VERTEX PHARMACEUTICALS INC / MA
Form S-3ASR
March 13, 2009

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As filed with the Securities and Exchange Commission on March 13, 2009

Registration No. 333-

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM S-3

REGISTRATION STATEMENT
UNDER
THE SECURITIES ACT OF 1933

VERTEX PHARMACEUTICALS INCORPORATED

(Exact name of registrant as specified in its charter)

Massachusetts	**04-3039129**
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification Number)

130 Waverly Street
Cambridge, Massachusetts 02139
(617) 444-6100

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

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

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

With a copies to:

Michael L. Fantozzi, Esq.	**Kenneth S. Boger, Esq.**
Mintz, Levin, Cohn, Ferris,	**Senior Vice President and General Counsel**
Glovsky and Popeo, P.C.	**Vertex Pharmaceuticals Incorporated**
One Financial Center	**130 Waverly Street**
Boston, Massachusetts 02111	**Cambridge, Massachusetts 02139**
(617) 542-6000	**(617) 444-6100**

Approximate Date of Commencement of Proposed Sale to the Public: From time to time after the effective date of this registration statement.

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

If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, check the following box: ý

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. o

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. o

If this Form is a registration statement pursuant to General Instruction I.D. or a post-effective amendment thereto that shall become effective upon filing with the Commission pursuant to Rule 462(e) under the Securities Act, check the following box: ý

If this Form is a post-effective amendment to a registration statement filed pursuant to General Instruction I.D. filed to register additional securities or additional classes of securities pursuant to Rule 413(b) under the Securities Act, check the following box: o

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

Large accelerated filer ý	Accelerated filer o	Non-accelerated filer o (Do not check if a smaller reporting company)	Smaller reporting company o

CALCULATION OF REGISTRATION FEE

Title of Each Class of Securities to be Registered	**Amount to Be Registered**	**Proposed Maximum Offering Price Per Unit(2)**	**Proposed Maximum Aggregate Offering Price**	**Amount of Registration Fee**
Common Stock, $.01 par value per share(1)	10,733,527	$28.04	$300,968,097	$11,828

(1) Each share of common stock includes a right to purchase series A junior participating preferred stock of the Registrant, which are initially attached to and trade with the shares of the common stock being registered hereby. No separate consideration will be received for these rights.

(2) Estimated solely for the purpose of calculating the registration fee pursuant to Rule 457(c) under the Securities Act of 1933, as amended, based upon the average of the high and low prices for the common stock of the Registrant, on March 11, 2009, as reported on the Nasdaq Global Select Market.

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PROSPECTUS

VERTEX PHARMACEUTICALS INCORPORATED

10,733,527 SHARES

COMMON STOCK

This prospectus relates to the resale from time to time of a total of up to 10,733,527 shares of our common stock by certain of our stockholders. Such selling stockholders will be identified in one or more supplements to this prospectus to be filed with the Securities and Exchange Commission. The shares were issued to the selling stockholders in connection with our acquisition of ViroChem Pharma Inc., or ViroChem, on March 12, 2009. This prospectus relates to registration of the resale of the shares issued in the acquisition pursuant to the resale registration rights agreement by and among us and such holders.

The selling stockholders may offer and sell any of the shares of common stock from time to time at fixed prices, at market prices or at negotiated prices, and may engage a broker, dealer or underwriter to sell the shares. For additional information on the possible methods of sale that may be used by the selling stockholders, you should refer to the section entitled "Plan of Distribution" on page 27 of this prospectus. We will not receive any proceeds from the sale of the shares of common stock by the selling stockholders.

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

Our common stock is listed on the Nasdaq Global Select Market under the symbol "VRTX." On March 11, 2009, the last reported sale price for our common stock was $27.15 per share.

You should consider carefully the risks that we have described in "Risk Factors" beginning on page 3 of this prospectus before deciding whether to invest in our common stock.

Neither the Securities and Exchange Commission nor any state securities commission 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 March 13, 2009.

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ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement on Form S-3 that we filed with the Securities and Exchange Commission, or the SEC, utilizing a "shelf" registration process. Pursuant to this prospectus and any related prospectus supplements, the selling stockholders named in the prospectus supplements may sell up to a total of 10,733,527 shares of our common stock. This prospectus, any related prospectus supplement and the documents incorporated by reference herein include important information about us, the common stock being offered and other information you should know before investing. This prospectus does not contain all of the information included in the registration statement. For a more complete understanding of any offering of our common stock pursuant to this prospectus, you should refer to the registration statement, including its exhibits. The prospectus supplement may also add, update or change information contained in this prospectus. You should read both this prospectus and the applicable prospectus supplement together with additional information under the headings "Available Information" and "Incorporation by Reference." To the extent there are inconsistencies between any prospectus supplement, this prospectus and any documents incorporated by reference, the document with the most recent date will control. You should rely only on information contained in, or incorporated by reference into, this prospectus and any prospectus supplement. We have not authorized anyone to provide you with information different from that contained in, or incorporated by reference into, this prospectus. The information contained in this prospectus is accurate only as of the date on the front cover of the prospectus and information we have incorporated by reference in this prospectus is accurate only as of the date of the document incorporated by reference. You should not assume that the information contained in, or incorporated by reference into, this prospectus is accurate as of any other date.

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AVAILABLE INFORMATION

We are a public company and are required to file annual, quarterly and current reports, proxy statements and other information with the SEC pursuant to the Securities Exchange Act of 1934, as amended, or the Exchange Act. You may read and copy any document we file at the SEC's Public Reference Room at 100 F Street, N.E., Washington, D.C. 20549. You can request copies of these documents by writing to the SEC and paying a fee for the copying cost. Please call the SEC at 1-800-SEC-0330 for more information about the operation of the public reference room. Our SEC filings are also available to the public on the SEC's website at *www.sec.gov*. The information on the SEC's website or any other website is not part of this prospectus, and any references to this website or any other website are inactive textual references only. In addition, our stock is listed for trading on the Nasdaq Global Select Market. You can read and copy reports and other information concerning us at the offices of the Financial Industry Regulatory Authority located at 1735 K Street, Washington, D.C. 20006.

