prior to the corresponding interest payment date, we will make the interest payment to the record holder on the regular record date corresponding to such interest payment date instead of paying interest in connection with the provisional redemption.

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Upon any provisional redemption, we will make an additional payment (the "additional payment upon provisional redemption") with respect to the notes called for redemption to holders of record on the notice date in an amount equal to $ per $1,000 principal amount of notes (three years of interest on the notes), less the amount of any interest paid on the notes from their issuance, so that the interest paid by us on such notes, together with the additional payment upon provisional redemption, shall equal an amount corresponding to three years of interest on the applicable notes. We will be obligated to make the additional payment upon provisional redemption on all notes called for provisional redemption, including any notes converted after the notice date and before the provisional redemption date.

We may, at our option, pay the additional payment upon provisional redemption in our common stock instead of cash, as long as:

- our common stock is then listed on a national securities exchange and
- we register our delivery of common stock as payment under the Securities Act and applicable state securities laws, in each case to the extent required in order to deliver unrestricted common stock.

The number of shares we will be required to deliver to a holder if we pay the additional payment upon provisional redemption in our common stock would be equal to the cash amount otherwise payable divided by 98% of the 5-day volume-weighted average price of a share of our common stock on the date on which we give notice of a provisional redemption. "5-day volume-weighted average price" means the per share volume-weighted average price as displayed under the heading "Bloomberg VWAP" on Bloomberg page "VRTX.UQ <equity> AQR" (or its equivalent successor if such page is not available) in respect of the five trading day period from the scheduled open of trading on the trading day immediately following the provisional redemption notice date until the scheduled close of trading of the primary trading session on the last trading day of that five trading day period (or if such volume-weighted average price is unavailable, the market value of one share of our common stock during that five trading day period determined, using a volume-weighted average method, by a nationally recognized independent investment banking firm retained for this purpose by us). The "5-day volume-weighted average price" will be determined without regard to after hours trading or any other trading outside of the regular trading session trading hours.

We will pay cash based on the 5-day volume-weighted average price for all fractional shares of common stock otherwise deliverable in the event we elect to deliver common stock to satisfy our obligation to make the additional payment upon provisional redemption. If the conditions to payment of the additional payment upon provisional redemption in stock are not satisfied with respect to a holder prior to the close of business on the relevant redemption date, we will pay the additional payment upon provisional redemption in respect of the notes of that holder entirely in cash. To elect to pay the additional payment upon provisional redemption in our common stock, we must include notice of this election in our notice of redemption and may not change our election thereafter.

Optional Redemption. On and after October 1, 2013, we may redeem all or any portion of the notes, at once or over time, on not more than 60 nor less than 30 days' notice by mail, without regard to the closing price of our common stock. The notes may be redeemed for cash at the redemption prices set forth below, plus accrued and unpaid interest, if any, to, but excluding, the redemption date. However, if the redemption date occurs after a regular record date and on or prior to the corresponding interest payment date, we will instead make the interest payment to the record holder on the regular record date corresponding to such interest payment date. The following prices

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are for notes redeemed during the 12-month period commencing on October 1 of the years set forth below, and are expressed as percentages of principal amount:

Year	Redemption Price
2013	%
2014	%

Selection and Notice

If less than all the notes are to be redeemed at any time, selection of notes for redemption will be made by the trustee on a pro rata basis, by lot or by any other method that the trustee considers fair and appropriate. Notes and portions thereof will be redeemed in the amount of $1,000 or integral multiples of $1,000. The trustee will make the selection from notes outstanding and not previously called for redemption; *provided*, *however*, that if a portion of a holder's notes are selected for partial redemption and such holder thereafter converts a portion of such notes, such converted portion will be deemed to be taken from the portion selected for redemption.

Provisions of the indenture that apply to notes called for redemption also apply to portions of the notes called for redemption. If any note is to be redeemed in part, the notice of redemption will state the portion of the principal amount to be redeemed. In the event of any redemption of less than all the notes, we will not be required to:

(i) issue or register the transfer or exchange of any note during a period of 15 days before any selection of such notes for redemption, or

(ii) register the transfer or exchange of any note so selected for redemption, in whole or in part, except the unredeemed portion of any note being redeemed in part, in which case we will execute and the trustee will authenticate and deliver to the holder a new note equal in principal amount to the unredeemed portion of the note surrendered.

On and after the redemption date, unless we default in the payment of the redemption price interest will cease to accrue on the principal amount of the notes or portions of notes called for redemption and for which funds have been set aside for payment. In the case of notes or portions of notes redeemed on a redemption date which is also a regularly scheduled interest payment date, the interest payment due on such date will be paid to the person in whose name the note is registered at the close of business on the relevant regular record date.

Make-Whole Premium Upon a Fundamental Change

If a fundamental change described under clause (1) or (2) of the definition of a change in control described below under " Repurchase at Option of Holders Upon a Fundamental Change" occurs, we will pay a make-whole premium upon the conversion of the notes in connection with any such transaction by increasing the applicable conversion rate on such notes. The make-whole premium will be in addition to, and not in substitution for, any cash, securities or other assets otherwise due to holders of notes upon conversion. The make-whole premium will be determined by reference to the table below and is based on the date on which the fundamental change becomes effective, referred to as the "effective date," and the price, referred to as the "stock price," paid, or deemed to be paid, per share of our common stock in the transaction constituting the fundamental change, subject to adjustment as described below. If holders of our common stock receive only cash in the fundamental change, the stock price shall be the cash amount paid per share. In all other cases, the stock price shall be the average closing sale price of our common stock for the 15 trading days immediately prior to but not including the effective date.

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The following table shows what the make-whole premium would be for each hypothetical stock price and effective date set forth below, expressed as additional shares of common stock per $1,000 principal amount of notes.

	Effective Date					
Stock Price on Effective Date	**, 2010**	**October 1, 2011**	**October 1, 2012**	**October 1, 2013**	**October 1, 2014**	**October 1, 2015**
$						

The hypothetical stock prices and additional share amounts set forth above are based on a common stock price of $ per share on , 2010 and an initial conversion price of approximately $ per share.

The actual stock price and effective date may not be set forth on the table, in which case:

- if the actual stock price on the effective date is between two stock prices on the table or the actual effective date is between two effective dates on the table, the make-whole premium will be determined by a straight-line interpolation between the make-whole premiums set forth for the two stock prices and the two effective dates on the table based on a 365-day year, as applicable.

- if the stock price on the effective date exceeds $ per share, subject to adjustment as described below, no make-whole premium will be paid.

- if the stock price on the effective date is less than $ per share, subject to adjustment as described below, no make-whole premium will be paid.

The stock prices set forth in the first column of the table above will be adjusted as of any date on which the conversion rate of the notes is adjusted. The adjusted stock prices will equal the stock prices applicable immediately prior to such adjustment multiplied by a fraction, the numerator of which is the applicable conversion rate immediately prior to the adjustment giving rise to the stock price adjustment and the denominator of which is the conversion rate as so adjusted. The number of additional shares set forth in the table above will be adjusted in the same manner as the conversion rate as set forth above under " Adjustment of Conversion Rate."

A conversion of the notes by a holder will be deemed for these purposes to be "in connection with" a fundamental change if the conversion notice is received by the conversion agent on or subsequent to the date 20 calendar days prior to the date announced by us as the anticipated effective date of the fundamental change but before the close of business on the business day immediately preceding the related repurchase date. We will notify holders of notes of the anticipated effective date of any fundamental change as promptly as practicable following the date we publicly announce such fundamental change, but in no event less than 20 days prior to such date.

Notwithstanding the foregoing, in no event will the applicable conversion rate exceed per $1,000 principal amount of notes, subject to adjustments in the same manner as the

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conversion rate with respect to the events described under " Conversion Rights Adjustment of Conversion Rate."

The additional shares will be delivered upon the later of the settlement date for the conversion and promptly following the effective date of the fundamental change transaction.

If our obligation to pay the make-whole premium were construed as a penalty under applicable contract law, its enforceability would be subject to general principles of reasonableness of economic remedies.

Repurchase at Option of Holders Upon a Fundamental Change

If a fundamental change occurs, each holder of notes will have the right to require us to repurchase all or any portion of that holder's notes that is equal to $1,000 or a whole multiple of $1,000, on the date that is 45 days after the date we give notice of the occurrence of a fundamental change at a repurchase price, payable in cash, equal to 100% of the principal amount of the notes to be repurchased, together with interest accrued and unpaid to, but excluding, the repurchase date.

As promptly as practicable following the date we publicly announce such transaction, but in no event less than 20 days prior to the anticipated effective date of a fundamental change, we are required to give notice to all holders of notes, as provided in the indenture, of the occurrence of the fundamental change and of their resulting repurchase right. We must also deliver a copy of our notice to the trustee. To exercise the repurchase right, a holder of notes must deliver prior to or on the 30th day after the date of our notice irrevocable written notice to the trustee of the holder's exercise of its repurchase right, together with the notes with respect to which the right is being exercised. We will also disseminate a press release through Dow Jones & Company, Inc. or Bloomberg Business News announcing the occurrence of the fundamental change or publish that information in a newspaper of general circulation in New York City or on our website, or through such other public medium as we deem appropriate at that time.

A "fundamental change" will be deemed to have occurred upon a change in control or a termination of trading, each as defined below.

A "change in control" will be deemed to have occurred at such time after the original issuance of the notes when the following has occurred:

(1) the acquisition by any person, including any syndicate or group deemed to be a "person" under Section 13(d)(3) of the Securities Exchange Act of 1934, as amended (Exchange Act), of beneficial ownership, directly or indirectly, through a purchase, merger or other acquisition transaction or series of transactions of shares of our capital stock entitling that person to exercise 50% or more of the total voting power of all shares of our capital stock entitled to vote generally in elections of directors, other than any acquisition by us, any of our subsidiaries or any of our employee benefit plans;

(2) our consolidation or merger with or into any other person, any merger of another person into us, or any conveyance, transfer, sale, lease or other disposition of all or substantially all of our properties and assets to another person, other than:

any transaction that does not result in any reclassification, conversion, exchange or cancellation of outstanding shares of our capital stock, and

any transaction pursuant to which holders of our capital stock immediately prior to the transaction have the entitlement to exercise, directly or indirectly, 50% or more of the total voting power of all shares of our capital

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stock entitled to vote generally in the election of directors of the continuing or surviving person immediately after the transaction; or

any merger solely for the purpose of changing our jurisdiction of incorporation and resulting in a reclassification, conversion or exchange of outstanding shares of common stock solely into shares of common stock of the surviving entity;

However, a change in control will not be deemed to have occurred if, in the case of a merger or consolidation, at least 90% of the consideration (excluding cash payments for fractional shares and cash payments pursuant to dissenters' appraisal rights) in the merger or consolidation constituting the change in control consists of common stock traded on a U.S. national securities exchange (or which will be so traded when issued or exchanged in connection with such change in control) and as a result of such transaction or transactions the notes become convertible solely into such common stock.

(3) during any consecutive two-year period, individuals who at the beginning of that two-year period constituted our board of directors, together with any new directors whose election to our board of directors, or whose nomination for election by our stockholders, was approved by a vote of a majority of the directors then still in office who were either directors at the beginning of such period or whose election or nomination for election was previously so approved, cease for any reason to constitute a majority of our board of directors then in office; or

(4) our stockholders pass a resolution approving a plan of liquidation or dissolution.

