
**UNITED STATES
SECURITIES AND EXCHANGE COMMISSION**
Washington, D.C. 20549

FORM S-3

**REGISTRATION STATEMENT
UNDER
THE SECURITIES ACT OF 1933**

VERTEX PHARMACEUTICALS INCORPORATED

(Exact name of registrant as specified in its charter)

Massachusetts

(State or other jurisdiction of incorporation or organization)

04-3039129

(I.R.S. Employer Identification Number)

**130 Waverly Street
Cambridge, Massachusetts 02139
(617) 444-6100**

(Address, including zip code, and telephone number, including area code, of registrant's principal executive offices)

**Joshua S. Boger
Chief Executive Officer
Vertex Pharmaceuticals Incorporated
130 Waverly Street
Cambridge, Massachusetts 02139
(617) 444-6100**

(Name, address, including zip code, and telephone number, including area code, of agent for service)

With a copies to:

**Michael L. Fantozzi, Esq.
Mintz, Levin, Cohn, Ferris,
Glovsky and Popeo, P.C.
One Financial Center
Boston, Massachusetts 02111
(617) 542-6000**

**Kenneth S. Boger, Esq.
Senior Vice President and General Counsel
Vertex Pharmaceuticals Incorporated
130 Waverly Street
Cambridge, Massachusetts 02139
(617) 444-6100**

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

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

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

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

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

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

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

CALCULATION OF REGISTRATION FEE

Title of Each Class of Securities to be Registered	Amount to Be Registered	Proposed Maximum Offering Price Per Unit(2)	Proposed Maximum Aggregate Offering Price	Amount of Registration Fee
Common Stock, \$0.01 par value per share(1)	136,489	\$30.36	\$4,143,806	\$444

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

(2) Estimated solely for the purpose of calculating the registration fee pursuant to Rules 457(r) and 457(c) under the Securities Act of 1933, as amended, based upon the average of the high and low prices for the common stock of the Registrant, on August 10, 2006, as reported on the Nasdaq National Market.

PROSPECTUS

VERTEX PHARMACEUTICALS INCORPORATED

136,489 SHARES

COMMON STOCK

This prospectus relates to the resale from time to time of a total of up to 136,489 shares of our common stock by the selling stockholders described in the section entitled "Selling Stockholders" beginning on page 5 of this prospectus. The shares were issued to the selling stockholders in exchange for 5³/₄% convertible senior subordinated notes due in 2011 pursuant to exchange agreements by and between us and such holders. This prospectus relates to registration of the resale of the shares issued in the exchange transaction pursuant to resale registration rights agreements by and between us and such holders.

The selling stockholders may offer and sell any of the shares of common stock from time to time at fixed prices, at market prices or at negotiated prices, and may engage a broker, dealer or underwriter to sell the shares. For additional information on the possible methods of sale that may be used by the selling stockholders, you should refer to the section entitled "Plan of Distribution" on page 6 of this prospectus. We will not receive any proceeds from the sale of the shares of common stock by the selling stockholders.

Our common stock is listed on the Nasdaq National Market under the symbol "VRTX." On August 10, 2006, the last reported sale price for our common stock was \$30.44 per share.

You should consider carefully the risks that we have described in "Risk Factors" beginning on page 2 of this prospectus before deciding whether to invest in our common stock.

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 August 15, 2006

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ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement on Form S-3 that we filed with the Securities and Exchange Commission, or the SEC. Pursuant to this prospectus, the selling stockholders named on page 5 may sell up to a total of 136,489 shares of our common stock. This prospectus and the documents incorporated by reference herein include important information about us, the common stock being offered and other information you should know before investing. You should read this prospectus together with the additional information about us described in the sections below entitled "Available Information" and "Incorporation of Certain Information by Reference." You should rely only on information contained in, or incorporated by reference into, this prospectus. We have not authorized anyone to provide you with information different from that contained in, or incorporated by reference into, this prospectus. The information contained in this prospectus is accurate only as of the date on the front cover of the prospectus and information we have

AVAILABLE INFORMATION

We are a public company and are required to file annual, quarterly and current reports, proxy statements and other information with the SEC pursuant to the Securities Exchange Act of 1934, as amended (hereinafter referred to as the "Exchange Act"). You may read and copy any document we file at the SEC's Public Reference Room at 100 F Street, N.E., Washington, D.C. 20549. You can request copies of these documents by writing to the SEC and paying a fee for the copying cost. Please call the SEC at 1-800-SEC-0330 for more information about the operation of the public reference room. Our SEC filings are also available to the public on the SEC's web site at "<http://www.sec.gov>." In addition, our stock is listed for trading on the Nasdaq National Market. You can read and copy reports and other information concerning us at the offices of the National Association of Securities Dealers, Inc. located at 1735 K Street, Washington, D.C. 20006.

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

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

The Company's internet address is www.vrtx.com. The Company's 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 "Investors" 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 OF CERTAIN INFORMATION BY REFERENCE

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

- (a) Our Annual Report on Form 10-K for the year ended December 31, 2005 (filing date March 16, 2006: Commission File No. 000-19319);
- (b) Our Quarterly Report on Form 10-Q for the quarter ended March 31, 2006 (filing date May 9, 2006: Commission File No. 000-19319);
- (c) Our Quarterly Report on Form 10-Q for the quarter ended June 30, 2006 (filing date August 9, 2006: Commission File No. 000-19319);
- (d) Our Current Report on Form 8-K dated January 6, 2006 (filing date January 12, 2006), February 7, 2006 (filing date February 7, 2006, and as amended on Form 8-KA filed on February 13, 2006), March 8, 2006 (filing date March 9, 2006), March 17, 2006 (filing date March 23, 2006), May 11, 2006 (filing date May 15, 2006), June 26, 2006 (filing date June 26, 2006), June 30, 2006 (Item 1.01 only) (filing date June 30, 2006), and August 2, 2006 (filing date August 8, 2006);

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- (e) The portions of our definitive proxy statement on Schedule 14A that are deemed "filed" with the SEC under the Exchange Act (filing date March 31, 2006: Commission File No. 000-19319); and

- (f) 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.

You may request, orally or in writing, a copy of these documents, which will be provided to you at no cost, by contacting us at:

SUMMARY

This summary highlights only some of the information included or incorporated by reference in this prospectus. You should carefully read this prospectus together with the additional information about us described in the sections entitled "Available Information" and "Incorporation of Certain Information by Reference" before purchasing our common stock.

Vertex Pharmaceuticals

We are a biotechnology company in the business of discovering, developing and commercializing small molecule drugs for serious diseases, independently and with collaborators. We continue to make progress toward our goal of becoming a profitable pharmaceutical company with industry-leading capabilities in research, development and commercialization of products. We intend to continue investing in and building these capabilities as we advance our product candidates to market.