We filed a registration statement on Form S-3 under the Securities Act of 1933, as amended, or the Securities Act, with the SEC with respect to the common stock being offered pursuant to this prospectus. This prospectus is only part of the registration statement and omits certain information contained in the registration statement, as permitted by the SEC. You should refer to the registration statement, including the exhibits, for further information about us and the common stock being offered pursuant to this prospectus and any related prospectus supplement. Statements in this prospectus and any related prospectus supplement regarding the provisions of certain documents filed with, or incorporated by reference in, the registration statement are not necessarily complete and each statement is qualified in all respects by that reference. You may:

inspect a copy of the registration statement, including the exhibits and schedules, without charge at the public reference room;

obtain a copy from the SEC upon payment of the fees prescribed by the SEC; or

obtain a copy from the SEC website.

Our internet address is *www.vrtx.com*. Our annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K, and all amendments to those reports are also available to you free of charge through the "Finances/Investor Info" section of our website as soon as reasonably practicable after those materials have been electronically filed with, or furnished to, the SEC. Other than the documents filed with the SEC and incorporated by reference into this prospectus, the information contained on our website does not constitute a part of this prospectus.

INCORPORATION BY REFERENCE

The SEC allows us to "incorporate by reference" information that we file with them. Incorporation by reference allows us to disclose important information to you by referring you to those other documents. The information incorporated by reference is an important part of this prospectus, and any information incorporated by reference is considered part of this prospectus. Any reports filed by us with the SEC after the date of this prospectus and before the date that the offering of common stock by means of this prospectus is terminated will automatically update and, where applicable, supersede any information contained in this prospectus or incorporated by reference in this prospectus. We incorporate by reference into this prospectus the following documents or information filed with the SEC (other than, in each case, documents or information therein deemed to have been furnished and not filed in accordance with SEC rules):

(a) Our Annual Report on Form 10-K for the year ended December 31, 2008 (filing date February 17, 2009: Commission File No. 000-19319);

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(b) Our Current Reports on Form 8-K filed on March 13, 2009, March 9, 2009, February 19, 2009, February 10, 2009 and January 15, 2009 (with respect to Item 1.01 only) (Commission File No. 000-19319);

(c) The portions of our definitive proxy statement on Schedule 14A that are deemed "filed" with the SEC under the Securities Exchange Act of 1934, as amended (filing date April 8, 2008: Commission File No. 000-19319); and

(d) The description of our common stock and the outstanding series A junior participating preferred stock purchase rights contained in our Registration Statement on Form 8-A, including any amendment or report filed for the purpose of updating such description (filing date May 30, 1991: Commission File No. 000-19319).

In addition, all documents filed by us pursuant to Section 13(a), 13(c), 14 or 15(d) of the Exchange Act on or after the date of this prospectus and before the termination of offerings under this prospectus are deemed to be incorporated by reference into, and to be a part of, this prospectus.

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

Vertex Pharmaceuticals Incorporated
130 Waverly Street
Cambridge, Massachusetts 02139
Attn: Investor Relations
(617) 444-6100

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SUMMARY

This summary highlights information contained elsewhere in this prospectus or incorporated by reference in this prospectus. This summary does not contain all of the information that you should consider before deciding to invest in our common stock. You should read this entire prospectus carefully, including the "Risk Factors" section contained in this prospectus and our consolidated financial statements and the related notes and the other documents incorporated by reference in this prospectus, together with the additional information about us described in the sections entitled "Available Information" and "Incorporation by Reference," before purchasing our common stock. Unless we have indicated otherwise, or the context otherwise requires, references in this prospectus or the documents incorporated by reference herein and therein to "we," "us," "our," "Vertex," and the "Company," or similar terms are to Vertex Pharmaceuticals Incorporated, a Massachusetts corporation, and its subsidiaries.

Business Overview

We are in the business of discovering, developing and commercializing small molecule drugs for the treatment of serious diseases. Telaprevir, our lead drug candidate, is an oral hepatitis C protease inhibitor and one of the most advanced of a new class of antiviral treatments in clinical development that targets hepatitis C virus, or HCV, infection. Telaprevir is being evaluated in a fully-enrolled registration program focused on treatment-naïve and treatment-experienced patients with genotype 1 HCV. We currently intend to file a new drug application, or NDA, for telaprevir in the United States in the second half of 2010, assuming the successful completion of our ongoing registration program. We also are developing, among other compounds, VX-770, a drug candidate for the treatment of patients with cystic fibrosis, or CF. In the first half of 2009, we expect to begin a registration program for VX-770 that focuses on CF patients with the G551D mutation in the gene responsible for CF.

We have built a drug discovery capability that integrates biology, pharmacology, biophysics, chemistry, automation and information technologies in a coordinated manner, with the goal of more efficiently identifying promising drug candidates to address significant unmet medical needs. Using our drug discovery capability we have identified, among other drug candidates: telaprevir; VX-770; VX-813 and VX-985, two additional HCV protease inhibitors; VX-809, a drug candidate designed for patients with CF; and VX-509, a Janus Kinase 3, or JAK3, inhibitor that targets immune-mediated inflammatory diseases, or IMID. We intend to continue to invest in our research programs with the goal of adding promising new compounds to our drug development pipeline. We also co-discovered fosamprenavir calcium, an HIV protease inhibitor that is being marketed by GlaxoSmithKline plc as Lexiva in the United States and Telzir in Europe.

On March 12, 2009, we acquired ViroChem, a privately-held biotechnology company organized under the laws of Canada. ViroChem has two HCV polymerase inhibitors, VCH-222 and VCH-759, which are currently in Phase 1 clinical development. We expect to begin clinical evaluation of novel combination regimens of our HCV protease inhibitor telaprevir, currently in Phase 3 clinical development, with VCH-222 and/or VCH-759 in the second half of 2009. The acquisition was structured as a share purchase transaction among us, our wholly-owned subsidiary, Vertex Pharmaceuticals (Canada) Incorporated, ViroChem, the shareholders of ViroChem, and a representative of certain of the securityholders of ViroChem. We purchased all of the issued and outstanding securities of ViroChem from its former shareholders and paid an aggregate purchase price of $100 million in cash and 10,733,527 shares of our common stock.