A "termination of trading" will be deemed to have occurred if our common stock or other common stock into which the notes are convertible is neither listed for trading on a U.S. national securities exchange nor approved for listing on any U.S. system of automated dissemination of quotations of securities prices, or traded in over-the-counter securities markets.

The beneficial owner shall be determined in accordance with Rule 13d-3 promulgated by the SEC under the Exchange Act. The term "person" includes any syndicate or group which would be deemed to be a "person" under Section 13(d)(3) of the Exchange Act.

Rule 13e-4 under the Exchange Act requires the dissemination of certain information to security holders if an issuer tender offer occurs and may apply if the repurchase option becomes available to holders of the notes. We will comply with this rule to the extent applicable at that time.

We may, to the extent permitted by applicable law, at any time purchase the notes in the open market or by tender at any price or by private agreement. Any note so purchased by us may, to the extent permitted by applicable law, be reissued or resold or may be surrendered to the trustee for cancellation. Any notes surrendered to the trustee may not be reissued or resold and will be canceled promptly.

The preceding provisions would not necessarily protect holders of the notes if highly leveraged or other transactions involving us occur that may adversely affect holders.

Our ability to repurchase notes upon the occurrence of a fundamental change is subject to important limitations. The occurrence of a fundamental change could cause an event of default under, or be prohibited or limited by, the terms of existing or future senior debt. As a result, any repurchase of the notes would, absent a waiver, be prohibited under the subordination provisions of the indenture until the senior debt is paid in full.

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Further, we cannot assure you that we would have the financial resources, or would be able to arrange financing, to pay the repurchase price for all the notes that might be delivered by holders of notes seeking to exercise the repurchase right. Any failure by us to repurchase the notes when required following a fundamental change would result in an event of default under the indenture, whether or not such repurchase is permitted by the subordination provisions of the indenture. Any such default may, in turn, cause a default under existing or future senior debt. See " Ranking" above.

No Stockholder Rights for Holders of Notes

Before they convert their notes into common stock, holders of notes, as such, will not have any rights as our stockholders (including, without limitation, voting rights and rights to receive any dividends or other distributions on shares of our common stock), except in limited circumstances described above under " Adjustment of Conversion Rate."

Calculations in Respect of the Notes

Except as explicitly specified otherwise herein, we will be responsible for making all calculations required under the notes. These calculations include, but are not limited to, determinations of the conversion price and conversion rate applicable to the notes. We will make all these calculations in good faith and, absent manifest error, our calculations will be final and binding on holders of the notes. We will provide a schedule of our calculations to the trustee, and the trustee is entitled to rely upon the accuracy of our calculations without responsibility for independent verification thereof. The trustee will forward our calculations to any holder of notes upon written request.

Consolidation, Merger and Sale of Assets

We may, without the consent of the holders of notes, consolidate with, merge into or transfer all or substantially all of our assets to any corporation, limited liability company, partnership or trust organized under the laws of the U.S. or any of its political subdivisions, *provided* that:

the surviving entity assumes all our obligations under the indenture and the notes, as provided in the indenture;

at the time of such transaction, no event of default, and no event which, after notice or lapse of time, would become an event of default, shall have happened and be continuing;

if as a result of such transaction the notes become convertible into common stock or other securities issued by a third party, such third party fully and unconditionally agrees to deliver such common stock or other securities upon conversion under the notes and the indenture; and

an officers' certificate and an opinion of counsel, each stating that the consolidation, merger or transfer complies with the provisions of the indenture, have been delivered to the trustee.

Reporting Obligations

We will file in a timely fashion all reports and other information and documents which we are required to file with the SEC pursuant to Section 13 or 15(d) of the Exchange Act, including our Annual Report on Form 10-K and our Quarterly Reports on Form 10-Q, and deliver such reports to the trustee within 15 days after we are required to file such reports with the SEC. In the event we are at any time no longer subject to the reporting requirements of Section 13 or 15(d) of the Exchange Act, we shall, if required to do so under rules and regulations prescribed by the SEC, provide the trustee with such reports containing such information as would have been required to be filed with the SEC had we continued to have been subject to such reporting requirements, as may be prescribed in such rules and regulations. We will comply with the other provisions of Section 314(a) of the Trust

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Indenture Act. Furthermore, within 90 days after the end of each fiscal year, we will deliver to the trustee an officer's certificate stating whether the signatory knows of any default or event of default under the indenture, and describe any default or event of default and the efforts to remedy the same.

Events of Default

Each of the following will constitute an event of default under the indenture:

- our failure to pay when due the principal of or premium (including the additional payment upon provisional redemption, if applicable), if any, on any of the notes at maturity, upon redemption or exercise of a repurchase right or otherwise, whether or not such payment is prohibited by the subordination provisions of the indenture;

- our failure to pay an installment of interest on any of the notes for 30 days after the date when due, whether or not such payment is prohibited by the subordination provisions of the indenture;

- our failure to deliver shares of common stock, together with cash instead of fractional shares, when those shares of common stock or cash instead of fractional shares, are required to be delivered following conversion of a note, and that failure continues for 10 days;

- our failure to perform or observe any other term, covenant or agreement contained in the notes or the indenture for a period of 60 days after written notice of such failure, requiring us to remedy the same, shall have been given to us by the trustee or to us and the trustee by the holders of at least 25% in aggregate principal amount of the notes then outstanding;

- our failure to make any payment by the end of the applicable grace period, if any, after the maturity of any indebtedness for borrowed money in an amount in excess of $5.0 million, or there is an acceleration of indebtedness for borrowed money in an amount in excess of $5.0 million because of a default with respect to such indebtedness without such indebtedness having been discharged or such acceleration having been cured, waived, rescinded or annulled, in either case, for a period of 30 days after written notice to us by the trustee or to us and the trustee by holders of at least 25% in aggregate principal amount of the notes then outstanding;

- our failure to give you notice of your rights to require us to repurchase your notes upon a fundamental change; and

- certain events of our bankruptcy, insolvency or reorganization.

If an event of default specified in the seventh bullet point above occurs and is continuing, then the principal of all the notes and the interest thereon shall automatically become immediately due and payable. If an event of default occurs and is continuing, other than an event of default specified in the seventh bullet point above, the trustee or the holders, with written notice to the trustee, of at least 25% in aggregate principal amount of the notes then outstanding may declare the notes due and payable at their principal amount together with accrued interest, and thereupon the trustee may, at its discretion, proceed to protect and enforce the rights of the holders of notes by appropriate judicial proceedings. Such declaration may be rescinded and annulled with the written consent of the holders of a majority in aggregate principal amount of the notes then outstanding, subject to the provisions of the indenture.

Notwithstanding the foregoing, the indenture will provide that, to the extent elected by us, the sole remedy for an event of default relating to the failure to comply with the reporting obligations in the indenture with respect to SEC filings that are described above under the caption " Reporting Obligations," and for any failure to comply with the requirements of Section 314(a)(1) of the Trust Indenture Act, will for the first 180 days after the occurrence of such an event of default consist exclusively of the right to receive special interest on the notes at an annual rate equal to 1.0% of the

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outstanding principal amount of the notes. This special interest will be paid semi-annually in arrears, with the first semi-annual payment due on the first interest payment date following the date on which the special interest began to accrue on any notes. The special interest will accrue on all outstanding notes from and including the date on which an event of default relating to a failure to comply with the reporting obligations in the indenture first occurs to but not including the 180th day thereafter (or such earlier date on which the event of default shall have been cured or waived). On such 180th day (or earlier, if the event of default relating to the reporting obligations is cured or waived prior to such 180th day), such special interest will cease to accrue and, if the event of default relating to reporting obligations has not been cured or waived prior to such 180th day, the notes will be subject to acceleration as provided above. The provisions of the indenture described in this paragraph will not affect the rights of holders in the event of the occurrence of any other event of default. In the event we do not elect to pay special interest upon an event of default in accordance with this paragraph, the notes will be subject to acceleration as provided above.

The holders of a majority in aggregate principal amount of notes at the time outstanding through their written consent, or the holders of a majority in aggregate principal amount of notes then outstanding represented at a meeting at which a quorum is present by a written resolution, may waive any existing default or event of default and its consequences except any default or event of default:

- in any payment on the notes;
- in respect of the conversion rights of the notes; or
- in respect of the covenants or provisions in the indenture that may not be modified or amended without the consent of the holder of each note affected as described in " Modification, Waiver and Meetings" below.

Holders of a majority in aggregate principal amount of the notes then outstanding through their written consent, or the holders of a majority in aggregate principal amount of the notes then outstanding represented at a meeting at which a quorum is present by a written resolution, may direct the time, method and place of conducting any proceeding for any remedy available to the trustee or exercising any trust or power conferred upon the trustee, subject to the provisions of the indenture. The indenture contains a provision entitling the trustee, subject to the duty of the trustee during a default to act with the required standard of care, to be indemnified by the holders of notes before proceeding to exercise any right or power under the indenture at the request of such holders. The rights of holders of the notes to pursue remedies with respect to the indenture and the notes are subject to a number of additional requirements set forth in the indenture.

The right of any holder:

- to receive payment of principal, premium, if any, the fundamental change repurchase price, the redemption price or interest, in respect of the notes held by that holder on or after the respective due dates expressed in the notes;
- to convert those notes; or
- to bring suit for the enforcement of any such payment on or after the respective due dates expressed in the notes and the right to convert;

will not be impaired or affected without that holder's consent.

The indenture will provide that the trustee shall, within 90 days of the occurrence of a default, give to the registered holders of the notes notice of all uncured defaults known to it, but the trustee shall be protected in withholding such notice if it, in good faith, determines that the withholding of such notice is in the best interest of such registered holders, except in the case of a default in the

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payment of the principal of, or premium, if any, or interest on, any of the notes when due or in the payment of any repurchase or redemption obligation.

We are required to furnish annually to the trustee a written statement as to the fulfillment of our obligations under the indenture. In addition, we are required to file with the trustee a written notice of the occurrence of any default or event of default within five business days of our becoming aware of the occurrence of any default or event of default.

Modification, Waiver and Meetings

The indenture contains provisions for convening meetings of the holders of notes to consider matters affecting their interests.

The indenture (including the terms and conditions of the notes) may be modified or amended by us and the trustee, without the consent of the holder of any note, for the purposes of, among other things:

- adding to our covenants for the benefit of the holders of notes;
- surrendering any right or power conferred upon us;
- providing for conversion rights of holders of notes if any recapitalization, reclassification or change of our common stock or any consolidation, merger or sale, conveyance or lease of all or substantially all of our assets or a statutory share exchange occurs;
- providing for the assumption of our obligations to the holders of notes in the case of a merger, consolidation, conveyance, transfer or lease;
- providing for the addition of a guaranty of the notes by any other entity;
- increasing the applicable conversion rate, *provided* that the increase will not adversely affect the interests of holders of notes in any material respect;
- complying with the requirements of the SEC in order to effect or maintain the qualification of the indenture under the Trust Indenture Act of 1939, as amended;
- curing any ambiguity or correcting or supplementing any defective provision contained in the indenture, *provided* that such modification or amendment does not, in the good faith opinion of our board of directors and the trustee, adversely affect the interests of the holders of the notes in any material respect; and provided further, that no modification or amendment made to conform the terms of the indenture or the notes to the description thereof in this prospectus supplement and the accompanying prospectus shall be deemed to adversely affect the interests of the holders of the notes; or
- adding or modifying any other provisions which we and the trustee may deem necessary or desirable and which will not adversely affect the interests of the holders of notes in any material respect.