We have a number of drug candidates in development, including compounds targeting hepatitis C virus ("HCV") infection, rheumatoid arthritis ("RA"), cystic fibrosis, cancer, pain and HIV infection. Our corporate strategy is to retain principal responsibility for the development and commercialization of some of our proprietary drug candidates in certain major markets, concentrating a significant part of our overall development and commercialization resources on those drug candidates once we select them. We rely on collaborators to conduct development and commercialization of certain of our other drug candidates either worldwide or in markets upon which we are not currently focused. We are concentrating most of our drug development resources at the present time on three compounds: VX-950 (telaprevir) for the treatment of chronic HCV infection, VX-702 for the treatment of RA and VX-770 for the treatment of cystic fibrosis.

Collaborations will continue to be a key component of our corporate strategy. Collaborations provide us with financial support and other valuable resources for our research programs, development resources for our clinical drug candidates and marketing and sales support for our products and product candidates. In June 2006, we entered into a collaboration agreement with Janssen Pharmaceutica, N.V., which will provide funding to cover 50% of the costs incurred in developing VX-950 (telaprevir), and manufacture and commercialize VX-950 (telaprevir) worldwide except in the Far East, and in North America, where we have retained commercial rights.

We plan to continue to add promising potential products to our development pipeline through our continuing commitment to discovery research. Our drug design approach integrates biology, chemistry, biophysics, automation and information technologies to make the drug discovery process more efficient and productive. Our drug discovery expertise is a principal factor in the creation of our pipeline, which includes a number of potentially breakthrough compounds. In addition to our efforts to research and develop kinase inhibitors, we currently are conducting a productive research program in the area of ion channel modulation. We expect that future development candidates from our programs will be focused on the treatment of a wide variety of diseases and conditions.

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

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. Our internet address is www.vrtx.com.

The Offering

Securities offered by the selling stockholders

Up to 136,489 shares of our common stock.

Use of proceeds

We will not receive any proceeds from the sale of the common stock offered by this prospectus.

Nasdaq National Market Symbol

VRTX

RISK FACTORS

Investing in our common stock is very risky. Please carefully consider the risk factors described in our periodic reports filed with the SEC, including those set forth under the caption "Risk Factors" in our annual report on Form 10-K for the year ended December 31, 2005 (File No. 000-19319), and in our quarterly reports on Form 10-Q for the quarter ended March 31, 2006 and the quarter ended June 30, 2006, which are incorporated by reference in this prospectus. Before making an investment decision, you should carefully consider these risks as well as other information we include or incorporate by reference in this prospectus. You should be able to bear a complete loss of your investment.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

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

- our business strategy;

- our predicted development and commercial timelines;
- our financial outlook, including those contained in the reports we furnished to the SEC;
- the establishment, development and maintenance of collaborative relationships;
- our ability to identify and develop new potential products;
- our ability to achieve commercial acceptance of our products;
- our ability to scale up our manufacturing capabilities and facilities;
- the potential for the acquisition of new and complementary technologies, resources and products;
- our projected capital expenditures; and
- our liquidity.

In some cases, you can identify forward-looking statements by terminology such as “may,” “will,” “should,” “expects,” “anticipates,” “believes,” “estimates,” “predicts,” “potential” or “continue” or the negative of such terms or other comparable terminology. These statements are only predictions and involve known and unknown risks, uncertainties and other factors, including the risks outlined in the section of this prospectus entitled “Risk Factors,” that may cause our or our industry’s actual results to differ materially from the results, levels of activity, performance or achievements expressed or implied by such forward-looking statements. Before deciding to purchase our securities you should carefully consider the risks described in the “Risk Factors” section, in addition to the other information set forth in this prospectus and the documents incorporated by reference herein. Although we believe that the expectations reflected in the forward-looking statements are reasonable, we cannot guarantee future results, levels of activity, performance or achievements.

USE OF PROCEEDS

We will not receive any proceeds from the sale of the shares of our common stock by the selling stockholders.

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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 200,000,000 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 the 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 the net assets of Vertex 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 or conversion rights. The rights, preferences and privileges 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.

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, preferences, privileges and restrictions thereof, including dividend rights, conversion rights, voting rights, terms of redemption, liquidation preferences, sinking fund terms and the number of shares constituting any series or the designation of such 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.

Stockholders Rights Plan

Pursuant to our 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.

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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 Relating to a Change in Control and Certain Provisions of Massachusetts Law

Provisions of our articles of organization and by-laws and our Stockholder Rights Plan may discourage certain types of transactions involving an actual or potential change in control of Vertex that might be beneficial to the company 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 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 for monetary damages to us for breaches of their fiduciary duty as directors, unless they violated their duty of loyalty to us or our stockholders, acted in bad faith, knowingly or intentionally violated the law, authorized illegal dividends or redemptions, authorized a loan of any of our assets to one of our officers or directors that is not repaid or derived an improper personal benefit from their action as directors. 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

The Transfer Agent and Registrar for our common stock is Computershare Limited. The Transfer Agent’s address is P.O. Box 8040, Boston, Massachusetts 02266-8040, and its telephone number is (781) 575-3120.

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SELLING STOCKHOLDER

We have issued 136,489 shares of our common stock to the selling stockholder named below in exchange for 5³/₄% senior subordinated convertible notes due in 2011. We have filed this prospectus in order to permit the selling stockholder to resell to the public these shares of common stock issued in connection with that transaction.

The following table, to our knowledge, sets forth information regarding the beneficial ownership of our common stock by the selling stockholder as of August 15, 2006 and the number of shares being offered hereby by the selling stockholder. For purposes of the following description, the term “selling stockholder” includes pledgees, donees, permitted transferees or other permitted successors-in-interest selling shares received after the date of this prospectus from the selling stockholder. The information is based on information provided by or on behalf of the selling stockholder. Beneficial ownership is determined in accordance with the rules of the SEC, and includes voting or investment power with respect to shares, as well as any shares as to which the selling stockholder has the right to acquire beneficial ownership within sixty (60) days after August 15, 2006 through the exercise or conversion of any stock options, warrants, convertible debt or otherwise. Unless otherwise indicated below, the selling stockholder has sole voting and investment power with respect to its shares of common stock. The inclusion of any shares in this table does not constitute an admission of beneficial ownership for the selling stockholder. We will not receive any of the proceeds from the sale of our common stock by the selling stockholder.

Selling Stockholder	Shares Beneficially Owned Prior to Offering		Shares Being Offered	Shares Beneficially Owned After Offering(1)	
	Number	Percent(2)		Number	Percent(2)
Highbridge International LLC	822,000	*	136,489	685,511	*

* Less than 1%.

(1) We do not know when or in what amounts the selling stockholder may offer for sale the shares of common stock pursuant to this offering. The selling stockholder may choose not to sell any of the shares offered by this prospectus. Because the selling stockholder may offer all or some of the shares of common stock pursuant to this offering, and because there are currently no agreements, arrangements or undertakings with respect to the sale of any of the shares of common stock, we cannot estimate the number of shares of common stock that the selling stockholder will hold after completion of the offering. For purposes of this table, however, we have assumed that the selling stockholder will have sold all of the shares covered by this prospectus upon the completion of the offering.

