Registration No. 333-

## SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

# FORM S-8

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 of Principal Executive Offices)

AMENDED AND RESTATED 2006 STOCK AND OPTION PLAN

(Full Title of Plan)

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

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

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 definition of "large accelerated filer," "accelerated filer" and "smaller reporting company" in Rule 12b-2 of the Exchange Act. (Check one):

Large accelerated filer  $\boxtimes$ 

Accelerated filer o

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

Smaller reporting company o

#### **CALCULATION OF REGISTRATION FEE**

Title of Each Class of Securities to be Registered(1)	Amount to be Registered(2)	Proposed Maximum Offering Price Per Unit(3)	Proposed Maximum Aggregate Offering Price	Amount of Registration Fee
Common Stock, \$.01 par value	536,625	\$18.93	\$10,158,311	\$400
	6,063,375	\$26.59	\$161,225,141	\$6,336
Total				\$6,736

- (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.
- The number of shares of common stock, par value \$.01 per share, stated above consists of the aggregate number of additional shares that may be issued under the Vertex Pharmaceuticals Incorporated Amended and Restated 2006 Stock and Option Plan pursuant to an amendment to the plan that became effective on May 15, 2008. The maximum number of shares that may be issued under the plan is subject to adjustment in accordance with certain anti-dilution and other provisions of the plan. Accordingly, pursuant to Rule 416 under the Securities Act of 1933, as amended, this Registration Statement covers, in addition to the number of shares stated above, an indeterminate number of shares that may be subject to grant or otherwise issuable after the operation of any such anti-dilution and other provisions.

(i) in the case of shares of common stock that may be purchased upon exercise of outstanding options, the fee is calculated on the basis of the price a which the options may be exercised; and (ii) in the case of shares of common stock for which options have not yet been granted the fee is calculated on the average of the high and low prices of the Registrant's common stock as reported by the Nasdaq Global Select Market on May 9, 2008.

# PART I INFORMATION REQUIRED IN THE SECTION 10(A) PROSPECTUS

#### Item 1. Plan Information.

The information required by Item 1 is included in documents sent or given to participants in the plan covered by this registration statement pursuant to Rule 428(b)(1) of the Securities Act of 1933, as amended (the "Securities Act").

#### Item 2. Registrant Information and Employee Plan Annual Information.

The written statement required by Item 2 is included in documents sent or given to participants in the plan covered by this registration statement pursuant to Rule 428(b)(1) of the Securities Act.

# PART II INFORMATION REQUIRED IN THE REGISTRATION STATEMENT

#### Item 3. Incorporation of Documents by Reference.

The following documents filed by the Registrant with the Commission are incorporated herein by reference:

- (a) The Registrant's Annual Report on Form 10-K for the fiscal year ended December 31, 2007 (filing date February 11, 2008).
- (b) The Registrant's Quarterly Report on Form 10-Q for the quarter ended March 31, 2008 (filing date May 12, 2008).
- (c) All other reports filed pursuant to Section 13(a) or 15(d) of the Exchange Act since the end of the fiscal year covered by the document referred to in (a) above.
- (d) The description of the Common Stock and the Rights contained in the Registrant's Registration Statement on Form 8-A (filing date May 30, 1991), as amended from time to time.

All documents subsequently filed by the registrant pursuant to Sections 13(a), 13(c), 14 and 15(d) of the Exchange Act, prior to the filing of a post-effective amendment that indicates that all securities offered hereby have been sold or that deregisters all securities then remaining unsold, shall be deemed to be incorporated by reference in this registration statement and to be part hereof from the date of the filing of such documents. Any statement contained in a document incorporated or deemed to be incorporated by reference herein shall be deemed to be modified or superseded for the purposes of this registration statement to the extent that a statement contained herein or in any other subsequently filed document that also is or is deemed to be incorporated by reference herein modifies or supersedes such statement. Any statement so modified or superseded shall not be deemed, except as so modified or superseded, to constitute a part of this registration statement.

#### Item 4. Description of Securities.

Not applicable.

#### Item 5. Interests of Named Experts and Counsel.

The validity of the issuance of the shares of Common Stock registered under this Registration Statement has been passed upon for the Registrant by Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C.

#### Item 6. 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 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 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 7. Exemption From Registration Claimed.

Not applicable

## Item 8. Exhibits.

Exhibit Number	Exhibit Description	Filed with this Registration Statement	Incorporated by Reference herein from—Form or Schedule	Filing Date/ Period Covered	SEC File/ Reg. Number
3.1	Restated Articles of Organization of Vertex, filed with the Secretary of State of The Commonwealth of Massachusetts on July 31, 1991.		10-K (Exhibit 3.1)	March 26, 1998	000-19319
3.2	Certificate of Vote of Directors Establishing a Series of a Class of Stock, filed with the Secretary of State of The Commonwealth of Massachusetts on July 31, 1991.		10-K (Exhibit 3.3)	March 26, 1998	000-19319
3.3	Articles of Amendment of the Articles of Organization of Vertex, filed with the Secretary of State of The Commonwealth of Massachusetts on May 17, 1995.		S-3 (Exhibit 3.3)	April 1, 2005	333-123731
3.4	Articles of Amendment of the Articles of Organization of Vertex, filed with the Secretary of State of The Commonwealth of Massachusetts on June 4, 1997.		10-K (Exhibit 3.2)	March 26, 1998	000-19319
3.5	Articles of Amendment of the Articles of Organization of Vertex, filed with the Secretary of State of The Commonwealth of Massachusetts on May 21, 2001.		S-4 (Exhibit 3.4)	May 23, 2001	333-61480
3.6	Form of Articles of Amendment of the Articles of Organization of Vertex, to be filed with the Secretary of State of The Commonwealth of Massachusetts on May 16, 2008.	X			
3.7	By-laws of Vertex, as amended and restated as of May 11, 2005.		10-Q (Exhibit 3.1)	August 9, 2005	000-19319
4.1	Specimen stock certificate.		S-1 (Exhibit 4.1)	July 18, 1991	33-40966
4.2	Rights Agreement, dated as of July 1, 1991.		S-1 (Exhibit 4.2)	July 5, 1991	33-40966
4.3	First Amendment to Rights Agreement, dated as of February 21, 1997.		10-K (Exhibit 4.3)	March 28, 1997	000-19319
4.4	Second Amendment to Rights Agreement, dated as of June 30, 2001.		10-Q (Exhibit 4.4)	August 14, 2001	000-19319
5.1	Opinion of Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C. as to the legality of the shares being registered	X			
10.1	Vertex Pharmaceuticals Incorporated Amended and Restated 2006 Stock and Option Plan	X			
23.1	Consent of Independent Registered Public Accounting Firm Ernst & Young LLP.	X			
23.2	Consent of Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C. (included as part of Exhibit 5.1)	X			
24.1	Power of Attorney to file future amendments (set forth on signature page of this Registration Statement)	X			

