

VERTEX PHARMACEUTICALS INC / MA

Form S-3

October 28, 2004

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As filed with the Securities and Exchange Commission on October 28, 2004

Registration Statement No. 333-

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 No.)

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

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

**Joshua S. Boger
Chief Executive Officer
Vertex Pharmaceuticals Incorporated
130 Waverly Street
Cambridge, Massachusetts 02139-4242
617-444-6100**

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

Copies to:

Michael L. Fantozzi, Esq.

Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, PC
One Financial Center
Boston, MA 02111
617-542-6000

Kenneth S. Boger, Esq.

Senior Vice President and General Counsel
Vertex Pharmaceuticals Incorporated
130 Waverly Street
Cambridge, MA 02139
617-444-6100

APPROXIMATE DATE OF COMMENCEMENT OF PROPOSED SALE TO PUBLIC: As soon as practicable after this Registration Statement becomes effective.

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.

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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 delivery of the prospectus is expected to be made pursuant to Rule 434, please check the following box.

CALCULATION OF REGISTRATION FEE

| Title of Each Class of Securities To Be Registered | Amount To Be Registered | Proposed Maximum Offering Price Per Unit | Proposed Maximum Aggregate Offering Price | Amount of Registration Fee |
|--|-------------------------|--|---|----------------------------|
| 5 ³ /4% Convertible Senior Subordinated Notes due February 15, 2011 | \$79,313,000(1) | 100% | \$79,313,000 | \$10,049 |
| Common Stock, par value \$.01 per share | 5,308,800(2) | (3) | (3) | (3) |
| Rights to purchase Series A Junior Participating Preferred Stock | (4) | (4) | (4) | (4) |

- (1) Equals the aggregate principal amount of the notes being registered.
- (2) Represents the number of shares of common stock that are currently issuable upon conversion of the notes, based on the initial conversion price of \$14.94 per share (equivalent to 66.9344 shares of common stock for each \$1,000 principal amount of the notes). In addition, pursuant to Rule 416 under the Securities Act of 1933, the amount to be registered also includes an indeterminate number of shares of common stock that may be issued as a result of stock splits, stock dividends and antidilution provisions.
- (3) No additional consideration will be received for the common stock, and, therefore, no registration fee is required pursuant to Rule 457(i).
- (4) No separate consideration will be received for the rights.

The Registrant hereby amends this Registration Statement on such date or dates as may be necessary to delay its effective date until the Registrant shall file a further amendment which specifically states that this Registration Statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act of 1933, or until this Registration Statement shall become effective on such date as the SEC, acting pursuant to said Section 8(a), may determine.

THE INFORMATION IN THIS PROSPECTUS IS NOT COMPLETE AND MAY BE CHANGED. THE SELLING HOLDERS MAY NOT SELL THESE SECURITIES UNTIL THE REGISTRATION STATEMENT FILED WITH THE SECURITIES AND EXCHANGE COMMISSION IS EFFECTIVE. THIS PROSPECTUS IS NOT AN OFFER TO SELL THESE SECURITIES AND IT IS NOT SOLICITING AN OFFER TO BUY THESE SECURITIES IN ANY STATE WHERE THE OFFER OR SALE IS NOT PERMITTED.

Subject to Completion, dated October 28, 2004

VERTEX PHARMACEUTICALS INCORPORATED

\$79,313,000 5³/₄% Convertible Senior Subordinated Notes Due 2011

5,308,800 Shares of Common Stock Issuable Upon Conversion of the Notes

Noteholders may offer for sale the notes and the shares of our common stock issuable upon conversion of the notes. See "Plan of Distribution." The notes have the following terms:

Holders may convert their notes at any time prior to maturity into shares of our common stock at a conversion price of \$14.94 per share, which is subject to adjustment.

Holders may require us to repurchase all or a portion of their notes (plus accrued and unpaid interest) upon a change of control. We may, at our option, pay the change of control purchase price in cash, shares of our common stock (valued at 95% of the market price of our common stock), or a combination thereof.

We may redeem the notes for cash on or after February 15, 2007, in whole or in part, at a redemption price equal to 100% of the principal amount of the notes, plus accrued and unpaid interest, if any, up to, but excluding, the redemption date.

The notes are unsecured and subordinated to all of our existing and future senior indebtedness. The notes are senior to our 5% convertible subordinated notes due 2007, which we refer to as our "old notes". The notes are equal in right of payment with a separate series of outstanding 5³/₄% Convertible Senior Subordinated Notes Due 2011 issued by us on February 13, 2004, which we refer to as the "February notes."

Our common stock is quoted on the Nasdaq National Market under the symbol "VRTX." On October 22, 2004, the last sale price of our common stock was \$10.01 per share. The notes are currently eligible for trading in the PORTAL market.

INVESTING IN THE NOTES OR OUR COMMON STOCK INVOLVES RISKS THAT ARE DESCRIBED IN THE "RISK FACTORS" SECTION BEGINNING ON PAGE 6 OF THIS PROSPECTUS.

NEITHER THE SECURITIES AND EXCHANGE COMMISSION NOR ANY OTHER REGULATORY BODY HAS APPROVED OR DISAPPROVED OF THESE SECURITIES OR PASSED UPON THE ACCURACY OR ADEQUACY OF THIS PROSPECTUS. ANY REPRESENTATION TO THE CONTRARY IS A CRIMINAL OFFENSE.

The date of this prospectus is , 2004

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Except as otherwise indicated, the "Company," "Vertex," "we" and "us," as used in this prospectus, refer to Vertex Pharmaceuticals Incorporated, a Massachusetts corporation, and its subsidiaries.

"Vertex" is a registered trademark of Vertex. "Agenerase", "Lexiva", and "Telzir" are registered trademarks of GlaxoSmithKline. "Prozei" is a trademark of Kissei Pharmaceutical Co., Ltd. Other brands, names and trademarks contained in this prospectus are the property of their respective owners.

The securities offered hereby constitute a different series from the outstanding 5³/₄% Convertible Senior Subordinated Notes due 2011 that we issued on February 13, 2004 and have accordingly been assigned a different CUSIP number. Except where otherwise indicated, we refer to the 5³/₄% Convertible Senior Subordinated Notes due 2011 issued on February 13, 2004 as the "February notes."

SUMMARY

THIS SUMMARY MAY NOT CONTAIN ALL OF THE INFORMATION THAT YOU SHOULD CONSIDER BEFORE INVESTING IN THE NOTES OR THE SHARES OF COMMON STOCK ISSUABLE UPON THEIR CONVERSION. YOU SHOULD CAREFULLY READ THE ENTIRE PROSPECTUS AND THE DOCUMENTS WE HAVE INCORPORATED BY REFERENCE INTO THE PROSPECTUS.

We are a biotechnology company in the business of discovering, developing and commercializing small molecule drugs for serious diseases, including HIV infection, chronic hepatitis C virus (HCV) infection, inflammatory and autoimmune disorders and cancer, independently and with collaborators. Our principal focus is on the development and commercialization of new treatments for viral and inflammatory diseases. There are two Vertex-discovered products on the market now for the treatment of HIV and AIDS. Our pipeline of potential products includes several drug candidates targeting chronic HCV infection and inflammatory diseases such as rheumatoid arthritis, osteoarthritis, and psoriasis. We also have developed several drug candidates directed at cancer therapy.

Our goal is to mature into a profitable pharmaceutical company with industry-leading capabilities in research, development and commercialization of products. We have begun developing certain product candidates for the treatment of chronic HCV infection and inflammation. We believe that we can effectively commercialize products for the treatment of those diseases, while expending comparatively fewer resources through the use of a specialist-focused sales force. We have focused our independent commercialization efforts on North America. The most advanced product candidates for which we currently retain North American commercialization rights are:

merimepodib, an oral treatment for chronic HCV;

VX-950, an oral hepatitis C protease inhibitor for the treatment of HCV infection;

VX-702, an oral p38 MAP kinase inhibitor for the treatment of inflammatory diseases; and

VX-765, an oral ICE inhibitor for the treatment of inflammatory diseases.

We expect to continue to invest in our research and development capabilities as we advance our own product candidates to market.

Partnerships and collaborations will continue to be a key component of our corporate strategy. Collaborations provide us with financial support and other valuable resources for our research programs, development resources for our clinical drug candidates and marketing and sales support for our products. Our two marketed products to date, the HIV protease inhibitors Agenerase® and Lexiva® (marketed under the name Telzir® in the European Union) were developed and commercialized in collaboration with GlaxoSmithKline plc, and we have a third HIV protease inhibitor, VX-385 (also developed in collaboration with GlaxoSmithKline), in clinical development. In addition to our collaboration with GlaxoSmithKline, we have collaborations with Aventis Pharma S.A., Merck & Co. Inc., Mitsubishi Pharma Corp., Novartis Pharma AG, the Cystic Fibrosis Foundation Therapeutics Incorporated and other companies.

We plan to continue adding promising potential products to our development pipeline through the conduct of our research programs. Our drug design approach integrates biology, chemistry, biophysics, automation and information technologies to make the drug discovery process more efficient and productive. We believe that our drug discovery expertise is a distinguishing feature of Vertex. In addition to our efforts to research and develop kinase inhibitors, we currently are conducting a productive research program in the area of ion channel modulation. We expect that future development candidates from our programs will be focused on the treatment of wide variety of diseases and conditions, including cancer and neuropathic pain.

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

We were incorporated in Massachusetts in 1989, and our principal executive offices are located at 130 Waverly Street, Cambridge, Massachusetts 02139.

Our Business Strategy

Our strategy is to:

commercialize certain therapeutic compounds for which we believe we will be able to independently reach a large patient population with a specialist-focused sales force in North America;

continue to advance our pipeline of potential products targeting the treatment of viral and inflammatory diseases;

continue to collaborate with existing and new partners to develop and commercialize products for selected therapeutic areas;

utilize our state-of-the-art research capability and drug design approach to create a strong flow of new products into clinical development; and

license and acquire technologies and products that have the potential to strengthen our drug discovery platform and product pipeline.

Commercial Products and Clinical Development Programs

Our product pipeline is principally focused on viral diseases, inflammatory and autoimmune diseases, and cancer.

| Therapeutic Area and Product Candidate | Clinical Indications | Development Phase | Company With Marketing Rights (Region) |
|---|--|--------------------------|---|
| Viral Diseases | | | |
| Agenerase® (amprenavir) | HIV infection | Marketed | GlaxoSmithKline (Worldwide)* |
| Lexiva®/Telzir® (fosamprenavir calcium)** | HIV infection | Marketed | GlaxoSmithKline (Worldwide)* |
| VX-385 | HIV infection | Phase II | GlaxoSmithKline (Worldwide)* |
| Merimepodib (VX-497) | Chronic hepatitis C | Phase II | Vertex (Worldwide) |
| VX-950 | Chronic hepatitis C | Phase I | Mitsubishi (Far East); Vertex (R.O.W.) |
| Inflammation and Autoimmune Disease | | | |
| VX-765 | Inflammatory and autoimmune diseases | Phase I | Vertex (Worldwide) |
| VX-702 | Acute coronary syndromes and inflammatory diseases | Phase II | Kissei (Japan); Vertex (R.O.W.) |
| Pralnacasan (VX-740) | Rheumatoid arthritis (RA); osteoarthritis (OA); and other inflammatory and autoimmune diseases | Phase II | Aventis (Worldwide)* |
| Cancer | | | |
| VX-680 | Oncology | Preclinical | Merck (Worldwide) |
| VX-944 | Oncology | Phase I | Vertex (Worldwide) |

*

Vertex has co-promotion rights in the United States and the European Union. Kissei has marketing rights to amprenavir in Japan, where it is marketed under the name Prozei .

**

Fosamprenavir calcium is marketed under the name Lexiva® in North America and Telzir® in the European Union.

THE OFFERING

| | |
|---------------------------|---|
| Securities offered | The resale by the selling holders of \$79,313,000 (principal amount) of 5 ³ / ₄ % Convertible Senior Subordinated Notes due February 15, 2011 and the 5,308,800 shares of common stock into which they are convertible, which we refer to as the "new notes." The new notes offered hereby constitute a different series from our outstanding 5 ³ / ₄ % Convertible Senior Subordinated Notes due 2011 issued on February 13, 2004 and have accordingly been assigned a different CUSIP number. Except where otherwise indicated, we refer to the 5 ³ / ₄ % Convertible Senior Subordinated Notes due 2011 issued on February 13, 2004 as the "February notes." |
| Maturity of notes | February 15, 2011. |
| Interest | 5 ³ / ₄ % per annum on the principal amount, payable semiannually on February 15 and August 15, beginning on August 15, 2004. The interest rate may be re-set upon the occurrence of a Re-set Transaction described under "Description of the notes Interest rate adjustments." |
| Conversion rights | The notes are convertible, at the option of the holder, at any time on or prior to maturity, into shares of our common stock at an initial conversion price of \$14.94 per share, which is equal to an initial conversion rate of 66.9344 shares per \$1,000 principal amount of notes. The initial conversion price is subject to adjustment. |
| Ranking | The new notes are unsecured obligations and are (i) senior in right of payment to our 5% convertible subordinated notes due 2007, which we refer to as our "old notes" and any future obligations that are designated by us as subordinate to the new notes; (ii) equal in right of payment with the February notes and any other existing or future obligations that are designated by us as, or otherwise determined to be, on a parity with the new notes; and (iii) subordinated in right of payment to the prior payment in full of all our existing and future Senior Debt, as defined herein, each as described in the indenture for the new notes. The new notes constitute "Designated Senior Debt" for purposes of the indenture for the old notes. At June 30, 2004, we had approximately \$20 million of debt outstanding that would be senior to the new notes. Because the new notes are subordinated, in the event of bankruptcy, liquidation, dissolution or acceleration of payment on the senior debt, holders of the new notes will not receive any payment until holders of the senior debt have been paid in full. At June 30, 2004, we had approximately \$153,135,000 of debt outstanding that would be equal in right of payment with the new notes. The indenture under which the new notes will be issued will not prevent us or our subsidiaries from incurring additional senior debt or other obligations. |

Redemption of notes at our option

On or after February 15, 2007, we may, at our option, redeem the notes, in whole or in part, for cash, at a redemption price equal to 100% of the principal amount of notes to be redeemed, plus accrued and unpaid interest (including any liquidated damages), if any, up to, but excluding, the date of such redemption. See "Description of the notes Redemption of notes at our option."

Change of control

Upon a change of control event, each holder of the notes may require us to repurchase some or all of its notes at a purchase price equal to 100% of the principal amount of the notes plus accrued and unpaid interest (including any liquidated damages), if any. We may, at our option, instead of paying the change of control purchase price in cash, pay it in shares of our common stock valued at 95% of the average of the closing sale prices of our common stock for the five trading days immediately preceding and including the third trading day prior to the date we are required to repurchase the notes. We cannot pay the change of control purchase price in common stock unless we satisfy the conditions described in the indenture for the notes.

Use of proceeds

We will not receive any of the proceeds from the sale of securities by the selling holders under this prospectus.

Risk factors

See "Risk Factors" and the other information in this prospectus for a discussion of the factors you should carefully consider before deciding to invest in the notes or our common stock.

Trading

The notes are eligible for trading in the PORTAL market; however, we can provide no assurance as to the liquidity of, or trading markets for, the notes. Our common stock is traded on the Nasdaq National Market under the symbol "VRTX."

