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

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

VERTEX PHARMACEUTICALS INCORPORATED
(Exact name of registrant as specified in its charter)

Massachusetts
(State or other jurisdiction of
incorporation or organization)

04-3039129
(I.R.S. Employer
Identification Number)

**50 Northern Avenue
Boston, Massachusetts 02210
(617) 341-6100**
(Address, including zip code, and telephone number, including area code, of registrant's principal executive offices)

**Reshma Kewalramani
President and Chief Executive Officer
Vertex Pharmaceuticals Incorporated
50 Northern Avenue
Boston, Massachusetts 02210
(617) 341-6100**
(Name, address, including zip code, and telephone number, including area code, of agent for service)

With copies to:

**Zachary Blume
Ropes & Gray LLP
Prudential Tower
800 Boylston Street
Boston, Massachusetts 02199-3600
(617) 951-7000**

**Joy Liu, Esq.
Sabrina Yohai, Esq.
Vertex Pharmaceuticals Incorporated
50 Northern Avenue
Boston, Massachusetts 02210
(617) 341-6100**

Approximate date of commencement of proposed sale to the public: From time to time after the effective date of this registration statement.

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

If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, other than securities offered only in connection with dividend or interest reinvestment plans, 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, a smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company" and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer	<input checked="" type="checkbox"/>	Accelerated filer	<input type="checkbox"/>
Non-accelerated filer	<input type="checkbox"/>	Smaller reporting company	<input type="checkbox"/>
		Emerging growth company	<input type="checkbox"/>

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 7(a)(2)(B) of Securities Act.

Prospectus

VERTEX PHARMACEUTICALS INCORPORATED



Common Stock
Debt Securities
Preferred Stock
Warrants
Subscription Rights
Purchase Contracts
Purchase Units

We may offer, issue and sell, together or separately:

- shares of our common stock;
- debt securities, which may be issued in one or more series and which may be senior debt securities or subordinated debt securities;
- shares of our preferred stock, which may be issued in one or more series;
- warrants to purchase shares of our common stock, our debt securities or shares of our preferred stock;
- subscription rights to purchase shares of our common stock, our debt securities or shares of our preferred stock;
- purchase contracts to purchase shares of our common stock, our debt securities or shares of our preferred stock; and
- purchase units, each representing ownership of a purchase contract and debt securities, preferred securities or debt obligations of third-parties, including U.S. treasury securities, or any combination of the foregoing, securing the holder's obligation to purchase our common stock or other securities under the purchase contracts.

We will provide the specific prices and terms of these securities in one or more supplements to this prospectus at the time of offering. You should read this prospectus and the accompanying prospectus supplement carefully before you make your investment decision.

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

Investing in our securities involves a number of risks. See "[Risk Factors](#)" on page 3 before you make your investment decision.

We may offer securities through underwriting syndicates managed or co-managed by one or more underwriters or dealers, through agents or directly to purchasers. These securities also may be resold by selling securityholders. If required, the prospectus supplement for each offering of securities will describe the plan of distribution for that offering. For general information about the distribution of securities offered, please see "Plan of Distribution" in this prospectus.

Our common stock is listed on the Nasdaq Global Select Market under the trading symbol "VRTX." Each prospectus supplement will indicate whether the securities offered thereby will be listed on any securities exchange.

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

The date of this prospectus is February 9, 2022

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ABOUT THIS PROSPECTUS

This prospectus is part of an “automatic shelf” registration statement that we filed with the Securities and Exchange Commission (the “SEC”) as a “well-known seasoned issuer” as defined in Rule 405 under the Securities Act of 1933, as amended (the “Securities Act”), using a “shelf” registration process. Under this process, we may sell from time to time any combination of the securities described in this prospectus. This prospectus only provides you with a general description of the securities that we may offer. Each time we sell securities, we will provide a supplement to this prospectus that contains specific information about the terms of that offering, including the specific amounts, prices and terms of the securities offered. The prospectus supplement may also add, update or change information contained in this prospectus. You should carefully read both this prospectus, any accompanying prospectus supplement and any free writing prospectus prepared by or on behalf of us, together with the additional information described under the heading “Where You Can Find More Information.”

We have not authorized anyone to provide you with any information other than that contained in or incorporated by reference into this prospectus, any accompanying prospectus supplement and any free writing prospectus prepared by or on behalf of us. We take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. We are not making offers to sell the securities in any jurisdiction in which 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 an offer or solicitation.

The information in this prospectus is accurate as of the date on the front cover. You should not assume that the information contained in this prospectus is accurate as of any other date.

When used in this prospectus, the terms “Vertex,” the “Company,” “we,” “our” and “us” refer to Vertex Pharmaceuticals Incorporated and its consolidated subsidiaries, unless otherwise specified or the context otherwise requires.

WHERE YOU CAN FIND MORE INFORMATION

We file annual, quarterly and current reports, proxy statements and other information with the SEC under the Securities Exchange Act of 1934, as amended (the “Exchange Act”). Our SEC filings are available to the public at the SEC’s website at www.sec.gov. Please call the SEC at 1-800-SEC-0330 for further information about the Public Reference Room.

The SEC allows us to “incorporate by reference” information into this prospectus and any accompanying prospectus supplement, which means that we can disclose important information to you by referring you to another document filed separately with the SEC. The information incorporated by reference is deemed to be part of this prospectus and any accompanying prospectus supplement, except for any information superseded by information contained directly in this prospectus, any accompanying prospectus supplement, any subsequently filed document deemed incorporated by reference or any free writing prospectus prepared by or on behalf of us. This prospectus and any accompanying prospectus supplement incorporate by reference the documents set forth below that we have previously filed with the SEC (other than information deemed furnished and not filed in accordance with SEC rules, including Items 2.02 and 7.01 of Form 8-K):

- our Annual Report on [Form 10-K](#) for the fiscal year ended December 31, 2021, filed with the SEC on February 9, 2022;
- the information specifically incorporated by reference into our Annual Report on [Form 10-K](#) for the fiscal year ended December 31, 2020 from our definitive proxy statement on [Schedule 14A](#), filed with the SEC on April 8, 2021; and

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- the description of our common stock contained in our Registration Statement on Form 8-A, filed with the SEC on May 30, 1991, and any amendment or report filed for the purpose of updating such description.