Modifications and amendments to the indenture or to the terms and conditions of the notes may also be made, and non-compliance by us with any provision of the indenture or the notes may be waived, either:

with the written consent of the holders of at least a majority in aggregate principal amount of the notes at the time outstanding; or

by the adoption of a resolution at a meeting of holders at which a quorum is present by at least a majority in aggregate principal amount of the notes represented at such meeting.

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However, no such modification, amendment or waiver may, without the written consent or the affirmative vote of the holder of each note affected:

- change the maturity of the principal of or any installment of interest on any note; reduce the principal amount of, or any premium, if any, on any note;
- reduce the interest rate or interest on any note;
- change the currency of payment of principal of, premium, if any, or interest on any note;
- impair the right to institute suit for the enforcement of any payment on or with respect to, or the conversion of, any note;
- modify our obligations to maintain an office or agency in New York City;
- except as otherwise permitted or contemplated by provisions of the indenture concerning specified reclassifications or corporate reorganizations, adversely affect the conversion rights of holders of the notes;
- adversely affect the repurchase option of holders upon a fundamental change;
- modify the subordination provisions of the notes in a manner adverse to the holders of notes;
- reduce the percentage in aggregate principal amount of notes outstanding necessary to modify or amend the indenture or to waive any past default; or
- reduce the percentage in aggregate principal amount of notes outstanding required for the adoption of a resolution or the quorum required at any meeting of holders of notes at which a resolution is adopted.

The quorum at any meeting called to adopt a resolution will be persons holding or representing a majority in aggregate principal amount of the notes at the time outstanding.

Unclaimed Money

If money deposited with the trustee or paying agent for the payment of principal of, premium, if any, or accrued and unpaid interest on the notes remains unclaimed for two years, the trustee and paying agent will pay the money back to us upon our written request. However, the trustee and paying agent have the right to withhold paying the money back to us until they publish in a newspaper of general circulation in New York City, or mail to each holder, a notice stating that the money will be paid back to us if unclaimed after a date no less than 30 days from the publication or mailing. After the trustee or paying agent pays the money back to us, holders of notes entitled to the money must look to us for payment as general creditors, subject to applicable law, and all liability of the trustee and the paying agent with respect to the money will cease.

Book-Entry System

We will issue the notes in the form of one or more global securities. The global security will be deposited with the trustee as custodian for DTC and registered in the name of a nominee of DTC. Except as set forth below, the global security may be transferred, in whole and not in part, only to DTC or another nominee of DTC. You will hold your beneficial interests in the global security directly through DTC if you have an account with DTC or indirectly through organizations that have accounts with DTC.

Notes in definitive certificated form (called "certificated securities") will be issued only in certain limited circumstances described below.

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DTC has advised us that it is:

- a limited purpose trust company organized under the laws of the State of New York; a member of the Federal Reserve System;

- a "clearing corporation" within the meaning of the New York Uniform Commercial Code; and a "clearing agency" registered pursuant to the provisions of Section 17A of the Exchange Act.

DTC was created to hold securities of institutions that have accounts with DTC (called participants) and to facilitate the clearance and settlement of securities transactions among its participants in such securities through electronic book-entry changes in accounts of the participants, thereby eliminating the need for physical movement of securities certificates. DTC's participants include securities brokers and dealers, which may include the underwriter, banks, trust companies, clearing corporations and certain other organizations. Access to DTC's book-entry system is also available to others such as banks, brokers, dealers and trust companies (called, the indirect participants) that clear through or maintain a custodial relationship with a participant, whether directly or indirectly.

We expect that pursuant to procedures established by DTC upon the deposit of the global security with DTC, DTC will credit, on its book-entry registration and transfer system, the principal amount of notes represented by such global security to the accounts of participants. The accounts to be credited shall be designated by the underwriter. Ownership of beneficial interests in the global security will be limited to participants or persons that may hold interests through participants. Ownership of beneficial interests in the global security will be shown on, and the transfer of those beneficial interests will be effected only through, records maintained by DTC (with respect to participants' interests), the participants and the indirect participants.

The laws of some jurisdictions may require that certain purchasers of securities take physical delivery of such securities in definitive form. These limits and laws may impair the ability to transfer or pledge beneficial interests in the global security. Accordingly, the ability to transfer beneficial interests in the notes represented by the global security to those persons may be limited. In addition, because DTC can act only on behalf of its participants, who in turn act on behalf of persons who hold interests through participants, the ability of a person having a beneficial interest in notes represented by the global security to pledge or transfer those interests to persons or entities that do not participate in DTC's system, or otherwise to take actions in respect of such interest, may be affected by the lack of a physical definitive security in respect of such interest.

Owners of beneficial interests in global securities who desire to convert their interests for common stock should contact their brokers or other participants or indirect participants through whom they hold such beneficial interests to obtain information on procedures, including proper forms and cut-off times, for submitting requests for conversion. So long as DTC, or its nominee, is the registered owner or holder of a global security, DTC or its nominee, as the case may be, will be considered the sole owner or holder of the notes represented by the global security for all purposes under the indenture and the notes. In addition, no owner of a beneficial interest in a global security will be able to transfer that interest except in accordance with the applicable procedures of DTC.

Except as set forth below, as an owner of a beneficial interest in the global security, you will not be entitled to have the notes represented by the global security registered in your name, will not receive or be entitled to receive physical delivery of certificated securities and will not be considered to be the owner or holder of any notes under the global security. We understand that under existing industry practice, if an owner of a beneficial interest in the global security desires to take any action that DTC, as the holder of the global security, is entitled to take, DTC would authorize the participants to take such action. Additionally, in such case, the participants would authorize beneficial owners

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owning through such participants to take such action or would otherwise act upon the instructions of beneficial owners owning through them.

We will make payments of principal of, premium, if any, and interest on the notes represented by the global security registered in the name of and held by DTC or its nominee to DTC or its nominee, as the case may be, as the registered owner and holder of the global security. Neither we, the trustee nor any paying agent will have any responsibility or liability for any aspect of the records relating to or payments made on account of beneficial interests in the global security or for maintaining, supervising or reviewing any records relating to such beneficial interests.

We expect that DTC or its nominee, upon receipt of any payment of principal of, premium, if any, or interest on the global security, will credit participants' accounts with payments in amounts proportionate to their respective beneficial interests in the principal amount of the global security as shown on the records of DTC or its nominee. We also expect that payments by participants or indirect participants to owners of beneficial interests in the global security held through such participants or indirect participants will be governed by standing instructions and customary practices and will be the responsibility of such participants or indirect participants. We will not have any responsibility or liability for any aspect of the records relating to, or payments made on account of, beneficial interests in the global security for any note or for maintaining, supervising or reviewing any records relating to such beneficial interests or for any other aspect of the relationship between DTC and its participants or indirect participants or the relationship between such participants or indirect participants and the owners of beneficial interests in the global security owning through such participants.

Transfers between participants in DTC will be effected in the ordinary way in accordance with DTC rules and will be settled in same-day funds.

DTC has advised us that it will take any action permitted to be taken by a holder of notes only at the direction of one or more participants to whose account the DTC interests in the global security is credited and only in respect of such portion of the aggregate principal amount of notes as to which such participant or participants has or have given such direction. However, if DTC notifies us that it is unwilling to be a depositary for the global security or ceases to be a clearing agency or there is an event of default under the notes, DTC will convert global security for certificated securities which it will distribute to its participants and which will be legended, if required, as set forth under "Transfer Restrictions." Although DTC is expected to follow the foregoing procedures in order to facilitate transfers of interests in the global security among participants of DTC, it is under no obligation to perform or continue to perform such procedures, and such procedures may be discontinued at any time. Neither we nor the trustee will have any responsibility, or liability for the performance by DTC or the participants or indirect participants of their respective obligations under the rules and procedures governing their respective operations.

Satisfaction and Discharge

We may satisfy and discharge our obligations under the indenture by delivering to the registrar for cancellation all outstanding notes or by depositing with the trustee or delivering to the holders, as applicable, after the notes have become due and payable, whether at the stated maturity, any fundamental change purchase date or upon conversion, redemption or otherwise, cash (or in the case of conversions, shares of our common stock), sufficient to pay all of the outstanding notes and all other sums payable under the indenture by us. Such discharge is subject to terms contained in the indenture.

Form, Denomination and Registration

The notes are being issued in fully registered form, without coupons, in denominations of $1,000 principal amount and whole multiples of $1,000.

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Notices

Except as otherwise provided in the indenture, notices to holders of notes will be given by mail to the addresses of holders of the notes as they appear in the note register.

Governing Law

The indenture and the notes will be governed by, and construed in accordance with, the law of the State of New York.

Information Regarding the Trustee

U.S. Bank National Association, as trustee under the indenture, has been appointed by us as paying agent, conversion agent, registrar and custodian with regard to the notes. Computershare Investor Services is the transfer agent and registrar for our common stock. The trustee or its affiliates may from time to time in the future provide banking and other services to us in the ordinary course of their business.

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MATERIAL U.S. FEDERAL INCOME TAX CONSIDERATIONS

The following is a summary of certain material U.S. federal income tax considerations relating to the purchase, ownership and disposition of the notes and common stock into which the notes are convertible, but does not purport to be a complete analysis of all the potential tax considerations relating thereto. This summary is based upon the provisions of the Internal Revenue Code of 1986, as amended, or the Code, Treasury Regulations promulgated thereunder, administrative rulings and judicial decisions, all as of the date hereof. These authorities may be changed, possibly retroactively, so as to result in U.S. federal income tax consequences different from those set forth below. We have not sought any ruling from the Internal Revenue Service, or the IRS, with respect to the statements made and the conclusions reached in the following summary, and there can be no assurance that the IRS will agree with such statements and conclusions.

The following discussion of U.S. federal income tax considerations is for general information only. It is not tax advice. Each prospective investor should consult its own tax advisor regarding the particular U.S. federal, state, local and foreign tax consequences of purchasing, holding and disposing of our notes or common stock, including the consequences of any proposed change in applicable laws.

This summary is limited to holders who purchase notes upon their initial issuance at their initial issue price and who hold the notes and the common stock into which such notes are convertible as capital assets. This summary also does not address the tax considerations arising under the laws of any foreign, state or local jurisdiction or any federal estate or gift tax rules. In addition, this discussion does not address tax considerations applicable to an investor's particular circumstances or to investors that may be subject to special tax rules, including, without limitation:

- banks, insurance companies or other financial institutions;
- regulated investment companies or real estate investment trusts;
- persons subject to the alternative minimum tax;
- tax-exempt organizations;
- dealers in securities or currencies;
- traders in securities that elect to use a mark-to-market method of accounting for their securities holdings;
- persons who hold the notes or common stock through S-corporations, partnerships or other passthrough entities;
- certain former citizens or former long-term residents of the United States;
- persons whose functional currency is not the U.S. dollar;
- persons who hold the notes or common stock as a position in a hedging transaction, straddle, conversion transaction or other risk reduction transaction; or
- persons deemed to sell the notes or common stock under the constructive sale provisions of the Code.