RISK FACTORS

AN INVESTMENT IN THE SECURITIES OFFERED BY THIS PROSPECTUS INVOLVES A HIGH DEGREE OF RISK. YOU SHOULD CAREFULLY CONSIDER THE FOLLOWING FACTORS AND OTHER INFORMATION IN THIS PROSPECTUS BEFORE DECIDING TO PURCHASE THE NOTES OR OUR COMMON STOCK.

WE EXPECT TO INCUR FUTURE LOSSES AND WE MAY NEVER BECOME PROFITABLE.

We have incurred significant operating losses each year since our inception and expect to incur a significant operating loss in 2004. We believe that operating losses will continue beyond 2004, even if we receive significant future payments under our existing and future collaborative agreements, because we are planning to make significant investments in research and development, and because we will incur significant selling, general and administrative expenses for our potential products. We expect that losses will fluctuate from quarter to quarter and year to year, and that such fluctuations may be substantial. We cannot predict when we will become profitable, if at all.

WE DO NOT KNOW WHETHER LEXIVA®/TELZIR® WILL CONTINUE TO BE COMPETITIVE IN THE MARKET FOR PROTEASE INHIBITORS.

We currently recognize royalties from sales of Agenerase® and Lexiva®/Telzir®, two protease inhibitors that we discovered. We have noted a decrease in sales of Agenerase® since the launch of Lexiva®, which we attribute to the availability and acceptance of Lexiva®, and we anticipate that this trend will continue until Agenerase® is largely replaced by Lexiva® in the market. Our share of the worldwide protease inhibitor market may decrease due to competitive forces and market dynamics. Other HIV protease inhibitors and a number of other products, including Gilead's Viread®, Dupont's Sustiva® and GlaxoSmithKline's Ziagen®, are on the market for the treatment of HIV infection and AIDS. Other drugs are still in development by our competitors, including Bristol Myers Squibb and Boehringer Ingelheim, which may have better efficacy, fewer side effects, easier administration and/or lower costs than Lexiva®/Telzir®. Moreover, the growth in the worldwide market for HIV protease inhibitors has, to a certain extent, occurred as a result of early and aggressive treatment of HIV infection with a protease inhibitor-based regimen. Changes in treatment strategy, in which treatment is initiated later in the course of infection, or in which treatment is more often initiated with a regimen that does not include a protease inhibitor, may result in reduced use of HIV protease inhibitors. In addition, the clinical benefit of strategies used by clinicians to boost drug levels of Lexiva®/Telzir® by co-administering other antiretroviral agents may not prove to be effective, or may not result in increased revenues. As a result, the total market for protease inhibitors may decline, decreasing the sales potential of Agenerase® and Lexiva®/Telzir®. Further, although we co-promote Lexiva®/Telzir® in the U.S. and key markets in Europe, GlaxoSmithKline directs the majority of the marketing and sales efforts and we will have little control over the success of those efforts. GlaxoSmithKline has the right to terminate its agreement with us without cause upon twelve months' notice.

WE MAY NOT SUCCESSFULLY DEVELOP OUR DRUG PIPELINE.

All of the products that we are pursuing independently and with partners will require extensive additional development, testing and investment, as well as regulatory approvals, prior to commercialization. Our product research and development efforts may not be successful. Our drug candidates may not enter preclinical, nonclinical or clinical studies as or when anticipated and may not receive required regulatory approvals. Moreover, our products, if introduced, may not be commercially successful. The results of preclinical and initial clinical trials of products under development by us are not necessarily predictive of results that will be obtained from large-scale clinical testing. Clinical trials of products under development may not demonstrate the safety and efficacy of such products or result in a marketable product. Findings in nonclinical studies conducted concurrently with clinical studies

could adversely impact the development of our products. In addition, the administration, alone or in combination with other drugs, of any product developed by us may produce undesirable side effects in humans.

The failure to demonstrate adequately the safety and efficacy of a therapeutic drug under development could delay or prevent regulatory approval of the product and could have a material adverse effect on us. In addition, the FDA or regulatory authorities in other jurisdictions may require additional clinical or nonclinical studies, which could result in increased costs and significant development delays. While all or a portion of these additional costs may be covered by payments under our collaborative agreements, we bear all of the costs for our development candidates that are not partnered.

IF DELAYS IN PATIENT ENROLLMENT SLOW OUR DEVELOPMENT PROGRESS, WE MAY LOSE OUR COMPETITIVE ADVANTAGE OR BE UNABLE TO BRING OUR DRUGS TO MARKET.

The rate of completion of clinical trials of our products is dependent upon, among other factors, the rate of patient accrual. Patient accrual is a function of many factors, including the size of the patient population, the proximity of patients to clinical sites, the eligibility criteria for the trial, the level of compliance by the clinical sites to clinical trial protocols, and the availability of clinical trial material. Delays in patient enrollment in clinical trials may result in increased costs, program delays, or both, which could have a material adverse effect on us. While all or a portion of these additional costs may be covered by payments under our collaborative agreements, we bear all of the costs for our development candidates that are not partnered. If our clinical trials are not completed, we may not be able to submit a new drug application. If we are able to file a new drug application, such application may not be reviewed and approved in a timely manner, if at all.

IF WE DO NOT OBTAIN REGULATORY APPROVAL FOR OUR PRODUCTS ON A TIMELY BASIS, OR AT ALL, OUR REVENUES WILL BE NEGATIVELY IMPACTED.

The United States Food and Drug Administration and comparable agencies in foreign countries impose substantial requirements on the introduction of therapeutic pharmaceutical products through lengthy and detailed laboratory and clinical testing procedures, sampling activities and other costly and time-consuming procedures. Satisfaction of these requirements typically can take many years and may vary substantially based upon the type, complexity and novelty of the pharmaceutical product. Data obtained from preclinical, nonclinical and clinical activities are susceptible to varying interpretations, which could delay, limit or prevent regulatory approval. In addition, delays or rejections may be encountered based on changes in, or additions to, regulatory policies for drug approval during the period of product development and regulatory review. The effect of government regulation may be to delay or prevent the commencement of planned clinical trials for our drug candidates in clinical development, including merimepodib, VX-385, VX-950, VX-765 and VX-702. Their regulations may also impose costly procedures upon our activities and provide competitive advantages to companies more experienced in regulatory affairs that compete with us. Moreover, even if approval is granted, such approval may entail limitations on the indicated uses for which a product may be marketed.

IF WE ARE UNABLE TO ATTRACT AND RETAIN COLLABORATIVE PARTNERS FOR RESEARCH SUPPORT AND THE DEVELOPMENT AND COMMERCIALIZATION OF OUR PRODUCTS, WE MAY NOT BE ABLE TO FUND OUR RESEARCH AND DEVELOPMENT ACTIVITIES.

Our collaborative partners have agreed to fund portions of our research and development programs and/or to conduct certain research and development relating to specified products. In exchange, we have given them technology, product and marketing rights relating to those products. Some of our corporate partners, including Aventis, GlaxoSmithKline, Merck and Novartis, have rights to control the planning and execution of product development and clinical programs. Our collaborative

partners may exercise their control rights in ways that may negatively affect the timing and success of those programs. Our collaborations are subject to termination rights by the collaborators. If any of Aventis, GlaxoSmithKline, Merck or Novartis were to terminate its relationship with us, or fail to meet its contractual obligations, it could have a material adverse effect on our ability to undertake research, to fund related and other programs and to develop, manufacture and market any products that may have resulted from the collaboration. We expect to seek additional collaborative arrangements, which may not be available to us, to provide research support and to develop and commercialize our products in the future. For example, a significant portion of our overall research effort is conducted under our collaboration with Novartis. That collaboration will end by its terms in April 2006. If we are unable to enter into collaborative arrangements that would extend or replace the Novartis collaboration, or to find other means of financing the effort currently devoted to the Novartis collaboration, our ability to conduct our research, development and commercial activities could be adversely affected to a material degree. Even if we are able to establish acceptable collaborative arrangements in the future, they may not be successful. Under certain of our collaborative agreements, our collaborators have agreed to provide funding for only a portion of our research and development activities, and we are committed to investing our own capital to fund the remainder of the agreed-upon programs. However, we may not have adequate financial resources to satisfy those requirements.

IF WE LOSE OUR TECHNOLOGICAL ADVANTAGES, WE MAY NOT BE ABLE TO COMPETE IN THE MARKETPLACE.

We believe that our integrated drug discovery capability gives us a technological advantage over our competitors. However, the pharmaceutical research field is characterized by rapid technological progress and intense competition. As a result, we may not realize the expected benefits from these technologies. For example, a large pharmaceutical company, with significantly more resources than we have, could pursue a novel, systematic approach to discover drugs based on gene families using proprietary drug targets, compound libraries, compound approaches, structural protein analysis and information technologies. Such a company might identify broadly applicable compound classes faster and more effectively than we do, impeding our ability to develop and market drugs based on our approach. Further, we believe that interest in the application of structure-based drug design, parallel drug design and related approaches has accelerated as the strategies have become more widely understood. Businesses, academic institutions, governmental agencies and other public and private research organizations are conducting research to develop technologies that may compete with those we use. It is possible that our competitors could acquire or develop technologies that would render our technology obsolete or noncompetitive. For example, a competitor could develop information technologies that accelerate the atomic-level analysis of potential compounds that bind to the active site of a drug target, and predict the absorption, toxicity, and relative ease-of-synthesis of candidate compounds. If we were unable to access the same technologies at an acceptable price, our business could be adversely affected.

IF OUR COMPETITORS BRING SUPERIOR PRODUCTS TO MARKET OR BRING THEIR PRODUCTS TO MARKET BEFORE WE DO, WE MAY BE UNABLE TO FIND A MARKET FOR OUR PRODUCTS.

Our products in development may not be able to compete effectively with products that are currently on the market or new products that may be developed by others. There are many other companies developing products for the same indications that we are pursuing in development. In order to compete successfully in these areas, we must demonstrate improved safety, efficacy and ease of manufacturing and gain market acceptance over competing products that have received regulatory approval and are currently marketed. Many of our competitors, including major pharmaceutical companies such as Abbott, GlaxoSmithKline, Merck, and Novartis, have substantially greater financial, technical and human resources than we do. In addition, many of our competitors have significantly

greater experience than we do in conducting preclinical testing and human clinical trials of new pharmaceutical products, and in obtaining regulatory approvals of products. Accordingly, our competitors may succeed in obtaining regulatory approval for products more rapidly than we do. If we obtain regulatory approval and launch commercial sales of our products, we will also compete with respect to manufacturing efficiency and sales and marketing capabilities, areas in which we currently have limited experience.

THE LOSS OF THE SERVICES OF KEY EMPLOYEES OR THE FAILURE TO HIRE QUALIFIED EMPLOYEES WOULD NEGATIVELY IMPACT OUR BUSINESS AND FUTURE GROWTH.

Because our products are highly technical in nature, we require the services of highly qualified and trained scientists who have the necessary skills to develop our products. Our future success will depend in large part on the continued services of our key scientific and management personnel, including Dr. Joshua Boger, our Chief Executive Officer, and Dr. Vicki L. Sato, our President. While we have entered into employment agreements with Dr. Boger and Dr. Sato, they provide for termination by the employee upon six months' notice.

We face intense competition for our scientific personnel from our competitors, our collaborative partners and other companies throughout our industry. Moreover, the growth of local biotechnology companies and the expansion of major pharmaceutical companies into the Boston area has increased competition for the available pool of skilled employees, especially in technical fields, and the high cost of living in the Boston and San Diego areas makes it difficult to attract employees from other parts of the country. A failure to retain, as well as hire, train and effectively integrate into our organization a sufficient number of qualified scientists and professionals would negatively impact our business and our ability to grow our business. In addition, the level of funding under certain of our collaborative agreements, in particular the Novartis collaboration, depends on the number of our scientists performing research under those agreements. If we cannot hire and retain the required personnel, funding received under the agreements may be reduced.

IF WE FAIL TO MANAGE OUR GROWTH EFFECTIVELY, OUR BUSINESS MAY SUFFER.

We expect that if our clinical candidates continue to progress in development, we continue to build our commercial organization and our drug discovery efforts continue to generate drug candidates, we will require significant additional investment in personnel, management systems and resources. Our ability to commercialize our products, achieve our research and development objectives, and satisfy our commitments under our collaboration agreements depends on our ability to respond effectively to these demands and expand our internal organization to accommodate additional anticipated growth. If we are unable to manage our growth effectively, there could be a material adverse effect on our business.

WE DEPEND ON THIRD PARTY MANUFACTURERS, AND IF WE ARE UNABLE TO OBTAIN CONTRACT MANUFACTURING ON REASONABLE TERMS, WE MAY NOT BE ABLE TO DEVELOP OR COMMERCIALIZE OUR PRODUCTS.

Our ability to conduct clinical trials and our ability to commercialize our potential products will depend, in part, on our ability to manufacture our products on a large scale, either directly or through third parties, at a competitive cost and in accordance with regulatory requirements. We have no experience in manufacturing pharmaceuticals or other products, and we may not be able to develop such capabilities in the foreseeable future. In addition, some of our current corporate partners have manufacturing rights with respect to our products under development. We are, therefore, dependent on third party manufacturers and our collaborative partners for the production of our drug candidates for preclinical research, clinical trial purposes and commercial production. Accordingly, if we are not able to obtain contract manufacturing from these third parties on commercially reasonable terms, we may not be able to conduct or complete clinical trials or commercialize our products as planned. Further,

commercial formulation and manufacturing processes have yet to be developed for our drug candidates other than Agenerase® and Lexiva®/Telzir®. As a result, our collaborators or we may encounter difficulties developing commercial formulations and manufacturing processes for our drug candidates that could result in delays in clinical trials, regulatory submissions, regulatory approvals and commercialization of our products.

IF OUR PATENTS DO NOT PROTECT OUR PRODUCTS, OR OUR PRODUCTS INFRINGE THIRD-PARTY PATENTS, WE COULD BE SUBJECT TO LITIGATION AND SUBSTANTIAL LIABILITIES.

We have numerous patent applications pending in the United States, as well as foreign counterparts in other countries. Our success will depend, in significant part, on our ability to obtain and maintain United States and foreign patent protection for our products, their uses and our processes to preserve our trade secrets and to operate without infringing the proprietary rights of third parties. We do not know whether any patents will issue from any of our patent applications or, even if patents issue or have issued, that the issued claims will provide us with any significant protection against competitive products or otherwise be valuable commercially. Legal standards relating to the validity of patents and the proper scope of their claims in the biopharmaceutical field are still evolving, and there is no consistent law or policy regarding the valid breadth of claims in biopharmaceutical patents or the effect of prior art on them. If we are not able to obtain adequate patent protection, our ability to prevent competitors from making, using and selling competing products will be limited. Furthermore, our activities may infringe the claims of patents held by third parties. Defense and prosecution of infringement or other intellectual property claims, as well as participation in other inter-party proceedings, can be expensive and time-consuming, even in those instances in which the outcome is favorable to us. If the outcome of any such litigation or proceeding were adverse, we could be subject to significant liabilities to third parties, could be required to obtain licenses from third parties or could be required to cease sales of affected products, any of which outcomes could have a material adverse effect on our consolidated financial position.

WE MAY NEED TO RAISE ADDITIONAL CAPITAL THAT MAY NOT BE AVAILABLE.