#### Item 9. Undertakings.

- (a) 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 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.
    - (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:

- (A) Paragraphs (a)(1)(i) and (a)(1)(ii) of this section do not apply if the registration statement is on Form S-8, and 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 this 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.
- (b) The undersigned Registrant hereby undertakes 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 Section 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 this 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.
- (c) 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 Act and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the Registrant of expenses incurred or paid by a director, officer or controlling person of the 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, the 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 is against public policy as expressed in the Act and will be governed by the final adjudication of such issue.

#### **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-8 and has duly caused this Registration Statement to be signed on its behalf by the undersigned, thereunto duly authorized, in Cambridge, Massachusetts on May 15, 2008.

١	/FRTFX	PHARM	/ACFI	ITICAL	S INCORPO	RATED

By:	/s/ JOSHUA S. BOGER

Joshua S. Boger President and Chief Executive Officer

#### POWER OF ATTORNEY

Each person whose signature appears below constitutes and appoints Ian F. Smith and Valerie Andrews and each of them singly, his/her true and lawful attorneys-in-fact and agents, with full power of substitution and resubstitution in each of them singly, for him/her and in his/her name, place and stead, and in any and all capacities, to sign any and all amendments (including post-effective amendments) to this Registration Statement on Form S-8 of Vertex Pharmaceuticals Incorporated, and to file the same, with all exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, granting to the 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 or about the premises, as full to all intents and purposes as he might or could do in person, hereby ratifying and confirming all that the attorneys-in-fact and agents or any of each of them or their substitute may lawfully do or cause to be done by virtue hereof.

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

Signature		Title	Date	
By:	/s/ JOSHUA S. BOGER	Director, President and Chief Executive Officer (principal executive officer)	May 15, 2008	
	Joshua S. Boger			
By:	/s/ IAN F. SMITH	Executive Vice President and Chief Financial Officer (principal financial officer)	May 15, 2008	
By:	Ian F. Smith /s/ JOHANNA MESSINA POWER	Vice President and Corporate Controller (principal accounting officer)	May 15, 2008	
	Johanna Messina Power	uccomming officery		
By:	/s/ CHARLES A. SANDERS	Director, Chairman of the Board	May 15, 2008	
	Charles A. Sanders			
By:	/s/ ERIC K. BRANDT	Director	May 15, 2008	
	Eric K. Brandt	6		
		U		

By:	/s/ ROGER W. BRIMBLECOMBE	Director	May 15, 2008
	Roger W. Brimblecombe		
By:	/s/ STUART J. COLLINSON	Director	May 15, 2008
	Stuart J. Collinson		
By:	/s/ EUGENE H. CORDES	Director	May 15, 2008
	Eugene H. Cordes		
By:	/s/ MATTHEW W. EMMENS	Director	May 15, 2008
	Matthew W. Emmens		
By:	/s/ BRUCE I. SACHS	Director	May 15, 2008
	Bruce I. Sachs		
By:		Director	May 15, 2008
	Elaine S. Ullian	Direction	Wiay 15, 2000
		7	

# VERTEX PHARMACEUTICALS INCORPORATED INDEX TO EXHIBITS FILED WITH FORM S-8 REGISTRATION STATEMENT

Exhibit Number	Exhibit Description	Filed with this Registration Statement	Incorporated by Reference herein from—Form or Schedule	Filing Date/ Period Covered	SEC File/ Reg. Number
3.1	Restated Articles of Organization of Vertex, filed with the Secretary of State of The Commonwealth of Massachusetts on July 31, 1991.		10-K (Exhibit 3.1)	March 26, 1998	000-19319
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10.1	Vertex Pharmaceuticals Incorporated Amended and Restated 2006 Stock and Option Plan	X			
23.1	Consent of Independent Registered Public Accounting Firm Ernst & Young LLP.	X			
23.2	Consent of Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C. (included as part of Exhibit 5.1)	X			
24.1	Power of Attorney to file future amendments (set forth on signature page of this Registration Statement)	X			
		8			

## QuickLinks

#### PART I INFORMATION REQUIRED IN THE SECTION 10(A) PROSPECTUS

Item 1. Plan Information.

<u>Item 2. Registrant Information and Employee Plan Annual Information.</u>

#### PART II INFORMATION REQUIRED IN THE REGISTRATION STATEMENT

<u>Item 3. Incorporation of Documents by Reference.</u>

Item 4. Description of Securities.

<u>Item 5. Interests of Named Experts and Counsel.</u>

<u>Item 6. Indemnification of Directors and Officers.</u>

<u>Item 7. Exemption From Registration Claimed.</u>

Item 8. Exhibits.

Item 9. Undertakings.

#### **SIGNATURES**

**POWER OF ATTORNEY** 

VERTEX PHARMACEUTICALS INCORPORATED INDEX TO EXHIBITS FILED WITH FORM S-8 REGISTRATION STATEMENT

Exhibit 3.6

D PC

#### The Commonwealth of Massachusetts William Francis Galvin

Secretary of the Commonwealth One Ashburton Place, Boston, Massachusetts 02108-1512

FORM MUST BE TYPED

Articles of Amendment (General Laws Chapter 156D, Section 10.06; 950 CMR 113.34) FORM MUST BE TYPED

- (1) Exact name of corporation: Vertex Pharmaceuticals Incorporated
- (2) Registered office address: **130 Waverly Street, Cambridge, Massachusetts 02139** (number, street, city or town, state, zip code)
- (3) These articles of amendment affect article(s): 3

(specify the number(s) of article(s) being amended (I-VI))

(4) Date adopted: May 15, 2008

(month, day, year)

(5) Approved by:

(check appropriate box)

- o the incorporators.
- o the board of directors without shareholder approval and shareholder approval was not required.
- the board of directors and the shareholders in the manner required by law and the articles of organization.
- (6) State the article number and the text of the amendment. Unless contained in the text of the amendment, state the provisions for implementing the exchange, reclassification or cancellation of issued shares.