You are urged to consult your tax advisor with respect to the application of the U.S. federal income tax laws to your particular situation, as well as any tax consequences of the purchase, ownership and disposition of the notes and common stock arising under the federal estate or gift tax rules or under the laws of any state, local, foreign or other taxing jurisdiction or under any applicable tax treaty.

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Consequences to U.S. Holders

The following is a summary of certain material U.S. federal income tax consequences that will apply to you if you are a U.S. holder of the notes or the common stock. Certain consequences to non-U.S. holders of the notes or common stock are described under " Consequences to Non-U.S. Holders" below. "U.S. holder" means a beneficial owner of our notes or our common stock that is:

- an individual citizen or resident of the United States;
- a corporation or other entity taxable as a corporation for U.S. federal income tax purposes, created or organized in the United States or under the laws of the United States, any state thereof, or the District of Columbia;
- an estate, the income of which is subject to U.S. federal income taxation regardless of its source; or
- a trust that (i) is subject to the primary supervision of a U.S. court and the control of one or more U.S. persons or (ii) has a valid election in effect under applicable Treasury Regulations to be treated as a U.S. person.

If a partnership holds our notes or common stock, the tax treatment of a partner will generally depend upon the status of the partner and the activities of the partnership. If you are a partner in a partnership (or member of a limited liability company taxed as a partnership for U.S. federal income tax purposes) holding the notes, you should consult your own tax advisor.

Payment of Interest

You will be required to include interest paid on the notes as ordinary income at the time it is paid or accrued, depending upon your regular method of accounting for U.S. federal income tax purposes.

Sale, Exchange, Repurchase or Redemption of the Notes

Upon the sale, exchange, repurchase or redemption of a note, you generally will recognize capital gain or loss equal to the difference between the amount you receive (including the amount of cash and the fair market value of any property other than common stock received upon conversion of the notes as discussed below in " Conversion of the Notes") and your adjusted tax basis in the notes. A portion of the proceeds may be attributable to accrued interest and should not be taken into account when computing capital gain or loss. Instead, that portion should be recognized as ordinary interest income to the extent such accrued interest has not been previously included in income. Any gain you recognize generally will be treated as long-term capital gain or loss if you held the notes for more than one year. The deductibility of capital losses is subject to limitations.

Special rules apply in determining the tax basis of a note. Your basis in a note will generally equal your original purchase price for the notes.

Conversion of the Notes

You generally will not recognize gain or loss upon conversion of the notes into our common stock, except with respect to any cash received in lieu of fractional shares. The receipt of cash for fractional shares generally will result in the recognition of gain or loss equal to the difference between the cash received and your adjusted tax basis in the fractional share.

Your tax basis in common stock received upon conversion of a note will generally equal your adjusted tax basis in the note at the time of the conversion, reduced by any basis allocable to a

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fractional share. Your holding period for the common stock received will generally include the holding period for the note converted.

Constructive Dividends

Holders of convertible debt instruments such as the notes may, in certain circumstances, be deemed to have received distributions of stock if the conversion price of such instruments is adjusted with the effect of increasing your proportionate interest in our assets and earnings (including on payment of the make-whole premium). However, adjustments to the conversion price made pursuant to a bona fide reasonable adjustment formula which has the effect of preventing the dilution of the interest of the holders of the debt instruments will generally not be deemed to result in a constructive distribution of stock. Certain of the possible adjustments provided in the notes, including, without limitation, adjustments in respect of taxable dividends to our stockholders, may not qualify as being pursuant to a bona fide reasonable adjustment formula. If such adjustments are made, you will be deemed to have received constructive distributions (in an amount equal to the value of the additional shares issuable upon conversion) includible in your income in the manner described under " Dividends" below even though you have not received any cash or property as a result of such adjustments. In certain circumstances, the failure to provide for such an adjustment may also result in a constructive distribution to you. Any constructive dividend deemed paid would not be eligible for the lower capital gains rate applicable to certain dividends for tax years beginning prior to January 1, 2011 and corporate holders would not be entitled to claim the dividends received deduction with respect to any constructive dividends.

In addition, we may be required to report to the IRS and to holders the amount of such constructive dividends taking place on or after January 1, 2013. It is anticipated that such constructive dividends would be reported to you in the same manner as actual dividends.

Dividends

Distributions, if any, made on our common stock held by you in connection with the conversion of the notes generally will be included in your income as ordinary dividend income to the extent of our current or accumulated earnings and profits as determined for U.S. federal income tax purposes. With respect to non-corporate taxpayers for taxable years beginning before January 1, 2011, such dividends are generally taxed at the lower applicable capital gains rate provided certain holding period requirements are satisfied, and Congress is currently considering legislation that would extend this favorable treatment beyond 2010. Distributions in excess of our current and accumulated earnings and profits will be treated as a return of capital to the extent of your adjusted tax basis in the common stock and thereafter as capital gain from the sale or exchange of such common stock. Dividends received by a corporate U.S. holder may be eligible for a dividends received deduction, subject to applicable limitations.

Sale, Exchange, Redemption of Common Stock

Upon the sale, exchange or redemption of our common stock held by you in connection with the conversion of the notes, you generally will recognize capital gain or loss equal to the difference between (i) the amount of cash and the fair market value of any property received upon the sale, exchange or redemption and (ii) your adjusted tax basis in the common stock. Such capital gain or loss will be long-term capital gain or loss if your holding period in the common stock is more than one year at the time of the sale, exchange or redemption. Your adjusted tax basis and holding period in common stock received in connection with the conversion of notes are determined as discussed above under " Conversion of the Notes." The deductibility of capital losses is subject to limitations.

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Backup Withholding and Information Reporting

Certain noncorporate U.S. holders may be subject to IRS information reporting and backup withholding (which is currently imposed at a 28% rate through December 31, 2010) on payments of interest on the notes, dividends on common stock (including constructive dividends) and proceeds from the sale or other disposition of the notes or common stock. Backup withholding should only be imposed where the noncorporate U.S. holder is not otherwise exempt and:

- fails to furnish its taxpayer identification number, or TIN;
- furnishes an incorrect TIN;
- is notified by the IRS that he or she has failed to properly report payments of interest or dividends; or
- under certain circumstances, fails to certify, under penalties of perjury, that he or she has furnished a correct TIN and has not been notified by the IRS that he or she is subject to backup withholding.

You generally will be entitled to credit any amounts withheld under the backup withholding rules against your U.S. federal income tax liability provided that the required information is furnished to the IRS in a timely manner.

Consequences to Non-U.S. Holders

The following is a summary of certain material U.S. federal income tax consequences that will apply to you if you are a non-U.S. holder of the notes. For purposes of this discussion, a "non-U.S. holder" means a beneficial owner of our notes that is not a U.S. holder.

Special rules may apply to certain non-U.S. holders such as "controlled foreign corporations," "passive foreign investment companies," corporations that accumulate earnings to avoid federal income tax or, in certain circumstances, individuals who are U.S. expatriates. Such non-U.S. holders should consult their own tax advisors to determine the U.S. federal, state, local and other tax consequences that may be relevant to them in their particular circumstances.

Payments of Interest

Generally, all payments of interest made to you on the notes will be subject to a 30% U.S. federal withholding tax. However, the interest may be exempt from withholding tax if it qualifies as "portfolio interest." You may be entitled to the exemption if:

- you do not own, actually or constructively, 10% or more of the total combined voting power of all classes of our stock entitled to vote;
- you are not a "controlled foreign corporation" with respect to which we are, directly or indirectly, a "related person"; and
- you provide your name and address, and certify, under penalties of perjury, that you are not a U.S. person, which certification may be made on an IRS Form W-8BEN or successor form, or that you hold your notes through certain intermediaries, and you and the intermediaries satisfy the certification requirements of applicable Treasury Regulations.

Prospective investors should consult their tax advisors regarding the certification requirements for non-U.S. holders.

If you can not satisfy the requirements described above, you will be subject to the 30% U.S. federal withholding tax with respect to payments of interest, or payments treated as interest, on the notes, unless you provide us with a properly executed (1) IRS Form W-8BEN or successor form

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claiming an exemption from or reduction in withholding under the benefit of an applicable U.S. income tax treaty or (2) IRS Form W-8ECI or successor form stating that interest paid on the note is not subject to withholding tax because it is effectively connected with the conduct of a U.S. trade or business.

If you are engaged in a trade or business in the United States and interest on a note is effectively connected with your conduct of that trade or business, you generally will be subject to U.S. federal income tax on that interest in the same manner as if you were a U.S. person as defined under the Code, although you will be exempt from the 30% withholding tax, provided the certification requirements described above are satisfied. In addition, if you are a foreign corporation, you may be subject to a branch profits tax equal to 30%, or lower rate as may be prescribed under an applicable U.S. income tax treaty, of your earnings and profits for the taxable year, subject to adjustments, that are effectively connected with your conduct of a trade or business in the United States. For this purpose, interest will be included in your earnings and profits.

Conversion of the Notes

A non-U.S. holder will generally not recognize any gain or loss on the conversion of the notes into common stock. To the extent you receive cash upon conversion of a note in lieu of fractional shares, you generally will be subject to the rules described under " Sale, Exchange, Repurchase of Other Disposition of Notes or Common Stock" below.

Sale, Exchange, Repurchase or Other Disposition of Notes or Common Stock

Any gain that a non-U.S. holder realizes upon the sale, exchange, repurchase or other disposition of our notes (except to the extent a portion is attributable to accrued interest) or our common stock generally will not be subject to U.S. federal income tax unless:

- the gain is effectively connected with your conduct of a trade or business in the United States; or
- you are an individual who is present in the United States for 183 days or more in the taxable year of sale, exchange, repurchase or other disposition and certain conditions are met.

If your gain is described in the first bullet point above, you generally will be subject to U.S. federal income tax on the net gain derived from the sale. If you are a corporation, then any such effectively connected gain received by you may also, under certain circumstances, be subject to the branch profits tax at a 30% rate, or such lower rate as may be prescribed under an applicable U.S. income tax treaty. If you are an individual described in the second bullet point above, you will be subject to a flat 30% U.S. federal income tax on the gain derived from the sale, which may be offset by U.S. source capital losses, even though you are not considered a resident of the United States. Such holders are urged to consult their tax advisors regarding the tax consequences of the acquisition, ownership and disposition of the notes or the common stock.

In the case of the sale or disposition of common stock after December 31, 2012, you may be subject to a 30% withholding tax on the gross proceeds of the sale or disposition unless you hold the common stock through a foreign financial institution or entity that has entered into an agreement with the U.S. government to collect and provide to the U.S. tax authorities information about its accountholders (including certain investors in such institution or entity) and, if required, you have provided the withholding agent with a certification identifying your direct and indirect U.S. owners. Investors are encouraged to consult with their own tax advisors regarding the possible implications of these withholding requirements on their investment in the notes or common stock and the potential for a refund or credit in the case of any withholding tax.