We expect to incur substantial research and development and related supporting expenses as we design and develop existing and future compounds and undertake clinical trials of potential drugs resulting from such compounds. We also expect to incur substantial administrative and commercialization expenditures in the future and substantial expenses related to the filing, prosecution, defense and enforcement of patent and other intellectual property claims. We anticipate that we will finance these substantial cash needs with:

cash received from our existing collaborative agreements;

cash received from new collaborative agreements;

Lexiva®/Telzir® royalty revenue;

existing cash reserves, together with interest earned on those reserves; and

future product sales to the extent that we market products directly.

We expect that funds from these sources will be sufficient to fund our planned activities for at least the next eighteen months. If not, it will be necessary to raise additional funds through public offerings or private placements of equity or debt securities or other methods of financing. Any equity financings could result in dilution to our then-existing securityholders. Any debt financing, if available at all, may be on terms that, among other things, restrict our ability to pay dividends and interest (although we do not intend to pay dividends for the foreseeable future). The required interest payments associated with any significant additional debt financing could materially adversely impact our

ability to service our convertible subordinated notes and convertible senior subordinated notes. The terms of any additional debt financing may also, under certain circumstances, restrict or prohibit us from making interest payments on our convertible subordinated notes and convertible senior subordinated notes. If adequate funds are not available, we may be required to curtail significantly or discontinue one or more of our research, drug discovery or development programs (including clinical trials), or attempt to obtain funds through arrangements with collaborative partners or others that may require us to relinquish rights to certain of our technologies or products in research or development. Additional financing may not be available on acceptable terms, if at all.

OUR SALES AND MARKETING EXPERIENCE IS LIMITED.

We have little experience in marketing and selling pharmaceutical products. We must either develop a marketing and sales force or enter into arrangements with third parties to market and sell any of our product candidates that are approved by regulatory authorities. We do not know whether we will be able to enter into marketing and sales agreements with others on acceptable terms, if at all. We may not be able to successfully develop our own sales and marketing force for drug candidates for which we have retained marketing or co-promotion rights. If we develop our own marketing and sales capability, we may be competing with other companies that currently have experienced and well-funded marketing and sales operations. We have granted exclusive marketing rights for Agenerase® and Lexiva®/Telzir® to GlaxoSmithKline worldwide (except for amprenavir in Japan), and for pralnacasan to Aventis worldwide. Kissei has exclusive marketing rights to Prozei (amprenavir) and VX-702 in Japan. Mitsubishi Pharma Corp. has exclusive marketing rights to VX-950 in Japan and certain Far East countries. Even though we retain some co-promotion rights, to the extent that our collaborative partners have commercial rights to our products, any revenues we receive from those products will depend primarily on the sales and marketing efforts of others.

IF WE INCUR PRODUCT LIABILITY EXPENSES, OUR EARNINGS COULD BE NEGATIVELY IMPACTED.

Our business will expose us to potential product liability risks that arise from the testing, manufacturing and sales of our products. In addition to direct expenditures for damages, settlement and defense costs, there is the possibility of adverse publicity as a result of product liability claims. These risks will increase as our products receive regulatory approval and are commercialized. We currently carry \$15 million of product liability insurance. This level of insurance may not be sufficient. Moreover, we may not be able to maintain our existing levels of insurance or be able to obtain or maintain additional insurance that we may need in the future on acceptable terms.

In addition, our research and development activities may from time to time involve the controlled use of hazardous materials, including hazardous chemicals and radioactive materials. Accordingly, we are subject to federal, state and local laws governing the use, handling and disposal of these materials. Although we believe that our safety procedures for handling and disposing of hazardous materials comply with regulatory requirements, we cannot completely eliminate the risk that accidental contamination or injury from these materials could expose us to significant liability.

WE HAVE ADOPTED ANTI-TAKEOVER PROVISIONS THAT MAY FRUSTRATE ANY ATTEMPT TO REMOVE OR REPLACE OUR CURRENT MANAGEMENT.

Our corporate charter and by-law provisions and stockholder rights plan may discourage certain types of transactions involving an actual or potential change of control of Vertex which might be beneficial to the company or its securityholders. Our charter provides for staggered terms for the members of the Board of Directors. Our by-laws grant the directors a right to adjourn annual meetings of stockholders, and certain provisions of the by-laws may be amended only with an 80% stockholder vote. Pursuant to our stockholder rights plan, each share of common stock has an associated preferred share purchase right. The rights will not trade separately from the common stock until, and are exercisable only upon, the acquisition or the potential acquisition through tender offer by a person or group of 15% or more of the outstanding common stock. 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. As a result, shareholders or other parties may find it more difficult to remove or replace our current management.

OUR STOCK PRICE MAY FLUCTUATE BASED ON FACTORS BEYOND OUR CONTROL.

Market prices for securities of companies such as Vertex are highly volatile. Within the twelve months ended June 30, 2004, our common stock traded between \$7.83 and \$16.77. The market for our stock, like that of other companies in the biotechnology field, has from time to time experienced significant price and volume fluctuations that are unrelated to our operating performance. The future market price of our securities could be significantly and adversely affected by factors such as:

announcements of results of clinical or nonclinical trials;

announcements of financial results and other operating performance measures, or capital structuring activities;

technological innovations or the introduction of new products by our competitors;

government regulatory action;

public concern as to the safety of products developed by others;

developments in patent or other intellectual property rights or announcements relating to these matters;

developments in domestic and international governmental policy or regulation, for example relating to intellectual property rights; and

developments and market conditions for pharmaceutical and biotechnology stocks, in general.

OUR OUTSTANDING INDEBTEDNESS MAY MAKE IT MORE DIFFICULT TO OBTAIN ADDITIONAL FINANCING OR REDUCE OUR FLEXIBILITY TO ACT IN OUR BEST INTERESTS.

As of June 30, 2004, we had approximately \$335.0 million in long-term debt, including \$161.9 million of our 5% Convertible Notes due 2007 (referred to as our "old notes"). The notes offered hereby were issued in a transaction completed on September 17, 2004, in which we exchanged approximately \$79.3 million of our old notes for approximately \$79.3 million of our new notes. Immediately following that exchange, we had \$82.6 million in aggregate principal amount of our old notes outstanding and \$232.4 million in aggregate principal amount of our 5³/₄% Convertible Senior Subordinated Notes due 2011 outstanding (consisting of \$79.3 million of the new notes and \$153.1 million in aggregate principal amount of 5³/₄% Convertible Senior Subordinated Notes due 2011

issued on which were issued as part of a separate series) February 13, 2004. The high level of our indebtedness will impact us by:

exposing us to fixed rates of interest, which may be in excess of prevailing market rates;

making it more difficult to obtain additional financing for working capital, capital expenditures, debt service requirements or other purposes;

constraining our ability to react quickly in an unfavorable economic climate or to changes in our business, or the pharmaceutical industry; and

requiring the dedication of a substantial portion of our expected cash flow to service of our indebtedness, thereby reducing the amount of expected cash flow available for other purposes.

IF WE ARE NOT ABLE TO RESTRUCTURE OUR KENDALL SQUARE LEASE ON ACCEPTABLE TERMS, OR AT ALL, WE COULD BE OBLIGATED TO PAY AS MUCH AS THE FULL AMOUNT DUE UNDER THE LEASE, AS AND WHEN DUE UNDER THE LEASE AGREEMENT.

We have decided not to occupy a facility located in Kendall Square, Cambridge, Massachusetts that we lease under a 15-year agreement expiring in 2018. We have estimated our liability to restructure the lease, using assumptions and estimates we consider appropriate, to be \$56.7 million as of June 30, 2004. To date, we have subleased 45,000 square feet of the 290,000 square foot facility. If we are unable to find a tenant or tenants willing to sublease the balance of the facility on the terms we have incorporated into our estimate, including the rental rate, timing and term of any such sublease(s), or if the market for specialized laboratory space in Cambridge, Massachusetts or other real estate fundamentals should change before we are able to secure a sublease of the balance of the space, or if any of our other assumptions and estimates are inaccurate or circumstances bearing upon the potential restructuring should change before we are able to restructure the lease, or if we are unable to reach agreement with the landlord on the terms of any such restructuring, our estimated liability could increase to as much as the full amount due under the lease. Our future obligations under the lease could be as much as \$312,500,000, as set forth in "Off-Balance Sheet Commitments and Obligations at December 31, 2003" on page 5 of our Annual Report on Form 10-K/A (Amendment No. 1) for the fiscal year ended December 31, 2003, which was filed with the Securities and Exchange Commission on September 8, 2004.

OUR REVENUE DEPENDS AND WILL LIKELY CONTINUE TO DEPEND ON A LIMITED NUMBER OF PRODUCTS.

We derive a portion of our revenue from royalties earned from the sale of our two marketed products. We believe that royalties from the sales of a limited number of products will continue to constitute a portion of our revenue for the foreseeable future. Accordingly, any factor adversely affecting sales of any of these products could also have a material adverse effect on our business, financial condition and results of operations.

MARKET ACCEPTANCE OF OUR PRODUCTS WILL BE LIMITED IF USERS OF OUR PRODUCTS ARE UNABLE TO OBTAIN ADEQUATE REIMBURSEMENT FROM THIRD-PARTY PAYORS.

The commercial success of Lexiva®/Telzir® will depend in part on the availability of reimbursement from third-party payors, including government health administrators, managed care providers and private health insurers. Third-party payors are increasingly challenging the pricing of pharmaceutical products. Additionally, third-party payors may conclude that Lexiva®/Telzir® is less safe, less effective or less cost-effective than existing products. We cannot assure you that third-party payors will provide reimbursement for Lexiva®/Telzir®, in whole or in part. If third-party payors do not provide adequate

reimbursement for Lexiva®/Telzir®, the sale of that product may not be profitable to our partners and they may stop selling Lexiva®/Telzir®, thus terminating the royalties we receive on sales of these products.

THE RECENT MEDICARE PRESCRIPTION DRUG COVERAGE LEGISLATION AND FUTURE LEGISLATIVE OR REGULATORY REFORM OF THE HEALTHCARE SYSTEM MAY AFFECT OUR PARTNERS' ABILITY TO SELL AGENERASE OR LEXIVA PROFITABLY.

In the United States, there have been a number of legislative and regulatory proposals to change the healthcare system in ways that could affect our partners' ability to market and sell Lexiva® profitably. Pursuant to recent Medicare prescription drug coverage legislation, the Centers for Medicare and Medicaid Services, or CMS, the agency within the Department of Health and Human Services that administers Medicare and is responsible for reimbursement of the cost of drugs, has asserted the authority of Medicare to elect not to cover particular drugs if CMS determines that the drugs are not "reasonable and necessary" for Medicare beneficiaries or to elect to cover a drug at a lower rate similar to that of drugs that CMS considers to be "therapeutically comparable". Further federal and state proposals and healthcare reforms are likely and legislation and regulations affecting the pricing of pharmaceuticals may change in ways adverse to us. For example, the potential for importation of lower-priced drugs from foreign sources may limit or erode sales of Lexiva®, negatively impacting the amount of royalties we receive.

GOVERNMENT INVESTIGATIONS OR LITIGATION AGAINST OUR PARTNERS COULD IMPACT OUR BUSINESS.

The federal government, certain state governments and private payors are investigating and have begun to file actions against numerous pharmaceutical and biotechnology companies alleging that the reporting of prices for pharmaceutical products has resulted in a false and overstated Average Wholesale Price, or AWP, which in turn is alleged to have improperly inflated the reimbursement paid by Medicare beneficiaries, insurers, state Medicaid programs, medical plans and others to health care providers who prescribed and administered those products. Some payors are also alleging that pharmaceutical and biotechnology companies are not reporting their "best price" to the states under the Medicaid program. In any AWP cases where our partners are named as defendants, the outcome of the case could have an adverse effect on our financial results.

SALES OF ADDITIONAL SHARES OF OUR COMMON STOCK COULD CAUSE THE PRICE OF OUR COMMON STOCK TO DECLINE.

Sales of substantial amounts of our common stock in the open market, or the availability of such shares for sale, could adversely affect the price of our common stock. As of October 22, 2004, we had 80,227,506 shares of common stock outstanding, excluding shares reserved for issuance upon the exercise of outstanding stock options, employee stock purchase and 401(k) plans. As of October 22, 2004, we had granted stock options to purchase 16,319,075 shares of our common stock at a weighted average exercise price of \$22.57 per share, subject to adjustment in certain circumstances. Of this total, 10,846,375 were currently exercisable at an average exercise price of approximately \$23.89 per share. The shares of our common stock that may be issued under the options will be freely tradable or transferable pursuant to an effective registration statement.

THE NOTES ARE SUBORDINATED TO ANY EXISTING AND FUTURE SENIOR DEBT.

The notes are unsecured and contractually subordinated in right of payment to our existing and future senior debt. As of June 30, 2004, we had approximately \$20.0 million of debt outstanding that would be senior to the notes. The indenture under which the notes were issued does not limit the creation of additional senior debt or any other indebtedness. Any significant additional senior debt

incurred may materially adversely impact our ability to service our debt, including the notes. Due to subordination provisions contained in the indenture under which the notes were issued and other agreements relating to our senior debt, in the event of our bankruptcy, liquidation, dissolution or acceleration of payment on senior debt, funds which we would otherwise use to pay the holders of the notes will be used to pay the holders of senior debt to the extent necessary to pay the senior debt in full. As a result of these payments, our general creditors may recover less, ratably, than the holders of our senior debt and such general creditors may recover more, ratably, than the holders of our notes or our other subordinated indebtedness. In addition, the holders of senior debt may, under certain circumstances, restrict or prohibit us from making payments on the notes.

OUR ABILITY TO REPURCHASE NOTES, IF REQUIRED, MAY BE LIMITED.

In certain circumstances involving a change of control, each holder of the notes may require us to repurchase some or all of the holder's notes. If certain conditions described in the indenture are met, we may, at our option, pay the change of control purchase price in shares of our common stock instead of cash. Purchasing the notes with a payment of stock may not be possible, and if the change in control purchase price is to be made in cash, we may not have sufficient financial resources at such time and we may not be able to arrange financing to pay the repurchase price of the notes. Our ability to repurchase the notes in such event may be limited by law, the indenture, by the terms of other agreements relating to our senior debt and as such indebtedness and agreements may be entered into, replaced, supplemented or amended from time to time. We may be required to refinance our senior debt in order to make such payments.

IF AN ACTIVE TRADING MARKET FOR THE NOTES IS NOT SUSTAINED THE VALUE OF THE NOTES MAY DECREASE.

Although the notes are eligible for trading in the PORTAL market, an active trading market for the notes may not be sustained. If an active market for the notes fails to be sustained, the trading price of the notes could fall. Whether or not the notes will trade at lower prices depends on many factors, including:

prevailing interest rates and the markets for similar securities;

general economic conditions; and

our financial condition, historic financial performance and future prospects.

ANY RATING OF THE NOTES MAY CAUSE THEIR TRADING PRICE TO FALL.

If the rating agencies rate the notes, they may assign a lower rating than expected by investors. Rating agencies may also lower ratings on the notes in the future. If the rating agencies assign a lower than expected rating or reduce their ratings in the future, the trading price of the notes could decline.