All documents filed by us pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act after the date of this prospectus and before the termination of the offering also shall be deemed to be incorporated herein by reference. We are not, however, incorporating by reference any documents or portions thereof that are not deemed “filed” with the SEC, including any information furnished pursuant to Items 2.02 or 7.01 of Form 8-K.

If requested, we will provide to each person, including any beneficial owner, to whom a prospectus is delivered, a copy of any or all of the information that has been incorporated by reference in the prospectus but not delivered with the prospectus. Exhibits to the filings will not be sent, however, unless those exhibits have specifically been incorporated by reference into such documents. To obtain a copy of these filings at no cost, you may write or telephone us at the following address:

Vertex Pharmaceuticals Incorporated
50 Northern Avenue
Boston, Massachusetts 02210
Attn: Investor Relations
(617) 341-6100

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus and any accompanying prospectus supplement and any documents incorporated by reference contain statements that are “forward-looking” within the meaning of the Private Securities Litigation Reform Act of 1995.

Any or all of our forward-looking statements in this prospectus and any accompanying prospectus supplement and any documents incorporated by reference may turn out to be wrong. They can be affected by inaccurate assumptions or by known or unknown risks and uncertainties. Many factors mentioned in this prospectus and any accompanying prospectus supplement and any documents incorporated by reference will be important in determining future results. Consequently, no forward-looking statement can be guaranteed. Actual future results may vary materially from expected results. We also provide a cautionary discussion of risks and uncertainties under “Risk Factors” in our most recent Annual Report on Form 10-K (together with any changes contained in subsequently filed Quarterly Reports on Form 10-Q) and those contained in our other filings with the SEC that are incorporated by reference in this prospectus and any accompanying prospectus supplement. These are factors and uncertainties that we think could cause our actual results to differ materially from expected results. Other factors and uncertainties besides those listed there could also adversely affect us.

Without limiting the foregoing, the words “believes,” “anticipates,” “plans,” “intends,” “expects” and similar expressions are intended to identify forward-looking statements. There are a number of factors and uncertainties that could cause actual events or results to differ materially from those indicated by such forward-looking statements, many of which are beyond our control. In addition, any forward-looking statements contained herein represent our estimate only as of the date of such statement and should not be relied upon as representing our estimate as of any subsequent date. While we may elect to update these forward-looking statements at some point in the future, we specifically disclaim any obligation to do so to reflect actual results, changes in assumptions or changes in other factors affecting such forward-looking statements.

THE COMPANY

We invest in scientific innovation to create transformative medicines for people with serious diseases with a focus on specialty markets. We have four approved medicines to treat cystic fibrosis (“CF”), a life-threatening genetic disease, and are focused on increasing the number of people with CF eligible and able to receive our medicines through label expansions, approval of new medicines and expanded reimbursement. We are broadening our pipeline into additional disease areas through internal research efforts and accessing external innovation through business development transactions.

Our triple combination regimen, TRIKAFTA/KAFTRIO (elexacaftor/tezacaftor/ivacaftor and ivacaftor) was approved in 2019 in the United States, or U.S., and in 2020 in the European Union. Collectively, our four medicines are being used by the majority of the approximately 83,000 people with CF in North America, Europe and Australia. We are evaluating our medicines in additional patient populations, including younger children, with the goal of having small molecule treatments for approximately 90% of people with CF.

We continue to research and develop product candidates for the treatment of serious diseases, including genetic therapies to address the remaining approximately 10% of people with CF, sickle cell disease, beta thalassemia, APOL1-mediated kidney disease, type 1 diabetes, pain, alpha-1 antitrypsin deficiency, Duchenne muscular dystrophy, and myotonic dystrophy type 1.

Our principal executive office is located at 50 Northern Avenue, Boston, Massachusetts 02210 and our telephone number is (617) 341-6100. We maintain a website at www.vrtx.com. The information on our website is not incorporated by reference in this prospectus or any accompanying prospectus supplement, and you should not consider it a part of this prospectus or any accompanying prospectus supplement.

RISK FACTORS

Investing in our securities involves risk. See the risk factors described in our most recent Annual Report on Form 10-K (together with any changes contained in subsequently filed Quarterly Reports on Form 10-Q) and those contained in our other filings with the SEC that are incorporated by reference in this prospectus and any accompanying prospectus supplement. Before making an investment decision, you should carefully consider these risks as well as other information we include or incorporate by reference in this prospectus and any accompanying prospectus supplement. These risks could materially affect our business, financial condition or results of operations and cause the value of our securities to decline. You could lose all or part of your investment.

USE OF PROCEEDS

Except as otherwise set forth in any accompanying prospectus supplement, we expect to use the net proceeds from the sale of securities for general corporate purposes, including the financing of our operations, the possible repayment of indebtedness, and possible business acquisitions.

Unless set forth in an accompanying prospectus supplement, we will not receive any proceeds if securities are sold by a selling security holder.

DESCRIPTION OF SECURITIES

This prospectus contains summary descriptions of the common stock, debt securities, preferred stock, warrants, subscription rights, purchase contracts and purchase units that may be offered and sold from time to

time. These summary descriptions are not meant to be complete descriptions of each security. However, at the time of an offering and sale, this prospectus together with the accompanying prospectus supplement will contain the material terms of the securities being offered.

