

Use these links to rapidly review the document

[TABLE OF CONTENTS](#)

[Table of Contents](#)

As filed with the Securities and Exchange Commission on September 17, 2008

Registration No. 333-

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

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**FORM S-3**  
REGISTRATION STATEMENT  
UNDER  
THE SECURITIES ACT OF 1933

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**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)

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

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

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With copies to:

**Michael L. Fantozzi, Esq.  
Scott A. Samuels, 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**

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**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:

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, or a smaller reporting company. See the definitions of "large accelerated filer," "accelerated filer" and "smaller reporting company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer

Accelerated filer

Non-accelerated filer   
(Do not check if a smaller reporting company)

Smaller reporting company

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**CALCULATION OF REGISTRATION FEE**

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

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- (1) Each share of common stock includes a right to purchase our series A junior participating preferred stock, which is initially attached to and trades with the shares of the common stock being registered hereby. No separate consideration will be received for these rights.
  - (2) An unspecified and indeterminate aggregate initial offering price and number or amount of common stock is being registered as may from time to time be sold at indeterminate prices. In accordance with Rule 456(b) and Rule 457(r), we are deferring payment of all of the registration fee, except for \$578.62 that has already been paid with respect to \$18,847,500 aggregate initial offering price of securities that were previously registered pursuant to Registration Statement No. 333-147277 filed on November 9, 2007, and were not sold thereunder. Pursuant to Rule 457(p), such unutilized filing fee may be applied to the filing fee payable pursuant to this Registration Statement.
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**PROSPECTUS**



**VERTEX PHARMACEUTICALS INCORPORATED**

**Common Stock**

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This prospectus will allow us to issue shares of our common stock from time to time at prices and on terms to be determined at or prior to the time of the offering. We will provide specific terms of any offering in one or more supplements to this prospectus filed with the Securities and Exchange Commission.

We may sell the common stock to or through one or more underwriters, dealers and agents, or directly to purchasers, on a continued or delayed basis. We will set forth the names of any underwriters, dealers or agents and their compensation in the accompanying prospectus supplement.

This prospectus may not be used to sell any shares of common stock unless accompanied by a prospectus supplement.

Our common stock is listed on the Nasdaq Global Select Market under the symbol "VRTX." The last reported sale price of our common stock on the Nasdaq Global Select Market on September 16, 2008 was \$28.15 per share. Prospective purchasers of our securities are urged to obtain current information as to the market prices of our common stock.

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

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The date of this prospectus is September 17, 2008.

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**TABLE OF CONTENTS**

	<u>Page</u>
<a href="#">About this Prospectus</a>	1
<a href="#">Where You Can Find More Information</a>	1
<a href="#">Incorporation by Reference</a>	2
<a href="#">Use of Proceeds</a>	3
<a href="#">Description of Capital Stock</a>	3
<a href="#">Legal Matters</a>	5
<a href="#">Experts</a>	5

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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 shares of our common stock in one or more offerings. Each time our common stock is 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 any offering of our common stock pursuant to this prospectus, 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 our common stock 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 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 website at [www.sec.gov](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 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's website.

Our internet address is [www.vrtx.com](http://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 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, 2007 (filing date February 11, 2008: Commission File No. 000-19319);
- (b) Our Quarterly Reports on Form 10-Q for the quarters ended March 31, 2008 and June 30, 2008 (filing dates May 12, 2008 and August 11, 2008: Commission File No. 000-19319);
- (c) Our Current Reports on Form 8-K filed on February 14, 2008 (Items 1.01 and 9.01), February 25, 2008 (Items 1.01, 2.03 and 9.01), March 31, 2008 (Items 8.01 and 9.01), May 16, 2008 (Items 1.01, 1.02 and 9.01), June 4, 2008 (Items 1.01 and 2.01), June 18, 2008 (Item 5.02) and September 12, 2008 (Item 5.02) (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 Exchange Act (filing date April 8, 2008: 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).

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 [www.sec.gov](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

## USE OF PROCEEDS

Except as otherwise provided in the applicable prospectus supplement, 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, clinical trial expenditures and other development expenses for telaprevir and our other drug candidates, and investment in our research programs and manufacture and supply of drug substances, and which may include capital expenditures, investments and potentially acquisitions. 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.

## 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 or 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.

### 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.

### 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.

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 our 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 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.

#### **LEGAL MATTERS**

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

#### **EXPERTS**

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



**VERTEX PHARMACEUTICALS INCORPORATED**

**Common Stock**

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**PROSPECTUS**

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**September 17, 2008**

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**PART II****INFORMATION NOT REQUIRED IN PROSPECTUS****Item 14. Other Expenses of Issuance and Distribution.**

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

SEC registration fee	\$	*
Legal fees and expenses	100,000	
Accounting fees and expenses	75,000	
Printing fees	50,000	
Miscellaneous fees and expenses	50,000	
Total	<u>\$275,000</u>	

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

**Item 15. Indemnification of Directors and Officers.**

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

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

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

holders of a majority of the outstanding stock at the time entitled to vote for directors, voting as a single class, exclusive of any stock owned by any interested director or officer.

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

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

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

\* To be filed as an exhibit to a Current Report on Form 8-K and incorporated herein by reference.