We were incorporated in Massachusetts in 1989. Our principal executive offices are located at 130 Waverly Street, Cambridge, Massachusetts 02139. Our telephone number is (617) 444-6100.

"Vertex" and the Vertex logo in the form appearing on the cover page of this prospectus are registered trademarks of Vertex. Other brands, names and trademarks contained in this prospectus or the documents incorporated by reference herein and therein are the property of their respective owners.

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The Offering

Securities offered by the selling stockholders	Up to 10,733,527 shares of our common stock.
Use of proceeds	We will not receive any proceeds from the sale of the common stock offered by this prospectus.
Nasdaq Global Select Market Symbol	VRTX

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RISK FACTORS

Investing in our common stock involves a high degree of risk. You should carefully consider the following risk factors and all other information contained in this prospectus and incorporated by reference herein before purchasing our common stock. The risks and uncertainties described below are not the only ones facing us. Additional risks and uncertainties that we are unaware of, or that we currently deem immaterial, also may become important factors that affect us. If any of such risks or the risks described below occur, our business, financial condition or results of operations could be materially and adversely affected. In that case, the trading price of our common stock could decline, and you may lose some or all of your investment. You should also consider the risks, uncertainties and assumptions discussed under the heading "Risk Factors" included in our most recent annual report on Form 10-K, which is on file with the SEC and is incorporated herein by reference, and which may be amended, supplemented or superseded from time to time by other reports we file with the SEC in the future.

Risks Related to Our Business

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

We have incurred significant operating losses each year since our inception, including net losses of $459.9 million, $391.3 million and $206.9 million during 2008, 2007 and 2006, respectively, and expect to incur a significant operating loss in 2009. We expect to incur operating losses until we are able to obtain approval for and successfully commercialize telaprevir, because we are continuing to incur significant operating expenses as we continue the late-stage development of our advanced drug candidates, including telaprevir and VX-770, and continue to invest in research activities. As a result, we believe that it is likely that our expenses will exceed our revenues at least until we begin receiving substantial product revenues. There can be no assurance that any of our drug candidates will be approved or, if approved, will be commercially successful. Our net losses have had and will continue to have an adverse effect on, among other things, our stockholders' equity, total assets and working capital. 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 ever.

WE DEPEND HEAVILY ON THE SUCCESS OF OUR LEAD DRUG CANDIDATE, TELAPREVIR, WHICH IS STILL UNDER DEVELOPMENT. IF WE ARE UNABLE TO COMMERCIALIZE TELAPREVIR, OR EXPERIENCE DELAYS IN DOING SO, OUR BUSINESS WILL BE MATERIALLY HARMED.

We are investing a substantial portion of our personnel and financial resources in the development of telaprevir, and we believe that a significant portion of the value of our company relates to the commercial potential of telaprevir. The clinical development and commercial success of telaprevir will depend on several factors, including the following:

- successful completion of clinical trials with favorable outcomes relative to current standards of care and future competitive therapies;
- receipt and timing of marketing approvals for telaprevir from the United States Food and Drug Administration, or FDA, and similar foreign regulatory authorities;
- receipt and timing of marketing approvals from the FDA and similar foreign regulatory authorities for products being developed for the treatment of HCV by our competitors, including Schering-Plough's boceprevir;
- additional discussions with the FDA and similar foreign authorities regarding the scope and design of our clinical trials, the quality of our manufacturing process for telaprevir and our clinical trial results;

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establishing and maintaining commercial manufacturing arrangements for telaprevir with third-party manufacturers that are subject to extensive regulation by the FDA, and successfully monitoring those manufacturing operations to ensure they meet our standards and those of regulatory authorities, including the FDA, that extensively monitor pharmaceutical manufacturing facilities;

our ability to establish telaprevir if approved, as a significant component of any oral combination therapies that may be approved as a treatment for HCV;

launching commercial sales of telaprevir by us and our collaborators;

the efficacy and other characteristics, including the side effect profile, of telaprevir relative to existing and future treatments for HCV;

our ability to increase awareness of the benefits of early treatment for HCV if telaprevir is approved, and to increase the rates of diagnosis of currently undiagnosed patients with HCV infection; and

acceptance of telaprevir by patients, and in the medical community and with third-party payors.

If the data from our ongoing clinical trials or non-clinical studies regarding the safety or efficacy of telaprevir are not favorable, we may be forced to delay or terminate the clinical development of telaprevir, which would materially harm our business. Further, even if we gain marketing approvals from the FDA and comparable foreign regulatory authorities in a timely manner, we cannot be sure that telaprevir will be commercially successful in the pharmaceutical market. If the results of clinical trials of telaprevir, the anticipated or actual timing of marketing approvals for telaprevir, or the market acceptance of telaprevir, if approved, including treatment reimbursement levels agreed to by third-party payors, do not meet the expectations of investors or public market analysts, the market price of our common stock would likely decline.

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

We expect to incur substantial expenses as we design and develop existing and future compounds, undertake clinical trials of drug candidates resulting from such compounds, and build our drug supply, regulatory, development and commercial capabilities. We also expect to incur substantial administrative and commercialization expenses in the future. In particular, we expect the continuing development and commercialization of telaprevir to require additional capital beyond our current resources. We anticipate that we will finance these substantial cash needs with some combination of:

public offerings or private placements of our debt or equity securities or other methods of financing;

cash received from our existing collaborative agreements;

cash received from future collaborative agreements;

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

future product sales.

While we believe that our current cash, cash equivalents and marketable securities would be sufficient to fund our operations for the next twelve months, we may raise additional capital through public offerings or private placements of our debt or equity securities. Any such capital transactions may or may not be similar to the transactions that we have completed in the past. Any equity financings could result in dilution to

our then-existing security holders. Any debt financing may be on terms that, among other things, restrict our ability to pay interest and dividends although we do not intend to pay dividends for the foreseeable future. If adequate funds are not available on acceptable terms, or at all, we may be required to curtail significantly or discontinue one or more of our research, drug discovery or development programs, including clinical trials, incur significant cash exit costs, or

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attempt to obtain funds through arrangements with collaborators or others that may require us to relinquish rights to certain of our technologies, drugs or drug candidates. Based on many factors, including general economic conditions, additional financing may not be available on acceptable terms, if at all.