DESCRIPTION OF CAPITAL STOCK

General

The following summary description of our capital stock is based on the provisions of the Massachusetts Business Corporation Act (the “MBCA”), our articles of organization, as amended, and our by-laws, as amended. This description does not purport to be complete and is qualified in its entirety by reference to the full text of the MBCA, as it may be amended from time to time, and to the terms of our articles of organization and by-laws, as each may be amended from time to time, which are incorporated by reference as exhibits to the registration statement of which this prospectus is a part. See “Where You Can Find More Information.” As used in this “Description of Capital Stock,” the terms “Vertex,” the “Company,” “we,” “our” and “us” refer only to Vertex Pharmaceuticals Incorporated, a Massachusetts corporation, and do not, unless otherwise specified, include our subsidiaries.

Our authorized capital stock consists of 500,000,000 shares of common stock, par value \$0.01 per share, and 1,000,000 shares of preferred stock, par value \$0.01 per share. The number of authorized shares of any class may be increased or decreased by an amendment to our articles of organization proposed by our board of directors and approved by a majority of voting shares voted on the issue at a meeting at which a quorum exists.

Common Stock

Each stockholder of record of our common stock is entitled to one vote for each share held on every matter properly submitted to the stockholder for their vote. Holders of our common stock do not have cumulative voting rights. After satisfaction of any dividend rights of holders of preferred stock, holders of common stock are entitled ratably to any dividend declared by our board of directors out of funds legally available for this purpose.

Upon our liquidation, dissolution or winding up, the holders of our common stock are entitled to receive ratably our net assets available, if any, after the payment of all debts and other liabilities and subject to the prior rights of any outstanding preferred stock.

Holders of our common stock have no preemptive, subscription, redemption, conversion or exchange rights and no sinking fund provisions.

The rights, preferences and privileges of holders of common stock are subject to, and may be adversely affected by, the rights of the holders of shares of any series of preferred stock that we may designate and issue in the future.

Preferred Stock

This section describes the general terms and provisions of preferred stock that we are authorized to issue. An accompanying prospectus supplement will describe the specific terms of the shares of preferred stock offered through that prospectus supplement, as well as any general terms described in this section that will not apply to those shares of preferred stock. We will file a copy of the certificate of amendment to our articles of organization that contains the terms of each new series of preferred stock with the Secretary of The Commonwealth of Massachusetts and with the SEC each time we issue a new series of preferred stock. Each such certificate of amendment will establish the number of shares included in a designated series and fix the designation, powers, privileges, preferences and rights of the shares of each series as well as any applicable qualifications, limitations or restrictions. You should refer to the applicable certificate of amendment as well as our articles of organization before deciding to buy shares of our preferred stock as described in any accompanying prospectus supplement.

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Our board of directors has been authorized to provide for the issuance of up to 1,000,000 shares of our preferred stock in multiple series without the approval of stockholders. With respect to each series of our preferred stock, our board of directors has the authority to fix the following terms:

- the designation of the series;
- the number of shares within the series;
- whether dividends are cumulative and, if cumulative, the dates from which dividends are cumulative;
- the rate of any dividends, any conditions upon which dividends are payable, and the dates of payment of dividends;
- whether the shares are redeemable, the redemption price and the terms of redemption;
- the amount payable for each share if we dissolve or liquidate;
- whether the shares are convertible or exchangeable, the price or rate of conversion or exchange, and the applicable terms and conditions;
- any restrictions on issuance of shares in the same series or any other series;
- voting rights applicable to the series of preferred stock; and
- any other rights, priorities, preferences, restrictions or limitations of such series.

The right of a holder of preferred stock to receive payment in respect thereof upon any liquidation, dissolution or winding up of us will be subordinate to the rights of our general creditors.

Anti-Takeover Effects of Provisions of the Articles of Organization, By-laws and Other Agreements

Provisions of our articles of organization and by-laws may discourage specific types of transactions involving an actual or potential change in control of Vertex that might be beneficial to Vertex or its stockholders. Our by-laws grant the directors a right to adjourn annual meetings of stockholders. We may issue shares of any class or series of preferred stock in the future without stockholder approval and upon such terms as our board of directors may determine. The rights of the holders of common stock will be subject to, and may be adversely affected by, the rights of the holders of any class or series of preferred stock that may be issued in the future.

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.

Listing

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

Transfer Agent and Registrar

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

DESCRIPTION OF DEBT SECURITIES

We may offer debt securities in one or more series, which may be senior debt securities or subordinated debt securities and which may be convertible into another security.

The following description briefly sets forth certain general terms and provisions of the debt securities. The particular terms of the debt securities offered by any prospectus supplement and the extent, if any, to which the following general terms and provisions may apply to the debt securities, will be described in an accompanying prospectus supplement. Unless otherwise specified in an accompanying prospectus supplement, our debt securities will be issued in one or more series under an indenture to be entered into between us and a trustee to be named therein. A form of the indenture is incorporated by reference as an exhibit to the registration statement of which this prospectus forms a part. The terms of the debt securities will include those set forth in the indenture and those made a part of the indenture by the Trust Indenture Act of 1939 (“TIA”). You should read the summary below, any accompanying prospectus supplement and the provisions of the indenture in their entirety before investing in our debt securities.

The aggregate principal amount of debt securities that may be issued under the indenture is unlimited. The prospectus supplement relating to any series of debt securities that we may offer will contain the specific terms of the debt securities. These terms may include, among others, the following:

- the title and aggregate principal amount of the debt securities and any limit on the aggregate principal amount of such series;
- any applicable subordination provisions for any subordinated debt securities;
- the maturity date(s) or method for determining same;
- the interest rate(s) or the method for determining same;
- the dates on which interest will accrue or the method for determining dates on which interest will accrue and dates on which interest will be payable and whether interest will be payable in cash, additional securities or some combination thereof;
- whether the debt securities are convertible or exchangeable into other securities and any related terms and conditions;
- redemption or early repayment provisions;
- authorized denominations;
- if other than the principal amount, the principal amount of debt securities payable upon acceleration;
- place(s) where payment of principal and interest may be made, where debt securities may be presented and where notices or demands upon the company may be made;
- the form or forms of the debt securities of the series including such legends as may be required by applicable law;
- whether the debt securities will be issued in whole or in part in the form of one or more global securities and the date as of which the securities are dated if other than the date of original issuance;