VOTED: To increase the number of shares of Common Stock, \$.01 par value per share, that the Corporation shall have authorized to issue from 200,000,000 shares to 300,000,000 shares; and that ARTICLE 3 of the Corporation's Restated Articles of Organization be, and hereby is, amended to read as follows:

3. The total number of shares and the par value, if any, of each class of stock that the Corporation shall be authorized to issue is as follows; 1,000,000 shares of Preferred Stock, \$.01 par value per share, and 300,000,000 shares of Common Stock, \$.01 par value per share.

	he number of shares and the par value, * if any, of the corporation is authorized to issue, complete		or series, of stock, or change a designation	of class or seri	es of
	Chapter 156D eliminate the concept of par value the comments relative thereto.	e, however a corporation may spe	ecify par value in Article III. See G.L. Chapt	ter 156D, Secti	on 6.21,
Total author	rized prior to amendment:  WITHOUT PAR VALUE		WITH PAR VALUE		
ТҮРЕ	NUMBER OF SHARES	ТҮРЕ	NUMBER OF SHARES	PAR	VALUE
		Common: Preferred:	200,000,000 1,000,000	\$ \$	.01 .01
Total author	rized after amendment:				
	WITHOUT PAR VALUE		WITH PAR VALUE		
ТҮРЕ	NUMBER OF SHARES	ТҮРЕ	NUMBER OF SHARES	PAR	VALUE
		Common: Preferred:	300,000,000 1,000,000	\$ \$	.01 .01
	amendment shall be effective at the time and on time of filing is specified:	the date approved by the Division	ı, unless a later effective date not more than	90 days from t	he date
Signed by:		/s/ Joshua S	. Boger		
		(signature of author	ized individual)		
0	Chairman of the board of directors,				
$\boxtimes$	President,				
0	Other officer,				
0	Court-appointed fiduciary,				
on this 15th	day of <b>May, 2008.</b>				

#### **COMMONWEALTH OF MASSACHUSETTS**

#### **William Francis Galvin**

Secretary of the Commonwealth One Ashburton Place, Boston, Massachusetts 02108-1512

#### Articles of Amendment (General Laws Chapter 156D, Section 10.06; 950 CMR 113.34)

I hereby certify that upon examination of these articles of amendment, it appears that the provisions of the General Laws relative thereto have been complied with, and the filing fee in the amount of \$ having been paid, said articles are deemed to have been filed with me this day of May, 2008, at a.m./p.m.

time

Effective date: , 2008

(must be within 90 days of date submitted)

WILLIAM FRANCIS GALVIN Secretary of the Commonwealth

Filing fee: Minimum filing fee \$100 per article amended, stock increases \$100 per 100,000 shares, plus \$100 for each additional 100,000 shares or any fraction thereof.

Examiner

TO BE FILLED IN BY CORPORATION

Name approval Contact Information:

Kenneth S. Boger

M Senior Vice President and General Counsel

Vertex Pharmaceuticals Incorporated

Telephone: (617) 444-6417

Email: Ken\_Boger@vrtx.com

Upon filing, a copy of this filing will be available at www.sec.state.ma.us/cor. If the document is rejected, a copy of the rejection sheet and rejected document will be available in the rejected queue.

QuickLinks

Exhibit 3.6

#### **EXHIBIT 5.1**

#### MINTZ LEVIN LETTERHEAD

May 15, 2008

Vertex Pharmaceuticals Incorporated 130 Waverly Street Cambridge, Massachusetts 02139-4242

#### 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-8 (the "Registration Statement"), pursuant to which the Company is registering the issuance under the Securities Act of 1933, as amended, of a total of 6,600,000 shares (the "Shares") of its common stock, \$.01 par value per share (the "Common Stock"). This opinion is being rendered in connection with the filing of the Registration Statement. All capitalized terms used herein and not otherwise defined shall have the respective meanings given to them in the Registration Statement. All capitalized terms used herein and not otherwise defined shall have the respective meanings given to them in the Registration Statement.

In connection with this opinion, we have examined the Company's Restated Articles of Organization, as amended, and By-Laws, as amended and restated, 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.

Based upon the foregoing, we are of the opinion that (i) the Shares have been duly and validly authorized by the Company and (ii) the Shares, when sold, will have been duly and validly issued, fully paid and non-assessable shares of the Common Stock, free of preemptive rights.

Our opinion is limited to the General Corporation Laws of the State of Massachusetts and the reported judicial decisions interpreting those laws, and we express no opinion with respect to the laws of any other jurisdiction. 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.

We understand that you wish to file this opinion as an exhibit to the Registration Statement, and we hereby consent thereto.

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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EXHIBIT 5.1

#### Appendix A

# VERTEX PHARMACEUTICALS INCORPORATED AMENDED AND RESTATED 2006 STOCK and OPTION PLAN

#### 1. DEFINITIONS

Unless otherwise specified or unless the context otherwise requires, the following terms, as used in this Vertex Pharmaceuticals Incorporated Amended and Restated 2006 Stock and Option Plan, have the following meanings:

**Administrator** means the Board of Directors and/or a committee of the Board of Directors to which the Board of Directors has delegated power to act on its behalf in administering this Plan in whole or in part.

Affiliate means a corporation that, for purposes of Section 424 of the Code, is a parent or subsidiary of the Company, direct or indirect.

**Board of Directors** means the Board of Directors of the Company.

Code means the United States Internal Revenue Code of 1986, as amended.

**Common Stock** means shares of the Company's common stock, \$.01 par value.

Company means Vertex Pharmaceuticals Incorporated, a Massachusetts corporation.

**Employee** means an employee of the Company or of an Affiliate (including, without limitation, an employee who is also serving as an officer or director of the Company or of an Affiliate), designated by the Administrator to be eligible to be granted one or more Stock Rights under the Plan.

Exchange Act means the Securities Exchange Act of 1934, as amended.

**Fair Market Value** of a Share of Common Stock on a particular date shall be the mean between the highest and lowest quoted selling prices on such date (the "valuation date") on the securities market where the Common Stock is traded, or if there were no sales on the valuation date, on the next preceding date within a reasonable period (as determined in the sole discretion of the Administrator) on which there were sales. If there were no sales in such a market within a reasonable period, the fair market value shall be as determined in good faith by the Administrator in its sole discretion. The Fair Market Value as determined in this paragraph shall be rounded down to the next lower whole cent if the foregoing calculation results in fractional cents.