FORWARD-LOOKING STATEMENTS

This prospectus contains some forward-looking statements. Forward-looking statements give our current expectations or forecasts of future events. You can identify these statements by the fact that they do not relate strictly to historical or current facts. Such statements may include words such as "anticipate," "estimate," "expect," "project," "intend," "plan," "believe" and other words and terms of similar meaning in connection with any discussion of future operating or financial performance. In particular, these statements include, among other things, statements relating to:

our business strategy;

our predicted development and commercial timelines;

the selection, development and approval of our products;

the establishment, development and maintenance of collaborative partnerships;

our ability to identify and develop new potential products;

our ability to achieve commercial acceptance of our products;

our ability to scale up our manufacturing capabilities and facilities;

our estimates regarding liabilities associated with our Kendall Square lease;

the potential for the acquisition of new and complementary technologies, resources and products;

our projected capital expenditures; and

our liquidity.

Any or all of our forward-looking statements in this prospectus may turn out to be wrong. They can be affected by inaccurate assumptions we might make or by known or unknown risks and uncertainties. Many factors mentioned in our discussion in this prospectus will be important in determining future results. Consequently, no forward-looking statement can be guaranteed. Actual future results may vary materially.

We note that we provide a cautionary discussion of risks and uncertainties under "Risk Factors" beginning on page 6 of this prospectus. These are factors that we think could cause our actual results to differ materially from expected results. Other factors besides those listed there could also adversely affect us.

RATIO OF EARNINGS TO FIXED CHARGES

We present below the ratio of our earnings to our fixed charges. Earnings consist of loss from continuing operations before cumulative effects of changes in accounting principles and loss of equity investee plus fixed charges. Fixed charges consist of interest expense and amortization of deferred issuance costs and that portion of rental obligations we believe to be representative of interest.

| Ratio of earnings to fixed charges | Year ended December 31, | | | | | Six months ended June 30, 2004 |
|--|-------------------------|------|------|------|------|---|
| | 1999 | 2000 | 2001 | 2002 | 2003 | |
| | (1) | (1) | (1) | (1) | (1) | (1) |

(1)

Due to our loss from continuing operations for the years ended December 31, 1999, 2000, 2001, 2002, 2003, and for the six months ended June 30, 2004 earnings were insufficient to cover fixed charges by \$47.6 million, \$41.4 million, \$79.6 million, \$137.0 million, \$266.4 million, and \$84.7 million, respectively. For this reason, no ratios are provided.

USE OF PROCEEDS

We will not receive any of the proceeds from the sale by the selling holders of the notes or of our common stock under this prospectus.

DESCRIPTION OF THE NOTES

The notes were issued under an indenture between us and US Bank National Association, as trustee, dated September 17, 2004. We will make copies of the indenture, notes and registration rights agreement available to prospective investors in the notes upon request to us. A copy of the indenture was filed with the Securities and Exchange Commission on September 17, 2004 as Exhibit 10.2 to a Current Report on Form 8-K, and is incorporated into the registration statement to which this prospectus is a part. We have summarized portions of the indenture below. This summary is not complete. We urge you to read the indenture because it defines your rights as a holder of the notes. Terms not defined in this description have the meanings given them in the indenture. In this section, "Vertex," "we," "our" and "us" each refers only to Vertex Pharmaceuticals Incorporated and not to any existing or future subsidiary.

General

The notes are unsecured, senior subordinated obligations of Vertex and will be convertible into our common stock as described under "Conversion rights" below. There is no sinking fund for the notes.

The notes bear interest at the rate of 5³/₄% per year from the date of issuance of the notes, or from the most recent date to which interest had been paid or provided for, subject to adjustment upon the occurrence of a Re-set Transaction. See "Interest rate adjustments" below. Interest is payable semi-annually on February 15 and August 15 of each year, commencing August 15, 2004, to holders of record at the close of business on the preceding February 1 and August 1, respectively. Interest is computed on the basis of a 360-day year comprised of twelve 30-day months. In the event of the maturity, conversion, purchase by us at the option of the holder, or redemption of a note, interest will cease to accrue on the note under the terms of and subject to the conditions of the indenture.

Principal will be payable, and notes may be presented for conversion, registration of transfer and exchange, without service charge, at our office or agency in New York City, which shall initially be the office or agency of the trustee in New York, New York.

The indenture does not contain any financial covenants or any restrictions on the payment of dividends, the incurrence of senior debt or other indebtedness, or the issuance or repurchase of securities by us. The indenture contains no covenants or other provisions to protect holders of the notes in the event of a highly leveraged transaction or a change in control, except to the extent described under " Interest rate adjustments" and under " Change of control requires purchase of notes at the option of the holder" below.

The notes and the common stock issuable upon conversion of the notes may not be sold or otherwise transferred except in compliance with the provisions set forth under "Restrictions on transfer of the notes."

Interest rate adjustment

If a Re-set Transaction occurs, the interest rate will be adjusted to the Adjusted Interest Rate from the effective date of the Re-set Transaction up to, but not including, the effective date of any succeeding Re-set Transaction.

A "Re-set Transaction" means:

a merger, consolidation or share exchange to which the entity that is the issuer of the common stock into which the notes are convertible into is a party;

a sale of all or substantially all of the assets of that entity;

a recapitalization of that common stock; or

certain dividends or other distributions to all holders of our common stock of shares of our capital stock or evidences of our indebtedness or certain securities;

after the effective date of which transaction or distribution, the new notes would be convertible into (i) shares of an entity, the common stock of which had a dividend yield for the four fiscal quarters of such entity immediately preceding the public announcement of the transaction or distribution that was more than 2.5% higher than the dividend yield on our common stock (or other common stock then issuable upon conversion of the notes) for the four fiscal quarters preceding the public announcement of the transaction or distribution; or (ii) shares of an entity that announces a dividend policy prior to the effective date of the transaction or distribution, which policy, if implemented, would result in a dividend yield on that entity's common stock for the next four fiscal quarters that would result in such a 2.5% increase.

The "Adjusted Interest Rate" with respect to any Re-set Transaction will be the rate per year that is the arithmetic average of the rates quoted by two dealers engaged in the trading of convertible securities selected by us or our successor as the rate at which interest should accrue so that the fair market value, expressed in dollars, of a new note immediately after the later of the public announcement of the Re-set Transaction; or the public announcement of a change in dividend policy in connection with the Re-set Transaction, will equal the average Trading Price of a new note for the twenty trading days preceding the date of public announcement of the Re-set Transaction.

However, the Adjusted Interest Rate will not be less than $5\frac{3}{4}\%$ per year.

For purposes of the definition of Re-set Transaction, the "dividend yield" on any security for any period means the dividends paid or proposed to be paid pursuant to an announced dividend policy on the security for that period divided by, if with respect to dividends paid on that security, the average Closing Price (as defined in the indenture) of the security during that period and, if with respect to dividends proposed to be paid on the security, the Closing Price of such security on the effective date of the related Re-set Transaction.

The "Trading Price" of a security on any date of determination means:

the closing sale price (or, if no closing sale price is reported, the last reported sale price) of a security (regular way) on the New York Stock Exchange ("NYSE") on that date;

if that security is not listed on the NYSE on that date, the closing sale price as reported in the composite transactions for the principal U.S. securities exchange on which that security is listed;

if that security is not so listed on a U.S. national or regional securities exchange, the closing sale price as reported by the Nasdaq National Market;

if that security is not so reported, the last price quoted by Interactive Data Corporation for that security or, if Interactive Data Corporation is not quoting such price, a similar quotation service selected by us, if that security is not so quoted, the average of the mid-point of the last bid and ask prices for that security from at least two dealers recognized as market-makers for that security; or

if that security is not so quoted, the average of the last bid and ask prices for that security from a dealer engaged in the trading of convertible securities.

Subordination

The new notes offered hereby are unsecured obligations and are (i) senior in right of payment to our 5% convertible subordinated notes due 2007, which we refer to as our "old notes" and any future obligations that are designated by us as subordinate to the notes; (ii) equal in right of payment with the February notes and any other existing or future obligations that are designated by us as, or otherwise determined to be, on a parity with the new notes; and (iii) subordinated in right of payment to the prior payment in full of all our existing and future Senior Debt, as defined herein, each as described in the indenture for the new notes. The new notes constitute "Designated Senior Debt" for purposes of the indenture for the old notes.

At June 30, 2004, we had approximately \$20.0 million of debt outstanding that would be senior to the notes. The indenture does not restrict the incurrence by us or our subsidiaries of indebtedness or other obligations.

The term "Senior Debt" is defined in the indenture to mean the principal of, premium, if any, interest (including all interest accruing subsequent to the commencement of any bankruptcy or similar proceeding, whether or not a claim for post-petition interest is allowable as a claim in any such proceeding) and rent payable on or termination payment with respect to or in connection with, and all fees, costs, expenses and other amounts accrued or due on or in connection with, our Indebtedness, whether outstanding on the date of the indenture or subsequently created, incurred, assumed, guaranteed or in effect guaranteed by us (including all deferrals, renewals, extensions or refundings of, or amendments, modifications or supplements to, the foregoing), except for:

any Indebtedness that by its terms expressly provides that such Indebtedness shall not be senior in right of payment to the notes or expressly provides that such Indebtedness is equal with or junior to the notes;

any Indebtedness represented by the old notes; and

any Indebtedness between or among us and/or any of our subsidiaries, a majority of the voting stock of which we directly or indirectly own, or any of our affiliates.

The term "Indebtedness" is defined in the indenture to mean, with respect to any person: (1) all indebtedness, obligations and other liabilities (contingent or otherwise) of that person for borrowed money (including obligations in respect of overdrafts, foreign exchange

contracts, currency exchange agreements, interest rate protection agreements, and any loans or advances from banks, whether or not

evidenced by notes or similar instruments) or evidenced by bonds, debentures, notes or other instruments for the payment of money, or incurred in connection with the acquisition of any property, services or assets (whether or not the recourse of the lender is to the whole of the assets of such person or to only a portion thereof), other than any account payable or other accrued current liability or obligation to trade creditors incurred in the ordinary course of business in connection with the obtaining of materials or services; (2) all reimbursement obligations and other liabilities (contingent or otherwise) of that person with respect to letters of credit, bank guarantees, bankers' acceptances, surety bonds, performance bonds or other guaranty of contractual performance; (3) all obligations and liabilities (contingent or otherwise) in respect of (A) leases of such person required, in conformity with generally accepted accounting principles, to be accounted for as capitalized lease obligations on the balance sheet of such person, and (B) any lease or related documents (including a purchase agreement) in connection with the lease of real property which provides that such person is contractually obligated to purchase or cause a third party to purchase the leased property and thereby guarantee a minimum residual value of the leased property to the landlord and the obligations of such person under such lease or related document to purchase or to cause a third party to purchase the leased property; (4) all obligations of such person (contingent or otherwise) with respect to an interest rate or other swap, cap or collar agreement or other similar instrument or agreement or foreign currency hedge, exchange, purchase or similar instrument or agreement; (5) all direct or indirect guaranties or similar agreements by that person in respect of, and obligations or liabilities (contingent or otherwise) of that person to purchase or otherwise acquire or otherwise assure a creditor against loss in respect of, indebtedness, obligations or liabilities of another person of the kind described in clauses (1) through (4); (6) any indebtedness or other obligations described in clauses (1) through (4) secured by any mortgage, pledge, lien or other encumbrance existing on property which is owned or held by such person, regardless of whether the indebtedness or other obligation secured thereby shall have been assumed by such person; and (7) any and all deferrals, renewals, extensions, refinancings, replacements, restatements and refundings of, or amendments, modifications or supplements to, any indebtedness, obligation or liability of the kind described in clauses (1) through (6).

Any Senior Debt will continue to be Senior Debt and will be entitled to the benefits of the subordination provisions irrespective of any amendment, modification or waiver of any of its terms.

The indenture provides that in the event of any payment or distribution of our assets upon our dissolution, winding up, liquidation or reorganization, the holders of our Senior Debt shall first be paid in respect of all Senior Debt, in full, in cash or other payment satisfactory to the holders of Senior Debt before we make any payments of principal of, or premium, if any, and interest (including liquidated damages, if any) on the notes. In addition, if the notes are accelerated because of an event of default, the holders of any Senior Debt would be entitled to payment in full in cash or other payment satisfactory to the holders of Senior Debt of all obligations in respect of Senior Debt before the holders of the notes are entitled to receive any payment or distribution. Under the indenture, we must promptly notify holders of Senior Debt if payment of the notes is accelerated because of an event of default.

The indenture further provides if any default by us has occurred and is continuing in the payment of principal of, premium, if any, or interest on, rent or other payment obligations in respect of, any Senior Debt, then no payment shall be made on account of principal of, premium, if any, or interest (including liquidated damages, if any) on the notes, or to acquire any of the notes, until all such payments due in respect of that Senior Debt have been paid in full in cash or other payment satisfactory to the holders of that Senior Debt.

During the continuance of any event of default with respect to any Designated Senior Debt, as described below, (other than a default in payment of the principal of, or premium, if any, or interest on, rent or other payment obligations in respect of, any Designated Senior Debt), permitting the holders thereof to accelerate the maturity thereof (or, in the case of any lease, permitting the landlord

either to terminate the lease or to require us to make an irrevocable offer to terminate the lease following an event of default thereunder), no payment may be made by us, directly or indirectly, with respect to principal of, premium, if any, or interest (including liquidated damages, if any) on the notes for 179 days following written notice to us, from any holder, representative or trustee under any agreement pursuant to which that Designated Senior Debt may have been issued, that such an event of default has occurred and is continuing, unless such event of default has been cured or waived or that Designated Senior Debt has been paid in full in cash or other payment satisfactory to the holders of that Designated Senior Debt. However, if the maturity of that Designated Senior Debt is accelerated (or, in the case of a lease, as a result of such event of default, the landlord under the lease has given us notice of its intention to terminate the lease or to require us to make an irrevocable offer to terminate the lease following an event of default thereunder), no payment may be made on the notes until that Designated Senior Debt has been paid in full in cash or other payment satisfactory to the holders of that Designated Senior Debt or such acceleration (or termination, in the case of the lease) has been cured or waived.

The term "Designated Senior Debt" means our Senior Debt which, at the date of determination, has an aggregate amount outstanding of, or under which, at the date of determination, the holders thereof are committed to lend up to, at least \$20 million and is specifically designated in the instrument evidencing or governing that Senior Debt as "Designated Senior Debt" for purposes of the indenture. However, the instrument may place limitations and conditions on the right of that Senior Debt to exercise the rights of Designated Senior Debt. At June 30, 2004, we had no Designated Senior Debt outstanding.

By reason of these subordination provisions, in the event of insolvency, funds which we would otherwise use to pay the holders of notes will be used to pay the holders of Senior Debt to the extent necessary to pay Senior Debt in full in cash or other payment satisfactory to the holders of Senior Debt.

The notes will be effectively subordinated to all existing and future liabilities of our subsidiaries. Any right we have to receive assets of any of our existing and future subsidiaries upon the latter's liquidation or reorganization (and the consequent right of the holders of the notes to participate in those assets) will be effectively subordinated to the claims of that subsidiary's creditors, except to the extent that we are ourselves recognized as a creditor of that subsidiary, in which case our claims would still be subordinate to any security interests in the assets of that subsidiary and any indebtedness of that subsidiary senior to that held by us. There are no restrictions in the indenture on the ability of our subsidiaries to incur Indebtedness or other liabilities. As of June 30, 2004, none of our existing subsidiaries had outstanding indebtedness.