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- whether the debt securities are secured and the terms of such security;
- the amount of discount or premium, if any, with which the debt securities will be issued;
- any covenants applicable to the particular debt securities being issued;
- any additions or changes in the defaults and events of default applicable to the particular debt securities being issued;
- the guarantors of each series, if any, and the extent of the guarantees (including provisions relating to seniority, subordination and release of the guarantees), if any;
- the currency, currencies or currency units in which the purchase price for, the principal of and any premium and any interest on, the debt securities will be payable;
- the time period within which, the manner in which and the terms and conditions upon which we or the holders of the debt securities can select the payment currency;
- our obligation or right to redeem, purchase or repay debt securities under a sinking fund, amortization or analogous provision;
- any restriction or conditions on the transferability of the debt securities;
- provisions granting special rights to holders of the debt securities upon occurrence of specified events;
- additions or changes relating to compensation or reimbursement of the trustee of the series of debt securities;
- provisions relating to the modification of the indenture both with and without the consent of holders of debt securities issued under the indenture and the execution of supplemental indentures for such series; and
- any other terms of the debt securities (which terms shall not be inconsistent with the provisions of the TIA, but may modify, amend, supplement or delete any of the terms of the indenture with respect to such series of debt securities).

General

We may sell the debt securities, including original issue discount securities, at par or at a substantial discount below their stated principal amount. Unless we inform you otherwise in a prospectus supplement, we may issue additional debt securities of a particular series without the consent of the holders of the debt securities of such series or any other series outstanding at the time of issuance. Any such additional debt securities, together with all other outstanding debt securities of that series, will constitute a single series of securities under the indenture.

We will describe in an accompanying prospectus supplement any other special considerations for any debt securities we sell that are denominated in a currency or currency unit other than U.S. dollars. In addition, debt securities may be issued where the amount of principal and/or interest payable is determined by reference to one or more currency exchange rates, commodity prices, equity indices or other factors. Holders of such securities may receive a principal amount or a payment of interest that is greater than or less than the amount of principal or interest otherwise payable on such dates, depending upon the value of the applicable currencies, commodities, equity indices or other factors. Information as to the methods for determining the amount of principal or interest, if any, payable on any date, and the currencies, commodities, equity indices or other factors to which the amount payable on such date is linked will be described in an accompanying prospectus supplement.

United States federal income tax consequences and special considerations, if any, applicable to any such series will be described in an accompanying prospectus supplement.

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We expect most debt securities to be issued in fully registered form without coupons and in denominations of \$2,000 and any integral multiple of \$1,000 in excess thereof. Subject to the limitations provided in the indenture and in an accompanying prospectus supplement, debt securities that are issued in registered form may be transferred or exchanged at the designated corporate trust office of the trustee, without the payment of any service charge, other than any tax or other governmental charge payable in connection therewith.

Global Securities

Unless we inform you otherwise in an accompanying prospectus supplement, the debt securities of a series may be issued in whole or in part in the form of one or more global securities that will be deposited with, or on behalf of, a depository identified in an accompanying prospectus supplement. Unless and until a global security is exchanged in whole or in part for the individual debt securities, a global security may not be transferred except as a whole by the depository for such global security to a nominee of such depository or by a nominee of such depository to such depository or another nominee of such depository or by such depository or any such nominee to a successor of such depository or a nominee of such successor.

Governing Law

The indenture and the debt securities shall be construed in accordance with and governed by the laws of the State of New York.

DESCRIPTION OF WARRANTS

We may issue warrants for the purchase of shares of our common stock, our debt securities or shares of our preferred stock. We may issue warrants independently or together with other securities, and they may be attached to or separate from the other securities. Each series of warrants will be issued under a separate warrant agreement that we will enter into with a bank or trust company, as warrant agent, as detailed in an accompanying prospectus supplement. The warrant agent will act solely as our agent in connection with the warrants and will not assume any obligation, or agency or trust relationship, with you.

The prospectus supplement relating to a particular issue of warrants will describe the terms of those warrants, including, when applicable:

- the offering price;
- the currency or currencies, including composite currencies, in which the purchase price and/or exercise price of the warrants may be payable;
- the number of warrants offered;
- the exercise price and the amount of securities you will receive upon exercise;
- the procedure for exercise of the warrants and the circumstances, if any, that will cause the warrants to be automatically exercised;
- the rights, if any, we have to redeem the warrants;
- the date on which the right to exercise the warrants will commence and the date on which the warrants will expire;
- the name of the warrant agent; and
- any other material terms of the warrants.

After warrants expire they will become void. The prospectus supplement may provide for the adjustment of the exercise price of the warrants.

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Warrants may be exercised at the appropriate office of the warrant agent or any other office indicated in an accompanying prospectus supplement. Before the exercise of warrants, holders will not have any of the rights of holders of the securities purchasable upon exercise and will not be entitled to payments made to holders of those securities.

The description in an accompanying prospectus supplement of any warrants we offer will not necessarily be complete and will be qualified in its entirety by reference to the applicable warrant agreement, which will be filed with the SEC if we offer warrants. For more information on how you can obtain copies of any warrant agreement if we offer warrants, see “Where You Can Find More Information.” We urge you to read the applicable warrant agreement and any accompanying prospectus supplement in their entirety.

DESCRIPTION OF SUBSCRIPTION RIGHTS

We may issue subscription rights to purchase shares of our common stock, our debt securities or shares of our preferred stock. We may issue subscription rights independently or together with any other offered security, which may or may not be transferable by the stockholder. In connection with any offering of subscription rights, we may enter into a standby arrangement with one or more underwriters or other purchasers pursuant to which the underwriters or other purchasers may be required to purchase any securities remaining unsubscribed for after such offering.