ALL OF OUR DRUG CANDIDATES REMAIN SUBJECT TO CLINICAL TESTING AND REGULATORY APPROVAL. IF WE ARE UNABLE TO SUCCESSFULLY DEVELOP AND TEST OUR DRUG CANDIDATES, WE WILL NOT BE SUCCESSFUL.

The success of our business depends primarily upon our ability, and our collaborators' ability, to develop and commercialize our drug candidates, including telaprevir, successfully. Due to the development efforts of our competitors, in order to be successful in a therapeutic area it is often necessary to develop follow-on compounds and/or develop new combination therapies. Our drug candidates are in various stages of development and must satisfy rigorous standards of safety and efficacy before they can be approved by the FDA or other regulatory authorities for sale. To satisfy these standards, we and/or our collaborators must allocate our resources among our various development programs and must engage in expensive and lengthy testing of our drug candidates. These discovery and development efforts for a new pharmaceutical product, including follow-on compounds, are resource-intensive, and may take 10 to 15 years or more. Despite our efforts, our drug candidates may not:

offer therapeutic or other improvement over existing competitive drugs;

be proven safe and effective in clinical trials;

meet applicable regulatory standards;

be capable of being produced in commercial quantities at acceptable costs; or

if approved for commercial sale, be successfully marketed as pharmaceutical products.

Positive results in preclinical studies of a drug candidate may not be predictive of similar results in humans during clinical trials, and promising results from earlier clinical trials of a drug candidate may not be replicated in later clinical trials. Findings, including toxicology findings, in nonclinical studies conducted concurrently with clinical trials could result in abrupt changes in our development activities, including the possible cessation of development activities associated with a particular drug candidate or program. Furthermore, results from our clinical trials may not meet the level of statistical significance required by the FDA or other regulatory authorities for approval of a drug candidate.

We and many other companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late-stage clinical trials even after achieving promising results in earlier-stage clinical trials. Accordingly, the results from the completed preclinical studies and clinical trials and ongoing clinical trials for our drug candidates may not be predictive of the results we may obtain in later stage trials, and may not be predictive of the likelihood of approval of a drug candidate for commercial sale. In addition, from time to time, we report interim data from our clinical trials, including with respect to telaprevir data regarding patients' HCV RNA levels during treatment, at the end-of-treatment or 12 weeks after completing treatment. Interim data are subject to change, and there can be no assurances that interim data will be confirmed upon the analysis of final data. In addition, interim data with respect to a patient's HCV RNA levels may not be predictive of the final SVR rates that will be achieved in the clinical trial.

IF WE ARE UNABLE TO OBTAIN UNITED STATES AND/OR FOREIGN REGULATORY APPROVAL, WE WILL BE UNABLE TO COMMERCIALIZE OUR DRUG CANDIDATES.

Our drug candidates are subject to extensive governmental regulations relating to their development, clinical trials, manufacturing and commercialization. Rigorous preclinical testing and

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clinical trials and an extensive regulatory approval process are required in the United States and in most other countries prior to the commercial sale of our drug candidates. Satisfaction of these and other regulatory requirements is costly, time consuming, uncertain and subject to unanticipated delays. It is possible that none of the drug candidates we are developing independently, or in collaboration with others, will be approved for marketing.

We have limited experience in conducting and managing the late-stage clinical trials necessary to obtain regulatory approvals, including approval by the FDA. The time required to complete clinical trials and to satisfy the FDA and other countries' regulatory review processes is uncertain and typically takes many years. Our analysis of data obtained from preclinical and clinical activities is subject to confirmation and interpretation by regulatory authorities, which could delay, limit or prevent regulatory approval. We may also encounter unanticipated delays or increased costs due to government regulation from future legislation or administrative action or changes in FDA policy during the period of drug development, clinical trials and FDA regulatory review.

Any delay in obtaining or failure to obtain required approvals could materially adversely affect our ability to successfully commercialize any drug candidate. Furthermore, any regulatory approval to market a drug may be subject to limitations that we do not currently expect on the indicated uses for which we may market the drug. Any such limitations could limit the size of the market for the drug.

We are also subject to numerous foreign regulatory requirements governing the conduct of clinical trials, manufacturing and marketing authorization, pricing and third-party reimbursement. The foreign regulatory approval process includes all of the risks associated with the FDA approval process described above, as well as risks attributable to the satisfaction of foreign requirements. Approval by the FDA does not ensure approval by regulatory authorities outside the United States. Foreign jurisdictions may have different approval procedures than those required by the FDA and may impose additional testing requirements for our drug candidates.

WE ARE INVESTING SIGNIFICANT RESOURCES IN OUR DEVELOPMENT PROGRAM FOR VX-770, BASED PRIMARILY ON DATA FROM A RELATIVELY SMALL CLINICAL TRIAL IN WHICH PATIENTS RECEIVED VX-770 OVER A SHORT DURATION. IF WE ARE UNABLE TO SHOW THE SAFETY AND EFFICACY OF VX-770, OR EXPERIENCE DELAYS IN DOING SO, OUR BUSINESS COULD BE MATERIALLY HARMED.

We are increasing the resources that we are investing in the development of VX-770 and expect to begin a registration program for VX-770 focused on CF patients with the G551D mutation in the first half of 2009. We are initiating this registration program based primarily on data from a Phase 2a clinical trial of VX-770 in 39 patients with CF, in which patients received VX-770 over 14-day and 28-day periods. In order to receive approval for VX-770, we will need to show that it is safe and effective in a larger number of patients than were involved in the Phase 2a clinical trial over significantly longer dosing periods. In addition, our registration program for VX-770 will include two pediatric patient populations in which VX-770 has not previously been studied. Since a substantial portion of the CF population is under age 18, VX-770 potential commercial success will be dependent on not only being able to obtain approval for adult patients, but also for pediatric patients. If we are unable to show the safety and efficacy of VX-770, or experience delays in doing so, our business could be materially harmed.

WE MAY NOT BE SUCCESSFUL IN DEVELOPING ANY OF THE DRUG CANDIDATES WE RECENTLY ACQUIRED FROM VIROCHEM AND, AS A RESULT, MAY NOT REALIZE ANY BENEFITS OF THIS ACQUISITION.

