

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

**SCHEDULE 13G**  
**(Amendment No. 2)**

Under the Securities Exchange Act of 1934

Vertex Pharmaceuticals Incorporated  
(Name of Issuer)

Common Stock, \$0.01 par value  
(Title of Class of Securities)

92532F100  
(CUSIP Number)

December 31, 2009  
(Date of Event Which Requires Filing of this Statement)

Check the following box to designate the rule pursuant to which the Schedule is filed:

- Rule 13d-1(b)
- Rule 13d-1(c)
- Rule 13d-1(d)

\* The remainder of this cover page shall be filled out for a reporting person's initial filing on this form with respect to the subject class of securities, and for any subsequent amendment containing information which would alter the disclosures provided in a prior cover page.

The information required in the remainder of this cover page shall not be deemed to be "filed" for the purpose of Section 18 of the Securities Exchange Act of 1934 ("Act") or otherwise subject to the liabilities of that section of the Act but shall be subject to all other provisions of the Act (however, see the Notes).

---

1. **Names of Reporting Persons**  
**I.R.S. Identification Nos. of above persons (entities only)**  
D. E. Shaw Valence Portfolios, L.L.C.  
13-4046559
2. **Check the Appropriate Box if a Member of a Group (See Instructions)**  
(a)  0  
(b)  0
3. **SEC Use Only**
4. **Citizenship or Place of Organization**  
Delaware

<b>Number of Shares Beneficially Owned by Each Reporting Person With</b>	5.	<b>Sole Voting Power</b> -0-
	6.	<b>Shared Voting Power</b> 6,972,857 (1)
	7.	<b>Sole Dispositive Power</b> -0-
	8.	<b>Shared Dispositive Power</b> 6,972,857 (1)
9.	<b>Aggregate Amount Beneficially Owned by Each Reporting Person</b> 6,972,857 (1)	
10.	<b>Check if the Aggregate Amount in Row (9) Excludes Certain Shares (See Instructions)</b> <input type="radio"/>	
11.	<b>Percent of Class Represented by Amount in Row (9)</b> 3.6% (2)	
12.	<b>Type of Reporting Person (See Instructions)</b> OO	

1 Includes bonds convertible into 123,298 shares.

2 Based on 193,898,858 shares of outstanding common stock as reported in the Issuer's Prospectus Supplement filed on December 3, 2009, and including the 123,298 shares from the potential conversion of the bonds for a total of 194,022,156 shares outstanding.

---

1. **Names of Reporting Persons**  
**I.R.S. Identification Nos. of above persons (entities only)**  
D. E. Shaw & Co., L.P.  
13-3695715
2. **Check the Appropriate Box if a Member of a Group (See Instructions)**  
(a)   
(b)
3. **SEC Use Only**
4. **Citizenship or Place of Organization**  
Delaware

<b>Number of Shares Beneficially Owned by Each Reporting Person With</b>	5.	<b>Sole Voting Power</b> -0-
	6.	<b>Shared Voting Power</b> 7,131,460 (1)
	7.	<b>Sole Dispositive Power</b> -0-
	8.	<b>Shared Dispositive Power</b> 7,131,460 (1)
9.	<b>Aggregate Amount Beneficially Owned by Each Reporting Person</b> 7,131,460 (1)	
10.	<b>Check if the Aggregate Amount in Row (9) Excludes Certain Shares (See Instructions)</b> <input type="radio"/>	
11.	<b>Percent of Class Represented by Amount in Row (9)</b> 3.7% (2)	
12.	<b>Type of Reporting Person (See Instructions)</b> IA, PN	

1 Includes bonds convertible into 281,429 shares.

2 Based on 193,898,858 shares of outstanding common stock as reported in the Issuer's Prospectus Supplement filed on December 3, 2009, and including the 281,429 shares from the potential conversion of the bonds for a total of 194,180,287 shares outstanding.

---

1. **Names of Reporting Persons**  
**I.R.S. Identification Nos. of above persons (entities only)**  
David E. Shaw
2. **Check the Appropriate Box if a Member of a Group (See Instructions)**  
(a)   
(b)
3. **SEC Use Only**
4. **Citizenship or Place of Organization**  
United States

<b>Number of Shares Beneficially Owned by Each Reporting Person With</b>	5.	<b>Sole Voting Power</b> -0-
	6.	<b>Shared Voting Power</b> 7,131,460 (1)
	7.	<b>Sole Dispositive Power</b> -0-
	8.	<b>Shared Dispositive Power</b> 7,131,460 (1)

9. **Aggregate Amount Beneficially Owned by Each Reporting Person**  
7,131,460 (1)
10. **Check if the Aggregate Amount in Row (9) Excludes Certain Shares (See Instructions)**
11. **Percent of Class Represented by Amount in Row (9)**  
3.7% (2)
12. **Type of Reporting Person (See Instructions)**  
IN

1 Includes bonds convertible into 281,429 shares.

2 Based on 193,898,858 shares of outstanding common stock as reported in the Issuer's Prospectus Supplement filed on December 3, 2009, and including the 281,429 shares from the potential conversion of the bonds for a total of 194,180,287 shares outstanding.