**ISO** means an option intended to qualify as an incentive stock option under Code Section 422.

Non-Employee Director means a member of the Board of Directors who is not an employee of the Company or any Affiliate.

Non-Qualified Option means an option that is not intended to qualify as an ISO.

**Option** means an ISO or Non-Qualified Option granted under the Plan.

**Participant** means an Employee, Non-Employee Director, consultant or advisor of the Company or an Affiliate to whom one or more Stock Rights are granted under the Plan. As used herein, "Participant" shall include "Participant's Survivors" and a Participant's permitted transferees where the context requires.

**Participant's Survivors** means a deceased Participant's legal representatives and/or any person or persons who acquires the Participant's rights to a Stock Right by will or by the laws of descent and distribution.

Plan means this Vertex Pharmaceuticals Incorporated Amended and Restated 2006 Stock and Option Plan, as amended from time to time.

**Shares** means shares of the Common Stock as to which Stock Rights have been or may be granted under the Plan or any shares of capital stock into which the Shares are changed or for which they are exchanged within the provisions of Section 3 of the Plan. The Shares subject to Stock Rights granted under the Plan may be authorized and unissued shares or shares held by the Company in its treasury, or both.

**Stock Agreement** means an agreement between the Company and a Participant delivered pursuant to the Plan with respect to a Stock Right, in such form as the Administrator shall approve.

Stock-Based Award means a grant by the Company under the Plan of an equity award or equity-based award that is not an Option or Stock Grant.

**Stock Grant** means a grant by the Company of Shares under the Plan.

**Stock Right** means a right to Shares or the value of Shares of the Company granted pursuant to the Plan as an ISO, a Non-Qualified Option, a Stock Grant or a Stock-Based Award.

#### 2. PURPOSES OF THE PLAN

The Plan is intended to encourage ownership of Shares by Employees, Non-Employee Directors and certain consultants and advisors to the Company in order to attract such persons, to induce them to work for the benefit of the Company or of an Affiliate and to provide additional incentive for them to promote the success of the Company or of an Affiliate. The Plan provides for the granting of Stock Rights to Employees, Non-Employee Directors, consultants and advisors of the Company.

#### 3. SHARES SUBJECT TO THE PLAN

The number of Shares subject to this Plan as to which Stock Rights may be granted from time to time shall be 13,902,380 or the equivalent of such number of Shares after the Administrator, in its sole discretion, has interpreted the effect of any stock split, stock dividend, combination, recapitalization or similar transaction in accordance with Section 17 of this Plan. The number of Shares subject to this Plan shall be reduced, share for share, by the number of shares underlying Stock Rights, if any, that are granted under the Company's 2007 New Hire Stock and Option Plan after March 17, 2008.

If an Option granted hereunder ceases to be outstanding, in whole or in part (other than by exercise), or if the Company shall reacquire (at no more than its original issuance price) any Shares issued pursuant to a Stock Grant, or if any Stock Right expires or is forfeited, cancelled or otherwise terminated or results in any Shares not being issued, the unissued Shares that were subject to such Stock Right shall again be available for issuance from time to time pursuant to this Plan; provided that, the following Shares may not again be made available for issuance as Awards under the Plan: (i) Shares that are not issued or delivered as a result of the net settlement of an outstanding Stock-Based Award or Option and (ii) Shares that the Company acquires from a Participant for a price that is more than the original issuance price of the Share, including any Share acquired by the Company to fund employee payroll tax withholding obligations on a Stock Grant or Shares applied to payment of the exercise price for an Option.

After May 14, 2008, the number Shares that may be subject to or delivered pursuant to any form of Stock Right other than an Option shall not exceed 20% of the aggregate of (A) the number of Shares available as to which Stock Rights may be granted under this Plan on May 15, 2008 (taking in account the Shares added on such date, but which amount does not include those 536,625 Shares as to which the Company granted Options on February 7, 2008, subject to obtaining subsequent stockholder

approval of such Options) and (B) any Shares that again become available for issuance on or after May 15, 2008 pursuant to the preceding paragraph.

#### 4. ADMINISTRATION OF THE PLAN

The Administrator shall administer the Plan. Subject to the provisions of the Plan, the Administrator is authorized to:

- a. Interpret the provisions of the Plan and of any Stock Right or Stock Agreement and to make all rules and determinations that it deems necessary or advisable for the administration of the Plan;
- b. Determine which Employees, Non-Employee Directors, consultants and advisors of the Company and its Affiliates shall be granted Stock Rights;
- c. Determine the number of Shares and exercise price for which a Stock Right shall be granted;
- d. Specify the terms and conditions upon which a Stock Right or Stock Rights may be granted;
- e. In its discretion, accelerate:
  - (i) the date of exercise of any installment of any Option; provided that the Administrator shall not, without the consent of the Option holder accelerate the exercise date of any installment of any Option granted to any Employee as an ISO (and not previously converted into a Non-Qualified Option pursuant to Section 20) if such acceleration would violate the annual vesting limitation contained in Section 422(d) of the Code, as described in Section 6.2.3; or
  - (ii) the date or dates of vesting of Shares, or lapsing of Company repurchase rights with respect to any Shares, under any Stock Rights; and
- f. In its discretion, extend the exercise date for any Option;

provided, however, that all such interpretations, rules, determinations, terms and conditions shall be made and prescribed in the context of preserving the tax status under Code Section 422 of those Options which are designated as ISOs (unless the holder of any such Option otherwise agrees). Subject to the foregoing, the interpretation and construction by the Administrator of any provisions of the Plan or of any Stock Right granted under it shall be final, unless otherwise determined by the Board of Directors, if the Administrator is other than the Board of Directors.

The Administrator may employ attorneys, consultants, accountants or other persons, and the Administrator, the Company and its officers and directors shall be entitled to rely upon the advice, opinions or valuations of such persons. All actions taken and all interpretations and determinations made by the Administrator in good faith shall be final and binding upon the Company, all Participants, and all other interested persons. No member or agent of the Administrator shall be personally liable for any action, determination, or interpretation made in good faith with respect to this Plan or grants hereunder. Each member of the Administrator shall be indemnified and held harmless by the Company against any cost or expense (including counsel fees) reasonably incurred by him or her or any liability (including any sum paid in settlement of a claim with the approval of the Company) arising out of any act or omission to act in connection with this Plan unless arising out of such member's own fraud or bad faith. Such indemnification shall be in addition to any rights of indemnification the members of the Administrator may have as directors or otherwise under the by-laws of the Company, or any agreement, vote of stockholders or disinterested directors, or otherwise.