(2) Percentages are based on 111,801,481 shares of common stock that were issued and outstanding as of August 7, 2006.

PLAN OF DISTRIBUTION

The selling stockholders may, from time to time, sell any or all of their shares of common stock on any stock exchange, market or trading facility on which the shares are traded or in private transactions. These sales may be at fixed or negotiated prices. The selling stockholders may use any one or more of the following methods when selling shares:

- ordinary brokerage transactions and transactions in which the broker-dealer solicits purchasers;
- block trades in which the broker-dealer will attempt to sell the shares as agent but may position and resell a portion of the block as principal to facilitate the transaction;
- purchases by a broker-dealer as principal and resale by the broker-dealer for its account;
- an exchange distribution in accordance with the rules of the applicable exchange;
- privately negotiated transactions;
- short sales;
- broker-dealers may agree with the selling stockholders to sell a specified number of such shares at a stipulated price per share;
- a combination of any such methods of sale; and
- any other method permitted pursuant to applicable law.

The selling stockholders may also sell shares under Rule 144 under the Securities Act, if available, rather than under this prospectus.

The selling stockholders may also engage in short sales against the box, puts and calls and other transactions in our securities or derivatives of our securities and may sell or deliver shares in connection with these trades.

Broker-dealers engaged by the selling stockholders may arrange for other brokers-dealers to participate in sales. Broker-dealers may receive commissions or discounts from the selling stockholders (or, if any broker-dealer acts as agent for the purchaser of shares, from the purchaser) in amounts to be negotiated. The selling stockholders do not expect these commissions and discounts to exceed what is customary in the types of transactions involved. Any profits on the resale of shares of common stock by a broker-dealer acting as principal might be deemed to be underwriting discounts or commissions under the Securities Act. Discounts, concessions, commissions and similar selling expenses, if any, attributable to the sale of shares will be borne by a selling stockholder. The selling stockholders may agree to indemnify any agent, dealer or broker-dealer that participates in transactions involving sales of the shares if liabilities are imposed on that person under the Securities Act.

The selling stockholders may from time to time pledge or grant a security interest in some or all of the shares of common stock owned by them and, if they default in the performance of their secured obligations, the pledgees or secured parties may offer and sell the shares of common stock from time to time under this prospectus after we have filed a prospectus supplement amending the list of selling stockholders to include the pledgee, transferee or other successors in interest as selling stockholders under this prospectus.

The selling stockholders also may transfer the shares of common stock in other circumstances, in which case the transferees, pledgees or other successors in interest will be the selling beneficial owners for purposes of this prospectus and may sell the shares of common stock from time to time under this prospectus after we have filed a prospectus supplement amending the list of selling stockholders to include the pledgee, transferee or other successors in interest as selling stockholders under this prospectus.

The selling stockholders and any broker-dealers or agents that are involved in selling the shares of common stock may be deemed to be “underwriters” within the meaning of the Securities Act in connection with such sales. In such event, any commissions received by such broker-dealers or agents and any profit on the resale of the shares of common stock purchased by them may be deemed to be underwriting commissions or discounts under the Securities Act.

The selling stockholders have advised us that they have not entered into any agreements, understandings or arrangements with any underwriters or broker-dealers regarding the sale of their shares of common stock, nor is there an underwriter or coordinating broker acting in connection with a proposed sale

of shares of common stock by any selling stockholder. If we are notified by any selling stockholder that any material arrangement has been entered into with a broker-dealer for the sale of shares of common stock, we will file a supplement to this prospectus if required. If the selling stockholders use this prospectus for any sale of the shares of common stock, they will be subject to the prospectus delivery requirements of the Securities Act.

The anti-manipulation rules of Regulation M under the Securities Exchange Act of 1934 may apply to sales of our common stock and activities of the selling stockholders.

LEGAL MATTERS

The validity of the common stock offered in this prospectus will be passed upon for us by Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C., Boston, Massachusetts.

EXPERTS

The consolidated financial statements of Vertex Pharmaceuticals Incorporated at December 31, 2005 and for the year then ended appearing in Vertex Pharmaceuticals Incorporated's Annual Report (Form 10-K) for the year ended December 31, 2005, and Vertex Pharmaceuticals Incorporated management's assessment of the effectiveness of internal control over financial reporting as of December 31, 2005 included therein, 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 and management's assessment are incorporated herein by reference in reliance upon such reports given on the authority of such firm as experts in accounting and auditing.

The consolidated financial statements of Vertex Pharmaceuticals Incorporated as of December 31, 2004 and for the years ended December 31, 2004 and 2003 incorporated in this prospectus by reference to the Annual Report on Form 10-K for the year ended December 31, 2005 have been so incorporated in reliance on the report of PricewaterhouseCoopers LLP, an independent registered public accounting firm, given on the authority of said firm as experts in auditing and accounting.

PART II

INFORMATION NOT REQUIRED IN PROSPECTUS

Item 14. Other Expenses of Issuance and Distribution

The following table sets forth our estimates (other than the SEC registration fee) of the expenses in connection with the issuance and distribution of the securities being registered, other than underwriting discounts and commissions.

Item	Amount
SEC registration fee	\$ 444
Legal fees and expenses	5,000
Accounting fees and expenses	15,000
Printing fees	5,000
Miscellaneous fees and expenses	4,556
Total	\$ 30,000

Item 15. Indemnification of Directors and Officers.

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

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

As to any matter disposed of by a compromise payment by any such person, pursuant to a consent decree or otherwise, Article V of the Registrant's By-laws provides that no indemnification shall be provided to such person for such payment or for any other expenses unless such compromise has been approved as in the best interests of the Registrant, after notice that it involves such indemnification (i) by a disinterested majority of the directors then in office or (ii) by a majority of the disinterested directors then in office provided there has been obtained an opinion in writing of independent legal counsel to the effect that such director or officer appeared to have acted in good faith in the reasonable belief that such person's action as in the best interest of the Registrant, or (iii) by the holders of a majority of the outstanding stock at the time entitled to vote for directors, voting as a single class, exclusive of any stock owned by any interested director or officer.

Article V of the Registrant's By-laws provides that expenses, including counsel fees, reasonably incurred by any director or officer in connection with the defense or disposition of any such action, suit or other proceeding may be paid from time to time by the Registrant at the discretion of a majority of

the disinterested directors then in office, in advance of the final disposition thereof, upon receipt of an undertaking by such director or officer to repay the Registrant the amounts so paid if it is ultimately determined that indemnification for such expenses is not authorized under Article V of the By-laws, which undertaking may be accepted by the Registrant without reference to the financial ability of such director or officer to make repayment.