The prospectus supplement relating to any subscription rights we may offer will contain the specific terms of the subscription rights. These terms may include the following:

- the price, if any, for the subscription rights;
- the number and terms of each share of common stock or preferred stock or debt securities which may be purchased per each subscription right;
- the exercise price payable for each share of common stock or preferred stock or debt securities upon the exercise of the subscription rights;
- the extent to which the subscription rights are transferable;
- any provisions for adjustment of the number or amount of securities receivable upon exercise of the subscription rights or the exercise price of the subscription rights;
- any other terms of the subscription rights, including the terms, procedures and limitations relating to the exchange and exercise of the subscription rights;
- the date on which the right to exercise the subscription rights shall commence, and the date on which the subscription rights shall expire;
- the extent to which the subscription rights may include an over-subscription privilege with respect to unsubscribed securities; and
- if applicable, the material terms of any standby underwriting or purchase arrangement entered into by us in connection with the offering of subscription rights.

The description in an accompanying prospectus supplement of any subscription rights we offer will not necessarily be complete and will be qualified in its entirety by reference to the applicable subscription rights certificate or subscription rights agreement, which will be filed with the SEC if we offer subscription rights. For more information on how you can obtain copies of any subscription rights certificate or subscription rights agreement if we offer subscription rights, see “Where You Can Find More Information.” We urge you to read the applicable subscription rights certificate, the applicable subscription rights agreement and any accompanying prospectus supplement in their entirety.

DESCRIPTION OF PURCHASE CONTRACTS AND PURCHASE UNITS

We may issue purchase contracts, including contracts obligating holders to purchase from us, and obligating us to sell to the holders, a specified number of shares of our common stock, our debt securities or shares of our preferred stock at a future date or dates, which we refer to in this prospectus as purchase contracts. The price of the securities and the number of securities may be fixed at the time the purchase contracts are issued or may be determined by reference to a specific formula set forth in the purchase contracts, and may be subject to adjustment under anti-dilution formulas. The purchase contracts may be issued separately or as part of units consisting of a stock purchase contract and debt securities, preferred securities or debt obligations of third parties, including U.S. treasury securities, or any combination of the foregoing, securing the holders' obligations to purchase the securities under the purchase contracts, which we refer to herein as purchase units. The purchase contracts may require holders to secure their obligations under the purchase contracts in a specified manner. The purchase contracts also may require us to make periodic payments to the holders of the purchase contracts or the purchase units, as the case may be, or vice versa, and those payments may be unsecured or pre-funded in whole or in part.

The description in an accompanying prospectus supplement of any purchase contract or purchase unit we offer will not necessarily be complete and will be qualified in its entirety by reference to the applicable purchase contract or purchase unit, which will be filed with the SEC if we offer purchase contracts or purchase units. For more information on how you can obtain copies of any purchase contract or purchase unit we may offer, see "Where You Can Find More Information." We urge you to read the applicable purchase contract or applicable purchase unit and any accompanying prospectus supplement in their entirety.

SELLING SECURITYHOLDERS

Information about selling securityholders, where applicable, will be set forth in a prospectus supplement, in a post-effective amendment or in filings we make with the SEC under the Exchange Act which are incorporated by reference into this prospectus.

PLAN OF DISTRIBUTION

We or the selling securityholders may sell the securities being offered hereby in one or more of the following ways from time to time:

- to underwriters for resale to purchasers;
- directly to purchasers; or
- through agents or dealers to purchasers.

In addition, we may enter into derivative or hedging transactions with third parties, or sell securities not covered by this prospectus to third parties in privately negotiated transactions. In connection with such a transaction, the third parties may sell securities covered by and pursuant to this prospectus and any accompanying prospectus supplement. If so, the third party may use securities borrowed from us or others to settle such sales and may use securities received from us to close out any related short positions. We may also loan or pledge securities covered by this prospectus and any accompanying prospectus supplement to third parties, who may sell the loaned securities or, in an event of default in the case of a pledge, sell the pledged securities pursuant to this prospectus and any accompanying prospectus supplement.

We will identify the specific plan of distribution, including any underwriters, dealers, agents or direct purchasers and their compensation in a prospectus supplement.

LEGAL MATTERS

Unless otherwise indicated in any accompanying prospectus supplement, Ropes & Gray LLP will provide opinions regarding the authorization and validity of the securities. Ropes & Gray LLP may also provide opinions regarding certain other matters. Any underwriters will be advised about legal matters by their own counsel, which will be named in an accompanying prospectus supplement.

EXPERTS

The consolidated financial statements of Vertex Pharmaceuticals Incorporated appearing in Vertex Pharmaceuticals Incorporated's Annual Report on Form 10-K for the year ended December 31, 2021, and the effectiveness of Vertex Pharmaceuticals Incorporated's internal control over financial reporting as of December 31, 2021, have been audited by Ernst & Young LLP, independent registered public accounting firm, as set forth in their reports thereon included therein, and incorporated herein by reference. Such financial statements are, and audited financial statements to be included in subsequently filed documents will be, incorporated herein in reliance upon the reports of Ernst & Young LLP pertaining to such financial statements and the effectiveness of our internal control over financial reporting as of the respective dates (to the extent covered by consents filed with the Securities and Exchange Commission) given on the authority of such firm as experts in accounting and auditing.

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

The expenses relating to the registration of the securities will be borne by the registrant.

Securities and Exchange Commission Registration Fee	\$ *
Accounting Fees and Expenses	\$ **
Legal Fees and Expenses	\$ **
Printing Fees	\$ **
Transfer Agents and Trustees' Fees and Expenses	\$ **
Rating Agency Fees	\$ **
Stock Exchange Listing Fees	\$ **
Miscellaneous	\$ **
Total	\$—

* Deferred in reliance on Rules 456(b) and 457(r) under the Securities Act.

** Since an indeterminate amount of securities is covered by this registration statement, the expenses in connection with the issuance and distribution of the securities are not currently determinable.