---

**Item 1.**

- (a) **Name of Issuer:**  
Vertex Pharmaceuticals Incorporated
- (b) **Address of Issuer's Principal Executive Offices:**  
130 Waverly Street  
Cambridge, MA 02139

**Item 2.**

- (a) **Name of Person Filing:**  
D. E. Shaw Valence Portfolios, L.L.C.  
D. E. Shaw & Co., L.P.  
David E. Shaw
- (b) **Address of Principal Business Office or, if none, Residence:**  
The business address for each reporting person is:  
120 W. 45<sup>th</sup> Street, Tower 45, 39<sup>th</sup> Floor  
New York, NY 10036
- (c) **Citizenship:**  
D. E. Shaw Valence Portfolios, L.L.C. is a limited liability company organized under the laws of the state of Delaware.  
D. E. Shaw & Co., L.P. is a limited partnership organized under the laws of the state of Delaware.  
David E. Shaw is a citizen of the United States of America.
- (d) **Title of Class of Securities:**  
Common Stock, \$0.01 par value
- (e) **CUSIP Number:**  
92532F100

**Item 3. If this statement is filed pursuant to Rule 13d-1(b) or 13d-2(b) or (c), check whether the person filing is a:**

Not Applicable

**Item 4. Ownership**

As of December 31, 2009:

**(a) Amount beneficially owned:**

D. E. Shaw Valence Portfolios, L.L.C.:	6,972,857 shares This is composed of (i) 6,801,559 shares in the name of D. E. Shaw Valence Portfolios, L.L.C., (ii) 48,000 shares that D. E. Shaw Valence Portfolios, L.L.C. has the right to acquire through the exercise of listed call options, and (iii) 123,298 shares that D. E. Shaw Valence Portfolios, L.L.C. has the right to acquire through the conversion of convertible bonds.
D. E. Shaw & Co., L.P.:	7,131,460 shares This is composed of (i) 6,801,559 shares in the name of D. E. Shaw Valence Portfolios, L.L.C., (ii) 48,000 shares that D. E. Shaw Valence Portfolios, L.L.C. has the right to acquire through the exercise of listed call options, (iii) 123,298 shares that D. E. Shaw Valence Portfolios, L.L.C. has the right to acquire through the conversion of convertible bonds, (iv) 158,131 shares that D. E. Shaw Oculus Portfolios, L.L.C. has the right to acquire through the conversion of convertible bonds, and (v) 472 shares in the name of D. E. Shaw Synoptic Portfolios 2, L.L.C.
David E. Shaw:	7,131,460 shares This is composed of (i) 6,801,559 shares in the name of D. E. Shaw Valence Portfolios, L.L.C., (ii) 48,000 shares that D. E. Shaw Valence Portfolios, L.L.C. has the right to acquire through the exercise of listed call options, (iii) 123,298 shares that D. E. Shaw Valence Portfolios, L.L.C. has the right to acquire through the conversion of convertible bonds, (iv) 158,131 shares that D. E. Shaw Oculus Portfolios, L.L.C. has the right to acquire through the conversion of convertible bonds, and (v) 472 shares in the name of D. E. Shaw Synoptic Portfolios 2, L.L.C.

---

(b) Percent of class:		
	D. E. Shaw Valence Portfolios, L.L.C.:	3.6%
	D. E. Shaw & Co., L.P.:	3.7%
	David E. Shaw:	3.7%

(c) Number of shares to which the person has:

(i)	Sole power to vote or to direct the vote:	
	D. E. Shaw Valence Portfolios, L.L.C.:	-0- shares
	D. E. Shaw & Co., L.P.:	-0- shares
	David E. Shaw:	-0- shares
(ii)	Shared power to vote or to direct the vote:	
	D. E. Shaw Valence Portfolios, L.L.C.:	6,972,857 shares
	D. E. Shaw & Co., L.P.:	7,131,460 shares
	David E. Shaw:	7,131,460 shares
(iii)	Sole power to dispose or to direct the disposition of:	
	D. E. Shaw Valence Portfolios, L.L.C.:	-0- shares
	D. E. Shaw & Co., L.P.:	-0- shares
	David E. Shaw:	-0- shares
(iv)	Shared power to dispose or to direct the disposition of:	
	D. E. Shaw Valence Portfolios, L.L.C.:	6,972,857 shares
	D. E. Shaw & Co., L.P.:	7,131,460 shares
	David E. Shaw:	7,131,460 shares