In March 2009, we acquired ViroChem, a privately-held biotechnology company organized under the laws of Canada, for $100 million in cash and 10,733,527 shares of our common stock. We acquired ViroChem primarily in order to acquire two HCV polymerase inhibitors, VCH-222 and VCH-759, as

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part of our strategy to pursue drug candidates that could potentially be developed in combination with telaprevir or our earlier-stage protease inhibitors. VCH-222 and VCH-759 are still in Phase 1 clinical development and have only been evaluated in preclinical studies and in a limited number of patients with HCV. While we believe the data from the clinical trials to date, together with studies in animal models and in vitro data, support the development of combination therapies, there are numerous reasons why we may not be able to successfully develop a combination involving either VCH-222 or VCH-759, including:

- data from trials involving drug candidates separately may not be predictive of results involving drug candidates dosed in combination, including as a result of unforeseen drug interactions; and

- positive results in small clinical trials and preclinical studies may not be predictive of results in clinical trials involving large numbers of patients.

There can be no assurance that we will be able to successfully develop either VCH-222 or VCH-759 in combination with telaprevir or our other HCV protease inhibitors, or at all, and if we are not successful in developing VCH-222 or VCH-759, we are unlikely to realize any benefits from our recently completed acquisition.

ISSUANCES 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, including the shares that may be sold by the selling stockholders pursuant to this prospectus, could adversely affect the price of our common stock. In addition, the issuance of restricted common stock or common stock upon exercise of any outstanding option would be dilutive, and may cause the market price for a share of our common stock to decline. As of March 9, 2009, we had approximately 162.2 million shares of common stock issued and outstanding. As of March 9, 2009, we also had outstanding options to purchase approximately 18.7 million shares of common stock with a weighted-average exercise price of $29.81 per share and 12.4 million shares of common stock issuable upon conversion of our outstanding 2013 Notes at a conversion price of approximately $23.14 of aggregate principal amount per share. Outstanding vested options could be exercised if the market price of our common stock exceeds the applicable exercise price. In addition, we may issue additional common stock or restricted securities in the future as part of our financing activities or business development activities and any such issuances may have a dilutive effect on existing shareholders.

IF WE ACQUIRE OR LICENSE TECHNOLOGIES, RESOURCES OR DRUG CANDIDATES, WE WILL INCUR A VARIETY OF COSTS AND MAY NEVER REALIZE BENEFITS FROM THE TRANSACTION.

If appropriate opportunities become available, we might attempt to license or acquire technologies, resources and drugs or drug candidates, including potentially complimentary HCV therapies. The process of negotiating the license or acquisition might result in operating difficulties and expenditures and, whether or not any such transaction is ever consummated, might require significant management attention that would otherwise be available for ongoing development of our business. Moreover, even if we complete a license or other transaction, we might never realize the anticipated benefits of the transaction. Future licenses or acquisitions could result in potentially dilutive issuances of equity securities, the incurrence of debt, contingent liabilities, or impairment expenses related to goodwill, and impairment or amortization expenses related to other intangible assets, which could harm our financial condition.

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

As of December 31, 2008, we had outstanding $287.5 million in aggregate principal amount of 2013 Notes. The level of our indebtedness could affect 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; or
- requiring the dedication of substantial cash to service the semi-annual interest payments on our outstanding debt, thereby reducing the amount of cash available for other purposes.

THE RESULTS FROM OUR CLINICAL DEVELOPMENT ACTIVITIES AND THE CLINICAL DEVELOPMENT ACTIVITIES OF OUR COMPETITORS ARE RELEASED PERIODICALLY, AND HAVE OFTEN RESULTED IN SIGNIFICANT VOLATILITY IN THE PRICE OF OUR COMMON STOCK.

We, our collaborators and our competitors periodically provide updates regarding drug development programs typically through press releases, conference calls and presentations at medical conferences. These periodic updates often include interim or final results from clinical trials conducted by us, our collaborators or our competitors and/or information about our or our competitor's expectations regarding future clinical development of our drug candidates or potentially competitive drugs or drug candidates. The timing of the release of information by us regarding our drug development programs is often beyond our control and is influenced by when we receive data from our clinical trials and by the general preference among pharmaceutical companies to disclose clinical data during medical conferences. In addition, because clinical trials of drug candidates for the treatment of HCV often occur over two years, the information that we, our collaborators and our competitors disclose is often based on interim data and subject to significant interpretation by investors. Any new information regarding our drug candidates or potentially competitive drugs or drug candidates, and in particular any new information regarding telaprevir and potentially competitive HCV drug candidates, can substantially affect investors' perceptions regarding our future prospects.

IF CLINICAL TRIALS FOR OUR DRUG CANDIDATES ARE PROLONGED OR DELAYED, WE MAY BE UNABLE TO COMMERCIALIZE OUR DRUG CANDIDATES ON A TIMELY BASIS, WHICH WOULD REQUIRE US TO INCUR ADDITIONAL COSTS, WOULD DELAY OUR RECEIPT OF ANY PRODUCT REVENUE AND COULD HARM OUR COMPETITIVE POSITION.

We cannot predict whether or not we will encounter problems with any of our completed, ongoing or planned clinical trials that will cause us or regulatory authorities to delay or suspend clinical trials, or delay the analysis of data from our completed or ongoing clinical trials. Any of the following could delay the clinical development of our drug candidates:

- ongoing discussions with the FDA or comparable foreign authorities regarding the scope or design of our clinical trials and the number of clinical trials we must conduct;
- delays in receiving or the inability to obtain required approvals from Institutional Review Boards at one or more of the institutions at which a clinical trial is conducted or other reviewing entities at clinical sites selected for participation in our clinical trials;

delays in enrolling volunteers or patients into clinical trials, including as a result of low numbers of patients that meet the eligibility criteria for the trial;

a lower than anticipated retention rate of volunteers or patients in clinical trials;

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the need to repeat clinical trials as a result of inconclusive results or unforeseen complications in testing;

inadequate supply or deficient quality of drug candidate materials or other materials necessary for the conduct of our clinical trials;

unfavorable FDA inspection and review of a manufacturing facility for a drug candidate or its relevant manufacturing records or a clinical trial site or records of any clinical or preclinical investigation;

serious and unexpected drug-related side effects experienced by participants in our clinical trials; or

the placement by the FDA of a clinical hold on a trial.