Article V of the Registrant's By-laws gives the Board of Directors of the Registrant the power to authorize the purchase and maintenance of insurance, in such amounts as the Board of Directors may from time to time deem appropriate, on behalf of

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any person who is or was a director, officer, or agent of the Registrant, or who is or was serving at the request of the Registrant as a director, officer or agent of another organization in which the Registrant has any interest, direct or indirect, as a shareholder, creditor or otherwise, or with respect to any employee benefit plan, against any liability incurred by such person in any such capacity, or arising out of such person's status as such agent, whether or not such person is entitled to indemnification by the Registrant pursuant to Article V of otherwise and whether or not the Registrant would have the power to indemnify the person against such liability.

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

Sections 8.30 and 8.42 of the MBCA provide that if an officer or director discharges his or her duties in good faith and with the care that a person in a like position would reasonably exercise under similar circumstances and in a manner the officer or director reasonably believes to be in the best interests of the corporation, he or she will not be liable for such actions.

Item 16. Exhibits

(a) Exhibits.

Exhibit Number	Description of Document
3.1*	Restated Articles of Organization, filed with the Secretary of the Commonwealth of Massachusetts on July 31, 1991 (filed as Exhibit 3.1).
3.2*	Certificate of Vote of Directors Establishing a Series of a Class of Stock, filed with the Secretary of the Commonwealth of Massachusetts on July 31, 1991 (filed as Exhibit 3.3).
3.3**	Articles of Amendment, filed with the Secretary of the Commonwealth of Massachusetts on May 17, 1995 (filed as Exhibit 3.3).
3.4*	Articles of Amendment, filed with the Secretary of the Commonwealth of Massachusetts on June 4, 1997 (filed as Exhibit 3.2).
3.5*	Articles of Amendment, filed with the Secretary of the Commonwealth of Massachusetts on May 21, 2001 (filed as Exhibit 3.4).
3.6***	By-laws, as amended and restated as of May 11, 2005 (filed as Exhibit 3.1).
4.1****	Specimen common stock certificate (filed as Exhibit 4.1).
4.2*****	Stockholder Rights Agreement, dated as of July 1, 1991 (filed as Exhibit 4.2).
4.3*****	First Amendment to Rights Agreement, dated as of February 21, 1997 (filed as Exhibit 4.3).
4.4*****	Second Amendment to Rights Agreement, dated as of June 30, 2001 (filed as Exhibit 4.4).
4.5	Form of Registration Rights Agreement between Vertex Pharmaceuticals Incorporated and Highbridge International LLC (filed herewith).
5.1	Opinion of Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C. regarding legality of securities being registered (filed herewith).
23.1	Consent of PricewaterhouseCoopers LLP (filed herewith).
23.2	Consent of Ernst & Young LLP (filed herewith).
23.3	Consent of Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C. (included in the opinion filed as Exhibit 5.1).
24.1	Power of Attorney (included on signature page).

* Previously filed with the Commission as Exhibits to, and incorporated herein by reference from, the Registrant's Registration Statement on Form S-4, Registration No. 333-61480.

** Previously filed with the Commission as Exhibits to, and incorporated herein by reference from, the Registrant's Registration Statement on Form S-3, Registration No. 333-123731.

*** Previously filed with the Commission as an Exhibit to, and incorporated herein by reference from, the Registrant's Form 10-Q for the quarter ended June 30, 2005, File No. 000-19319.

**** Previously filed with the Commission as Exhibits to, and incorporated herein by reference from, the Registrant's Registration Statement on Form S-1, Registration No. 33-40966.

***** Previously filed with the Commission as an Exhibit to, and incorporated herein by reference from, the Registrant's Form 10-Q for the quarter ended June 30, 2001, File No. 000-19319.

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Item 17. Undertakings

The undersigned Registrant hereby undertakes:

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

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

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

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

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

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

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

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

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

(ii) Each prospectus required to be filed pursuant to Rule 424(b)(2), (b)(5) or (b)(7) as part of a registration statement in reliance on Rule 430B relating to an offering made pursuant to Rule 415(a)(1)(i), (vii) or (x) for the purpose of providing the information required by Section 10(a) of the Securities Act of 1933 shall be deemed to be part of and included in the registration statement as of the earlier of the date such form of prospectus is first used after effectiveness or the date of the first contract of sale of securities in the offering described in the prospectus. As provided in Rule 430B, for liability purposes of the issuer and any person that is at that date an underwriter, such date shall be deemed to be a new effective date of the registration statement relating to the securities in the registration statement to which the prospectus relates, and the offering of such securities at that time shall be deemed to be the initial *bona fide* offering thereof. *Provided, however*, that no statement made in a registration statement or prospectus that is part of the registration statement or made in a document incorporated or deemed incorporated by reference into the registration statement or prospectus that is part of the registration statement will, as to a purchaser with a time of contract of sale prior to such effective date, supersede or modify any statement that was made in the registration statement or prospectus that was part of the registration statement or made in any such document immediately prior to such effective date.

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

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(6) Insofar as indemnification for liabilities arising under the Securities Act of 1933 may be permitted to directors, officers and controlling persons of the Registrant pursuant to the foregoing provisions, or otherwise, the Registrant has been advised that in the opinion of the Securities and Exchange Commission such indemnification is against public policy as expressed in the Securities Act of 1933 and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by a Registrant of expenses incurred or paid by a director, officer or controlling person of a Registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, that Registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it against public policy as expressed in the Securities Act of 1933 and will be governed by the final adjudication of such issue.

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SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, the Registrant certifies that it has reasonable grounds to believe that it meets all of the requirements for filing on Form S-3 and has duly caused this Registration Statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of Cambridge, The Commonwealth of Massachusetts, on August 15, 2006.

VERTEX PHARMACEUTICALS INCORPORATED

By: /s/ Joshua S. Boger
Joshua S. Boger
President and Chief Executive Officer

We, the undersigned officers and directors of Vertex Pharmaceuticals Incorporated, hereby severally constitute and appoint Joshua S. Boger, Ian F. Smith and Valerie L. Andrews, and each of them singly (with full power to each of them to act alone), our true and lawful attorneys-in-fact and agents, with full power of substitution and resubstitution in each of them for him and in his name, place and stead, and in any and all capacities, to sign any and all amendments (including post-effective amendments) to this Registration Statement, and to file the same, with all exhibits thereto and other documents in

connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing requisite or necessary to be done in and about the premises, as full to all intents and purposes as he might or could do in person, hereby ratifying and confirming all that said attorneys-in-fact and agents or any of them or their or his substitute or substitutes may lawfully do or cause to be done by virtue hereof.