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 MBCA, 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, and advance funds to pay for or reimburse the reasonable expenses incurred by, its directors and the officers that have been appointed by the board of directors (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) to the fullest extent permitted by law, and may indemnify, and advance funds to pay for or reimburse the reasonable expenses incurred by, such other employees and agents as are identified by the board of directors.

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 stockholder, 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 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

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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.

The registrant also has indemnification agreements with its directors and officers. In addition, the registrant maintains liability insurance for its directors and officers.

Item 16. List of Exhibits.

The Exhibits to this registration statement are listed in the Index to Exhibits on page II-5.

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 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 SEC pursuant to Rule 424(b) if, in the aggregate, the changes in volume and price represent no more than a 20 percent 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 paragraphs (i), (ii) and (iii) of this section 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 SEC 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, or is contained in a form of prospectus filed pursuant to Rule 424(b) that is part of 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.
- (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 this registration statement as of the date the filed prospectus was deemed part of and included in this 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

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10(a) of the Securities Act of 1933 shall be deemed to be part of and included in this 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 that 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 this registration statement or made in a document incorporated or deemed incorporated by reference into this registration statement or prospectus that is part of this 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 this registration statement or prospectus that was part of this 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 the 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.

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 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.

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 SEC 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.

The undersigned registrant hereby undertakes to file an application for the purpose of determining the eligibility of the trustee to act under subsection (a) of Section 310 of the Trust Indenture Act in accordance with the rules and regulations prescribed by the SEC under Section 305(b)(2) of the Act.

EXHIBIT INDEX

<u>Exhibit No.</u>	<u>Description of Exhibits</u>
1.1*	Form of Underwriting Agreement.
3.1	Restated Articles of Organization of the registrant, as amended on May 17, 2018 (incorporated by reference to Exhibit 3.1 to the registrant's Form 10-Q filed on July 26, 2018).
3.2	Amended and Restated By-Laws of Vertex Pharmaceuticals Incorporated, as subsequently amended on April 28, 2020 (incorporated by reference to Exhibit 3.2 to the registrant's Form 10-Q filed on May 1, 2020).
3.3*	Form of Certificate of Amendment with respect to any preferred stock issued hereunder.
4.1	Specimen of Common Stock Certificate (incorporated by reference to Exhibit 4.1 to the registrant's Form 10-K filed on February 15, 2018).
4.2	Form of Indenture for debt securities between the registrant and the trustee to be named therein. (incorporated by reference to Exhibit 4.2 to the registrant's Form S-3ASR filed on May 3, 2016).
4.3*	Form of Warrant Agreement (including form of Warrant Certificate).
4.4*	Form of Subscription Rights Agreement (including form of Subscription Rights Certificate).
4.5*	Form of Purchase Contract Agreement (including form of Purchase Contract Certificate).
4.6*	Form of Purchase Unit Agreement (including form of Purchase Unit Certificate).
5.1	Opinion of Ropes & Gray LLP.
23.1	Consent of Ernst & Young LLP, Independent Registered Public Accounting Firm.
23.2	Consent of Ropes & Gray LLP (included in Exhibit 5.1).
24.1	Powers of Attorney (included on signature pages hereto).
25.1*	Statement of Eligibility on Form T-1 of trustee under the Indenture.
107	Filing Fee Table

* To be filed by amendment to the Registration Statement or incorporated by reference from documents filed or to be filed with the SEC under the Securities Exchange Act of 1934, as amended.

SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, the registrant certifies that it has reasonable grounds to believe that it meets all of the requirements for filing on Form S-3 and has duly caused this registration statement on Form S-3 to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of Boston, The Commonwealth of Massachusetts on February 9, 2022.

VERTEX PHARMACEUTICALS INCORPORATED

By: /s/ Reshma Kewalramani

Name: Reshma Kewalramani

Title: President and Chief Executive Officer

In accordance with the requirements of the Securities Act of 1933, as amended, this Registration Statement has been signed by the following persons in the capacities and on the dates stated. Each person whose signature appears below constitutes and appoints Reshma Kewalramani and Joy Liu and each of them severally, as his or her true and lawful attorney-in-fact and agent, each acting along with full power of substitution and resubstitution, for him or her and in his or her name, place and stead, in any and all capacities, to sign any or all amendments (including post-effective amendments) and exhibits to the Registration Statement on Form S-3, and to any registration statement filed under SEC Rule 462, and to file the same, with all exhibits thereto, and all documents in connection therewith, with the SEC, granting unto said attorney-in-fact and agent, full power and authority to do and perform each and every act and thing requisite and necessary to be done in and about the premises, as fully to all intents and purposes as he or she might or could do in person, hereby ratifying and confirming all that said attorney-in-fact and agent, or his or her substitute or substitutes, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Act of 1933, this registration statement on Form S-3 has been signed by the following persons in the capacities indicated on February 9, 2022.

<u>Signature</u>	<u>Title</u>	<u>Date</u>
<u>/s/ Reshma Kewalramani</u> Reshma Kewalramani	President, Chief Executive Officer (Principal Executive Officer) and Director	February 9, 2022
<u>/s/ Charles F. Wagner Jr.</u> Charles F. Wagner Jr.	Executive Vice President and Chief Financial Officer (Principal Financial Officer)	February 9, 2022
<u>/s/ Kristen C. Ambrose</u> Kristen C. Ambrose	Senior Vice President and Chief Accounting Officer (Principal Accounting Officer)	February 9, 2022
<u>/s/ Jeffrey M. Leiden</u> Jeffrey M. Leiden	Executive Chairman	February 9, 2022
<u>/s/ Sangeeta N. Bhatia</u> Sangeeta N. Bhatia	Director	February 9, 2022
<u>/s/ Lloyd Carney</u> Lloyd Carney	Director	February 9, 2022