Our clinical trials of telaprevir involve the administration of telaprevir with interferon and ribavirin, and in the future may include one of our newly-acquired HCV polymerase inhibitors VCH-222 or VCH-759. Any clinical trial that calls for the administration of two or more drugs or drug candidates involves an increased potential for adverse events that might not be observed if only one drug or drug candidate were involved. The occurrence of adverse events may be particularly unpredictable if the clinical trial treatment regimen includes more than one investigational drug candidate, which could be the case with any clinical trial involving telaprevir and another compound that is a specifically targeted antiviral therapy for HCV, or STAT-C, such as VCH-222 or VCH-759. In the case of an unexpected adverse event in any combination therapy clinical trial, it may be difficult to attribute the adverse event to a particular drug or drug candidate administered in the clinical trial, which could result in a delay due to regulatory requirements for further testing or adverse labeling for either or both of the combination drugs, or other consequences that could delay or hinder registration.

Our ability to enroll patients in our clinical trials in sufficient numbers and on a timely basis will be subject to a number of factors, including the size of the patient population, the nature of the protocol, the proximity of patients to clinical sites, the availability of effective treatments for the relevant disease, the number of other clinical trials competing for patients in the same indication and the eligibility criteria for the clinical trial. In addition, subjects may drop out of our clinical trials or may be lost to follow-up medical evaluation after treatment ends, and this could possibly impair the validity or statistical significance of the trials. Delays in patient enrollment or unforeseen drop-out rates may result in increased costs and longer development times. 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 for which we have no financial support from a collaborator.

We, our collaborators, the FDA or other applicable regulatory authorities may suspend clinical trials of a drug candidate at any time if we or they believe the subjects or patients participating in such clinical trials are being exposed to unacceptable health risks or for other reasons. Any such suspension could materially adversely affect the development of a particular drug candidate and our business.

In addition, it is impossible to predict whether legislative changes will be enacted, or whether FDA regulations, guidance or interpretations will be changed, or what the impact of such changes, if any, may be. If we experience any such problems, we may not have the financial resources to continue development of the drug candidate that is affected or the development of any of our other drug candidates. Any delay in the approval of any of our drug candidates, including telaprevir, could have a material adverse impact on our ability to effectively commercialize the drug candidate after approval if one or more of our competitors are able to bring competing therapies to market before or in closer proximity to our drug candidates.

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IF WE ARE UNABLE TO DEVELOP EFFECTIVE INDEPENDENT SALES AND MARKETING CAPABILITIES OR ESTABLISH THIRD-PARTY RELATIONSHIPS FOR THE COMMERCIALIZATION OF OUR DRUG CANDIDATES, WE WILL NOT BE ABLE TO SUCCESSFULLY COMMERCIALIZE OUR DRUG CANDIDATES, AND IN PARTICULAR TELAPREVIR, EVEN IF WE ARE ABLE TO OBTAIN REGULATORY APPROVAL.

We currently have limited experience as a company in sales and marketing or with respect to pricing and obtaining adequate third-party reimbursement for drugs. We will need to either develop marketing capabilities and an independent sales force or enter into arrangements with third parties to sell and market our drug candidates, if they are approved for sale by regulatory authorities.

In order to market telaprevir in North America if it is approved, we intend to build a marketing organization and a specialized sales force, which will require substantial efforts and significant management and financial resources. In addition, if VX-770 is approved, we would also need to establish a small sales force in North America and Europe for VX-770. While we intend to stage our commitments to the extent possible in consideration of the development timelines, in order to support an effective launch of telaprevir, we will need to make significant financial commitments to our marketing organization prior to receiving regulatory approval. We will need to devote significant effort, in particular, to recruiting individuals with experience in the sales and marketing of pharmaceutical products. Competition for personnel with these skills is very high and may be particularly difficult for us since telaprevir is still an investigational drug candidate and we will be competing with companies that are currently marketing successful drugs. As a result, we may not be able to successfully develop our own marketing capabilities or independent sales force for telaprevir in North America in order to support an effective launch of telaprevir if it is approved for sale.

We have granted commercialization rights to other pharmaceutical companies with respect to certain of our drug candidates in specific geographic locations, including telaprevir, Aurora kinase inhibitors and AVN-944 (VX-944). To the extent that our collaborators have commercial rights to our drugs, any revenues we receive from any approved drugs will depend primarily on the sales and marketing efforts of others. We do not know whether we will be able to enter into additional third-party sales and marketing arrangements with respect to any of our other drug candidates on acceptable terms, if at all, or whether we will be able to leverage the sales and marketing capabilities we intend to build for telaprevir in order to market and sell any other drug candidate if it is approved for sale.

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

Our drug candidates in development may not be able to compete effectively with drugs that are currently on the market or new drugs that may be developed by others. No assurances can be given that telaprevir will be approved for marketing prior to competing therapies, including Schering-Plough's boceprevir, or at all. There are many other companies developing drugs for the same indications that we are pursuing in development in particular for the treatment of HCV infection. In order to compete successfully in these areas, we must demonstrate improved safety, efficacy and ease of manufacturing and gain market acceptance over competing drugs that may receive regulatory approval before or after our drug candidates, and over those that currently are marketed. Many of our competitors, including major pharmaceutical companies such as Schering-Plough, GlaxoSmithKline, Wyeth, Pfizer, Roche, Amgen, Novartis and Johnson & Johnson possess substantially greater financial, technical and human resources than we possess. In addition, many of our competitors have significantly greater experience than we have in conducting preclinical and nonclinical testing and human clinical trials of drug candidates, scaling up manufacturing operations and obtaining regulatory approvals of drugs and manufacturing facilities. Accordingly, our competitors may succeed in obtaining regulatory approval for drugs more rapidly than we do. If we obtain regulatory approval and launch commercial sales of our

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drug candidates, we also will compete with respect to manufacturing efficiency and sales and marketing capabilities, areas in which we currently have limited experience.