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

<u>Signature</u>	<u>Title</u>	<u>Date</u>
By: <u>/s/ Joshua S. Boger</u> Joshua S. Boger	Director, President and Chief Executive Officer (principal executive officer)	August 15, 2006.
By: <u>/s/ Ian F. Smith</u> Ian F. Smith	Chief Financial Officer (principal financial officer)	August 15, 2006.
By: <u>/s/ Johanna Messina Power</u> Johanna Messina Power	Controller (principal accounting officer)	August 15, 2006.
By: <u>/s/ Eric K. Brandt</u> Eric K. Brandt	Director	August 15, 2006.
By: <u>/s/ Roger W. Brimblecombe</u> Roger W. Brimblecombe	Director	August 15, 2006.
By: <u>/s/ Stuart J.M. Collinson</u> Stuart J.M. Collinson	Director	August 15, 2006.
By: <u>/s/ Eugene H. Cordes</u> Eugene H. Cordes	Director	August 15, 2006.
By: <u>/s/ Matthew W. Emmens</u> Matthew W. Emmens	Director	August 15, 2006.
By: <u>/s/ Bruce I. Sachs</u> Bruce I. Sachs	Director	August 15, 2006.
By: <u>/s/ Charles A. Sanders</u> Charles A. Sanders	Director, Chairman	August 15, 2006.
By: <u>/s/ Eve E. Slater</u> Eve E. Slater	Director	August 15, 2006.
By: <u>/s/ Elaine S. Ullian</u> Elaine S. Ullian	Director	August 15, 2006.

RESALE REGISTRATION RIGHTS AGREEMENT

Resale Registration Rights Agreement (this "Agreement"), dated August 2, 2006, between Vertex Pharmaceuticals Incorporated, a Massachusetts corporation (together with any successor entity, the "Issuer"), and Highbridge International LLC (the "Investor").

Pursuant to the Exchange Agreement, dated August 2, 2006, between the Issuer and the Investor (the "Exchange Agreement"), the Issuer has agreed to issue 136,489 restricted shares (the "Shares") of common stock, par value \$0.01 per share, of the Issuer (the "Common Stock") to Investor in exchange for \$2,000,000 principal amount of 5¾% Convertible Senior Subordinated Notes due 2011. In connection with the exchange, the Issuer has agreed to provide the registration rights set forth in this Agreement.

The parties hereby agree as follows:

1. DEFINITIONS. As used in this Agreement, the following capitalized terms shall have the following meanings:

AGREEMENT: As defined in the preamble hereto.

BUSINESS DAY: A day other than a Saturday or Sunday or any federal holiday in the United States.

COMMISSION: Securities and Exchange Commission.

COMMON STOCK: As defined in the preamble hereto.

EFFECTIVENESS PERIOD: As defined in Section 2(ii) hereof.

EXCHANGE ACT: Securities Exchange Act of 1934, as amended.

ISSUER: As defined in the preamble hereto.

PERSON: An individual, partnership, corporation, unincorporated organization, trust, joint venture or a government or agency or political subdivision thereof.

PROSPECTUS: The prospectus included in a Shelf Registration Statement, as amended or supplemented by any prospectus supplement and by all other amendments thereto, including post-effective amendments, and all material incorporated by reference into such Prospectus.

SECURITIES ACT: Securities Act of 1933, as amended.

SHELF REGISTRATION STATEMENT: As defined in Section 2(i) hereof.

SUSPENSION PERIOD: As defined in Section 4(b)(i) hereof.

TRANSFER RESTRICTED SECURITIES: Each Share until the earlier of:

- (i) the date on which such Share has been effectively registered under the Securities

Act and disposed of in accordance with the Shelf Registration Statement;

- (ii) the earlier of (i) the date on which such Share is transferred in compliance with Rule 144 under the Securities Act or may be sold or transferred pursuant to Rule 144(k) under the Securities Act (or any other similar provision then in force) or (ii) November 30, 2007; or

- (iii) the date on which such Share ceases to be outstanding (whether as a result of redemption, repurchase and cancellation, conversion or otherwise).

2. SHELF REGISTRATION.

The Issuer shall:

- (i) not later than August 16, 2006, cause to be filed an automatic shelf registration statement, as defined in Rule 405 under the Securities Act, or an automatically effective, post-effective amendment to a currently effective registration statement (the "Shelf Registration Statement"), which Shelf Registration Statement shall, among other things, provide for resales of all Transfer Restricted Securities held by the Investor (it being understood that the Shelf Registration Statement may include other securities of the Issuer with respect to registration rights have been granted in connection with other exchanges);

- (ii) use its best efforts to keep the Shelf Registration Statement continuously effective, supplemented and amended as required by the provisions of Section 3(b) hereof to the extent necessary to ensure that (A) it is available for resales by the Investor of Transfer Restricted Securities entitled to the benefit of this Agreement and (B) conforms with the requirements of this Agreement and the Securities Act and the rules and regulations of the Commission promulgated thereunder as announced from time to time for a period (the "Effectiveness Period") of:

- (1) up to November 30, 2007; or

(2) such shorter period that will terminate when (X) the Investor is able to sell all Transfer Restricted Securities immediately without restriction pursuant to Rule 144(k) under the Securities Act or any successor rule thereto, (Y) when all Transfer Restricted Securities have ceased to be outstanding (whether as a result of repurchase and cancellation or otherwise) or (Z) all Transfer Restricted Securities registered under the Shelf Registration Statement have been sold.

3. REGISTRATION PROCEDURES.

(a) In connection with the Shelf Registration Statement, the Issuer shall comply with all the provisions of Section 3(b) hereof and shall use its commercially reasonable efforts to effect such registration to permit the sale of the Transfer Restricted Securities being

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sold in accordance with the intended method or methods of distribution thereof, and pursuant thereto, shall as expeditiously as possible prepare and file with the Commission a Shelf Registration Statement relating to the registration on any appropriate form under the Securities Act.

(b) In connection with the Shelf Registration Statement and any Prospectus required by this Agreement to permit the sale or resale of Transfer Restricted Securities, the Issuer shall:

(i) Subject to any notice by the Issuer in accordance with this Section 3(b) of the existence of any fact or event of the kind described in Section 4(b)(iii)(D), use its commercially reasonable efforts to keep the Shelf Registration Statement continuously effective during the Effectiveness Period. Upon the occurrence of any event that would cause the Shelf Registration Statement or the Prospectus contained therein (A) to contain a material misstatement or omission or (B) not be effective and usable for resale of Transfer Restricted Securities during the Effectiveness Period, the Issuer shall file promptly an appropriate amendment to the Shelf Registration Statement or a report filed with the Commission pursuant to Section 13(a), 13(c), 14 or 15(d) of the Exchange Act, in the case of clause (A), correcting any such misstatement or omission, and, in the case of either clause (A) or (B), use its commercially reasonable efforts to cause any such amendment to be declared effective and the Shelf Registration Statement and the related Prospectus to become usable for their intended purposes as soon as practicable thereafter. Notwithstanding the foregoing, the Issuer may suspend the effectiveness of the Shelf Registration Statement by written notice to the Investor for a period not to exceed an aggregate of 45 days in any 90-day period (each such period, a "Suspension Period") if:

(x) an event occurs and is continuing as a result of which the Shelf Registration Statement would, in the Issuer's reasonable judgment, contain an untrue statement of a material fact or omit to state a material fact required to be stated therein or necessary to make the statements therein not misleading; and

(y) the Issuer reasonably determines that the disclosure of such event at such time would have a material adverse effect on the business of the Issuer (and its subsidiaries, if any, taken as a whole);

PROVIDED that in the event the disclosure relates to a previously undisclosed proposed or pending material business transaction, the disclosure of which would impede the Issuer's ability to consummate such transaction, the Issuer may extend a Suspension Period from 45 days to 60 days; PROVIDED, HOWEVER, that Suspension Periods shall not exceed an aggregate of 90 days in any 360-day period.