We are obligated to pay reasonable compensation to the trustee and to indemnify the trustee against any losses, liabilities or expenses incurred by it in connection with its duties relating to the notes. The trustee's claims for such payments will be senior to those of holders of the notes in respect of all funds collected or held by the trustee.

Conversion rights

The holders of notes may, at any time prior to the close of business on the final maturity date of the notes, convert any outstanding notes (or portions thereof) into shares of our common stock, initially at the conversion price set forth on the cover page of this prospectus subject to adjustment as described below. Holders may convert notes only in denominations of \$1,000 and whole multiples of \$1,000. Except as described below, no payment or other adjustment will be made on conversion of any notes for interest accrued thereon or dividends paid on any common stock. Accrued and unpaid interest on the notes at the time of conversion will be treated as paid in stock rather than cancelled.

If notes are converted after a record date for an interest payment but prior to the next interest payment date, those notes must be accompanied by funds equal to the interest payable to the record holder on the next interest payment date on the principal amount so converted, provided that no such payment will be required from a holder if such notes have been called for redemption. We will not issue fractional shares of common stock upon conversion of notes and instead will pay a cash adjustment based upon the market price of our common stock on the last business day before the date of the conversion. In the case of notes called for redemption, conversion rights will expire at the close of business on the business day preceding the date fixed for redemption, unless we default in payment of the redemption price.

A holder may exercise the right of conversion by delivering the new note to be converted to the specified office of a conversion agent, with a completed notice of conversion, together with any funds that may be required as described in the preceding paragraph. The conversion date will be the date on which the notes, the notice of conversion and any required funds have been so delivered. A holder delivering a note for conversion will not be required to pay any taxes or duties relating to the issuance or delivery of the common stock for such conversion, but will be required to pay any tax or duty which may be payable relating to any transfer involved in the issuance or delivery of the common stock in a name other than the holder of the note. Certificates representing shares of common stock will be issued or delivered only after all applicable taxes and duties, if any, payable by the holder have been paid. If any note is converted within two years after its original issuance, the common stock issuable upon conversion will not be issued or delivered in a name other than that of the holder of the note unless the applicable restrictions on transfer have been satisfied. See "Restrictions on transfer of the notes."

The initial conversion price will be adjusted for certain events, including: (1) the issuance of our common stock as a dividend or distribution on our common stock; (2) certain subdivisions and combinations of our common stock; (3) the issuance to all holders of our common stock of certain rights or warrants to purchase our common stock (or securities convertible into our common stock) at less than (or having a conversion price per share less than) the current market price of our common stock; (4) the dividend or other distribution to all holders of our common stock of shares of our capital stock (other than common stock) or evidences of our indebtedness or our assets (including securities, but excluding those rights and warrants referred to in clause (3) above and dividends and distributions in connection with a reclassification, change, merger, consolidation, statutory share exchange, combination, sale or conveyance resulting in a change in the conversion consideration pursuant to the second succeeding paragraph below and dividends or distributions paid exclusively in cash); (5) dividends or other distributions consisting exclusively of cash to all holders of our common stock (excluding any cash that is distributed upon a reclassification, change, merger, consolidation, statutory share exchange, combination, sale or conveyance as described in the second succeeding paragraph hereof or as part of a distribution referred to in clause (4) above) to the extent that such distributions, combined together with (A) all other such all-cash distributions made within the preceding twelve months for which no adjustment has been made plus (B) any cash and the fair market value of other consideration paid for any tender or exchange offers by us or any of our subsidiaries for our common stock concluded within the preceding twelve months for which no adjustment has been made, exceeds 10% of our market capitalization on the record date for such distribution (market capitalization is the product of the then current market price of our common stock times the number of shares of our common stock then outstanding); and (6) payments to holders of our common stock pursuant to a tender or exchange offer made by us or any of our subsidiaries to the extent that the same involves aggregate consideration that, together with (A) any cash and the fair market value of any other consideration paid in any other tender or exchange offer by us or any of our subsidiaries for our common stock expiring within the twelve months preceding such tender or exchange offer for which no adjustment has been made plus (B) the aggregate amount of any all-cash distributions referred to in clause (5) above to all holders of our common stock within twelve months preceding the expiration of

such tender or exchange offer for which no adjustments have been made, exceeds 10% of our market capitalization on the expiration of such tender or exchange offer.

No adjustment in the conversion price will be required unless such adjustment would require a change of at least 1% in the conversion price then in effect at such time. Any adjustment that would otherwise be required to be made shall be carried forward and taken into account in any subsequent adjustment. Except as stated above, the conversion price will not be adjusted for the issuance of our common stock or any securities convertible into or exchangeable for our common stock or carrying the right to purchase any of the foregoing.

In the case of:

any recapitalization, reclassification or change of our common stock (other than changes in par value or resulting from a subdivision or combination);

a merger, consolidation, statutory share exchange or combination involving us; or

a sale, conveyance or lease to another corporation of all or substantially all of our property and assets,

in each case as a result of which holders of our common stock are entitled to receive stock, other securities, other property or assets (including cash or any combination thereof) with respect to or in exchange for our common stock, the holders of the notes then outstanding will be entitled thereafter to convert those notes into the kind and amount of shares of stock, other securities or other property or assets (including cash or any combination thereof) which they would have owned or been entitled to receive upon such recapitalization, reclassification, change, merger, consolidation, statutory share exchange, combination, sale or conveyance had such notes been converted into our common stock immediately prior to such recapitalization, reclassification, change, merger, consolidation, statutory share exchange, combination, sale or conveyance. We may not become a party to any such transaction unless its terms are consistent with the foregoing.

If a taxable distribution to holders of our common stock or other transaction occurs which results in any adjustment of the conversion price, the holders of notes may, in certain circumstances, be deemed to have received a distribution subject to United States income tax as a dividend. In certain other circumstances, the absence of an adjustment may result in a taxable dividend to the holders of common stock. In particular, any adjustment in the conversion rate to compensate holders of notes for taxable distributions of cash on any of our outstanding common stock will be treated as a deemed distribution of stock to the holders, which will be taxable as a dividend. See "Certain U.S. federal income tax consequences."

We may from time to time, to the extent permitted by law or applicable NASDAQ Marketplace Rules, reduce the conversion price of the notes by any amount for any period of at least 20 days. In that case, we will give at least 15 days' notice of such decrease. We may make such reductions in the conversion price in compliance with applicable NASDAQ Marketplace Rules, in addition to those set forth above, as our board of directors deems advisable to avoid or diminish any income tax to holders of our common stock resulting from any dividend or distribution of stock (or rights to acquire stock) or from any event treated as such for income tax purposes.

Redemption of the notes at our option

Prior to February 15, 2007, we cannot redeem the notes. We may redeem the notes at our option, in whole or in part, at any time on or after February 15, 2007, on any date not less than 30 nor more than 60 days after the mailing of a redemption notice to each holder of notes to be redeemed at the address of the holder appearing in the security register, at a redemption price, payable in cash, equal to 100% of the principal amount of the notes to be redeemed plus accrued and unpaid interest (including

any liquidated damages), if any, to, but excluding, the redemption date. However, if a redemption date is an interest payment date, the semi-annual payment of interest becoming due on such date will be payable to the holder of record at the close of business on the relevant record date, and the redemption price shall not include such interest payment.

If the paying agent holds money sufficient to pay the redemption price due on a new note on the redemption date in accordance with the terms of the indenture, then, on and after the redemption date, the new note will cease to be outstanding, and interest on such new note will cease to accrue, whether or not the new note is delivered to the paying agent. Thereafter, all other rights of the holder terminate, other than the right to receive the redemption price upon delivery of the new note.

If we do not redeem all of the notes, the trustee will select the notes to be redeemed in principal amounts of \$1,000 or whole multiples of \$1,000 by lot, on a pro rata basis or in accordance with any other method the trustee considers fair and appropriate. If any notes are to be redeemed in part only, a new note or notes in principal amount equal to the unredeemed portion thereof will be issued. If a portion of a holder's notes is selected for partial redemption and the holder converts a portion of its notes, the converted portion will be deemed to be taken from the portion selected for redemption.

Change of control requires purchase of notes at the option of the holder

If a Change of Control occurs, each holder of notes will have the right to require us to repurchase all of that holder's notes not previously called for redemption, or any portion of those notes that is equal to \$1,000 or a whole multiple of \$1,000, on the date that is 45 days after the date we give notice at a repurchase price equal to 100% of the principal amount of the notes to be repurchased, together with interest (including liquidated damages, if any) accrued and unpaid to, but excluding, the repurchase date.

Instead of paying the repurchase price in cash, we may pay the repurchase price in common stock. The number of shares of common stock a holder will receive will equal the repurchase price divided by 95% of the average of the closing sale prices of our common stock for the five trading days immediately preceding and including the third trading day prior to the repurchase date. However, we may not pay the repurchase price in common stock unless we satisfy certain conditions prior to the repurchase date as provided in the indenture.

Within 30 days after the occurrence of a Change of Control, we are required to give notice to all holders of notes, as provided in the indenture, of the occurrence of the Change of Control and of their resulting repurchase right. We must also deliver a copy of our notice to the trustee. To exercise the repurchase right, a holder of notes must deliver prior to or on the 30th day after the date of our notice irrevocable written notice to the trustee of the holder's exercise of its repurchase right, together with the notes with respect to which the right is being exercised.

Under the indenture, a "Change of Control" will be deemed to have occurred at such time after the original issuance of the notes when the following has occurred:

the acquisition by any person of beneficial ownership, directly or indirectly, through a purchase, merger or other acquisition transaction or series of transactions of shares of our capital stock entitling that person to exercise 50% or more of the total voting power of all shares of our capital stock entitled to vote generally in elections of directors, other than any acquisition by us, any of our subsidiaries or any of our employee benefit plans;

our consolidation or merger with or into any other person, any merger of another person into us, or any conveyance, transfer, sale, lease or other disposition of all or substantially all of our properties and assets to another person, other than: any transaction (A) that does not result in any reclassification, conversion, exchange or cancellation of outstanding shares of our capital stock and (B) pursuant to which holders of our capital stock immediately prior to the transaction

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are entitled to exercise, directly or indirectly, 50% or more of the total voting power of all shares of our capital stock entitled to vote generally in the election of directors of the continuing or surviving person immediately after the transaction; or any merger solely for the purpose of changing our jurisdiction of incorporation and resulting in a reclassification, conversion or exchange of outstanding shares of common stock solely into shares of common stock of the surviving entity;

during any consecutive two-year period, individuals who at the beginning of that two-year period constituted our board of directors (together with any new directors whose election to our board of directors, or whose nomination for election by our stockholders, was approved by a vote of a majority of the directors then still in office who were either directors at the beginning of such period or whose election or nomination for election was previously so approved) cease for any reason to constitute a majority of our board of directors then in office; or

we are liquidated or dissolved or our stockholders pass a resolution approving a plan of liquidation or dissolution.

The beneficial owner shall be determined in accordance with Rule 13d-3 promulgated by the SEC under the Exchange Act. The term "person" includes any syndicate or group that would be deemed to be a "person" under Section 13(d)(3) of the Exchange Act.

Rule 13e-4 under the Exchange Act, as amended, requires the dissemination of certain information to security holders if an issuer tender offer occurs and may apply if the repurchase option becomes available to holders of the notes. We will comply with this rule to the extent applicable at that time.

We may, to the extent permitted by applicable law, at any time purchase the notes in the open market or by tender at any price or by private agreement. Any note so purchased by us may, to the extent permitted by applicable law, be reissued or resold or may be surrendered to the trustee for cancellation. Any notes surrendered to the trustee may not be reissued or resold and will be canceled promptly.

The foregoing provisions would not necessarily protect holders of the notes if highly leveraged or other transactions involving us that may adversely affect holders occur.

Our ability to repurchase notes upon the occurrence of a Change of Control is subject to important limitations. The occurrence of a Change of Control could cause an event of default under, or be prohibited or limited by, the terms of existing or future Senior Debt. As a result, any repurchase of the notes would, absent a waiver, be prohibited under the subordination provisions of the indenture until the Senior Debt is paid in full. Further, we cannot assure you that we would have the financial resources, or would be able to arrange financing, to pay the repurchase price for all the notes that might be delivered by holders of notes seeking to exercise the repurchase right. Any failure by us to repurchase the notes when required following a Change of Control would result in an event of default under the indenture, whether or not such repurchase is permitted by the subordination provisions of the indenture. Any such default may, in turn, cause a default under existing or future Senior Debt. See " Subordination" above.

Consolidation, merger and transfer of assets

We may, without the consent of the holders of notes, consolidate with, merge into or transfer all or substantially all of our assets to any corporation, limited liability company, partnership or trust organized under the laws of the United States or any of its political subdivisions provided that;

the surviving entity assumes all our obligations under the indenture and the notes;

at the time of such transaction, no event of default, and no event which, after notice or lapse of time, would become an event of default, shall have happened and be continuing; and

an officers' certificate and an opinion of counsel, each stating that the consolidation, merger or transfer complies with the provisions of the indenture, have been delivered to the trustee.

Information requirement

We have agreed, during any period in which we are not subject to the reporting requirements of the Exchange Act, to make available to holders of the notes, or beneficial owners of interests therein, or any prospective purchaser of the notes, the information required by Rule 144A(d)(4) of the Securities Act in connection with the sale of notes or beneficial interests in the notes. We are not required, however, to furnish such information in connection with any request made on or after the date that is two years from the later of the date such notes were last acquired by us or an affiliate.

Events of default

Each of the following constitutes an event of default under the indenture:

- (1) our failure to pay when due the principal of or premium, if any, on any of the notes at maturity, upon redemption or exercise of a repurchase right or otherwise, whether or not such payment is prohibited by the subordination provisions of the indenture;
- (2) our failure to pay an installment of interest (including liquidated damages, if any) on any of the notes for 30 days after the date when due, whether or not such payment is prohibited by the subordination provisions of the indenture;
- (3) our failure to deliver shares of common stock, together with cash instead of fractional shares, when those shares of common stock or cash instead of fractional shares are required to be delivered following conversion of a new note, and that failure continues for 10 days;
- (4) our failure to perform or observe any other term, covenant or agreement contained in the notes or the indenture for a period of 60 days after written notice of such failure, requiring us to remedy the same, shall have been given to us by the trustee or to us and the trustee by the holders of at least 25% in aggregate principal amount of the notes then outstanding;
- (5) our failure to make any payment by the end of the applicable grace period, if any, after the maturity of any Indebtedness for borrowed money in an amount in excess of \$5 million, or there is an acceleration of Indebtedness for borrowed money in an amount in excess of \$5 million because of a default with respect to such Indebtedness without such Indebtedness having been discharged or such acceleration having been cured, waived, rescinded or annulled, in either case, for a period of 30 days after written notice to us by the trustee or to us and the trustee by holders of at least 25% in aggregate principal amount of the notes then outstanding; and
- (6) certain events of our bankruptcy, insolvency or reorganization.