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<u>Signature</u>	<u>Title</u>	<u>Date</u>
<u>/s/ Alan Garber</u> Alan Garber	Director	February 9, 2022
<u>/s/ Terrence C. Kearney</u> Terrence C. Kearney	Director	February 9, 2022
<u>/s/ Yuchun Lee</u> Yuchun Lee	Director	February 9, 2022
<u>/s/ Margaret G. McGlynn</u> Margaret G. McGlynn	Director	February 9, 2022
<u>/s/ Diana McKenzie</u> Diana McKenzie	Director	February 9, 2022
<u>/s/ Bruce I. Sachs</u> Bruce I. Sachs	Director	February 9, 2022



ROPES & GRAY LLP
PRUDENTIAL TOWER
800 BOYLSTON STREET
BOSTON, MA 02199-3600
WWW.ROPESGRAY.COM

February 9, 2022

Vertex Pharmaceuticals Incorporated
50 Northern Avenue
Boston, MA 02210

Re: Registration of Securities by Vertex Pharmaceuticals Incorporated

Ladies and Gentlemen:

We have acted as counsel to Vertex Pharmaceuticals Incorporated, a Massachusetts corporation (the "Company"), in connection with the registration statement on Form S-3 (the "Registration Statement") filed on the date hereof by the Company with the Securities and Exchange Commission (the "Commission") under the Securities Act of 1933, as amended (the "Securities Act"), relating to the registration under the Securities Act and the proposed issuance and sale from time to time pursuant to Rule 415 under the Securities Act of:

- (i) shares of the Company's common stock, \$0.01 par value per share (the "Common Stock");
- (ii) one or more series of debt securities of the Company (the "Debt Securities"), which Debt Securities may include senior debt securities or subordinated debt securities issued under an indenture, including any supplemental indenture related thereto, and may be convertible into or exchangeable for other Securities (as defined below);
- (iii) shares of preferred stock of the Company, \$0.01 par value per share (the "Preferred Stock");
- (iv) warrants to purchase shares of Common Stock, shares of Preferred Stock or Debt Securities (the "Warrants");
- (v) subscription rights to purchase shares of Common Stock, shares of Preferred Stock or Debt Securities (the "Subscription Rights");
- (vi) purchase contracts (the "Purchase Contracts") obligating the holders thereof to purchase from the Company, and the Company to sell to such holders, shares of Common Stock, shares of Preferred Stock or Debt Securities at a future date or dates; and
- (vii) purchase units of the Company (the "Purchase Units"), each consisting of Purchase Contracts and shares of Preferred Stock, Debt Securities or debt obligations of third parties, including U.S. treasury securities, or any combination of the foregoing.

The Common Stock, the Debt Securities, the Preferred Stock, the Warrants, the Subscription Rights, the Purchase Contracts and the Purchase Units are referred to herein collectively as the "Securities."

In connection with this opinion letter, we have examined such certificates, documents and records and have made such investigation of fact and such examination of law as we have deemed appropriate in order to enable us to render the opinions set forth herein. In conducting such investigation, we have relied, without independent verification, upon certificates of officers of the Company, public officials and other appropriate persons.

The opinions expressed below are limited to the laws of the State of New York and the Massachusetts Business Corporation Act (the "MBCA").

Based upon and subject to the foregoing and the assumptions, qualifications and limitations set forth below, we are of the opinion that:

1. When (i) the issuance and sale of any shares of Common Stock have been duly authorized by all necessary corporate action of the Company and (ii) such shares have been issued and delivered against payment of the purchase price therefor (in an amount in excess of the par value thereof) in accordance with the applicable purchase, underwriting or other agreement, and as contemplated by the Registration Statement, such shares of Common Stock will be validly issued, fully paid and nonassessable. The Common Stock covered in the opinion in this paragraph includes any shares of Common Stock that may be issued upon exercise, conversion or exchange pursuant to the terms of any other Securities.

2. When (i) the terms of any Debt Securities and their issuance and sale have been duly authorized by all necessary corporate action of the Company and (ii) such Debt Securities have been duly executed, authenticated and delivered against payment of the purchase price therefor in accordance with the applicable definitive purchase, underwriting or similar agreement, as contemplated by the Registration Statement, and in the manner provided for in the applicable indenture, such Debt Securities will constitute valid and binding obligations of the Company enforceable against the Company in accordance with their respective terms. The Debt Securities covered in the opinion in this paragraph include any Debt Securities that may be issued upon exercise, conversion or exchange pursuant to the terms of any other Securities.

3. When (i) the terms of any Preferred Stock of a particular series and their issuance and sale have been duly authorized by all necessary corporate action of the Company, (ii) a certificate of amendment to the Company's articles of organization with respect to such series of Preferred Stock has been duly adopted by the Company and filed with the Secretary of the Commonwealth of Massachusetts in accordance with the MBCA and (iii) such shares of Preferred Stock have been issued and delivered against payment of the purchase price therefor (in an amount in excess of the par value thereof) in accordance with the applicable purchase, underwriting or other agreement, and as contemplated by the Registration Statement, such shares of Preferred Stock will be validly issued, fully paid and nonassessable. The Preferred Stock covered in the opinion in this paragraph includes any shares of Preferred Stock that may be issued upon exercise, conversion or exchange pursuant to the terms of any other Securities.

4. When (i) the terms of any Warrants and their issuance and sale have been duly authorized by all necessary corporate action of the Company and (ii) such Warrants have been duly executed, countersigned and delivered in accordance with the applicable warrant agreement and against payment of the purchase price therefor in accordance with the applicable purchase, underwriting or other agreement, and as contemplated by the Registration Statement, such Warrants will constitute valid and binding obligations of the Company enforceable against the Company in accordance with their terms.

5. When (i) the terms of any Subscription Rights and their issuance and sale have been duly authorized by all necessary corporate action of the Company and (ii) such Subscription Rights have been duly issued and delivered in accordance with the applicable rights agreement and against payment of the purchase price therefor in accordance with the applicable purchase, underwriting or other agreement, and as contemplated by the Registration Statement, such Subscription Rights will constitute valid and binding obligations of the Company enforceable against the Company in accordance with their terms.