We are aware of a number of companies that are developing new treatments for HCV infection including protease inhibitor compounds like telaprevir, such as Schering-Plough's boceprevir, polymerase inhibitor compounds and advanced interferons. Even if we are able to obtain marketing approval for telaprevir, it is possible that one or more of these therapies could be approved prior to or shortly after we obtain such approval for telaprevir, which we believe may negatively impact telaprevir sales.

IF PHYSICIANS, PATIENTS AND THIRD-PARTY PAYORS DO NOT ACCEPT OUR FUTURE DRUGS, WE MAY BE UNABLE TO GENERATE SIGNIFICANT REVENUE, IF ANY.

Even if our drug candidates obtain regulatory approval, they may not gain market acceptance among physicians, patients and health care payors. We believe that effectively marketing telaprevir will require substantial efforts, both prior to launch and after approval. Physicians may elect not to recommend our drugs for a variety of reasons including:

- the anticipated market introduction of competitive drugs;
- lower demonstrated clinical safety and efficacy compared to other drugs;
- lack of cost-effectiveness;
- lack of availability of reimbursement from third-party payors;
- convenience and ease of administration;
- prevalence and severity of adverse side effects;
- other potential advantages of alternative treatment methods; and
- ineffective marketing and distribution support.

If our approved drugs fail to achieve market acceptance, we will not be able to generate significant revenue.

IF THE GOVERNMENT AND OTHER THIRD-PARTY PAYORS FAIL TO PROVIDE COVERAGE AND ADEQUATE PAYMENT RATES FOR OUR FUTURE DRUGS, OUR REVENUE AND PROSPECTS FOR PROFITABILITY WILL BE HARMED.

In both domestic and foreign markets, our sales of any future drugs will depend in part upon the availability of reimbursement from third-party payors. Such third-party payors include government health programs such as Medicare, managed care providers, private health insurers and other organizations. These third-party payors are increasingly attempting to contain health care costs by demanding price discounts or rebates and limiting both the types and variety of drugs that they will cover and the amounts that they will pay for these drugs. As a result, they may not cover or provide adequate payment for our future drugs. We might need to conduct post-marketing studies in order to demonstrate the cost-effectiveness of any future drugs to such payors' satisfaction. Such studies might require us to commit a significant amount of management time and financial and other resources. Our future drugs might not ultimately be considered cost-effective. Adequate third-party reimbursement might not be available to enable us to maintain price levels sufficient to realize an appropriate return on investment in product development.

Reimbursement rates may vary according to the use of the drug and the clinical setting in which it is used, may be based on payments allowed for lower-cost products that are already reimbursed, may be incorporated into existing payments for other products or services, and may reflect budgetary

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constraints and/or imperfections in Medicare or Medicaid data used to calculate these rates. Net prices for drugs may be reduced by mandatory discounts or rebates required by government health care programs. In addition, legislation has been introduced in Congress that, if enacted, would permit more widespread importation of drugs from foreign countries into the United States, which may include importation from countries where the drugs are sold at lower prices than in the United States. Such legislation, or similar regulatory changes or relaxation of laws that restrict imports of drugs from other countries, could reduce the net price we receive for our marketed drugs.

IF OUR PROCESSES AND SYSTEMS ARE NOT COMPLIANT WITH REGULATORY REQUIREMENTS, WE COULD BE SUBJECT TO DELAYS IN FILING NDAs OR RESTRICTIONS ON MARKETING OF DRUGS AFTER THEY HAVE BEEN APPROVED.

We currently are developing drug candidates for regulatory approval for the first time since our inception, and are in the process of implementing regulated processes and systems required to obtain and maintain regulatory approval for our drug candidates. Certain of these processes and systems for conducting clinical trials and manufacturing material must be compliant with regulatory requirements before we can apply for regulatory approval for our drug candidates. These processes and systems will be subject to continual review and periodic inspection by the FDA and other regulatory bodies. If we are unable to achieve compliance in a timely fashion, or if compliance issues are identified at any point in the development and approval process, we may experience delays in filing for regulatory approval for our drug candidates, or delays in obtaining regulatory approval after filing. In addition, any later discovery of previously unknown problems or safety issues with approved drugs or manufacturing processes, or failure to comply with regulatory requirements, may result in restrictions on such drugs or manufacturing processes, withdrawal of drugs from the market, the imposition of civil or criminal penalties or a refusal by the FDA and/or other regulatory bodies to approve pending applications for marketing approval of new drugs or supplements to approved applications, any of which could have a material adverse effect on our business. In addition, we are a party to agreements that transfer responsibility for complying with specified regulatory requirements, such as filing and maintenance of marketing authorizations and safety reporting or compliance with manufacturing requirements, to our collaborators and third-party manufacturers. If our collaborators or third-party manufacturers do not fulfill these regulatory obligations, any drugs for which we or they obtain approval may be withdrawn from the market, which would have a material adverse effect on our business.

IF WE OBTAIN REGULATORY APPROVALS, OUR DRUG CANDIDATES WILL BE SUBJECT TO ONGOING REGULATORY REVIEW. IF WE FAIL TO COMPLY WITH CONTINUING UNITED STATES AND APPLICABLE FOREIGN REGULATIONS, WE COULD LOSE THOSE APPROVALS, AND OUR BUSINESS WOULD BE SERIOUSLY HARMED.

If we receive regulatory approval of any drug candidates that we are developing, we will be subject to continuing regulatory review, including the review of clinical results that are reported after our drug candidates become commercially available, approved drugs. Drugs are more widely used by patients once approval has been obtained, therefore side effects and other problems may be observed after approval that were not seen or anticipated during pre-approval clinical trials. In addition, the manufacturers and the manufacturing facilities we engage to make any of our drug candidates will also be subject to periodic review and inspection by the FDA. The subsequent discovery of previously unknown problems with the drug, manufacturers or manufacturing facilities may result in restrictions on the drug, manufacturers or manufacturing facilities, including withdrawal of the drug from the market or our inability to use the facilities to make our drug. If we fail to comply with applicable continuing regulatory requirements, we may be subject to fines, suspension or withdrawal of regulatory approval, product recalls and seizures, operating restrictions and criminal prosecutions.