(ii) Prepare and file with the Commission such amendments and post-effective amendments to the Shelf Registration Statement as may be necessary to keep the Shelf Registration Statement effective during the Effectiveness Period; cause the Prospectus to be supplemented by any required Prospectus supplement,

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and as so supplemented to be filed pursuant to Rule 424 under the Securities Act, and to comply fully with the applicable provisions of Rules 424, 430A and 430B under the Securities Act in a timely manner; and comply with the provisions of the Securities Act with respect to the disposition of all securities covered by the Shelf Registration Statement during the applicable period in accordance with the intended method or methods of distribution by the sellers thereof set forth in the Shelf Registration Statement or Prospectus supplement.

(iii) Advise the Investor promptly:

(A) with respect to the Shelf Registration Statement or any post-effective amendment thereto, when the same has become effective, and when the Prospectus or any Prospectus supplement or post-effective amendment has been filed,

(B) of any request by the Commission for amendments to the Shelf Registration Statement or amendments or supplements to the Prospectus or for additional information relating thereto,

(C) of the issuance by the Commission of any stop order suspending the effectiveness of the Shelf Registration Statement under the Securities Act or of the suspension by any state securities commission of the qualification of the Transfer Restricted Securities for offering or sale in any jurisdiction, or the initiation of any proceeding for any of the preceding purposes, or

(D) of the existence of any fact or the happening of any event, during the Effectiveness Period, that makes any statement of a material fact made in the Shelf Registration Statement or the Prospectus, any amendment or supplement thereto, or any document incorporated by reference therein untrue, or that requires the making of any additions to or changes in the Shelf Registration Statement or the Prospectus in order to make the statements therein not misleading.

If at any time the Commission shall issue any stop order suspending the effectiveness of the Shelf Registration Statement, or any state securities commission or other regulatory authority shall issue an order suspending the qualification or exemption from qualification of the Transfer Restricted

Securities under state securities or Blue Sky laws, the Issuer shall use its commercially reasonable efforts to obtain the withdrawal or lifting of such order at the earliest possible time.

(iv) Furnish to the Investor a copy of the Shelf Registration Statement and copies of any Prospectus included therein or any amendments or supplements to the Shelf Registration Statement or Prospectus (other than documents incorporated by reference after the initial filing of the Shelf Registration Statement).

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(v) Make available at reasonable times for inspection by the Investor and any attorney or accountant retained by the Investor, all financial and other records, pertinent corporate documents and properties of the Issuer as shall be reasonably necessary to enable them to exercise any applicable due diligence responsibilities, and cause the Issuer's officers, directors, managers and employees to supply all information reasonably requested by any such representative or representatives of the Investor, attorney or accountant in connection with the Shelf Registration Statement after the filing thereof and before its effectiveness; PROVIDED, HOWEVER, that any information designated by the Issuer as confidential at the time of delivery of such information shall be kept confidential by the recipient thereof.

(vi) If requested by the Investor, promptly incorporate in the Shelf Registration Statement or Prospectus, pursuant to a supplement or post-effective amendment if necessary, such information as the Investor may reasonably request to have included therein, including, without limitation: (1) information relating to the "Plan of Distribution" of the Transfer Restricted Securities, and (2) any other terms of the offering of the Transfer Restricted Securities to be sold in such offering; and make all required filings of such Prospectus supplement or post-effective amendment as soon as reasonably practicable after the Issuer is notified of the matters to be incorporated in such Prospectus supplement or post-effective amendment. Notwithstanding the foregoing, following the effective date of the Shelf Registration Statement, the Issuer shall not be required to file more than one such supplement or post-effective amendment to reflect changes in the amount of Transfer Restricted Securities held by the Investor at the request of such Investor in any 30-day period.

(vii) Furnish to the Investor without charge, at least one copy of the Shelf Registration Statement, as first filed with the Commission, and of each amendment thereto (and any documents incorporated by reference therein or exhibits thereto (or exhibits incorporated in such exhibits by reference) as the Investor may request).

(viii) Deliver to the Investor, without charge, as many copies of the Prospectus (including each preliminary prospectus) and any amendment or supplement thereto as the Investor reasonably may request; subject to any notice by the Issuer in accordance with this Section 3(b) of the existence of any fact or event of the kind described in Section 3(b)(iii)(D), the Issuer hereby consents to the use of the Prospectus and any amendment or supplement thereto by the Investor, in connection with the offering and the sale of the Transfer Restricted Securities covered by the Prospectus or any amendment or supplement thereto.

(ix) Cooperate with the Investor to facilitate the timely preparation and delivery of certificates representing Transfer Restricted Securities to be sold and not bearing any restrictive legends (unless required by applicable securities laws); and enable such Transfer Restricted Securities to be in such denominations and

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registered in such names as the Investor may request at least two Business Days before any sale of Transfer Restricted Securities made by the Investor.

(x) Use its commercially reasonable efforts to cause the Transfer Restricted Securities covered by the Shelf Registration Statement to be registered with or approved by such other U.S. governmental agencies or authorities as may be necessary to enable the seller or sellers thereof or the underwriter(s), if any, to consummate the disposition of such Transfer Restricted Securities.

(xi) Subject to Section 3(b)(i) hereof, if any fact or event contemplated by Section 3(b)(iii)(D) hereof shall exist or have occurred, use its reasonable commercially reasonable efforts to prepare a supplement or post-effective amendment to the Shelf Registration Statement or related Prospectus or any document incorporated therein by reference or file any other required document so that, as thereafter delivered to the purchasers of Transfer Restricted Securities, the Prospectus will not contain an untrue statement of a material fact or omit to state any material fact required to be stated therein or necessary to make the statements therein not misleading.

(xii) Provide CUSIP numbers for all Transfer Restricted Securities not later than the effective date of the Shelf Registration Statement.

(xiii) Otherwise use its commercially reasonable efforts to comply with all applicable rules and regulations of the Commission and all reporting requirements under the rules and regulations of the Exchange Act.

(c) The Investor agrees by acquisition of a Transfer Restricted Security that, upon receipt of any notice from the Issuer of the existence of any fact of the kind described in Section 3(b)(iii)(D) hereof, the Investor will discontinue disposition of Transfer Restricted Securities pursuant to the Shelf Registration Statement, and hold the content of such notice from the Issuer in confidence, until:

(i) the Investor has received copies of the supplemented or amended Prospectus contemplated by Section 3(b)(viii) hereof; or

(ii) the Investor is advised in writing by the Issuer that the use of the Prospectus may be resumed, and has received copies of any additional or supplemental filings that are incorporated by reference in the Prospectus.