6. When (i) the terms of any Purchase Contracts or Purchase Units and their issuance and sale have been duly authorized by all necessary corporate action of the Company and (ii) such Purchase Contracts or Purchase have been duly executed and delivered in accordance with the applicable purchase, underwriting or other agreement, and as contemplated by the Registration Statement, such Purchase Contracts and Purchase Units will constitute valid and binding obligations of the Company, enforceable against the Company in accordance with their terms.

In rendering the opinions set forth above, we have assumed that (i) the Registration Statement will have become effective under the Securities Act, a prospectus supplement will have been prepared and filed with the Commission describing the Securities offered thereby and such Securities will have been issued and sold in accordance with the terms of such prospectus supplement; (ii) a definitive purchase, underwriting or similar agreement and any applicable indenture (including any supplemental indenture) or warrant agreement pursuant to which such Securities may be issued, will have been duly authorized, executed and delivered by the Company and the other parties thereto, and the specific terms of such Securities will have been duly established in conformity with the applicable agreement and the articles of organization and bylaws of the Company (if applicable); (iii) at the time of the issuance of any Securities, the Company will be a validly existing corporation under the law of its jurisdiction of incorporation; (iv) the number of shares of Common Stock issued pursuant to the Registration Statement, together with the number of shares outstanding or reserved at the time of issuance, will not exceed the respective number of shares authorized by the Company's articles of organization in effect at the time of such issuance; (v) the number of shares of Preferred Stock issued pursuant to the Registration Statement, together with the number of shares outstanding or reserved at the time of issuance, will not exceed the respective number of shares authorized by the Company's articles of organization in effect at the time of such issuance; and (vi) all the foregoing actions to be taken by the Company will have been taken so as not to violate any applicable law and so as to comply with any requirement or restriction imposed by any court or governmental or regulatory body having jurisdiction over the Company or any of its property.

Our opinions set forth above are subject to (a) bankruptcy, insolvency, reorganization, moratorium, fraudulent conveyance and similar laws affecting the rights and remedies of creditors generally and (b) general principles of equity. Our opinions are also subject to the qualification that the enforceability of provisions in any applicable indenture (including any supplemental indenture thereto) providing for indemnification or contribution, broadly worded waivers, waivers of rights to damages or defenses, waivers of unknown or future claims, and waivers of statutory, regulatory or constitutional rights may be limited on public policy or statutory grounds. In addition, we express no opinion with respect to the enforceability of rights to receive prepayment premiums or the unaccrued portion of original issue discount upon acceleration of any Debt Securities, in each case to the extent determined to be unreasonable or to constitute unmaturing interest or judgment currency provisions.

We hereby consent to the filing of this opinion letter as an exhibit to the Registration Statement and to the use of our name therein and in the related prospectus under the caption "Legal Matters." In giving such consent, we do not thereby admit that we are in the category of persons whose consent is required under Section 7 of the Securities Act or the rules and regulations of the Commission thereunder.

Very truly yours,

/s/ Ropes & Gray LLP

Ropes & Gray LLP

Consent of Independent Registered Public Accounting Firm

We consent to the reference to our firm under the caption “Experts” in the Registration Statement (Form S-3) and related Prospectus of Vertex Pharmaceuticals Incorporated for the registration of common stock, debt securities, preferred stock, warrants, subscription rights, purchase contracts, and purchase units and to the incorporation by reference therein of our reports dated February 9, 2022, 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, 2021, filed with the Securities and Exchange Commission.

/s/ Ernst & Young LLP

Boston, Massachusetts

February 9, 2022

Calculation of Filing Fee Tables

Form S-3
(Form Type)Vertex Pharmaceuticals Incorporated
(Exact Name of Registrant as Specified in its Charter)

Table 1: Newly Registered Securities

	Security Type	Security Class Title(1)	Fee Calculation or Carry Forward Rule	Amount Registered	Proposed Maximum Offering Price Per Unit	Maximum Aggregate Offering Price	Fee Rate	Amount of Registration Fee
Newly Registered Securities								
Fees to Be Paid	Equity	Common stock, \$0.01 par value per share	Rule 456(b) and Rule 457(r)(3)	(2)	(2)	(2)	(3)	(3)
	Equity	Preferred stock, \$0.01 par value per share	Rule 456(b) and Rule 457(r)(3)	(2)	(2)	(2)	(3)	(3)
	Debt	Debt securities	Rule 456(b) and Rule 457(r)(3)	(2)	(2)	(2)	(3)	(3)
	Other	Warrants	Rule 456(b) and Rule 457(r)(3)	(2)	(2)	(2)	(3)	(3)
	Other	Subscription rights	Rule 456(b) and Rule 457(r)(3)	(2)	(2)	(2)	(3)	(3)
	Other	Purchase contracts	Rule 456(b) and Rule 457(r)(3)	(2)	(2)	(2)	(3)	(3)
	Other	Purchase units	Rule 456(b) and Rule 457(r)(3)	(2)	(2)	(2)	(3)	(3)
Fees Previously Paid	N/A	N/A	N/A	N/A	N/A	N/A		N/A

- (1) Securities registered hereunder may be sold separately, together or as units with other securities registered hereunder.
- (2) Omitted pursuant to Form S-3 General Instruction II.E. We are registering an indeterminate number of shares of common stock or preferred stock and amount of debt securities as may be issued upon conversion, exchange or exercise, as applicable, of any preferred stock, debt securities, warrants or subscription rights or settlement of any purchase contracts or purchase units, including such shares of common stock or preferred stock as may be issued pursuant to anti-dilution adjustments determined at the time of offering.
- (3) In accordance with Rules 456(b) and 457(r) under the Securities Act, the registrant is deferring payment of the entire registration fee.