If an event of default specified in clause (6) above occurs and is continuing, then the principal of all the notes and the interest thereon (including liquidated damages, if any) shall automatically become immediately due and payable. If an event of default shall occur and be continuing, other than with respect to clause (6) above, the trustee or the holders of at least 25% in aggregate principal amount of the notes then outstanding may declare the notes due and payable at their principal amount together with accrued interest (including liquidated damages, if any), and thereupon the trustee may, at its discretion, proceed to protect and enforce the rights of the holders of notes by appropriate judicial proceedings. Such declaration may be rescinded and annulled with the written consent of the holders of a majority in aggregate principal amount of the notes then outstanding, subject to the provisions of the indenture.

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The holders of a majority in aggregate principal amount of notes at the time outstanding through their written consent, or the holders of a majority in aggregate principal amount of notes then outstanding represented at a meeting at which a quorum is present by a written resolution, may waive any existing default or event of default and its consequences except any default or event of default:

in any payment on the notes;

in respect of the conversion rights of the notes; or

in respect of the covenants or provisions in the indenture that may not be modified or amended without the consent of the holder of each new note affected as described in "Modification, waiver and meetings," below.

Holders of a majority in aggregate principal amount of the notes then outstanding through their written consent, or the holders of a majority in aggregate principal amount of the notes then outstanding represented at a meeting at which a quorum is present by a written resolution, may direct the time, method and place of conducting any proceeding for any remedy available to the trustee or exercising any trust or power conferred upon the trustee, subject to the provisions of the indenture. The indenture contains a provision entitling the trustee, subject to the duty of the trustee during a default to act with the required standard of care, to be indemnified by the holders of notes before proceeding to exercise any right or power under the indenture at the request of such holders. The rights of holders of the notes to pursue remedies with respect to the indenture and the notes are subject to a number of additional requirements set forth in the indenture.

The right of any holder:

to receive payment of principal, premium, if any, the Change of Control purchase price and interest (including liquidated damages, if any) in respect of the notes held by that holder on or after the respective due dates expressed in the notes;

to convert those notes;

to bring suit for the enforcement of any such payment on or after the respective due dates expressed in the notes; or

and the right to convert the notes;

will not be impaired or affected without that holder's consent.

The indenture will provide that the trustee shall, within 90 days of the occurrence of a default of which the trustee has received written notice, give to the registered holders of the notes notice of all uncured defaults known to it, but the trustee shall be protected in withholding such notice if it, in good faith, determines that the withholding of such notice is in the best interest of such registered holders, except in the case of a default in the payment of the principal of, or premium, if any, or interest (including liquidated damages, if any) on, any of the notes when due or in the payment of any redemption or repurchase obligation.

We are required to furnish annually to the trustee a statement as to the fulfillment of our obligations under the indenture. In addition, we are required to file with the trustee a written notice of the occurrence of any default or event of default within five business days of our becoming aware of the occurrence of any default or event of default.

Modification, waiver and meetings

The indenture contains provisions for convening meetings of the holders of notes to consider matters affecting their interests.

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The indenture (including the terms and conditions of the notes) may be modified or amended by us and the trustee, without the consent of the holder of any note, for the purposes of, among other things:

adding to our covenants for the benefit of the holders of notes;

surrendering any right or power conferred upon us;

providing for conversion rights of holders of notes if any reclassification or change of our common stock or any consolidation, merger or sale of all or substantially all of our assets occurs;

providing for the assumption of our obligations to the holders of notes in the case of a merger, consolidation, conveyance, transfer or lease;

reducing the conversion price, provided that the reduction will not adversely affect the interests of holders of notes in any material respect;

complying with the requirements of the SEC in order to effect or maintain the qualification of the indenture under the Trust Indenture Act of 1939, as amended;

making any changes or modifications to the indenture necessary in connection with the registration of the notes under the Securities Act as contemplated by the registration rights agreement, provided that this action does not adversely affect the interests of the holders of the notes in any material respect;

curing any ambiguity or correcting or supplementing any defective provision contained in the indenture, provided that such modification or amendment does not, in the good faith opinion of our board of directors and the trustee, adversely affect the interests of the holders of the notes in any material respect; or

desirable and which will not adversely affect the interests of the holders of notes in any material respect.

Modifications and amendments to the indenture or to the terms and conditions of the notes may also be made, and noncompliance by us with any provision of the indenture or the notes may be waived, either:

with the written consent of the holders of at least a majority in aggregate principal amount of the notes at the time outstanding; or

by the adoption of a resolution by the holders of a majority in aggregate principal amount of notes then outstanding represented at a meeting of holders at which a quorum is present.

However, no such modification, amendment or waiver may, without the written consent or the affirmative vote of the holder of each note affected:

change the maturity of the principal of or any installment of interest on any note (including any payment of liquidated damages);

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reduce the principal amount of, or any premium, if any, on any new note; reduce the interest rate or interest (including any liquidated damages) on any note;

change the currency of payment of principal of, premium, if any, or interest (including any liquidated damages) on any note;

impair the right to institute suit for the enforcement of any payment on or with respect to, or the conversion of, any note;

modify our obligations to maintain an office or agency in New York City;

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except as otherwise permitted or contemplated by provisions of the indenture concerning specified reclassifications or corporate reorganizations, adversely affect the conversion rights of holders of the notes;

adversely affect the repurchase option of holders upon a Change of Control;

modify the subordination provisions of the notes in a manner adverse to the holders of notes;

reduce the percentage in aggregate principal amount of notes outstanding necessary to modify or amend the indenture or to waive any past default; or

reduce the percentage in aggregate principal amount of notes outstanding required for the adoption of a resolution or the quorum required at any meeting of holders of notes at which a resolution is adopted.

The quorum at any meeting called to adopt a resolution will be persons holding or representing a majority in aggregate principal amount of the notes at the time outstanding.

Satisfaction and discharge

We may discharge our obligations under the indenture while notes remain outstanding, subject to certain conditions, if:

all outstanding notes will become due and payable at their scheduled maturity within one year; or

all outstanding notes are scheduled for redemption within one year,

and, in either case, we have deposited with the trustee an amount sufficient to pay and discharge all outstanding notes on the date of their scheduled maturity or the scheduled date of redemption.

Form, denomination and registration

The notes will be issued in fully registered form, without coupons, in denominations of \$1,000 principal amount and whole multiples of \$1,000.

Global Notes: Book-Entry Form. Except as provided below, the notes will be evidenced by one or more global notes deposited with the trustee as custodian for DTC, and registered in the name of Cede & Co., as DTC's nominee. The global notes and any notes issued in exchange therefor will be subject to certain restrictions on transfer set forth in the global notes and in the indenture and will bear the legend regarding such restrictions set forth under "Restrictions on transfer of the notes." Record ownership of the global notes may be transferred, in whole or in part, only to another nominee of DTC or to a successor of DTC or its nominee, except as set forth below.

A qualified institutional buyer or "QIB," as defined in the Securities Act, may hold its interests in a global note directly through DTC if such QIB is a participant in DTC, or indirectly through organizations that are direct DTC participants. Transfers between direct DTC participants will be effected in the ordinary way in accordance with DTC's rules and will be settled in same-day funds. QIBs may also beneficially own interests in the global notes held by DTC through certain banks, brokers, dealers, trust companies and other parties that clear through or maintain a custodial relationship with a direct DTC participant, either directly or indirectly.

So long as Cede & Co., as nominee of DTC, is the registered owner of the global notes, Cede & Co. will generally be considered the sole holder of the global notes. Except as provided below and in the indenture, owners of beneficial interests in the global notes will not be entitled to have certificates registered in their names, will not receive or be entitled to receive physical delivery of certificates in definitive form, and will not be considered holders thereof. The laws of some states require that certain persons take physical delivery of securities in definitive form. Consequently, the ability to transfer a beneficial interest in the global notes to such persons may be limited.

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We will wire, through the facilities of the trustee, principal, premium, if any, and interest payments on the global notes to Cede & Co., the nominee for DTC, as the registered owner of the global notes. Vertex, the trustee and any paying agent will have no responsibility or liability for paying amounts due on the global notes to owners of beneficial interests in the global notes.

It is DTC's current practice, upon receipt of any payment of principal of and premium, if any, and interest on the global notes, to credit participants' accounts on the payment date in amounts proportionate to their respective beneficial interests in the notes represented by the global notes, as shown on the records of DTC, unless DTC believes that it will not receive payment on the payment date. Payments by DTC participants to owners of beneficial interests in notes represented by the global notes held through DTC participants will be the responsibility of DTC participants, as is now the case with securities held for the accounts of customers registered in "street name."

If you would like to convert your notes into common stock pursuant to the terms of the notes, you should contact your broker or other direct or indirect DTC participant to obtain information on procedures, including proper forms and cut-off times, for submitting those requests.

Because DTC can only act on behalf of DTC participants, who in turn act on behalf of indirect DTC participants and other banks, your ability to pledge your interest in the notes represented by global notes to persons or entities that do not participate in the DTC system, or otherwise take actions in respect of such interest, may be affected by the lack of a physical certificate.

Neither Vertex nor the trustee (nor any registrar, paying agent or conversion agent under the indenture) will have any responsibility for the performance by DTC or direct or indirect DTC participants of their obligations under the rules and procedures governing their operations. DTC has advised us that it will take any action permitted to be taken by a holder of notes, including, without limitation, the presentation of notes for conversion as described below, only at the direction of one or more direct DTC participants to whose account with DTC interests in the global notes are credited and only for the principal amount of the notes for which directions have been given.

DTC has advised us as follows: DTC is a limited purpose trust company organized under the laws of the State of New York, a member of the Federal Reserve System, a "clearing corporation" within the meaning of the Uniform Commercial Code and a "clearing agency" registered pursuant to the provisions of Section 17A of the Exchange Act. DTC was created to hold securities for DTC participants and to facilitate the clearance and settlement of securities transactions between DTC participants through electronic book-entry changes to the accounts of its participants, thereby eliminating the need for physical movement of certificates. Participants include securities brokers and dealers, banks, trust companies and clearing corporations and may include certain other organizations such as the dealer manager. Certain DTC participants or their representatives, together with other entities, own DTC. Indirect access to the DTC system is available to others such as banks, brokers, dealers and trust companies that clear through, or maintain a custodial relationship with, a participant, either directly or indirectly.

Although DTC has agreed to the foregoing procedures in order to facilitate transfers of interests in the global notes among DTC participants, it is under no obligation to perform or continue to perform such procedures, and such procedures may be discontinued at any time. If DTC is at any time unwilling or unable to continue as depositary and a successor depositary is not appointed by us within 90 days, we will cause notes to be issued in definitive form in exchange for the global notes. None of Vertex, the trustee or any of their respective agents will have any responsibility for the performance by DTC, direct or indirect DTC participants of their obligations under the rules and procedures governing their operations, including maintaining, supervising or reviewing the records relating to, or payments made on account of, beneficial ownership interests in global notes.

According to DTC, the foregoing information with respect to DTC has been provided to its participants and other members of the financial community for informational purposes only and is not intended to serve as a representation, warranty or contract modification of any kind.

Certificated Notes. The notes represented by a global note will be exchangeable for notes in definitive form of like tenor as that global note in denominations of \$1,000 and in any greater amount that is an integral multiple of \$1,000 if:

DTC notifies us in writing that it is unwilling or unable to continue as depositary for that global note or if at any time DTC ceases to be a clearing agency registered under the Exchange Act and a successor depositary is not appointed by us within 90 days;

we, at our option, notify the trustee in writing that we elect to issue the notes in definitive form in exchange for all or any part of the notes represented by the global note; or

there is, or continues to be, an event of default with respect to the notes and the registrar has received a request from DTC or the holder of the global note for the issuance of definitive notes in exchange for the global note.

Any new note that is exchangeable pursuant to the preceding sentence is exchangeable for notes registered in the names which DTC will instruct the Trustee. It is expected that DTC's instructions may be based upon directions received by DTC from its participants with respect to ownership of beneficial interests in that global note. Subject to the foregoing, a global note is not exchangeable except for a global note or global notes of the same aggregate denominations to be registered in the name of DTC or its nominee.

Restrictions on Transfer; Legends. The notes will be subject to certain transfer restrictions as described under "Restrictions on transfer of the notes" and certificates evidencing the notes will bear a legend to such effect.

Notices

Except as otherwise provided in the indenture, notices to holders of notes will be given by mail to the addresses of holders of the notes as they appear in the note register.

Governing law

The indenture, the notes and the registration rights agreement will be governed by, and construed in accordance with, the law of the State of New York.

Information regarding the trustee

US Bank National Association, as trustee under the indenture, has been appointed by us as paying agent, conversion agent, registrar and custodian with regard to the notes. Equiserve Trust Company, N.A. is the transfer agent and registrar for our common stock. The trustee or its affiliates may from time to time in the future provide banking and other services to us in the ordinary course of their business.

Registration rights of holders of the notes

When we issued the notes, we entered into a registration rights agreement with the initial holders of the notes. As required under that agreement, we have filed with the Securities and Exchange Commission, at our expense, a shelf registration statement, of which this prospectus forms a part, covering resales by holders of the notes and the common stock issuable upon conversion of the notes. Under the terms of the registration rights agreement, we have agreed to use our best efforts to keep the registration statement effective until September 17, 2006 (or such earlier date when the holders of

the notes and the common stock issuable upon conversion of the notes are able to sell all such securities immediately without restriction pursuant to the volume limitation provisions of Rule 144 under the Securities Act or any successor rule thereto or otherwise).

We will provide to each registered holder copies of this prospectus and take certain other actions as are required to permit unrestricted re-sales of the notes and the common stock issuable upon conversion of the notes. A holder who sells securities pursuant to the shelf registration statement of which this prospectus forms a part generally will be required to be named as a selling stockholder in this prospectus (or a supplement or amendment to this prospectus) and to deliver this prospectus (together with any prospectus supplement or amendment) to purchasers and will be bound by the provisions of the registration rights agreement, which are applicable to that holder (including certain indemnification provisions). We may suspend the holder's use of the prospectus for a reasonable period not to exceed 45 days (60 days under certain circumstances relating to a proposed or pending material business transaction, the disclosure of which would impede our ability to consummate such transaction) in any 90-day period, and not to exceed an aggregate of 90 days in any 12-month period, if we, in our reasonable judgment, believe we may possess material non-public information the disclosure of which would have a material adverse effect on us and our subsidiaries taken as a whole. Each holder, by its acceptance of a new note, agrees to hold any communication by us regarding suspension of the holder's use of the prospectus in confidence.

If:

the registration statement of which this prospectus forms a part shall cease to be effective or fail to be usable without being succeeded within five business days by a post-effective amendment or a report filed with the SEC pursuant to the Exchange Act that cures the failure of the registration statement to be effective or usable; or

on the 45th or 60th day, as the case may be, of any period that the prospectus has been suspended as described in the preceding paragraph, such suspension has not been terminated (each, a "registration default"),

additional interest as liquidated damages will accrue on the notes, from and including the day following the registration default to but excluding the day on which the registration default has been cured. Liquidated damages will be paid semi-annually in arrears, with the first semi-annual payment due on the first interest payment date, as applicable, following the date on which such liquidated damages begin to accrue, and will accrue at a rate per year equal to:

an additional 0.25% of the principal amount to and including the 90th day following such registration default; and

an additional 0.5% of the principal amount from and after the 91st day following such registration default.

In no event will liquidated damages accrue at a rate per year exceeding 0.5%. If a holder has converted some or all of its notes into common stock, the holder will be entitled to receive equivalent amounts based on the principal amount of the notes converted.