If so directed by the Issuer, the Investor will deliver to the Issuer all copies, other than permanent file copies then in the Investor's possession, of the Prospectus covering such Transfer Restricted Securities that was current at the time of receipt of such notice of suspension.

(d) (1) The Investor shall furnish to the Issuer in writing such information regarding the Investor and the proposed distribution by the Investor of its Transfer Restricted Securities as the Issuer may reasonably request for use in connection with the Shelf Registration Statement or Prospectus or preliminary Prospectus included therein. The Investor shall promptly furnish to the Issuer in writing such other information as the Issuer may from time to time

reasonably request in writing. The Investor agrees to furnish promptly to the Issuer all information required to be disclosed in order to make information previously furnished to the Issuer by the Investor not materially misleading. The Issuer shall take action so that the Investor is permitted to deliver the Prospectus forming a part thereof as of such time to purchasers of the Investor's Transfer Restricted Securities in accordance with applicable law.

4. REGISTRATION EXPENSES.

(a) All expenses incident to the Issuer's performance of or compliance with this Agreement shall be borne by the Issuer regardless of whether a Shelf Registration Statement becomes effective, including, without limitation:

- (i) all registration and filing fees and expenses;
- (ii) all fees and expenses of compliance with federal securities and state Blue Sky or securities laws;
- (iii) all expenses of printing (including printing of Prospectuses, messenger and delivery services and telephone);
- (iv) all fees and disbursements of counsel to the Issuer;
- (v) all application and filing fees in connection with listing (or authorizing for quotation) the Common Stock on a national securities exchange or automated quotation system pursuant to the requirements hereof; and
- (vi) all fees and disbursements of independent certified public accountants of the Issuer (including the expenses of any special audit and comfort letters required by or incident to such performance).

The Issuer shall bear its internal expenses (including, without limitation, all salaries and expenses of its officers and employees performing legal, accounting or other duties), the expenses of any annual audit and the fees and expenses of any Person, including special experts, retained by the Issuer.

5. INDEMNIFICATION AND CONTRIBUTION.

(a) The Issuer agrees to indemnify and hold harmless the Investor and each Person, if any, who controls the Investor within the meaning of either Section 15 of the Securities Act or Section 20 of the Exchange Act against any and all loss, liability, claim, damage and expense whatsoever, as incurred, arising out of any untrue statement or alleged untrue statement of a material fact contained in any Shelf Registration Statement (or any amendment or supplement thereto), including all documents incorporated therein by reference, or the omission or alleged omission therefrom of a material fact required to be stated therein or necessary to make the statements therein not misleading, or arising out of any untrue statement or alleged untrue statement of a material fact contained in any Prospectus (or any amendment or supplement thereto) or the omission or alleged omission therefrom of a material fact necessary in order to make the statements therein, in the light of the circumstances under which they were

made, not misleading; PROVIDED, HOWEVER, that this indemnity agreement shall not apply to any loss, liability, claim, damage or expense to the extent arising out of any untrue statement or omission or alleged untrue statement or omission made in reliance upon and in conformity with written information furnished to the Issuer by the Investor expressly for use in a Shelf Registration Statement (or any amendment thereto) or any Prospectus (or any amendment or supplement thereto).

(b) The Investor agrees to indemnify and hold harmless the Issuer, and each Person, if any, who controls the Issuer, within the meaning of Section 15 of the Securities Act or Section 20 of the Exchange Act, against any and all loss, liability, claim, damage and expense described in the indemnity contained in Section 5(a) hereof, as incurred, but only with respect to untrue statements or omissions, or alleged untrue statements or omissions, made in any Shelf Registration Statement (or any amendment or supplement thereto) or any Prospectus (or any amendment or supplement thereto) in reliance upon and in conformity with written information with respect to the Investor furnished to the Issuer by the Investor expressly for use in the Shelf Registration Statement (or any amendment thereto) or such Prospectus (or any amendment or supplement thereto); PROVIDED, HOWEVER, that the Investor shall not be liable for any claims hereunder in excess of the amount of net proceeds received by the Investor from the sale of Transfer Restricted Securities pursuant to such Shelf Registration Statement.

(c) Each indemnified party shall give notice as promptly as reasonably practicable to each indemnifying party of any action or proceeding commenced against it in respect of which indemnity may be sought hereunder, but failure so to notify an indemnifying party shall not relieve such indemnifying party from any liability hereunder to the extent it is not materially prejudiced as a result thereof and in any event shall not relieve it from any liability which it may have otherwise than on account of this indemnity agreement. An indemnifying party may participate at its own expense in the defense of such action; PROVIDED, HOWEVER, that counsel to the indemnifying party shall not (except with the consent of the indemnified party) also be counsel to the indemnified party. In no event shall the indemnifying party or parties be liable for the fees and expenses of more than one counsel (in addition to any local counsel) separate from their own counsel for all indemnified parties in connection with any one action or separate but similar or related actions in the same jurisdiction arising out of the same general allegations or circumstances.

For purposes of this Section 5, each Person, if any, who controls the Investor within the meaning of Section 15 of the Securities Act or Section 20 of the Exchange Act shall have the same rights to contribution as the Investor, and each director of the Issuer, and each Person, if any, who controls the Issuer within the meaning of Section 15 of the Securities Act or Section 20 of the Exchange Act shall have the same rights to contribution as the Issuer.

6. MISCELLANEOUS.

(a) NO INCONSISTENT AGREEMENTS. The Issuer will not, on or after the date of this Agreement, enter into any agreement with respect to its securities that is inconsistent with the rights granted to the Investor in this Agreement or otherwise conflicts with the provisions hereof.

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(b) AMENDMENTS AND WAIVERS. This Agreement may not be amended, modified or supplemented, and waivers or consents to or departures from the provisions hereof may not be given, unless the Issuer has obtained the written consent of the Investor.

(c) NOTICES. All notices and other communications provided for or permitted hereunder shall be made in writing by hand-delivery, first-class mail (registered or certified, return receipt requested), telex, telecopier, or air courier guaranteeing overnight delivery:

(i) if to the Investor:

Highbridge Capital Management, LLC
9 West 57th Street
New York, NY 10019
Facsimile: (212) 287-4915

(ii) if to the Issuer:

Vertex Pharmaceuticals Incorporated 130 Waverly Street
Cambridge, Massachusetts 02139
Attention: Investor Relations

With a copy to:

Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C.
One Financial Center Boston, Massachusetts 02111
Attention: Michael Fantozzi, Esq.

All such notices and communications shall be deemed to have been duly given: at the time delivered by hand, if personally delivered; five Business Days after being deposited in the mail, postage prepaid, if mailed; when answered back, if telexed; when receipt acknowledged, if telecopied; and on the next Business Day, if timely delivered to an air courier guaranteeing overnight delivery.