#### 5. ELIGIBILITY FOR PARTICIPATION

The Administrator shall, in its sole discretion, name the Participants in the Plan, provided, however, that each Participant must be a Employee, Non-Employee Director, consultant or advisor of the Company or of an Affiliate at the time a Stock Right is granted. Notwithstanding the foregoing, the Administrator may authorize the grant of a Stock Right to a person not then an Employee, Non-Employee Director, consultant or advisor of the Company or of an Affiliate; provided, however, that the actual grant of such Stock Right shall be conditioned upon such person becoming eligible to become a Participant at or prior to the time of execution of the Stock Agreement evidencing such Stock Right. ISOs may be granted only to Employees. The granting of any Stock Right to any individual shall neither entitle that individual to, nor disqualify him or her from, participation in other grants of Stock Rights.

#### 6. TERMS AND CONDITIONS OF OPTIONS

- 6.1 *General*. Each Option shall be set forth in writing in a Stock Agreement, duly executed by the Company and, to the extent required by law or requested by the Company, by the Participant. The Administrator may provide that Options be granted subject to such terms and conditions, consistent with the terms and conditions specifically required under this Plan, as the Administrator may deem appropriate including, without limitation, subsequent approval by the stockholders of the Company of this Plan or any amendments thereto. Each Stock Agreement shall state the option price (per share) of the Shares covered by each Option, the number of Shares to which it pertains, the date or dates on which it first is exercisable and the date after which it may no longer be exercised (subject to Sections 11, 12 and 13 of this Plan). Option rights may accrue or become exercisable in installments over a period of time, or upon the achievement of certain conditions or the attainment of stated goals or events. The Option Price per share of Shares covered by an Option (including both ISOs and Non-Qualified Options) shall not be less than one hundred percent (100%) of the Fair Market Value per share of the Common Stock on the date of grant.
- 6.2 *ISOs.* Each Option intended to be an ISO shall be issued only to Employees. In addition to the minimum standards set forth in Section 6.1, ISOs shall be subject to the following terms and conditions, with such additional restrictions or changes as the Administrator determines are appropriate but not in conflict with Code Section 422 and relevant regulations and rulings of the Internal Revenue Service:
  - 6.2.1 *ISO Option Price*. In addition to the limitation set forth in Section 6.1, the Option price per share of the Shares covered by each ISO granted to a Participant who owns, directly or by reason of the applicable attribution rules in Code Section 424(d), more than ten percent (10%) of the total combined voting power of all classes of stock of the Company or an Affiliate shall not be less than one hundred ten percent (110%) of the Fair Market Value on the date of grant.
  - 6.2.2 *Term of ISO*. Each ISO shall expire not more than ten (10) years from the date of grant; provided, however, that an ISO granted to a Participant who owns, directly or by reason of the applicable attribution rules in Code Section 424(d), more than ten percent (10%) of the total combined voting power of all classes of stock of the Company or an Affiliate shall expire not more than five (5) years from the date of grant.
  - 6.2.3 Annual Limit on Incentive Stock Options. To the extent required for "incentive stock option" treatment under Section 422 of the Code, the aggregate Fair Market Value (determined as of the time of grant) of the Shares with respect to which ISOs granted under this Plan and any other plan of the Company or its Affiliate become exercisable for the first time by a Participant during any calendar year shall not exceed the aggregate threshold for ISOs established by the Code (\$100,000 as of March 22, 2006). To the extent that any Option exceeds this limit, it shall constitute a Non-Qualified Option.

6.3 Non-Employee Directors' Options. Each Non-Employee Director, upon first being elected or appointed to the Board of Directors, shall be granted a Non-Qualified Option to purchase that number of Shares as shall be established for such Option grants from time to time by the Board of Directors. Each such Option shall (i) have an exercise price equal to the Fair Market Value (per share) on the date of grant of the Option, (ii) have a term of ten (10) years, and (ii) shall become cumulatively exercisable in sixteen (16) equal quarterly installments, upon completion of each full quarter of service on the Board of Directors after the date of grant. In addition, on June 1 of each year, each Non-Employee Director shall be granted a Non-Qualified Option to purchase that number of Shares as shall be established for such Option grants from time to time by the Board of Directors. Each such Option shall (i) have an exercise price equal to the Fair Market Value (per share) on the date of grant of such Option, (ii) have a term of ten (10) years, and (iii) be exercisable in full immediately on the date of grant. Any director entitled to receive an Option grant under this Section may elect to decline the Option. If a Non-Employee Director ceases to be any of an Employee, Non-Employee Director, consultant or advisor of the Company, Options granted under this Section 6.3 shall remain exercisable to the extent such Options are exercisable on the date of such termination of service, for their full term, and the provisions of Sections 11 and 13 below shall not apply to any such Options.

6.4 *Limitation on Number of Options Granted.* Notwithstanding anything in this Plan to the contrary, no Participant shall be granted an aggregate of Options and/or Stock-Based Awards under this Plan in any calendar year for more than an aggregate of 600,000 Shares (subject to adjustment pursuant to Section 17 to the extent consistent with Section 162(m) of the Code).

#### 7. TERMS AND CONDITIONS OF STOCK GRANTS

Each Stock Grant shall be set forth in a Stock Agreement, duly executed by the Company and, to the extent required by law or requested by the Company, by the Participant. The Stock Agreement shall be in the form approved by the Administrator, with such changes and modifications to such form as the Administrator, in its discretion, shall approve with respect to any particular Participant or Participants. The Stock Agreement shall contain terms and conditions that the Administrator determines to be appropriate and in the best interest of the Company; provided, however, that the purchase price per share of the Shares covered by each Stock Grant shall not be less than the par value per Share. Each Stock Agreement shall state the number of Shares to which the Stock Grant pertains and the terms of any right of the Company to reacquire the Shares subject to the Stock Grant, including the time and events upon which such rights shall accrue and the purchase price therefor, and any restrictions on the transferability of such Shares.