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Constructive Dividends

Under certain circumstances, a non-U.S. holder may be deemed to have received a constructive dividend. See "Consequences to U.S. Holders Constructive Dividends" above. Any constructive dividend deemed paid to a non-U.S. holder will be subject to withholding tax at a 30% rate or such lower rate as may be specified by an applicable income tax treaty. A non-U.S. holder who wishes to claim the benefit of an applicable treaty rate is required to satisfy applicable certification and other requirements. It is possible that U.S. federal tax on the constructive dividend would be withheld from interest or other distributions paid to the non-U.S. holder of the notes. A non-U.S. holder who is subject to withholding tax under such circumstances should consult its own tax advisor as to whether it can obtain a refund for all or a portion of the withholding tax.

As described above under "Consequences to U.S. Holders Constructive Dividends," we may be required to report to the IRS and to holders the amount of such constructive dividends taking place on or after January 1, 2013. As a result, if we make an adjustment to the conversion rate and the adjustment gives rise to a constructive dividend, non-U.S. holders should expect additional U.S. withholding on subsequent payments of interest or other distributions.

Dividends

In general, dividends, if any, received by a non-U.S. holder with respect to our common stock will be subject to withholding of U.S. federal income tax at a 30% rate, unless such rate is reduced by an applicable U.S. income tax treaty. Dividends that are effectively connected with your conduct of a trade or business in the United States. and, where a tax treaty applies, are attributable to a U.S. permanent establishment or fixed base, are not subject to the withholding tax, but instead are subject to U.S. federal income tax on a net income basis at applicable individual or corporate rates. As discussed above, certain certification and disclosure requirements must be complied with in order for effectively connected income to be exempt from withholding. Any such effectively connected dividends received by a non-U.S. holder that is a corporation may also, under certain circumstances, be subject to the branch profits tax at a 30% rate or such lower rate as may be prescribed under an applicable U.S. income tax treaty.

A non-U.S. holder of shares of common stock who wishes to claim the benefit of an applicable treaty rate is required to satisfy applicable certification and other requirements. If you are eligible for a reduced rate of U.S. withholding tax pursuant to an income tax treaty, you may obtain a refund of any excess amounts withheld by filing an appropriate claim for refund with the IRS.

In the case of actual or constructive dividends paid to a foreign entity after December 31, 2012, you will be subject to withholding of U.S. federal income tax at a 30% rate unless you hold the common stock through a foreign financial institution or entity that has entered into an agreement with the U.S. government to collect and provide to the U.S. tax authorities information about its accountholders (including certain investors in such institution or entity) and, if required, you have provided the withholding agent with a certification identifying your direct and indirect U.S. owners.

Backup Withholding and Information Reporting

In general, you will not be subject to backup withholding and information reporting with respect to payments that we make to you, provided that we do not have actual knowledge or reason to know that you are a U.S. person and you have given us an appropriate statement certifying, under penalties of perjury, that you are not a U.S. person. In addition, you will not be subject to backup withholding or information reporting with respect to the proceeds of the sale of a note or of a share of common stock within the United States or conducted through certain U.S.-related financial intermediaries, if the payor receives the statement described above and does not have actual knowledge or reason to know that you are a U.S. person or you otherwise establish an exemption. However, we

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may be required to report annually to the IRS and to you the amount of, and the tax withheld with respect to, any dividends paid to you, regardless of whether any tax was actually withheld. Copies of these information returns may also be made available under the provisions of a specific treaty or agreement to the tax authorities of the country in which you reside.

You generally will be entitled to credit any amounts withheld under the backup withholding rules against your U.S. federal income tax liability provided that the required information is furnished to the IRS in a timely manner.

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UNDERWRITING

Merrill Lynch, Pierce, Fenner & Smith Incorporated is acting as sole underwriter. Subject to the terms and conditions set forth in an underwriting agreement between us and the underwriter, we have agreed to sell to the underwriter, and the underwriter has agreed to purchase from us, $375,000,000 principal amount of notes.

Subject to the terms and conditions set forth in the underwriting agreement, the underwriter has agreed to purchase all of the notes sold under the underwriting agreement if any of these notes are purchased.

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

The underwriter is offering the notes, subject to prior sale, when, as and if issued to and accepted by it, subject to approval of legal matters by its counsel, including the validity of the notes, and other conditions contained in the underwriting agreement, such as the receipt by the underwriter of officer's certificates and legal opinions. The underwriter reserves the right to withdraw, cancel or modify offers to the public and to reject orders in whole or in part.

Commissions and Discounts

The representative has advised us that the underwriter proposes initially to offer the notes at a price of % of the principal amount of notes, plus accrued interest from the original issue date of the notes, if any, and to dealers at that price less a concession not in excess of % of the principal amount of the notes, plus accrued interest from the original issue date of the notes, if any. After the initial offering, the public offering price, concession or any other term of the offering may be changed.

The following table shows the public offering price, underwriting discount and proceeds before expenses to us. The information assumes either no exercise or full exercise by the underwriter of its option to purchase additional notes.

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

The expenses of the offering, not including the underwriting discount, are estimated at $400,000 and are payable by us.

Option to Purchase Additional Notes

We have granted an option to the underwriter to purchase up to an additional $25,000,000 principal amount of the notes at the public offering price, less the underwriting discount. The underwriter may exercise this option for 30 days from the date of this prospectus supplement.

New Issue of Notes

The notes are a new issue of securities with no established trading market. We do not intend to apply for listing of the notes on any national securities exchange or for inclusion of the notes on any automated dealer quotation system. We have been advised by the underwriter that it presently intends to make a market in the notes after completion of the offering. However, it is under no obligation to do so and may discontinue any market-making activities at any time without any notice. We cannot

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assure the liquidity of the trading market for the notes or that an active public market for the notes will develop. If an active public trading market for the notes does not develop, the market price and liquidity of the notes may be adversely affected. If the notes are traded, they may trade at a discount from their initial offering price, depending on prevailing interest rates, the market for similar securities, our operating performance and financial condition, general economic conditions and other factors. Our shares are listed on the Nasdaq Global Market under the symbol "VRTX."

No Sales of Similar Securities

We and our executive officers and directors have agreed, with certain limited exceptions, that we and they will not, for a period of 90 days, with respect to us, and 60 days, with respect to our executive officers and directors, after the date of this prospectus supplement, without first obtaining the prior written consent of Merrill Lynch, Pierce, Fenner & Smith Incorporated, directly or indirectly

offer, pledge, sell or contract to sell any common stock,

sell any option or contract to purchase any common stock,

purchase any option or contract to sell any common stock,

grant any option, right or warrant for the sale of any common stock,

otherwise dispose of or transfer any common stock, or

enter into any swap or other agreement that transfers, in whole or in part, directly or indirectly, the economic consequence of ownership of any common stock, or any of the options, contracts, rights or warrants listed above, whether any such swap or transaction is to be settled by delivery of shares or other securities, in cash or otherwise.

This lock-up provision applies to our common stock and to securities convertible into or exchangeable or exercisable for or repayable with our common stock. It also applies to common stock owned now or acquired later by the person executing the agreement or for which the person executing the agreement later acquires the power of disposition.

Price Stabilization, Short Positions

In connection with the offering, the underwriter may purchase and sell the notes or shares of our common stock in the open market. These transactions may include short sales, purchases on the open market to cover positions created by short sales and stabilizing transactions. Short sales involve the sale by the underwriter of a greater principal amount of notes than it is required to purchase in the offering. "Covered" short sales are sales made in an amount not greater than the underwriter's option to purchase additional notes described above. The underwriter may close out any covered short position by either exercising its option to purchase additional notes or purchasing notes in the open market. In determining the source of notes to close out the covered short position, the underwriter will consider, among other things, the price of notes available for purchase in the open market as compared to the price at which it may purchase notes through the option to purchase additional notes. "Naked" short sales are sales in excess of the option to purchase additional notes. The underwriter must close out any naked short position by purchasing notes in the open market. A naked short position is more likely to be created if the underwriter is concerned that there may be downward pressure on the price of the notes in the open market after pricing that could adversely affect investors who purchase in the offering. Stabilizing transactions consist of various bids for or purchases of notes or shares of our common stock made by the underwriter in the open market to peg, fix or maintain the price of the notes or our common stock prior to the completion of the offering.

Similar to other purchase transactions, the underwriter's purchases to cover short sales may have the effect of raising or maintaining the market price of the notes or preventing or retarding a

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decline in the market price of the notes. As a result, the price of the notes may be higher than the price that might otherwise exist in the open market.

Neither we nor the underwriter make any representation or prediction as to the direction or magnitude of any effect that the transactions described above may have on the price of the notes or our common stock. In addition, neither we nor the underwriter make any representation that the underwriter will engage in these transactions or that these transactions, once commenced, will not be discontinued without notice.

Other Relationships

The underwriter and its affiliates have engaged in, and may in the future engage in, investment banking and other commercial dealings in the ordinary course of business with us or our affiliates. They have received, or may in the future receive, customary fees and commissions for these transactions.

In addition, in the ordinary course of its business activities, the underwriter and its affiliates may make or hold a broad array of investments and actively trade debt and equity securities (or related derivative securities) and financial instruments (including bank loans) for their own account and for the accounts of their customers. Such investments and securities activities may involve securities and/or instruments of ours or our affiliates. The underwriter and its affiliates may also make investment recommendations and/or publish or express independent research views in respect of such securities or financial instruments and may hold, or recommend to clients that they acquire, long and/or short positions in such securities and instruments.

Electronic Offer, Sale and Distribution of Securities

In connection with the offering, the underwriter may distribute this prospectus supplement and the accompanying prospectus by electronic means, such as e-mail. In addition, Merrill Lynch, Pierce, Fenner & Smith Incorporated may facilitate Internet distribution for this offering to certain of its Internet subscription customers. Merrill Lynch, Pierce, Fenner & Smith Incorporated may allocate a limited principal amount of notes for sale to its online brokerage customers. An electronic prospectus supplement and the accompanying prospectus is available on the Internet web site maintained by Merrill Lynch, Pierce, Fenner & Smith Incorporated. Other than the prospectus supplement and the accompanying prospectus in electronic format, the information on the Merrill Lynch, Pierce, Fenner & Smith Incorporated web site is not part of this prospectus supplement.

Notice to Prospective Investors in the EEA

In relation to each Member State of the European Economic Area which has implemented the Prospectus Directive (each, a "Relevant Member State") an offer to the public of any securities which are the subject of the offering contemplated by this prospectus supplement and the accompanying prospectus (the "Securities") may not be made in that Relevant Member State once the prospectus supplement and the accompanying prospectus have been approved by the competent authority in such Member State and published in accordance with the Prospectus Directive as implemented except that an offer to the public in that Relevant Member State of any Securities may be made at any time under the following exemptions under the Prospectus Directive, if they have been implemented in that Relevant Member State:

(a) to legal entities which are authorised or regulated to operate in the financial markets or, if not so authorised or regulated, whose corporate purpose is solely to invest in securities;

(b) to any legal entity which has two or more of (1) an average of at least 250 employees during the last financial year; (2) a total balance sheet of more than €43,000,000 and

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(3) an annual net turnover of more than €50,000,000, as shown in its last annual or consolidated accounts;

(c) by the underwriter to fewer than 100 natural or legal persons (other than qualified investors as defined in the Prospectus Directive) subject to obtaining the prior consent of Merrill Lynch, Pierce, Fenner & Smith Incorporated for any such offer; or

(d) in any other circumstances falling within Article 3(2) of the Prospectus Directive,

provided that no such offer of Securities shall result in a requirement for the publication by Vertex or the underwriter of a prospectus pursuant to Article 3 of the Prospectus Directive.