**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 the purpose of determining liability of the Registrant under the Securities Act of 1933 to any purchaser in the initial distribution of the securities, the undersigned Registrant undertakes that in a primary offering of securities of the undersigned Registrant pursuant to this registration statement, regardless of the underwriting method used to sell the securities to the purchaser, if the securities are offered or sold to such purchaser by means of any of the following communications, the undersigned Registrant will be a seller to the purchaser and will be considered to offer or sell such securities to such purchaser:
- (i) Any preliminary prospectus or prospectus of the undersigned Registrant relating to the offering required to be filed pursuant to Rule 424;
  - (ii) Any free writing prospectus relating to the offering prepared by or on behalf of an undersigned Registrant or used or referred to by the undersigned Registrant;
  - (iii) The portion of any other free writing prospectus relating to the offering containing material information about the undersigned Registrant or its securities provided by or on behalf of the undersigned Registrant; and
  - (iv) Any other communication that is an offer in the offering made by the undersigned Registrant to the purchaser.
- (6) That, for purposes of determining any liability under the Securities Act of 1933, each filing of the Registrant's annual report pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934 (and, where applicable, each filing of an employee benefit plan's annual report pursuant to Section 15(d) of the Securities Exchange Act of 1934) that is incorporated by reference in the registration statement shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial *bona fide* offering thereof.
- (7) Insofar as indemnification for liabilities arising under the Securities Act of 1933 may be permitted to directors, officers and controlling persons of the Registrant pursuant to the foregoing provisions, or otherwise, the Registrant has been advised that in the opinion of the Securities and Exchange Commission such indemnification is against public policy as expressed in the Securities Act of 1933 and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by a Registrant of expenses incurred or paid by a director, officer or controlling person of a Registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, that Registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it against public policy as expressed in the Securities Act of 1933 and will be governed by the final adjudication of such issue.



By:	/s/ ROGER W. BRIMBLECOMBE	Director	September 17, 2008
	<hr/> <b>Roger W. Brimblecombe</b>		
By:	/s/ STUART J.M. COLLINSON	Director	September 17, 2008
	<hr/> <b>Stuart J.M. Collinson</b>		
By:	/s/ EUGENE H. CORDES	Director	September 17, 2008
	<hr/> <b>Eugene H. Cordes</b>		
By:	/s/ MATTHEW W. EMMENS	Director	September 17, 2008
	<hr/> <b>Matthew W. Emmens</b>		
By:	/s/ BRUCE I. SACHS	Director	September 17, 2008
	<hr/> <b>Bruce I. Sachs</b>		
By:	/s/ ELAINE S. ULLIAN	Director	September 17, 2008
	<hr/> <b>Elaine S. Ullian</b>		





[Mintz Levin Letterhead]

September 17, 2008

Vertex Pharmaceuticals Incorporated  
130 Waverly Street  
Cambridge, MA 02139

Re: *Automatic Registration Statement on Form S-3 for Shares of Common Stock*

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 (the "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"), shares (the "Shares") of the Company's common stock, \$0.01 par value per share (the "Common Stock"), which may be issued and sold 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 By-laws, 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 Shares under the securities or blue sky laws of any state or any foreign jurisdiction. The Shares 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. 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 are basing this opinion on our understanding that, prior to issuing any of the Shares, the Company will advise us in writing of the terms thereof and other information material thereto, will afford us an opportunity to review the operative documents pursuant to which such Shares are to be issued (including the Registration Statement, the prospectus prepared in connection with the Registration Statement, and any supplement or amendment thereto) and will file such supplement or amendment to this opinion (if any) as we may reasonably consider necessary or appropriate with respect to such Shares. However, we undertake no responsibility to monitor the Company's future compliance with applicable laws, rules or regulations of the Commission or other governmental body.

In connection with our opinion expressed below, we have assumed that, if any Shares are to be issued, they will only be issued pursuant to the underwriting agreement in the form filed with the Registration Statement as an exhibit and that, at the time of the offer, issuance and sale of any Shares, no stop order suspending the Registration Statement's effectiveness will have been issued and remain in effect and no proceedings for that purpose are pending before or contemplated by the Commission, and that there will not have occurred any change in law affecting the validity or enforceability of the Shares.

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Based upon the foregoing, we are of the opinion that the Shares to be issued and sold by the Company, when duly authorized by appropriate corporate action of the Company (including the Board of Directors of the Company or a committee thereof), and issued, sold and delivered in the manner and for the consideration stated in the Registration Statement, and in accordance with the resolutions adopted by the Board of Directors of the Company or a committee thereof, will be validly issued, fully paid and nonassessable.

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.

We hereby consent to (i) the reference to this firm 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.

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## QuickLinks

[Exhibit 5.1](#)

**Consent of Independent Registered Public Accounting Firm**

We consent to the reference to our firm under the caption "Experts" in this Registration Statement (Form S-3) and related Prospectus of Vertex Pharmaceuticals Incorporated for the registration of shares of its common stock and to the incorporation by reference therein of our reports dated February 11, 2008, with respect to the consolidated financial statements of Vertex Pharmaceuticals Incorporated 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, 2007, filed with the Securities and Exchange Commission.

/s/ Ernst & Young LLP

Boston, Massachusetts  
September 16, 2008

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## QuickLinks

[Exhibit 23.1](#)