#### 8. TERMS AND CONDITIONS OF OTHER STOCK-BASED AWARDS

The Administrator shall have the right to grant other Stock-Based Awards having such terms and conditions as the Administrator may determine, including, without limitation, the grant of Shares based upon certain conditions, the grant of securities convertible into Shares and the grant of stock appreciation rights, phantom stock awards or stock units. The principal terms of each Stock-Based Award shall be set forth in a Stock Agreement, duly executed by the Company and, to the extent required by law or requested by the Company, by the Participant. The Stock Agreement shall be in a form approved by the Administrator and shall contain terms and conditions that the Administrator determines to be appropriate.

#### 9. EXERCISE OF OPTIONS AND ISSUANCE OF SHARES

An Option (or any part or installment thereof) shall be exercised by giving written notice to the Company or its designee, together with provision for payment of the full purchase price in accordance with this Section for the Shares as to which the Option is being exercised, and upon compliance with any other condition(s) set forth in the Stock Agreement. Such notice shall be signed by the person

exercising the Option, shall state the number of Shares with respect to which the Option is being exercised and shall contain any representation required by the Plan or the Stock Agreement.

Payment of the purchase price for the Shares as to which such Option is being exercised shall be made (a) in United States dollars in cash or by check acceptable to the Administrator, or (b) at the discretion of the Administrator, (i) through delivery of shares of Common Stock not subject to any restriction under any plan and having a Fair Market Value equal as of the date of exercise to the cash exercise price of the Option, (ii) in accordance with a cashless exercise program established with a securities brokerage firm, and approved by the Company, (iii) by any other means (excluding, however, delivery of a promissory note of the Participant) that the Administrator determines to be consistent with the purpose of this Plan and applicable law, or (iv) by any combination of the foregoing. Notwithstanding the foregoing, the Administrator shall accept only such payment on exercise of an ISO as is permitted by Section 422 of the Code.

The Company shall then as soon as is reasonably practicable deliver the Shares as to which such Option was exercised to the Participant (or to the Participant's Survivors, as the case may be). It is expressly understood that the Company may delay the delivery of the Shares in order to comply with any law or regulation that requires the Company to take any action with respect to the Shares prior to their issuance. The Shares shall, upon delivery, be fully paid, non-assessable Shares.

#### 10. ASSIGNABILITY AND TRANSFERABILITY OF STOCK RIGHTS

By its terms, a Stock Right granted to a Participant shall not be transferable by the Participant other than by will or by the laws of descent and distribution or pursuant to a qualified domestic relations order as defined by the Code or Title I of the Employee Retirement Income Security Act or the rules thereunder or as approved by the Administrator in its discretion and set forth in the applicable Stock Agreement, provided, however, that the Administrator shall not approve any transfer of a Stock Right for consideration. Except as provided in the preceding sentence or as otherwise permitted under a Stock Agreement, a Stock Right shall be exercisable, during the Participant's lifetime only by such Participant (or by his or her legal representative) and shall not be assigned, pledged or hypothecated in any way (whether by operation of law or otherwise) and shall not be subject to execution, attachment or similar process. Any attempted transfer, assignment, pledge, hypothecation or other disposition of any Stock Right or of any rights granted thereunder contrary to the provisions of this Plan, or the levy of any attachment or similar process upon a Stock Right, shall be null and void.

#### 11. EFFECT ON STOCK RIGHTS OF TERMINATION OF SERVICE

- 11.1 Except as otherwise provided in the applicable Stock Agreement or as otherwise provided in Sections 12 or 13, if a Participant ceases to be an Employee, Non-Employee Director, consultant or advisor with the Company and its Affiliates (for any reason other than termination for "cause," or death) (a "Termination of Service") before the Participant has exercised all Stock Rights, the Participant may exercise any Stock Right granted to him or her to the extent that the Stock Right is exercisable on the date of such Termination of Service. Any such Stock Right must be exercised within three months after the date of the Participant's Termination of Service, unless otherwise provided in the applicable Stock Agreement, but in no event after the expiration of the term of the Stock Right.
- 11.2 The provisions of this Section, and not the provisions of Section 14, shall apply to a Participant who subsequently dies after the Termination of Service; provided, however, that in the case of a Participant's death within three (3) months after the Termination of Service, the Participant's Survivors may exercise the Stock Right within one (1) year after the date of the Participant's death, but in no event after the date of expiration of the term of the Stock Right.
- 11.3 Notwithstanding anything herein to the contrary, if subsequent to a Participant's Termination of Service, but prior to the exercise of a Stock Right, the Administrator determines that, either prior or

subsequent to the Participant's Termination of Service, the Participant engaged in conduct which would constitute "cause" (as defined in Section 12), then such Participant shall forthwith cease to have any right to exercise any Stock Right. Stock Rights that consist of Shares issued under Stock Grants for which any restrictions on transfer or Company repurchase right shall have lapsed, shall be deemed for all purposes to have been "exercised."

11.4 Absence from work with the Company or an Affiliate because of temporary disability or a leave of absence for any purpose, shall not, during the period of any such absence in accordance with Company policies, be deemed, by virtue of such absence alone, a Termination of Service, except as the Administrator may otherwise expressly provide.

11.5 Except as required by law or as set forth in a Participant's Stock Agreement, Stock Rights granted under the Plan shall not be affected by any change of a Participant's status within or among the Company and any Affiliates, so long as the Participant continues to be an employee, director, consultant or advisor of the Company or any Affiliate.

#### 12. EFFECT ON STOCK RIGHTS OF TERMINATION OF SERVICE FOR "CAUSE"

Except as otherwise provided in a Participant's Stock Agreement or as otherwise agreed in writing by the Administrator, if a Participant's service with the Company or an Affiliate is terminated for "cause," all outstanding and unexercised (vested or unvested) Stock Rights will immediately be forfeited as of the time the Participant is notified that his or her service is terminated for "cause." Stock Rights that consist of Shares issued under Stock Grants for which any restrictions on transfer or Company repurchase right shall have lapsed, shall be deemed for all purposes to have been "exercised." For purposes of this Plan, "cause" shall include (and is not limited to) dishonesty with respect to the Company and its Affiliates, insubordination, substantial malfeasance or non-feasance of duty, unauthorized disclosure of confidential information, breach by the Participant of any provision of any employment, consulting, advisory, nondisclosure, non-competition or similar agreement between the Participant and the Company, and conduct substantially prejudicial to the business of the Company or any Affiliate. The determination of the Administrator as to the existence of cause will be conclusive on the Participant and the Company. "Cause" is not limited to events that have occurred prior to a Participant's termination of service, nor is it necessary that the Administrator's finding of "cause" occur prior to termination of service. If the Administrator determines, subsequent to a Participant's termination of service but prior to the exercise of a Stock Right, that either prior or subsequent to the Participant's termination of service the Participant engaged in conduct which would constitute "cause," then the right to exercise any Stock Right shall be forfeited as set forth in this Section 12. Any definition in an agreement between a Participant and the Company or an Affiliate which contains a conflicting definition of "cause" for termination of service and which is in effect at the time of such termination of service sha