Any person making or intending to make any offer of securities within the EEA should only do so in circumstances in which no obligation arises for us or the underwriter to produce a prospectus for such offer. Neither we nor the underwriter has authorized, nor do we authorize, the making of any offer of securities through any financial intermediary, other than offers made by the underwriter which constitute the final offering of securities contemplated in this prospectus.

For the purposes of this provision, the expression an "offer to the public" in relation to any Securities in any Relevant Member State means the communication in any form and by any means of sufficient information on the terms of the offer and any Securities to be offered so as to enable an investor to decide to purchase any Securities, as the same may be varied in that Member State by any measure implementing the Prospectus Directive in that Member State and the expression "Prospectus Directive" means Directive 2003/71/EC and includes any relevant implementing measure in each Relevant Member State.

Each person in a Relevant Member State who receives any communication in respect of, or who acquires any securities under, the offer of securities contemplated by this prospectus will be deemed to have represented, warranted and agreed to and with us and the underwriter that:

(A) it is a "qualified investor" within the meaning of the law in that Relevant Member State implementing Article 2(1)(e) of the Prospectus Directive; and

(B) in the case of any securities acquired by it as a financial intermediary, as that term is used in Article 3(2) of the Prospectus Directive, (i) the securities acquired by it in the offering have not been acquired on behalf of, nor have they been acquired with a view to their offer or resale to, persons in any Relevant Member State other than "qualified investors" (as defined in the Prospectus Directive), or in circumstances in which the prior consent of the representative has been given to the offer or resale; or (ii) where securities have been acquired by it on behalf of persons in any Relevant Member State other than qualified investors, the offer of those securities to it is not treated under the Prospectus Directive as having been made to such persons.

In addition, in the United Kingdom, this document is being distributed only to, and is directed only at, and any offer subsequently made may only be directed at persons who are "qualified investors" (as defined in the Prospectus Directive) (i) who have professional experience in matters relating to investments falling within Article 19 (5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005, as amended (the "Order") and/or (ii) who are high net worth companies (or persons to whom it may otherwise be lawfully communicated) falling within Article 49(2)(a) to (d) of the Order (all such persons together being referred to as "relevant persons"). This document must not be acted on or relied on in the United Kingdom by persons who are not relevant persons. In the United Kingdom, any investment or investment activity to which this document relates is only available to, and will be engaged in with, relevant persons.

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Notice to Prospective Investors in Switzerland

This document as well as any other material relating to the securities which are the subject of the offering contemplated by this prospectus supplement and the accompanying prospectus (the "Securities") does not constitute an issue prospectus pursuant to Articles 652a and/or 1156 of the Swiss Code of Obligations. The Securities will not be listed on the SIX Swiss Exchange and, therefore, the documents relating to the Securities, including, but not limited to, this document, do not claim to comply with the disclosure standards of the listing rules of the SIX Swiss Exchange and corresponding prospectus schemes annexed to the listing rules of the SIX Swiss Exchange. The Securities are being offered in Switzerland by way of a private placement, i.e. to a small number of selected investors only, without any public offer and only to investors who do not purchase the Securities with the intention to distribute them to the public. The investors will be individually approached by us from time to time. This document as well as any other material relating to the Securities is personal and confidential and does not constitute an offer to any other person. This document may only be used by those investors to whom it has been handed out in connection with the offering described herein and may neither directly nor indirectly be distributed or made available to other persons without our express consent. It may not be used in connection with any other offer and shall in particular not be copied and/or distributed to the public in (or from) Switzerland.

Notice to Prospective Investors in the Dubai International Financial Centre

This prospectus supplement and the accompanying prospectus relate to an Exempt Offer in accordance with the Offered Securities Rules of the Dubai Financial Services Authority ("DFSA"). This prospectus supplement and the accompanying prospectus are intended for distribution only to persons of a type specified in the Offered Securities Rules of the DFSA. It must not be delivered to, or relied on by, any other person. The DFSA has no responsibility for reviewing or verifying any documents in connection with Exempt Offers. The DFSA has not approved this prospectus supplement and the accompanying prospectus nor taken steps to verify the information set forth herein and has no responsibility for the prospectus supplement and the accompanying prospectus. The securities to which this prospectus supplement and the accompanying prospectus relate may be illiquid and/or subject to restrictions on their resale. Prospective purchasers of the securities offered should conduct their own due diligence on the securities. If you do not understand the contents of this prospectus supplement and the accompanying prospectus you should consult an authorized financial advisor.

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LEGAL MATTERS

Certain legal matters relating to the issuance of the notes offered hereby will be passed upon for us by Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C., Boston, Massachusetts. Certain legal matters will be passed upon for the underwriter by Cleary Gottlieb Steen & Hamilton LLP, New York, New York.

EXPERTS

The consolidated financial statements of Vertex Pharmaceuticals Incorporated appearing in Vertex Pharmaceuticals Incorporated's Annual Report (Form 10-K) for the year ended December 31, 2009 and the effectiveness of Vertex Pharmaceuticals Incorporated's internal control over financial reporting as of December 31, 2009 have been audited by Ernst & Young LLP, independent registered public accounting firm, as set forth in their report thereon, included therein, and incorporated herein by reference. Such consolidated financial statements are incorporated herein by reference in reliance upon such report given on the authority of such firm as experts in accounting and auditing.

INCORPORATION BY REFERENCE

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

(a) Our Annual Report on Form 10-K for the year ended December 31, 2009 (filing date February 19, 2010: Commission File No. 000-19319);

(b) Our Quarterly Reports on Form 10-Q for the periods ended March 31, 2010 and June 30, 2010 (filing dates May 3, 2010 and August 3, 2010: Commission File No. 000-19319);

(c) Our Current Reports on Form 8-K filed on May 17, 2010 (Items 1.01, 5.02 and 5.07); May 25, 2010 (Items 8.01 and 9.01); July 13, 2010 (Item 5.02); August 10, 2010 (Items 8.01 and 9.01) and September 7, 2010 (Items 8.01 and 9.01) (Commission File No. 000-19319);

(d) The portions of our definitive proxy statement on Schedule 14A that are deemed "filed" with the SEC under the Securities Exchange Act of 1934, as amended (filing date April 15, 2010: Commission File No. 000-19319); and

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

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In addition, all documents filed by us pursuant to Section 13(a), 13(c), 14 or 15(d) of the Securities Exchange Act of 1934, as amended, on or after the date of this prospectus supplement and before the termination of the offering under this prospectus supplement are deemed to be incorporated by reference into, and to be a part of, this prospectus supplement.

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

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

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PROSPECTUS

VERTEX PHARMACEUTICALS INCORPORATED

COMMON STOCK
DEBT SECURITIES

Vertex Pharmaceuticals Incorporated may from time to time offer to sell common stock and/or debt securities. This prospectus describes some of the general terms that may apply to these securities. The specific terms of any securities to be offered will be set forth in a supplement to this prospectus. We may sell these securities to or through one or more underwriters, dealers and agents, or directly to purchasers, on a continued or delayed basis.

Our common stock is listed on the Nasdaq Global Select Market under the symbol "VRTX." On February 17, 2010, the last reported sale price for our common stock was $39.78 per share. Prospective purchasers of our securities are urged to obtain current information as to the market prices of our common stock. We have not yet determined whether any of the other securities that may be offered by this prospectus will be listed on any exchange, inter-dealer quotation system or over-the-counter market. If we decide to seek listing of any such securities, a prospectus supplement relating to those securities will disclose the exchange, quotation system or market on which the securities will be listed.

Investing in our securities involves risks. See "Risk Factors" in our most recent Annual Report on Form 10-K, and any subsequent Quarterly Reports on Form 10-Q, which are incorporated by reference into this prospectus.

This prospectus may not be used to offer and sell securities unless accompanied by a prospectus supplement.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed upon the accuracy or adequacy of this prospectus. Any representation to the contrary is a criminal offense.

The date of this prospectus is February 19, 2010

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ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement that we filed with the Securities and Exchange Commission, or SEC, utilizing a "shelf" registration process. Under this shelf process, we may sell any combination of the securities described in this prospectus in one or more offerings. Each time securities are offered under this prospectus, we will provide a prospectus supplement that will contain specific information about the terms of that offering.

This prospectus does not contain all of the information included in the registration statement. For a more complete understanding of the offering of the securities, you should refer to the registration statement, including its exhibits. The prospectus supplement may also add, update or change information contained in this prospectus. You should read both this prospectus and the applicable prospectus supplement together with additional information under the headings "Where you can Find More Information" and "Incorporation by Reference." To the extent there are inconsistencies between any prospectus supplement, this prospectus and any documents incorporated by reference, the document with the most recent date will control.

You should rely only on information contained in, or incorporated by reference into, this prospectus and any prospectus supplement. We have not authorized anyone to provide you with information different from that contained in this prospectus or incorporated by reference in this prospectus. We are not making offers to sell the securities in any jurisdiction in which such an offer or solicitation is not authorized or in which the person making such offer or solicitation is not qualified to do so or to anyone to whom it is unlawful to make such offer or solicitation.

The information contained in this prospectus is accurate only as of the date on the front cover of the prospectus and information we have incorporated by reference in this prospectus is accurate only as of the date of the document incorporated by reference. You should not assume that the information contained in, or incorporated by reference into, this prospectus is accurate as of any other date.

WHERE YOU CAN FIND MORE INFORMATION

We are a public company and are required to file annual, quarterly and current reports, proxy statements and other information with the SEC pursuant to the Securities Exchange Act of 1934, as amended, or the Exchange Act. You may read and copy any document we file with the SEC at the SEC's Public Reference Room at 100 F Street, N.E., Washington, D.C. 20549. You can request copies of these documents by writing to the SEC and paying a fee for the copying cost. Please call the SEC at 1-800-SEC-0330 for more information about the operation of the public reference room. Our SEC filings are also available to the public at the SEC's website at *http://www.sec.gov*. The information on the SEC's website is not part of this prospectus, and any references to this website or any other website are inactive textual references only.

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

- inspect a copy of the registration statement, including the exhibits thereto, without charge at the SEC's public reference room;
- obtain a copy from the SEC upon payment of the fees prescribed by the SEC; or
- obtain a copy from the SEC's website.

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Our internet address is *www.vrtx.com*. Our annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K, and all amendments to those reports are also available to you free of charge through the "Finances/Investor Info" section of our website as soon as reasonably practicable after those materials have been electronically filed with, or furnished to, the SEC. Other than the documents filed with the SEC and incorporated by reference into this prospectus, the information contained on our website does not constitute a part of this prospectus.