Additional notes

Pursuant to the indenture, we may, from time to time, without the consent of the holders of the new notes, create and issue additional notes which will have terms and conditions identical to those of the new notes, except that any such additional notes may have a different issue date from the new notes, may have a different amount of interest payable on the first interest payment date after issuance than is payable on other new notes, and may have additional terms and conditions required to conform to applicable provisions of the Securities Act of 1933, as amended, or any registration rights agreement to which such additional notes are subject. No such additional terms or conditions will adversely effect the holder of any new notes.

DESCRIPTION OF CAPITAL STOCK

Vertex's authorized capital stock consists of 200,000,000 shares of common stock, \$.01 par value, and 1,000,000 shares of preferred stock, \$.01 par value.

Common Stock

As of October 22, 2004, there were 80,227,506 shares of common stock outstanding held by approximately 1,112 stockholders of record.

Holders of common stock are entitled to one vote for each share held on all matters submitted to a vote of stockholders and do not have cumulative voting rights. Accordingly, holders of a majority of the shares of common stock entitled to vote in any election of directors may elect all of the directors standing for election. Holders of common stock are entitled to receive ratably such dividends, if any, as may be declared by the Board of Directors out of funds legally available therefor, subject to any preferential dividend rights of any outstanding preferred stock. Upon the liquidation, dissolution or winding up of Vertex, the holders of common stock are entitled to receive ratably the net assets of Vertex available after the payment of all debts and other liabilities and subject to any prior rights of any outstanding preferred stock. Holders of common stock have no preemptive, subscription, redemption or conversion rights. The shares of common stock issuable upon conversion of the notes, when issued and paid for, will be, fully paid and nonassessable. The rights, preferences and privileges of holders of common stock are subject to, and may be adversely affected by, the rights of the holders of shares of any series of preferred stock that we may designate and issue in the future.

Preferred Stock

Our Board of Directors has the authority, without further action by the stockholders, to issue up to 1,000,000 shares of Preferred Stock in one or more series and to fix the rights, preferences, privileges and restrictions thereof, including dividend rights, conversion rights, voting rights, terms of redemption, liquidation preferences, sinking fund terms and the number of shares constituting any series or the designation of such series, without any further vote or action by stockholders. The issuance of Preferred Stock could adversely affect the voting power of holders of our common stock and the likelihood that such holders will receive dividend payments and payments upon liquidation and could have the effect of delaying, deferring or preventing a change in control. We have no present plan to issue any shares of Preferred Stock.

Options

As of October 22, 2004, there were outstanding options for the purchase of 16,319,075 shares of our common stock at a weighted average exercise price of \$22.57 per share. Options for the purchase of 10,846,375 shares were exercisable as of that date.

Convertible Notes

As of October 22, 2004, there were outstanding notes convertible into 894,776 shares of common stock at a conversion price of \$92.26 and 15,558,768 shares of common stock at a conversion price of \$14.94 per share.

Stockholders Rights Plan

Pursuant to our Stockholder Rights Plan, each share of common stock has an associated preferred share purchase right. Each right entitles the holder to purchase from Vertex one half of one-hundredth of a share of Series A Junior Participating Preferred Stock, \$.01 par value, of Vertex at a price of \$135 per one half of one-hundredth of a Junior Preferred Share, subject to adjustment. The rights are not

exercisable until after acquisition by a person or group of 15% or more of the outstanding common stock (an "acquiring person") or after the announcement of an intention to make or commencement of a tender offer or exchange offer the consummation of which would result in the beneficial ownership by a person or group of 15% or more of the outstanding common stock (the earlier of such dates being called the "Distribution Date"). Until a right is exercised, the holder thereof will have no rights as a stockholder of Vertex. Until the Distribution Date (or earlier redemption or expiration of the Rights), the Rights will be transferred with and only with the common stock.

If any person or group becomes an acquiring person, each holder of a right, other than rights beneficially owned by the acquiring person, will thereafter have the right to receive upon exercise that number of shares of common stock having a market value of two times the purchase price, and if Vertex is acquired in a business combination transaction or 50% or more of its assets are sold, each holder of a right will thereafter have the right to receive upon exercise that number of shares of common stock of the acquiring company which at the time of the transaction will have a market value of two times the purchase price.

At any time after any person becomes an acquiring person and prior to the acquisition by such person or group of 50% or more of the outstanding common stock, our Board of Directors may cause the rights (other than rights owned by such person or group) to be exchanged, in whole or in part, for common stock or junior preferred shares, at an exchange rate of one share of common stock per right or one half of one-hundredth of a junior preferred share per right.

At any time prior to the acquisition by a person or group of beneficial ownership of 15% or more of the outstanding common stock, our Board of Directors may redeem the rights in whole at a price of \$.01 per right.

The rights have certain anti-takeover effects, in that they will cause substantial dilution to a person or group that attempts to acquire a significant interest in Vertex on terms not approved by the Board of Directors.

Provisions of our charter and by-laws relating to a change in control

Our corporate charter and by-law provisions and Stockholder Rights Plan may discourage certain types of transactions involving an actual or potential change in control of Vertex that might be beneficial to the company or its stockholders. Our charter provides for staggered terms for the members of the Board of Directors. Our by-laws grant the directors a right to adjourn annual meetings of stockholders, and certain provisions of the by-laws may be amended only with an 80% stockholder vote.

Transfer agent and registrar

The Transfer Agent and Registrar for our common stock is EquiServe Trust Company. The Transfer Agent's address is P.O. Box 8040, Boston, MA 02266-8040, and its telephone number is 781-575-3120.

UNITED STATES FEDERAL INCOME TAX CONSIDERATIONS

The following is a discussion of the material U.S. federal income tax considerations to a U.S. holder relating to the purchase, ownership and disposition of the notes and common stock into which the notes may be converted. This discussion is based upon the Internal Revenue Code of 1986, as amended, existing and proposed Treasury Regulations, and judicial decisions and administrative interpretations thereunder, as of the date hereof, all of which are subject to change, possibly with retroactive effect. There can be no assurance that the Internal Revenue Service will not challenge one or more of the tax results described herein, and we have not obtained, nor do we intend to obtain, a ruling from the IRS with respect to the U.S. federal tax consequences of acquiring or holding notes or common stock.

This discussion does not purport to address all tax considerations that may be important to a particular U.S. holder in light of the U.S. holder's particular circumstances (such as the alternative minimum tax provisions of the Code), or to certain categories of investors (such as certain financial institutions, tax-exempt organizations, dealers in securities, persons who hold the notes or common stock as part of a hedge, conversion or constructive sale transaction, or straddle or other risk reduction transaction or persons who are not U.S. holders) that may be subject to special rules. This discussion is limited to U.S. holders of notes who hold the notes and any common stock into which the notes are converted as capital assets. This discussion also does not address the tax consequences arising under the laws of any foreign, state or local jurisdiction.

PERSONS CONSIDERING THE PURCHASE OF A NOTE SHOULD CONSULT THEIR OWN TAX ADVISORS AS TO THE PARTICULAR TAX CONSEQUENCES TO THEM OF ACQUIRING, HOLDING, CONVERTING OR OTHERWISE DISPOSING OF THE NOTES AND COMMON STOCK, INCLUDING THE EFFECT AND APPLICABILITY OF STATE, LOCAL OR FOREIGN TAX LAWS. PERSONS THAT ARE NOT UNITED STATES PERSONS (WITHIN THE MEANING OF SECTION 7701(a)(30) OF THE CODE) THAT ARE CONSIDERING THE PURCHASE OF A NOTE SHOULD CONSULT THEIR OWN TAX ADVISORS AS TO THE UNITED STATES FEDERAL INCOME TAX CONSEQUENCES OF AN INVESTMENT IN THE NOTES, INCLUDING THE POTENTIAL APPLICATION OF THE UNITED STATES WITHHOLDING TAXES.

For purposes of this discussion, the term "U.S. holder" means a beneficial owner of a note or common stock that is for U.S. federal income tax purposes:

a natural person who is a citizen or resident of the United States;

a corporation or partnership created or organized in or under the laws of the United States or any state thereof; or

an estate or trust that is a United States person (within the meaning of section 7701(a)(30) of the Code).

Tax consequences to U.S. holders

We believe that the notes and the common stock into which the notes will be converted will be treated as described below. The description below assumes, and we believe, that the possibility of our making certain payments (other than principal and stated interest) with respect to the notes is remote, and also that the possibility of an additional payment in connection with a provisional redemption does not result in the notes being treated as "contingent payment debt instruments." Persons that are considering the purchase of a note should consult their own tax advisors as to the foregoing.

Payments of interest. Payments of stated interest on a note will be includable in the income of a U.S. holder as ordinary income at the time it accrues or is received in accordance with the U.S.

holder's method of accounting for federal income tax purposes. The notes will not be treated as bearing original issue discount for federal income tax purposes.

Sale, exchange or retirement of notes. Upon the sale, exchange or retirement of a note, a U.S. holder will recognize taxable gain or loss equal to the difference between such holder's adjusted tax basis in the note and the amount realized on the sale, exchange or retirement (including any additional payment received upon a provisional redemption but excluding amounts representing interest not previously included in income). A U.S. holder's adjusted tax basis in a note will generally equal the cost of the note to such holder. In general, gain or loss realized on the sale, exchange or retirement of a note will be capital gain or loss. Prospective investors should consult their tax advisers regarding the treatment of capital gains (which may be taxed at lower rates than ordinary income for taxpayers who are individuals, trust or estates and have held their notes for more than one year) and losses (the deductibility of which is subject to limitations).

Conversion of notes. A U.S. holder's conversion of a note into common stock will generally not be a taxable event, except for (i) any cash received instead of a fractional share of common stock, as described below, and (ii) any cash received as an additional payment following conversion of a note after receiving notice of a provisional redemption, to the extent described below. The receipt of cash in lieu of a fractional share of common stock should generally result in capital gain or loss (measured by the difference between the cash received for the fractional share interest and the U.S. holder's tax basis in the fractional share interest), the taxation of which is described above in "Sale, Exchange or Retirement of Notes." Although the treatment of any cash payment that we will be required to make in connection with a provisional redemption is unclear, it is likely that you will be required to recognize gain, if any, that you realize to the extent not in excess of such cash payment. Any gain so recognized will generally be capital gain. A U.S. holder's basis in the common stock received on conversion of a note generally will be the same as the U.S. holder's basis in the note at the time of conversion, increased by the amount of gain, if any, recognized or as a result of the additional payment in connection with a provisional redemption, and reduced by the amount of such additional payment and by any tax basis allocable to a fractional share. The holding period for the common stock received on conversion will include the holding period of the note converted. If we repurchase a note in exchange for common stock after a change of control, although the matter is not entirely clear, such exchange should be treated in the same manner as a conversion of the note as described in this paragraph (except with respect to any common stock received that is attributable to accrued interest on the notes).

Ownership and disposition of common stock. Dividends, if any, paid on the common stock generally will be includable in the income of a U.S. holder as ordinary income to the extent of the U.S. holder's ratable share of our current or accumulated earnings and profits. Upon the sale or exchange of common stock, a U.S. holder generally will recognize capital gain or capital loss equal to the difference between the amount realized on such sale or exchange and the holder's adjusted tax basis in such shares. Prospective investors should consult their tax advisers regarding the treatment of capital gains (which may be taxed at lower rates than ordinary income for taxpayers who are individuals, trust or estates and have held their common stock for more than one year) and losses (the deductibility of which is subject to limitations).

Adjustment of conversion price. If at the time we make a distribution to shareholders that would be taxable to such shareholders as a dividend for federal income tax purposes (for example, distributions of evidence of indebtedness or assets, but generally not stock dividends or rights to subscribe for common stock) and, pursuant to the anti-dilution provisions of the indenture, the Conversion Price of the notes is reduced, such reduction may be deemed to represent the payment of a taxable dividend to the U.S. holders of notes in a corresponding amount. If the Conversion Price is reduced at our discretion or in certain other circumstances, such reduction also may be deemed to represent the

payment of a taxable dividend to U.S. holders of notes in a corresponding amount. Moreover, in certain other circumstances, the absence of such an adjustment to the Conversion Price of the notes may result in a taxable dividend to the holders of common stock.

Information reporting requirements and backup withholding

Information reporting will apply to payments of interest or dividends made by us on, or the proceeds of the sale or other disposition of, the notes or shares of common stock with respect to certain non-corporate U.S. holders, and backup withholding at a rate of 28% may apply unless the recipient of such payment supplies a taxpayer identification number, certified under penalties of perjury, as well as certain other information or otherwise establishes an exemption from backup withholding. Any amount withheld under the backup withholding rules is allowable as a credit against the U.S. holder's federal income tax, provided that the required information is provided to the IRS.

SELLING HOLDERS

The notes offered hereby were originally issued in a transaction completed on September 17, 2004, in which we exchanged \$79,313,000 of our 5% Convertible Notes due 2007 (referred to as our "old notes") for \$79,313,000 of our new notes. Selling holders, including their transferees, pledgees or their successors, may from time to time offer and sell any or all of the notes and the common stock into which the notes are convertible pursuant to this prospectus. The selling holders may offer all, some or none of the notes and the common stock into which the notes are convertible.

The table below sets forth information, as of October 27, 2004, as updated by information provided to us by selling holders, with respect to the selling holders and the principal amounts of notes and amounts of common stock beneficially owned by each selling holder that may be offered under this prospectus by the selling holders. The information is based on information provided by or on behalf of the selling holders. The selling holders identified below may have sold, transferred or otherwise disposed of all or a portion of their notes or common stock since the date on which they provided the information regarding their notes or common stock in transactions exempt from the registration requirements of the Securities Act.

Because the selling holders may offer all or some portion of the notes or the common stock to be offered by them, we cannot estimate the amount of the notes or our common stock that will be held by the selling holders upon completion of any sales.

No selling holder named in the table below beneficially owns 1% or more of our common stock, assuming conversion of a selling holder's notes. None of the selling holders has had any material relationship with us or our affiliates within the past three years.

| Name of security holder | Principal Amount of Notes Beneficially Owned and Offered(1) | Number of shares of Common Stock Issuable Upon Conversion of the Notes that May Be Offered |
|------------------------------|---|---|
| UBS Securities LLC | \$ 265,000 | 17,738 |
| Unidentified Securityholders | \$ 79,048,000 | 5,291,062 |

- (1) The number of securities beneficially owned is determined under the rules of the Securities and Exchange Commission and the information is not necessarily indicative of beneficial ownership for any other purpose. Under those rules, beneficial ownership includes any securities as to which the individual has sole or shared voting power or investment power and also any securities which the individual has the right to acquire within 60 days after the date the selling holder provided this information, through the exercise of any stock option or other right. The inclusion in the table of securities, however, does not constitute an admission that the selling holders are direct or indirect beneficial owners of those securities. The selling holders have sole voting power and investment power with respect to all securities of capital stock listed as owned by the selling holders.

PLAN OF DISTRIBUTION

The selling holders and their successors, including their transferees, pledgees or donees or their successors, may sell the notes and our common stock into which the notes are convertible directly to purchasers or through underwriters, broker-dealers or agents, who may receive compensation in the form of discounts, concessions or commissions from the selling holders or the purchasers. These discounts, concessions or commissions as to any particular underwriter, broker-dealer or agent may be in excess of those customary in the types of transactions involved.