#### 13. EFFECT ON STOCK RIGHTS OF DEATH WHILE AN EMPLOYEE, DIRECTOR, CONSULTANT OR ADVISOR

Except as otherwise provided in a Participant's Stock Agreement, in the event of death of a Participant while the Participant is an Employee, Non-Employee Director, consultant or advisor of the Company or of an Affiliate, any Stock Rights granted to such Participant may be exercised by the Participant's Survivors to the extent exercisable but not exercised on the date of death. Any such Stock Right must be exercised within one (1) year after the date of death of the Participant but in no event after the date of expiration of the term of the Stock Right, notwithstanding that the decedent might have been able to exercise the Stock Right as to some or all of the Shares on a later date if he or she had not died and had continued to be an Employee, Non-Employee Director, consultant or advisor.

#### 14. RIGHTS AS A STOCKHOLDER

No Participant to whom a Stock Right (other than a Stock Grant) has been granted shall have rights as a stockholder with respect to any Shares covered by such Stock Right, except after due exercise thereof and/or tender of the full purchase price for the Shares being purchased pursuant to such exercise. The provisions of this Section 14 shall not be applicable to Shares issued pursuant to Stock Grants, provided that the Participant shall have tendered the purchase price therefore, notwithstanding the existence of stock transfer restrictions on or a Company repurchase right with respect to such Shares.

#### 15. EMPLOYMENT OR OTHER RELATIONSHIP

Nothing in this Plan or any Stock Agreement shall be deemed to prevent the Company or an Affiliate from terminating the employment, consultancy or director status of a Participant, or to prevent a Participant from terminating his or her own employment, consultancy or director status or to give any Participant a right to be retained in employment or other service by the Company or any Affiliate for any period of time.

#### 16. DISSOLUTION OR LIQUIDATION OF THE COMPANY

Upon the dissolution or liquidation of the Company (other than in connection with a transaction subject to the provisions of Section 17.2), all Stock Rights granted under this Plan which as of such date shall not have been exercised will terminate and become null and void; provided, however, that if the rights of a Participant or a Participant's Survivors have not otherwise terminated and expired, the Participant or Participant's Survivors will have the right immediately prior to such dissolution or liquidation to exercise any Stock Right to the extent that such Stock Right is exercisable as of the date immediately prior to such dissolution or liquidation. Upon the dissolution or liquidation of the Company, any outstanding Stock-Based Awards shall immediately terminate unless otherwise determined by the Administrator or specifically provided in the applicable Stock Agreement.

#### 17. ADJUSTMENTS

Upon the occurrence of any of the following events, a Participant's rights with respect to any Stock Right granted to him or her hereunder that have not previously been exercised in full shall be adjusted as hereinafter provided, unless otherwise specifically provided in the Stock Agreement or in any employment agreement between a Participant and the Company or an Affiliate:

- 17.1 Stock Dividends and Stock Splits. If the shares of Common Stock shall be subdivided or combined into a greater or smaller number of shares or if the Company shall issue any shares of Common Stock as a stock dividend on its outstanding Common Stock, the number of shares of Common Stock subject to or deliverable upon the exercise of a Stock Right shall be appropriately increased or decreased, and appropriate adjustments shall be made in the purchase price per Share to reflect such event. The number of Shares subject to Options to be granted to Non-Employee Directors pursuant to Section 6.3 and the number of Shares subject to the limitation in Section 6.4 shall also be proportionately adjusted upon the occurrence of such events.
- 17.2 *Consolidations or Mergers.* In the event of a consolidation or merger in which the Company is not the surviving corporation or which results in the acquisition of substantially all the Company's outstanding stock by a single person or entity or by a group of persons and/or entities acting in concert, or in the event of the sale or transfer of substantially all the Company's assets (any of the foregoing, an "Acquisition"), all then outstanding Stock Rights (excluding any Shares subject to Stock Grants as to which all Company repurchase rights shall have lapsed) shall terminate unless assumed pursuant to clause (i) below; provided that either (i) the Administrator shall provide for the surviving or acquiring entity or an affiliate thereof to assume the outstanding

Stock Rights or grant replacement stock rights in lieu thereof, any such replacement to be upon an equitable basis as determined by the Administrator, or (ii) if there is no such assumption or substitution, all outstanding Stock Rights shall become immediately and fully exercisable and all Company repurchase rights with respect to Stock Rights shall lapse, in each case immediately prior to the Acquisition, notwithstanding any restrictions or vesting conditions set forth therein.

- 17.3 *Recapitalization or Reorganization.* In the event of a recapitalization or reorganization of the Company (other than a transaction described in Section 17.2 above) pursuant to which securities of the Company or of another corporation are issued with respect to the outstanding shares of Common Stock, a Participant upon exercising a Stock Right shall be entitled to receive for the purchase price paid upon such exercise the securities he or she would have received if he or she had exercised such Stock Right prior to such recapitalization or reorganization.
- 17.4 Adjustments to Stock Grants and Stock-Based Awards. Upon the happening of any of the events described in Sections 17.1, 17.2 or 17.3, any outstanding Stock-Based Award and the Shares subject to any Stock Grant, vested or unvested, shall be appropriately adjusted to reflect the events described in such Sections. The Administrator shall determine the specific adjustments to be made under this Section 17.4.
- 17.5 *Modification of ISOs.* Notwithstanding the foregoing, any adjustments made pursuant to Section 17.1, 17.2 or 17.3 with respect to ISOs shall be made only after the Administrator determines whether such adjustments would constitute a "modification" of such ISOs (as that term is defined in Section 424(h) of the Code) or would cause any adverse tax consequences for the holders of such ISOs. If the Administrator determines that such adjustments made with respect to ISOs would constitute a modification of such ISOs, it may refrain from making such adjustments, unless the holder of an ISO specifically requests in writing that such adjustment be made and such writing indicates that the holder has full knowledge of the consequences of such "modification" on his or her income tax treatment with respect to the ISO.