INCORPORATION BY REFERENCE

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

- our annual report on Form 10-K for the year ended December 31, 2009 (filing date February 19, 2010: Commission File No. 000-19319);

- the portions of our definitive proxy statement on Schedule 14A that are deemed "filed" with the SEC under the Exchange Act (filing date April 8, 2009: Commission File No. 000-19319); and

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

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

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

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

RATIO OF EARNINGS TO FIXED CHARGES

Any time we offer debt securities pursuant to this prospectus, we will provide a table setting forth our ratio of earnings to fixed charges on a historical basis in the applicable prospectus supplement, if required.

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USE OF PROCEEDS

Except as otherwise provided in the applicable prospectus supplement, we intend to use the net proceeds from the sale of the securities covered by this prospectus for general corporate purposes. Additional information on the use of net proceeds from the sale of securities covered by this prospectus may be set forth in the prospectus supplement relating to the specific offering.

THE SECURITIES WE MAY OFFER

We may from time to time offer to sell common stock and/or debt securities. We will describe in the applicable prospectus supplement relating to any securities the particular terms of the securities offered by that prospectus supplement. We will also include in the prospectus supplement information, where applicable, about material United States federal income tax considerations relating to the securities, and the exchange, quotation system or market, if any, on which the securities will be listed.

DESCRIPTION OF CAPITAL STOCK

The following description of our capital stock and certain provisions of our articles of organization and by-laws is a summary and is qualified in its entirety by the provisions of our articles of organization and by-laws.

Our authorized capital stock consists of 300,000,000 shares of common stock, $0.01 par value, and 1,000,000 shares of preferred stock, $0.01 par value.

Common Stock

Holders of common stock are entitled to one vote for each share held on all matters submitted to a vote of stockholders and do not have cumulative voting rights. Accordingly, holders of a majority of the shares of common stock entitled to vote in any election of directors may elect all of the directors standing for election. Holders of common stock are entitled to receive ratably such dividends, if any, as may be declared by our Board of Directors out of funds legally available therefor, subject to any preferential dividend rights of any outstanding preferred stock. Upon the liquidation, dissolution or winding up of Vertex, the holders of common stock are entitled to receive ratably our net assets available after the payment of all debts and other liabilities and subject to any prior rights of any outstanding preferred stock. Holders of common stock have no preemptive, subscription, redemption, conversion or exchange rights. The rights, powers, preferences and terms of holders of common stock are subject to, and may be adversely affected by, the rights of the holders of shares of any series of preferred stock that we may designate and issue in the future.

Our common stock is listed on the Nasdaq Global Select Market under the symbol "VRTX."

Preferred Stock

Our Board of Directors has the authority, without further action by the stockholders, to issue up to 1,000,000 shares of preferred stock in one or more series and to fix the rights, powers, preferences and terms thereof, including dividend rights, conversion or exchange rights, voting rights, terms of redemption, liquidation preferences, sinking fund terms, the number of shares constituting any series or the designation of such series and any restrictions on the issue or reissue of any additional shares of such series or another series, without any further vote or action by stockholders. The issuance of preferred stock could adversely affect the voting power of holders of our common stock and the likelihood that such holders will receive dividend payments and payments upon liquidation and could have the effect of delaying, deferring or preventing a change in control.

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Stockholders Rights Plan

Pursuant to our Rights Agreement, as amended (the "Stockholder Rights Plan"), each share of common stock has an associated preferred share purchase right (each a "Right" and collectively, the "Rights"). Each Right entitles the holder to purchase from Vertex one half of one-hundredth of a share of series A junior participating preferred stock, $0.01 par value (the "Junior Preferred Stock"), of Vertex at a price of $135 per one half of one-hundredth of a share of the Junior Preferred Stock, subject to adjustment (the "Adjusted Purchase Price"). The Rights are not exercisable until after acquisition by a person or group of 15% or more of our outstanding common stock (an "acquiring person") or after the announcement of an intention to make or commencement of a tender offer or exchange offer the consummation of which would result in the beneficial ownership by a person or group of 15% or more of our outstanding common stock (the earlier of such dates being called the "Distribution Date"). Until the Distribution Date (or earlier redemption or expiration of the Rights), the Rights will be transferred with and only with the common stock. Until a Right is exercised, the Right will not entitle the holder thereof to any rights as a stockholder.

If any person or group becomes an acquiring person, each holder of a Right, other than Rights beneficially owned by the acquiring person, will thereafter have the right to receive upon exercise and payment of the Adjusted Purchase Price that number of shares of common stock having a market value of two times the Adjusted Purchase Price, and if Vertex is acquired in a business combination transaction or 50% or more of its assets are sold, each holder of a Right will thereafter have the right to receive upon exercise and payment of the Adjusted Purchase Price that number of shares of common stock of the acquiring company which at the time of the transaction will have a market value of two times the Adjusted Purchase Price.

At any time after any person becomes an acquiring person and prior to the acquisition by such person or group of 50% or more of the outstanding common stock, our Board of Directors may cause the Rights (other than Rights owned by such person or group) to be exchanged, in whole or in part, for common stock or junior preferred shares, at an exchange rate of one share of common stock per Right or one half of one-hundredth of a share of Junior Preferred Stock per Right.

At any time prior to the acquisition by a person or group of beneficial ownership of 15% or more of the outstanding common stock, our Board of Directors may redeem the Rights in whole at a price of $0.01 per Right.

The Rights have certain anti-takeover effects, in that they will cause substantial dilution to a person or group that attempts to acquire a significant interest in Vertex on terms not approved by the Board of Directors.

Provisions of Our Articles of Organization and By-laws and Massachusetts Law Relating to a Change in Control and Indemnification

Provisions of our articles of organization and by-laws and our Stockholder Rights Plan may discourage specific types of transactions involving an actual or potential change in control of Vertex that might be beneficial to Vertex or its stockholders. Our articles of organization provide for staggered terms for the members of the Board of Directors. Our by-laws grant the directors a right to adjourn annual meetings of stockholders, and certain provisions of the by-laws may be amended only with an 80% stockholder vote.

We are subject to Chapter 110F of the Massachusetts General Laws, an anti-takeover law. In general, this statute prohibits a publicly-held Massachusetts corporation from engaging in a "business combination" with an "interested stockholder" for a period of three years after the date of the transaction in which the person becomes an interested stockholder, unless (i) the interested stockholder obtains the approval of the board of directors prior to becoming an interested stockholder, (ii) the

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interested stockholder acquires 90% of the outstanding voting stock of the corporation (excluding shares held by certain affiliates of the corporation) at the time it becomes an interested stockholder or (iii) the business combination is approved by both the board of directors and the holders of two-thirds of the outstanding voting stock of the corporation (excluding shares held by the interested stockholder). Generally, an "interested stockholder" is a person who, together with affiliates and associates, owns (or at any time within the prior three years did own) 5% or more of the outstanding voting stock of the corporation. A "business combination" includes a merger, a stock or asset sale, and certain other transactions resulting in a financial benefit to the interested stockholders.

We are subject to Massachusetts General Laws Chapter 110D, entitled "Regulation of Control Share Acquisitions." In general, this statute provides that any stockholder of a corporation subject to this statute who acquires 20% or more of the outstanding voting stock of a corporation may not vote such stock unless the stockholders of the corporation so authorize. The Board of Directors may amend our by-laws to exclude us from this statute prospectively.

Our articles of organization provide that our directors will not be personally liable to us or our stockholders for monetary damages for breach of fiduciary duty as a director except for (i) any breach of such director's duty of loyalty to us or our stockholders, (ii) acts or omissions not in good faith or which involve intentional misconduct or a knowing violation of laws, (iii) the authorization of illegal dividends or redemptions, or the authorization of a loan of any of our assets to one of our officers or directors that is not repaid or (iv) any transactions from which such director derived an improper personal benefit. This provision does not eliminate director liability under federal securities laws or preclude non-monetary relief under state law. In addition, our by-laws provide that we may indemnify our directors and officers against all liabilities and expenses incurred in connection with service for us or on our behalf.

Transfer Agent and Registrar

Computershare Investor Services is the transfer agent and registrar for our common stock.

DESCRIPTION OF DEBT SECURITIES

The following description, together with the additional information we include in any applicable prospectus supplements, summarizes the material terms and provisions of the debt securities that we may offer under this prospectus. While the terms we have summarized below will apply generally to any future debt securities we may offer pursuant to this prospectus, we will describe the particular terms of any debt securities that we may offer in more detail in the applicable prospectus supplement. If we indicate in a prospectus supplement, the terms of any debt securities we offer under that prospectus supplement may differ from the terms we describe below.

We may sell from time to time, in one or more offerings under this prospectus, debt securities, which may be senior or subordinated. We will issue any such senior debt securities under a senior indenture that we will enter into with a trustee to be named in the senior indenture. We will issue any such subordinated debt securities under a subordinated indenture, which we will enter into with a trustee to be named in the subordinated indenture. We have filed forms of these documents as exhibits to the registration statement, which includes this prospectus. We use the term "indentures" to refer to both the senior indenture and the subordinated indenture. The indentures will be qualified under the Trust Indenture Act of 1939, as amended, or the Trust Indenture Act. We use the term "debenture trustee" to refer to either the trustee under the senior indenture or the trustee under the subordinated indenture, as applicable.

The following summaries of material provisions of the senior debt securities, the subordinated debt securities and the indentures are subject to, and qualified in their entirety by reference to, all the provisions of the indenture applicable to a particular series of debt securities.

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We conduct some of our operations through our subsidiaries. Our rights and the rights of our creditors, including holders of debt securities, to the assets of any subsidiary of ours upon that subsidiary's liquidation or reorganization or otherwise would be subject to the prior claims of that subsidiary's creditors, except to the extent that we may be a creditor with recognized claims against the subsidiary. Our subsidiaries' creditors would include trade creditors, debt holders, secured creditors and taxing authorities. Except as we may provide in a prospectus supplement, neither the debt securities nor the indentures restrict us or any of our subsidiaries from incurring indebtedness or from imposing restrictions on the ability of our subsidiaries to pay dividends to us or others. Under this caption, the phrase "the Company" refers solely to Vertex Pharmaceuticals Incorporated.

General

Each indenture provides that debt securities may be issued from time to time in one or more series and may be payable in currency of the United States or in foreign currencies or units based on or relating to foreign currencies. Neither indenture limits the amount of debt securities that may be issued thereunder, and each indenture provides that the specific terms of any series of debt securities shall be set forth in, or determined pursuant to, an authorizing resolution and/or a supplemental indenture, if any, relating to such series.

We will describe in each prospectus supplement the following terms relating to a series of debt securities:

the title;

the aggregate principal amount and any limit on the amount that may be issued;

the currency or units based on or relating to currencies in which debt securities of such series are denominated and the currency or units in which principal or interest or both will or may be payable;

whether we will issue the series of debt securities in global form, the terms of any global securities and who the depositary will be;

the maturity date and the date or dates on which principal will be payable;

the interest rate, which may be fixed or variable, or the method for determining the rate and the date interest will begin to accrue, the date or dates interest will be payable and the record dates for interest payment dates or the method for determining such dates;

the terms of the subordination of any series of subordinated debt;

the place or places where payments will be payable;

our right, if any, to extend the period of payment of interest and the maximum length of any such extension;

the date, if any, after which, and the price at which, we may, at our option, redeem debt securities of the series pursuant to any optional redemption provisions;

the date, if any, on which, and the price at which we are obligated, pursuant to any mandatory sinking fund provisions or otherwise, to redeem, or at the holder's option to purchase, debt securities of the series;

a discussion on any material or special United States federal income tax considerations applicable to a series of debt securities;

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the denominations in which we will issue the series of debt securities, if other than denominations of $1,000 and any integral multiple thereof; and

any other specific terms, preferences, rights or limitations of, or restrictions on, the debt securities.