The notes and common stock issuable upon conversion of the notes may be sold in one or more transactions at fixed prices, at prevailing market prices at the time of sale, at prices related to the prevailing market prices, at varying prices determined at the time of sale, or at negotiated prices. These sales may be effected in transactions, which may involve crosses or block transactions:

on any national securities exchange or U.S. inter-dealer system of a registered national securities association on which the notes or our common stock may be listed or quoted at the time of sale;

in the over-the-counter market;

otherwise than on these exchanges or systems or in the over-the-counter market;

through the writing of options, whether the options are listed on an options exchange or otherwise; or

through the settlement of short sales.

In connection with the sale of the notes and common stock issuable upon conversion of the notes, the selling holders may enter into hedging transactions with broker-dealers or other financial institutions, which may in turn engage in short sales of the notes or common stock in the course of hedging the positions they assume. The selling holders may also sell the notes or common stock issuable upon conversion of the notes short and deliver these securities to close out their short positions, or loan or pledge the notes or common stock to broker-dealers that in turn may sell these securities.

The aggregate proceeds to the selling holders from the sale of the notes or common stock offered by them will be the purchase price of the notes or common stock less discounts and commissions, if any. Each of the selling holders reserves the right to accept and, together with their agents from time to time, to reject, in whole or in part, any proposed purchase of notes or common stock to be made directly or through agents. We will not receive any of the proceeds from the sales by the selling holders.

Our common stock is quoted on the Nasdaq National Market under the symbol "VRTX." The notes are currently eligible for trading on the PORTAL market. However, we do not intend to list the notes for trading on any national securities exchange or on the Nasdaq National Market and can give no assurance about the development of any trading market for the notes.

In order to comply with the securities laws of some states, if applicable, the notes and common stock may be sold in these jurisdictions only through registered or licensed brokers or dealers. In addition, in some states the notes and common stock may not be sold unless they have been registered or qualified for sale or an exemption from registration or qualification requirements is available and is complied with.

The selling holders and any underwriters, broker-dealers or agents that participate in the sale of the notes and common stock may be "underwriters" within the meaning of Section 2(11) of the Securities Act. Any discounts, commissions, concessions or profit they earn on any resale of the shares may be underwriting discounts and commissions under the Securities Act. Selling holders who are "underwriters" within the meaning of Section 2(11) of the Securities Act will be subject to the

prospectus delivery requirements of the Securities Act. The selling holders have acknowledged that they understand their obligations to comply with the provisions of the Exchange Act and the rules thereunder relating to stock manipulation, particularly Regulation M.

In addition, any securities covered by this prospectus which qualify for sale pursuant to Rule 144 or Rule 144A of the Securities Act may be sold under Rule 144 or Rule 144A rather than under this prospectus. A selling holder may not sell any notes or common stock described in this prospectus and may not transfer, devise or gift these securities by other means not described in this prospectus.

To the extent required, the specific notes or shares of our common stock to be sold, the names of the selling holders, the respective purchase prices and public offering prices, the names of any agent, dealer or underwriter, and any applicable commissions or discounts with respect to a particular offer will be set forth in an accompanying prospectus supplement or, if appropriate, a post-effective amendment to the registration statement of which this prospectus is a part.

We entered into a resale registration rights agreement for the benefit of holders of the notes to register their notes and our common stock under applicable federal and state securities laws under specific circumstances and at specific times. The registration rights agreement provides for cross-indemnification of the selling holders and us and our respective directors, officers and controlling persons against specific liabilities in connection with the offer and sale of the notes and our common stock, including liabilities under the Securities Act. We will pay substantially all of the expenses incurred by the selling holders of incident to their offering and sale of the notes and our common stock. We estimate that our total expenses of the offering of the notes and common stock will be approximately \$1,805,604.

LEGAL MATTERS

Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, PC have passed upon the legality of the issuance of the notes and the shares of common stock offered in this prospectus on our behalf.

EXPERTS

The financial statements incorporated in this prospectus by reference to the Annual Report on Form 10-K for Vertex Pharmaceuticals Incorporated for the year ended December 31, 2003 filed with the Securities and Exchange Commission on March 15, 2004 have been so incorporated in reliance on the report of PricewaterhouseCoopers LLP, an independent registered public accounting firm, given on the authority of said firm as experts in auditing and accounting.

WHERE YOU CAN FIND MORE INFORMATION

We are subject to the information and reporting requirements of the Exchange Act, as amended, under which we file periodic reports, proxy statements and other information with the Securities and Exchange Commission. Copies of the reports, proxy statements and other information may be examined without charge at the Public Reference Room of the Securities and Exchange Commission, 450 Fifth Street, N.W. Room 1024, Washington, D.C. 20549 or on the Internet at www.sec.gov. Please call the Securities and Exchange Commission at 1-800-SEC-0330 for further information about the Public Reference Room.

The Company's internet address is www.vrtx.com. The Company's annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K, and all amendments to those reports are also available to you free of charge through the "Investors" section of our website as soon as reasonably practicable after those materials have been electronically filed with, or furnished to, the Securities and Exchange Commission. Other than the documents filed with the Securities and Exchange

Commission and incorporated by reference into this prospectus, the information contained on our website does not constitute a part of this prospectus.

We have agreed that if, at any time that the notes or the common stock issuable upon conversion of the notes are "restricted securities" within the meaning of the Securities Act and we are not subject to the information reporting requirements of the Exchange Act, we will furnish to holders of the notes and such common stock and to prospective purchasers designated by them the information required to be delivered pursuant to Rule 144A(d)(4) under the Securities Act to permit compliance with Rule 144A in connection with resales of the notes and such common stock.

INCORPORATION OF CERTAIN DOCUMENTS BY REFERENCE

The Securities and Exchange Commission allows us to "incorporate" into this prospectus information that we file with the SEC in other documents. This means that we can disclose important information to you by referring to other documents that contain that information. The information incorporated by reference is considered to be part of this prospectus. Information contained in this prospectus and information that we file with the SEC in the future and incorporate by reference in this prospectus automatically updates and supersedes previously filed information. We incorporate by reference the documents listed below and any future filings we make with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act, prior to the sale of all the notes and shares of our common stock covered by this prospectus; provided, however, that we are not incorporating any information furnished, but not filed, on any current report on Form 8-K.

1. Our Annual Report on Form 10-K for the year ended December 31, 2003 (Commission File No. 000-19319), filed with the Commission on March 15, 2004, as amended by our Amended Annual Report on Form 10-K/A for the year ended December 31, 2003, filed with the Commission on September 8, 2004 (Commission File No. 000-19319).
2. Our Quarterly Report on Form 10-Q for the quarter ended March 31, 2004 (Commission File No. 000-19319), filed with the Commission on May 10, 2004.
3. Our Quarterly Report on Form 10-Q for the quarter ended June 30, 2004 (Commission File No. 000-19319).
4. Our Current Report on Form 8-K (Commission File No. 000-19319), filed with the Commission on February 3, 2004.
5. Our Current Report on Form 8-K (Commission File No. 000-19319), filed with the Commission on February 13, 2004.
6. Our Current Report on Form 8-K (Commission File No. 000-19319), filed with the Commission on February 23, 2004.
7. Our Current Report on Form 8-K (Commission File No. 000-19319), filed with the Commission on May 10, 2004.
8. Our Current Report on Form 8-K (Commission File No. 000-19319), filed with the Commission on July 2, 2004, as amended by our Amended Current Report on Form 8-K/A (Commission File No. 000-19319), filed with the Commission on September 10, 2004.
9. Our Current Report on Form 8-K (Commission File No. 000-19319), filed with the Commission on July 19, 2004, as amended by our Amended Current Report on Form 8-K/A (Commission File No. 000-19319), filed with the Commission on September 10, 2004.
10. Our Current Report on Form 8-K (Commission File No. 000-19319), filed with the Commission on September 17, 2004.

11. Our Current Report on Form 8-K (Commission File No. 000-19319), filed with the Commission on October 13, 2004.
12. Our Definitive Proxy Statement filed with the SEC on March 25, 2004, as amended on March 30, 2004.
13. The description of our common stock contained in our Registration Statement on Form 8-A, as that description is amended from time to time.

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

Corporate Communications
Vertex Pharmaceuticals Incorporated
130 Waverly Street
Cambridge, MA 02139-4242
Telephone: (617) 444-6100

PART II
INFORMATION NOT REQUIRED IN PROSPECTUS

ITEM 14. OTHER EXPENSES OF ISSUANCE AND DISTRIBUTION.

The following table sets forth the various expenses to be incurred in connection with the registration of the securities being registered hereby, all of which will be borne by Vertex Pharmaceuticals Incorporated (except any underwriting discounts and commissions and expenses incurred by the selling stockholders for brokerage, accounting, tax or legal services or any other expenses incurred by the selling stockholders in disposing of the notes or the shares). All amounts shown are estimates except the Securities and Exchange Commission registration fee.

| | | |
|------------------------------|----|-----------|
| SEC registration fee | \$ | 10,049 |
| Legal fees and expenses | \$ | 296,459 |
| Accounting fees and expenses | \$ | 75,000 |
| Printing fees | \$ | 15,500 |
| Miscellaneous expenses | \$ | 1,408,596 |

ITEM 15. INDEMNIFICATION OF DIRECTORS AND OFFICERS.

Part D of Article 6 of the Restated 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 Bylaws 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 Bylaws, 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 of otherwise and whether or not the Registrant would have the power to indemnify the person against such liability.

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

Sections 8.30 and 8.92 of the MBCA provide that if an officer or director discharges his duties in good faith and with the care that a person in a like position would reasonably exercise under similar circumstances and in a manner the officer or director reasonably believes to be in the best interests of the corporation, he or she will not be liable for such actions.

ITEM 16. EXHIBITS.

| Exhibit Number | Description |
|-------------------|--|
| 4.1 | Indenture dated as of September 17, 2004 between the Registrant and US Bank National Association, as Trustee, including therein the forms of the notes (filed as Exhibit 10.2 to our Current Report on Form 8-K filed September 17, 2004 (SEC File No. 000-19319) and incorporated herein by reference). |
| 4.2 | Resale Registration Rights Agreement dated as of September 17, 2004, among the Registrant and UBS Securities LLC (filed as Exhibit 10.3 to our Current Report on Form 8-K filed September 17, 2004 (SEC File No. 000-19319) and incorporated herein by reference). |
| 5.1 | Opinion of Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, PC with respect to the legality of the securities being registered. |
| 12.1 | Computation of Ratio of Earnings to Fixed Charges, June 30, 2004 |
| 23.1 | Consent of PricewaterhouseCoopers LLP |
| 23.2 | Consent of Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, PC, included in Exhibit 5.1 |
| 24.1 | Powers of Attorney (on signature page) |
| 25 | Form T-1 Statement of Eligibility under the Trust Indenture Act of US Bank National Association |

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 this 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 this Registration Statement. Notwithstanding the foregoing, any increase or decrease in the 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 20 percent change in the maximum aggregate offering price set forth in the "Calculation of Registration Fee" table in the effective Registration Statement; and
 - (iii) To include any material information with respect to the plan of distribution not previously disclosed in this Registration Statement or any material change to such information in this Registration Statement;

PROVIDED, HOWEVER, that paragraphs (1)(i) and (1)(ii) do not apply if the information required to be included is a post-effective amendment by those paragraphs is contained in periodic reports filed by the Company 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 purposes of determining any liability under the Securities Act, each post-effective amendment that contains a form of prospectus shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at the 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.

The Registrant hereby undertakes that, for purposes of determining any liability under the Securities Act, each filing of the Registrant's annual report pursuant to Section 13(a) or 15(d) of the Exchange Act (and, where applicable, each filing of an employee benefit plan's annual report pursuant to Section 15(d) of the Exchange Act) 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 the time shall be deemed to be the initial bona fide offering thereof.

Insofar as indemnification for liabilities arising under the Securities Act may be permitted to directors, officers and controlling persons of the Registrant pursuant to the indemnification provisions described herein, or otherwise, the Registrant has been advised that in the opinion of the Securities and Exchange Commission such indemnification is against public policy as expressed in the Securities Act 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 Securities 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 Commission under Section 305(b)(2) of the Trust Indenture Act.

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SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, as amended, the Registrant certifies that it has reasonable grounds to believe that it meets all of the requirements for filing on Form S-3 and has duly caused this Registration Statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of Cambridge, The Commonwealth of Massachusetts, on October 28, 2004.

VERTEX PHARMACEUTICALS INCORPORATED

By: /s/ JOSHUA S. BOGER

Joshua S. Boger
Chairman of the Board of Directors and
Chief Executive Officer

Pursuant to 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 dated indicated.

The registrant and each person whose signature appears below constitutes and appoints Joshua S. Boger, Vicki L. Sato, Ian F. Smith and Kenneth S. Boger, and each of them singly, his, her or its true and lawful attorneys-in-fact and agents, with full power of substitution and resubstitution, for him, her or it and in his, her or its name, place and stead, in any and all capacities, to sign and file (i) any and all amendments (including post-effective amendments) to this Registration Statement, with all exhibits thereto, and other documents in connection therewith, and (ii) a registration statement, and any and all amendments thereto, relating to the offering covered hereby filed pursuant to Rule 462(b) under the Securities Act of 1933, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing requisite or necessary to be done in and about the premises, as fully to all intents and purposes as he, she, or it might or could do in person, hereby ratifying and confirming all that said attorneys-in-fact and agents or any of them, or their or his substitute or substitutes, may lawfully do or cause to be done by virtue hereof.

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Pursuant to 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 dated indicated.

| Name | Title | Date |
|---|---|------------------|
| <u>/s/ JOSHUA S. BOGER</u> Joshua S. Boger | Director, Chairman and Chief Executive Officer (Principal Executive Officer) | October 28, 2004 |
| <u>/s/ IAN F. SMITH</u> Ian F. Smith | Senior Vice President and Chief Financial Officer (Principal Financial Officer) | October 28, 2004 |
| <u>/s/ JOHANNA MESSINA POWER</u> Johanna Messina Power | Controller (Principal Accounting Officer) | October 28, 2004 |
| <u>/s/ ERIC K. BRANDT</u> Eric K. Brandt | Director | October 28, 2004 |
| <u>/s/ ROGER W. BRIMBLECOMBE</u> Roger W. Brimblecombe | Director | October 28, 2004 |
| <u>/s/ STUART J.M. COLLINSON</u> Stuart J.M. Collinson | Director | October 28, 2004 |
| <u>/s/ MATTHEW W. EMMENS</u> Matthew W. Emmens | Director | October 28, 2004 |
| <u>/s/ BRUCE I. SACHS</u> Bruce I. Sachs | Director | October 28, 2004 |
| <u>/s/ CHARLES A. SANDERS</u> Charles A. Sanders | Director | October 28, 2004 |
| <u>/s/ EVE E. SLATER</u> Eve E. Slater | Director | October 28, 2004 |
| <u>/s/ ELAINE S. ULLIAN</u> | Director | October 28, 2004 |

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Name

Title

Date

Elaine S. Ullian

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| Exhibit Number | Description |
|---------------------------|--|
| 4.1 | Indenture dated as of September 17, 2004 between the Registrant and US Bank National Association, as Trustee, including therein the forms of the notes (filed as Exhibit 10.2 to our Current Report on Form 8-K filed September 17, 2004 (SEC File No. 000-19319) and incorporated herein by reference). |
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