David E. Shaw does not own any shares directly. By virtue of David E. Shaw's position as President and sole shareholder of D. E. Shaw & Co., Inc., which is the general partner of D. E. Shaw & Co., L.P., which in turn is the managing member and investment adviser of D. E. Shaw Valence Portfolios, L.L.C., and the investment adviser of D. E. Shaw Oculus Portfolios, L.L.C. and D. E. Shaw Synoptic Portfolios 2, L.L.C., and by virtue of David E. Shaw's position as President and sole shareholder of D. E. Shaw & Co. II, Inc., which is the managing member of D. E. Shaw & Co., L.L.C., which in turn is the managing member of D. E. Shaw Oculus Portfolios, L.L.C. and D. E. Shaw Synoptic Portfolios 2, L.L.C., David E. Shaw may be deemed to have the shared power to vote or direct the vote of , and the shared power to dispose or direct the disposition of, the 7,131,460 shares as described above constituting 3.7% of the outstanding shares and, therefore, David E. Shaw may be deemed to be the beneficial owner of such shares. David E. Shaw disclaims beneficial ownership of such 7,131,460 shares.

**Item 5. Ownership of Five Percent or Less of a Class**

If this statement is being filed to report the fact that as of the date hereof the reporting person has ceased to be the beneficial owner of more than 5 percent of the class of securities, check the following [X].

**Item 6. Ownership of More than Five Percent on Behalf of Another Person**

Not Applicable

**Item 7. Identification and Classification of the Subsidiary Which Acquired the Security Being Reported on By the Parent Holding Company or Control Person**

Not Applicable

**Item 8. Identification and Classification of Members of the Group**

Not Applicable

**Item 9. Notice of Dissolution of Group**

Not Applicable

**Item 10. Certification**

By signing below, each of D. E. Shaw Valence Portfolios, L.L.C., D. E. Shaw & Co., L.P., and David E. Shaw certify that, to the best of such reporting person's knowledge and belief, the securities referred to above were not acquired and are not held for the purpose of or with the effect of changing or influencing the control of the issuer of the securities and were not acquired and are not held in connection with or as a participant in any transaction having such purposes or effect.

**SIGNATURE**

After reasonable inquiry and to the best of their knowledge and belief, the undersigned certify that the information set forth in this statement is true, complete and correct. A Power of Attorney, dated October 24, 2007, granted by David E. Shaw in favor of Rochelle Elias, is attached hereto.

Dated: February 16, 2010

D. E. Shaw Valence Portfolios, L.L.C.

By: /s/ Rochelle Elias

---

Rochelle Elias  
Authorized Signatory

D. E. Shaw & Co., L.P.

By: /s/ Rochelle Elias

---

Rochelle Elias  
Chief Compliance Officer

David E. Shaw

By: /s/ Rochelle Elias

---

Rochelle Elias  
Attorney-in-Fact for David E. Shaw

---

**Exhibit 1**

POWER OF ATTORNEY  
FOR CERTAIN FILINGS  
UNDER THE SECURITIES EXCHANGE ACT OF 1934

I, David E. Shaw, hereby make, constitute, and appoint each of:

Anne Dinning,

Rochelle Elias,

Julius Gaudio,

John Liftin,

Louis Salkind,

Stuart Steckler,

Maximilian Stone, and

Eric Wepsic,

acting individually, as my agent and attorney-in-fact, with full power of substitution, for the purpose of, from time to time, executing in my name and/or my capacity as President of D. E. Shaw & Co., Inc. (acting for itself or as the general partner of D. E. Shaw & Co., L. P. and general partner, managing member, or manager of other entities, any of which in turn may be acting for itself or other entities) all documents, certificates, instruments, statements, other filings, and amendments to the foregoing (collectively, "documents") determined by such person to be necessary or appropriate to comply with ownership or control-person reporting requirements imposed by any United States or non-United States governmental or regulatory authority, including without limitation Forms 3, 4, 5, and 13F and Schedules 13D and 13G required to be filed with the Securities and Exchange Commission; and delivering, furnishing, or filing any such documents to or with the appropriate governmental or regulatory authority. Any such determination shall be conclusively evidenced by such person's execution, delivery, furnishing, and/or filing of the applicable document.

This power of attorney shall be valid from the date hereof and replaces the power granted on February 24, 2004, which is hereby cancelled.

IN WITNESS HEREOF, I have executed this instrument as of the date set forth below.

Date: October 24, 2007

DAVID E. SHAW, as President of  
D. E. Shaw & Co., Inc.  
/s/ David E. Shaw  
New York, New York

---