(d) SUCCESSORS AND ASSIGNS. This Agreement shall inure to the benefit of and be binding upon the successors and assigns of each of the parties, PROVIDED, HOWEVER, that this Agreement shall not inure to the benefit of or be binding upon a successor or assign of the Investor unless and to the extent such successor or assign acquired Transfer Restricted Securities from the Investor. If any transferee of the Investor shall acquire Transfer Restricted Securities, in any manner, whether by operation of law or otherwise, such Transfer Restricted Securities shall be held subject to all of the terms of this Agreement, and by taking and holding such Transfer Restricted Securities such person shall be conclusively deemed to have agreed to be bound by and to perform all of the terms and provisions of this Agreement.

(e) COUNTERPARTS. This Agreement may be executed in any number of counterparts and by the parties hereto in separate counterparts, each of which when so executed

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shall be deemed to be an original and all of which taken together shall constitute one and the same agreement.

(f) HEADINGS. The headings in this Agreement are for convenience of reference only and shall not limit or otherwise affect the meaning hereof.

(g) GOVERNING LAW. This Agreement shall be governed by, and construed in accordance with, the law of the Commonwealth of Massachusetts, without regard to conflict of laws principles thereof.

(h) SEVERABILITY. If any one or more of the provisions contained herein, or the application thereof in any circumstance, is held invalid, illegal or unenforceable, the validity, legality and enforceability of any such provision in every other respect and of the remaining provisions contained herein shall not be affected or impaired thereby.

(i) ENTIRE AGREEMENT. This Agreement is intended by the parties as a final expression of their agreement and intended to be a complete and exclusive statement of the agreement and understanding of the parties hereto in respect of the subject matter contained herein. There are no restrictions, promises, warranties or undertakings, other than those set forth or referred to herein with respect to the registration rights granted by the Issuer with respect to the Transfer Restricted Securities. This Agreement supersedes all prior agreements and understandings between the parties with respect to such subject matter.

[REMAINDER OF PAGE INTENTIONALLY LEFT BLANK]

[SIGNATURES PAGE FOLLOWS]

[Counterpart signature page of Resale Registration Rights Agreement made as of the 2nd day of August, 2006, by and among Vertex Pharmaceuticals Incorporated and the undersigned.]

IN WITNESS WHEREOF, the parties have executed this Agreement as of the date first written above.

VERTEX PHARMACEUTICALS
INCORPORATED

By: /s/ Richard C. Garrison

Name: Richard C. Garrison
Title: Senior Vice President and Catalyst

HIGHBRIDGE INTERNATIONAL LLC

BY: HIGHBRIDGE CAPITAL MANAGEMENT, LLC

By: /s/ A. J. Starr

Authorized Signatory

MINTZ LEVIN LETTERHEAD

August 15, 2006

Vertex Pharmaceuticals Incorporated
130 Waverly Street
Cambridge, MA 02139

Ladies and Gentlemen:

We have acted as counsel to Vertex Pharmaceuticals Incorporated, a Massachusetts corporation (the "Company"), in connection with the preparation and filing with the Securities and Exchange Commission of a Registration Statement on Form S-3 (the "Registration Statement"), pursuant to which the Company is registering under the Securities Act of 1933, as amended (the "Securities Act"), 136,489 shares (the "Shares") of common stock, \$0.01 par value per share (the "Common Stock"), which may be sold by the selling stockholders named in the prospectus included in the Registration Statement (the "Selling Stockholders") from time to time on a delayed or continuous basis pursuant to Rule 415 under the Securities Act.

In connection with this opinion, we have examined the Company's Restated Articles of Organization, and the Company's ByLaws, both as currently in effect, such other records of the corporate proceedings of the Company and certificates of the Company's officers as we have deemed relevant; and the Registration Statement and the exhibits thereto.

In our examination, we have assumed the genuineness of all signatures, the legal capacity of natural persons, the authenticity of all documents submitted to us as originals, the conformity to original documents of all documents submitted to us as certified or photostatic copies and the authenticity of the originals of such copies.

Members of our firm are admitted to the Bar of the Commonwealth of Massachusetts, and we do not express any opinion as to the laws of any other jurisdiction other than the United States Federal Laws and the reported judicial decisions interpreting those laws. To the extent that any applicable document is stated to be governed by the laws of another jurisdiction, we have assumed for purposes of this opinion that the laws of such jurisdiction are identical to the state laws of the Commonwealth of Massachusetts. No opinion is expressed herein with respect to the qualification of the Securities under the securities or blue sky laws of any state or any foreign jurisdiction. The Securities may be issued from time to time on a delayed or continuous basis, but this opinion is limited to the laws, including the rules and regulations thereunder, as in effect on the date hereof.

Based upon the foregoing, we are of the opinion that, when sold by the Selling Stockholders pursuant to the Registration Statement (including any prospectus supplement relating thereto), and provided no stop order shall have been issued by the Commission relating thereto, the Shares will be validly issued, fully paid and non-assessable.

It is understood that this opinion is to be used only in connection with the offer and sale of the Shares while the Registration Statement is in effect.

Please note that we are opining only as to the matters expressly set forth herein, and no opinion should be inferred as to any other matters. This opinion is based upon currently existing statutes, rules, regulations and judicial decisions, and we disclaim any obligation to advise you of any change in any of these sources of law or subsequent legal or factual developments which might affect any matters or opinions set forth herein.

We hereby consent to (i) the reference to this firm under the under the caption "Legal Matters" in the Prospectus forming a part of the Registration Statement and (ii) the filing of this opinion as an exhibit to the Registration Statement.

Very truly yours,

/s/ Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C.

Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C.

Consent of Independent Registered Public Accounting Firm

We hereby consent to the incorporation by reference in this Registration Statement on Form S-3 of our report dated March 15, 2005 relating to the financial statements of Vertex Pharmaceuticals Incorporated as of December 31, 2004 and for the years ended December 31, 2004 and 2003, which appears in Vertex Pharmaceuticals Incorporated's Annual Report on Form 10-K for the year ended December 31, 2005. We also consent to the reference to us under the heading "Experts" in such Registration Statement.

/s/ PricewaterhouseCoopers LLP

Boston, Massachusetts

August 11, 2006.

Consent of Independent Registered Public Accounting Firm

We consent to the reference to our firm under the caption "Experts" in the Registration Statement (Form S-3) and related Prospectus of Vertex Pharmaceuticals Incorporated for the registration of 136,489 shares of its common stock and to the incorporation by reference therein of our reports dated March 8, 2006, with respect to the consolidated financial statements of Vertex Pharmaceuticals Incorporated, Vertex Pharmaceuticals Incorporated management's assessment of the effectiveness of internal control over financial reporting, and the effectiveness of internal control over financial reporting of Vertex Pharmaceuticals Incorporated, included in its Annual Report (Form 10-K) for the year ended December 31, 2005, filed with the Securities and Exchange Commission.

/s/ Ernst & Young LLP

Boston, Massachusetts
August 11, 2006