We may issue debt securities that provide for an amount less than their stated principal amount to be due and payable upon declaration of acceleration of their maturity pursuant to the terms of the indenture. We will provide you with information on the United States federal income tax considerations and other special considerations applicable to any of these debt securities in the applicable prospectus supplement.

Conversion or Exchange Rights

We will set forth in the prospectus supplement the terms, if any, on which a series of debt securities may be convertible into or exchangeable for our common stock or other securities of ours. We will describe whether conversion or exchange is mandatory, at the option of the holder or at our option. We may include provisions pursuant to which the number of shares of our common stock or other securities of ours that the holders of the series of debt securities receive would be subject to adjustment.

Consolidation, Merger or Sale; No Protection in Event of a Change of Control or Highly Leveraged Transaction

The indentures do not contain any covenant that restricts our ability to merge or consolidate, or sell, convey, transfer or otherwise dispose of all or substantially all of our assets. However, if we are not the surviving entity in any such transaction, our successor or the acquirer of such assets must assume all of our obligations under the indentures or the debt securities, as appropriate.

Unless we state otherwise in the applicable prospectus supplement, the debt securities will not contain any provisions that may afford holders of the debt securities protection in the event we have a change of control or in the event of a highly leveraged transaction (whether or not such transaction results in a change of control), which could adversely affect holders of debt securities.

Events of Default Under the Indenture

We will set forth in the applicable prospectus supplement the events of default under the indentures with respect to any series of debt securities that we may issue.

No event of default with respect to a particular series of debt securities necessarily constitutes an event of default with respect to any other series of debt securities. The occurrence of an event of default may constitute an event of default under any bank credit agreements we may have in existence from time to time. In addition, the occurrence of certain events of default or an acceleration under the indenture may constitute an event of default under certain of our other indebtedness outstanding from time to time.

If an event of default with respect to debt securities of any series at the time outstanding occurs and is continuing, then, if so specified in the applicable prospectus supplement, the trustee or the holders of not less than a majority in principal amount of the outstanding debt securities of that series may, by a notice in writing to us (and to the debenture trustee if given by the holders), declare to be due and payable immediately the principal (or, if the debt securities of that series are discount securities, that portion of the principal amount as may be specified in the terms of that series) of and premium and accrued and unpaid interest, if any, on all debt securities of that series. Before a judgment or decree for payment of the money due has been obtained with respect to debt securities of any series, the holders of a majority in principal amount of the outstanding debt securities of that series

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may rescind and annul the acceleration if all events of default, other than the non-payment of accelerated principal, premium, if any, and interest, if any, with respect to debt securities of that series, have been remedied or waived as provided in the applicable indenture (including payments or deposits in respect of principal, premium or interest that had become due other than as a result of such acceleration). We refer you to the prospectus supplement relating to any series of debt securities that are discount securities for the particular provisions relating to acceleration of a portion of the principal amount of such discount securities upon the occurrence of an event of default.

Subject to the terms of the indentures, if an event of default under an indenture shall occur and be continuing, the debenture trustee will be under no obligation to exercise any of its rights or powers under such indenture at the request or direction of any of the holders of the applicable series of debt securities, unless such holders have offered the debenture trustee reasonable security or indemnity. The holders of a majority in principal amount of the outstanding debt securities of any series will have the right to direct the time, method and place of conducting any proceeding for any remedy available to the debenture trustee, or exercising any trust or power conferred on the debenture trustee, with respect to the debt securities of that series, provided that:

- the direction so given by the holder is not in conflict with any law or the applicable indenture; and
- subject to its duties under the Trust Indenture Act, the debenture trustee need not take any action that might involve it in personal liability or might be unduly prejudicial to the holders not involved in the proceeding.

A holder of the debt securities of any series will only have the right to institute a proceeding under the indentures or to appoint a receiver or trustee, or to seek other remedies if:

- the holder previously has given written notice to the debenture trustee of a continuing event of default with respect to that series;
- the holders of at least a majority in aggregate principal amount of the outstanding debt securities of that series have made written request, and such holders have offered reasonable indemnity to the debenture trustee to institute the proceeding as trustee; and
- the debenture trustee does not institute the proceeding, and does not receive from the holders of a majority in aggregate principal amount of the outstanding debt securities of that series other conflicting directions within 60 days after the notice, request and offer.

These limitations do not apply to a suit instituted by a holder of debt securities if we default in the payment of the principal, premium, if any, or interest on, the debt securities.

Modification of Indenture; Waiver

The debenture trustee and we may change the applicable indenture without the consent of any holders with respect to specific matters, including:

- to fix any ambiguity, defect or inconsistency in the indenture; and
- to change anything that does not materially adversely affect the interests of any holder of debt securities of any series issued pursuant to such indenture.

In addition, under the indentures, the rights of holders of a series of debt securities may be changed by us and the debenture trustee with the written consent of the holders of at least a majority in aggregate principal amount of the outstanding debt securities of each series that is affected.

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However, the debenture trustee and we may make the following changes only with the consent of each holder of any outstanding debt securities affected:

extending the fixed maturity of the debt securities of a series;

reducing the principal amount, reducing the rate of interest, or reducing any premium payable upon the redemption of any debt securities; or

reducing the percentage of debt securities, the holders of which are required to consent to any amendment or waiver.

Except for certain specified provisions, the holders of at least a majority in principal amount of the outstanding debt securities of any series may on behalf of the holders of all debt securities of that series waive our compliance with provisions of the indenture. The holders of a majority in principal amount of the outstanding debt securities of any series may on behalf of the holders of all the debt securities of such series waive any past default under the indenture with respect to that series and its consequences, except a default in the payment of the principal of, premium or any interest on any debt security of that series or in respect of a covenant or provision, which cannot be modified or amended without the consent of the holder of each outstanding debt security of the series affected; *provided, however,* that the holders of a majority in principal amount of the outstanding debt securities of any series may rescind an acceleration and its consequences, including any related payment default that resulted from the acceleration.

Discharge

Each indenture provides that we can elect to be discharged from our obligations with respect to one or more series of debt securities, except for obligations to:

register the transfer or exchange of debt securities of the series;

replace stolen, lost or mutilated debt securities of the series;

maintain paying agencies;

hold monies for payment in trust;

compensate and indemnify the trustee; and

appoint any successor trustee.

In order to exercise our rights to be discharged with respect to a series, we must deposit with the trustee money or government obligations sufficient to pay all the principal of, any premium, if any, and interest on, the debt securities of the series on the dates payments are due.

Form, Exchange and Transfer

We will issue the debt securities of each series only in fully registered form and, unless we otherwise specify in the applicable prospectus supplement, in denominations of $1,000 and any integral multiple thereof. The indentures provide that we may issue debt securities of a series in temporary or permanent global form and as book-entry securities that will be deposited with, or on behalf of, The Depository Trust Company or another depositary named by us and identified in a prospectus supplement with respect to that series.

At the option of the holder, subject to the terms of the indentures and the limitations applicable to global securities described in the applicable prospectus supplement, the holder of the debt securities of any series can exchange the debt securities for other debt securities of the same series, in any authorized denomination and of like tenor and aggregate principal amount.

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Subject to the terms of the indentures and the limitations applicable to global securities set forth in the applicable prospectus supplement, holders of the debt securities may present the debt securities for exchange or for registration of transfer, accompanied by a written instrument of transfer if so required by us or the security registrar, at the office of the security registrar designated by us for this purpose. Unless otherwise provided in the debt securities that the holder presents for transfer or exchange or in the applicable indenture, we will make no service charge for any registration of transfer or exchange, but we may require payment of any taxes or other governmental charges.

We will name in the applicable prospectus supplement the security registrar that we initially designate for any debt securities.

If we elect to redeem the debt securities of any series, we will not be required to:

issue, register the transfer of, or exchange any debt securities of that series during a period beginning at the opening of business 15 days before the day of mailing of a notice of redemption of any debt securities that may be selected for redemption and ending at the close of business on the day of the mailing; or

register the transfer of or exchange any debt securities so selected for redemption, in whole or in part, except the unredeemed portion of any debt securities we are redeeming in part.

Information Concerning the Debenture Trustee

The debenture trustee, other than during the occurrence and continuance of an event of default under the applicable indenture, undertakes to perform only those duties as are specifically set forth in the applicable indenture. Upon an event of default under an indenture, the debenture trustee under such indenture must use the same degree of care as a prudent person would exercise or use in the conduct of his or her own affairs. Subject to this provision, the debenture trustee is under no obligation to exercise any of the powers given it by the indentures at the request of any holder of debt securities unless it is offered reasonable security and indemnity against the costs, expenses and liabilities that it might incur.

Payment and Paying Agents

Unless we otherwise indicate in the applicable prospectus supplement, we will make payment of the interest on any debt securities on any interest payment date to the person in whose name the debt securities, or one or more predecessor securities, are registered at the close of business on the regular record date for the interest.

We will pay principal of and any premium and interest on the debt securities of a particular series presented at the office or agency designated by us, except that unless we otherwise indicate in the applicable prospectus supplement, will we make interest payments by check which we will mail to the holder. We will name in the applicable prospectus supplement the office or agency that we initially designate for the debt securities of a particular series. We will maintain an office or agency in each place of payment for the debt securities of a particular series.

All money we pay to a paying agent or the debenture trustee for the payment of the principal of or any premium or interest on any debt securities which remains unclaimed at the end of two years after such principal, premium or interest has become due and payable will be repaid to us, and the holder of the security thereafter may look only to us for payment thereof.

Governing Law

The indentures and the debt securities will be governed by and construed in accordance with the laws of the State of New York, except to the extent that the Trust Indenture Act is applicable.

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Subordination of Subordinated Debt Securities

The obligations of the Company pursuant to any subordinated debt securities will be subordinate and junior in priority of payment to certain of our other indebtedness to the extent described in a prospectus supplement. The subordinated indenture does not limit the amount of senior indebtedness we may incur. It also does not limit us from issuing any other secured or unsecured debt.

LEGAL MATTERS

Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C., Boston, Massachusetts, will provide us with an opinion as to the legal matters in connection with the securities to be offered under this prospectus.

EXPERTS

The consolidated financial statements of Vertex Pharmaceuticals Incorporated appearing in Vertex Pharmaceuticals Incorporated's Annual Report (Form 10-K) for the year ended December 31, 2009 and the effectiveness of Vertex Pharmaceuticals Incorporated's internal control over financial reporting as of December 31, 2009 have been audited by Ernst & Young LLP, independent registered public accounting firm, as set forth in their reports thereon, included therein, and incorporated herein by reference. Such consolidated financial statements are incorporated herein by reference in reliance upon such reports given on the authority of such firm as experts in accounting and auditing.

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$375,000,000

Vertex Pharmaceuticals Incorporated

% Convertible Senior Subordinated Notes due 2015

PROSPECTUS SUPPLEMENT

BofA Merrill Lynch

September , 2010