#### 18. ISSUANCES OF SECURITIES

Except as expressly provided herein, no issuance (including for this purpose the delivery of shares held in treasury) by the Company of shares of stock of any class, or securities convertible into shares of stock of any class, shall affect, and no adjustment by reason thereof shall be made with respect to, the number or price of Shares subject to Stock Rights. Except as expressly provided herein, no adjustments shall be made for dividends paid in cash or in property (including without limitation, securities) of the Company.

#### 19. FRACTIONAL SHARES

No fractional share shall be issued under the Plan and the person exercising any Stock Right shall receive from the Company cash in lieu of any such fractional share equal to the Fair Market Value thereof.

#### 20. CONVERSION OF ISOs INTO NON-QUALIFIED OPTIONS: TERMINATION OF ISOs

Any Options granted under this Plan that do not meet the requirements of the Code for ISOs shall automatically be deemed to be Non-Qualified Options without further action on the part of the Administrator. The Administrator, at the written request of any Participant, may in its discretion take such actions as may be necessary to convert such Participant's ISOs (or any portion thereof) that have not been exercised on the date of conversion into Non-Qualified Options at any time prior to the expiration of such ISOs, regardless of whether the Participant is an employee of the Company or an Affiliate at the time of such conversion. At the time of such conversion, the Administrator (with the consent of the Participant) may impose such conditions on the exercise of the resulting Non-Qualified

Options as the Administrator in its discretion may determine, provided that such conditions shall not be inconsistent with this Plan. Nothing in the Plan shall be deemed to give any Participant the right to have such Participant's ISOs converted into Non-Qualified Options, and no such conversion shall occur until and unless the Administrator takes appropriate action. The Administrator, with the consent of the Participant, may also terminate any portion of any ISO that has not been exercised at the time of such termination.

#### 21. WITHHOLDING

If any federal, state, or local income taxes, employment taxes, Federal Insurance Contributions Act ("FICA") withholdings or other amounts are required by applicable law or governmental regulation to be withheld from the Participant's salary, wages or other remuneration in connection with the exercise of a Stock Right, the lapsing of a Company repurchase right or a Disqualifying Disposition (as defined in Section 22), the Company may withhold from the Participant' compensation, if any, or may require that the Participant advance in cash to the Company, or to any Affiliate of the Company which employs or employed the Participant, the amount of such withholdings unless a different withholding arrangement, including the use of shares of the Company's Common Stock, is authorized by the Administrator (and permitted by law). For purposes hereof, the Fair Market Value of any shares withheld for purposes of payroll withholding shall be determined in the manner provided in Section 1 above, as of the most recent practicable date prior to the date of exercise. If the Fair Market Value of the shares withheld is less than the amount of payroll withholdings required, the Participant may be required to advance the difference in cash to the Company or the Affiliate employer. The Administrator in its discretion may condition the exercise of an Option for less than the then Fair Market Value on the Participant's payment of such additional withholding. In no event shall shares be withheld from any award in satisfaction of tax withholding requirements in an amount that exceeds the statutory minimum amount of tax withholding required.

#### 22. NOTICE TO COMPANY OF DISQUALIFYING DISPOSITION

Each Employee who receives an ISO must agree to notify the Company in writing immediately after the Employee makes a "Disqualifying Disposition" of any Shares acquired pursuant to the exercise of an ISO. A Disqualifying Disposition is any disposition (as defined in Section 424(c) of the Code) of such Shares before the later of (a) two years from the date the Employee was granted the ISO, or (b) one year after the date the Employee acquired Shares by exercising the ISO. If the Employee has died before such Shares are sold, the notice provisions of this Section 22 shall not apply.

#### 23. EFFECTIVE DATE; TERMINATION OF THE PLAN

This Plan shall be effective on March 29, 2006, the date of its adoption by the Board of Directors, subject to approval by the shareholders of the Company. The Plan will terminate on March 28, 2016. The Plan also may be terminated at an earlier date by vote of the Board of Directors. Termination of this Plan will not affect any Stock Rights granted or Stock Agreements executed prior to the effective date of such termination.

#### 24. AMENDMENT OF THE PLAN; AMENDMENT OF STOCK RIGHTS

The Plan may be amended by the stockholders of the Company by affirmative vote of a majority of the votes cast at a meeting of the stockholders at which a quorum is present. The Plan also may be amended by the Board of Directors or the Administrator, including, without limitation, to the extent necessary to qualify any or all outstanding Stock Rights granted under the Plan or Stock Rights to be granted under the Plan for favorable federal income tax treatment (including deferral of taxation upon exercise) as may be afforded incentive stock options under Section 422 of the Code, and to the extent necessary to qualify the shares issuable upon exercise of any outstanding Stock Rights granted, or Stock

Rights to be granted, under the Plan for listing on any national securities exchange or quotation in any national automated quotation system of securities dealers. Any amendment approved by the Administrator that the Administrator determines is of a scope that requires stockholder approval shall be subject to stockholder approval. No modification or amendment of the Plan shall adversely affect a Participant's rights under a Stock Right previously granted to the Participant, without such Participant's consent.

In its discretion, the Administrator may amend any term or condition of any outstanding Stock Right, provided: (i) such term or condition is not prohibited by the Plan; (ii) if the amendment is adverse to the Participant, such amendment shall be made only with the consent of the Participant or the Participant's Survivors, as the case may be; and (iii) any such amendment of any ISO shall be made only after the Administrator determines whether such amendment would constitute a "modification" of any Stock Right which is an ISO (as that term is defined in Section 424(h) of the Code) or would cause any adverse tax consequences for the holder of such ISO (in which case, the Participant's or Participant's Survivors' consent to such amendment shall be required). Notwithstanding the foregoing, the Administrator shall not have the authority to reduce the exercise price of any Option after the date of grant, except for adjustments permitted under Section 17 of this Plan.

#### 25. GOVERNING LAW

This Plan shall be construed and enforced in accordance with the law of The Commonwealth of Massachusetts.

A-11

QuickLinks

Exhibit 10.1

Appendix A

**EXHIBIT 23.1** 

## Consent of Independent Registered Public Accounting Firm

We consent to the incorporation by reference in the Registration Statement on Form S-8 pertaining to the Amended and Restated 2006 Stock and Option Plan of Vertex Pharmaceuticals Incorporated, 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 May 12, 2008

# QuickLinks

EXHIBIT 23.1

Consent of Independent Registered Public Accounting Firm