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OUR DRUG DEVELOPMENT EFFORTS ARE DATA-DRIVEN AND THEREFORE POTENTIALLY SUBJECT TO ABRUPT CHANGES IN EXPECTED OUTCOMES.

Small molecule drug discovery and development involve, initially, the identification of chemical compounds that may have promise as treatments for specific diseases. Once identified as drug candidates, compounds are subjected to years of testing in a laboratory setting, in animals and in humans. Our ultimate objective is to determine whether the drug candidates have physical characteristics, both intrinsically and in animal and human systems, and a toxicological profile, that are compatible with clinical and commercial success in treatment of the disease being targeted. Throughout this process, experiments are conducted and data are gathered that could reinforce a decision to move to the next step in the investigation process for a particular drug candidate, could result in uncertainty over the proper course to pursue, or could result in the termination of further drug development efforts with respect to the compound being evaluated. We monitor the results of our discovery research and our nonclinical studies and clinical trials and regularly evaluate and re-evaluate our portfolio investments with the objective of balancing risk and potential return in view of new data and scientific, business and commercial insights. This process can result in relatively abrupt changes in focus and priority as new information comes to light and we gain additional insights into ongoing programs and potential new programs.

WE DEPEND ON OUR COLLABORATORS TO WORK WITH US TO DEVELOP, MANUFACTURE AND COMMERCIALIZE MANY OF OUR DRUG CANDIDATES.

We have granted development and commercialization rights to telaprevir to Janssen (worldwide other than North America and Far East) and to Mitsubishi Tanabe (Far East). We expect to receive significant financial support under our Janssen collaboration agreement, as well as meaningful technical and manufacturing contributions to the telaprevir program. The success of some of our key in-house programs, such as for telaprevir, is dependent upon the continued financial and other support that our collaborators have agreed to provide.

For some drug candidates on which we are not currently focusing our development efforts, we have granted worldwide rights to a collaborator, as in our collaborations with Merck & Co., Inc. and Avalon Pharmaceuticals, Inc.

The success of our collaborations depends on the efforts and activities of our collaborators. Each of our collaborators has significant discretion in determining the efforts and resources that it will apply to the collaboration. Our existing collaborations may not be scientifically or commercially successful, and we may fail in our attempts to establish further collaborations to develop our drug candidates on acceptable terms.

The risks that we face in connection with these existing and any future collaborations include the following:

Our collaboration agreements are subject to termination under various circumstances, including, as in the case of our agreements with Janssen and Merck, termination without cause. Any such termination could have an adverse material effect on our financial condition and/or delay the development and commercial sale of our drug candidates, including telaprevir.

Our collaborators may change the focus of their development and commercialization efforts or may have insufficient resources to effectively develop our drug candidates. Pharmaceutical and biotechnology companies historically have re-evaluated their development and commercialization priorities following mergers and consolidations, which have been common in recent years in these industries. The ability of some of our drug candidates to reach their potential could be limited if our collaborators decrease or fail to increase development or commercialization efforts related to those drug candidates.

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Our collaboration agreements may have the effect of limiting the areas of research and development that we may pursue, either alone or in collaboration with third parties.

Our collaborators may develop and commercialize, either alone or with others, drugs that are similar to or competitive with the drugs or drug candidates that are the subject of the collaboration with us.

IF WE ARE UNABLE TO ATTRACT AND RETAIN COLLABORATORS FOR THE DEVELOPMENT AND COMMERCIALIZATION OF OUR DRUGS AND DRUG CANDIDATES, WE MAY NOT BE ABLE TO FULLY FUND OUR DEVELOPMENT AND COMMERCIALIZATION ACTIVITIES.

Our collaborators have agreed to fund portions of our pharmaceutical development programs and/or to conduct the development and commercialization of specified drug candidates and, if they are approved, drugs. In exchange, we have given them technology and sales and marketing rights relating to those drugs and drug candidates. Some of our corporate collaborators have rights to control the planning and execution of drug development and clinical programs including for our Aurora kinase inhibitor drug candidates and AVN-944 (VX-944). Our collaborators 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 our collaborators were to terminate its relationship with us, or fail to meet its contractual obligations, that action could have a material adverse effect on our ability to develop, manufacture and market any drug candidates being developed under the collaboration and could adversely affect our revenues and net loss. As part of our ongoing strategy, we expect to seek additional collaborative arrangements, which may not be available to us on favorable terms, or at all, to develop and commercialize our drug candidates in the future. We plan to seek a collaborator for our JAK3 inhibitors, including VX-509. No assurance can be given that these efforts will be successful. Even if we are able to establish acceptable collaborative arrangements in the future, these collaborations may not be successful.

OUR INVESTMENT IN THE CLINICAL DEVELOPMENT AND MANUFACTURE OF A COMMERCIAL SUPPLY OF TELAPREVIR MAY NOT RESULT IN ANY BENEFIT TO US IF TELAPREVIR IS NOT APPROVED FOR COMMERCIAL SALE.

We are investing significant resources in the clinical development of telaprevir. Telaprevir is the first drug candidate for which we expect to perform all activities related to late-stage development, drug supply, registration and commercialization in a major market. We are planning for and investing significant resources now in preparation for application for marketing approval, commercial supply and sales and marketing. We also are incurring significant costs to obtain telaprevir commercial supply, including $17.4 million in 2008 and $75.4 million in 2007. Our engagement in these resource-intensive activities puts significant investment at risk if we do not obtain regulatory approval and successfully commercialize telaprevir in North America. There is no assurance that our development of telaprevir will lead successfully to regulatory approval, or that obtaining regulatory approval will lead to commercial success. If telaprevir is not approved for commercial sale or if its development is delayed for any reason, our full investment in telaprevir may be at risk, we may face significant costs to dispose of unusable inventory, and our business and financial condition could be materially adversely affected.

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WE DEPEND ON THIRD-PARTY MANUFACTURERS, INCLUDING SOLE SOURCE SUPPLIERS, TO MANUFACTURE CLINICAL TRIAL MATERIALS FOR CLINICAL TRIALS AND EXPECT TO CONTINUE TO RELY ON THEM TO MEET OUR COMMERCIAL SUPPLY NEEDS FOR ANY DRUG CANDIDATE THAT IS APPROVED FOR SALE. WE MAY NOT BE ABLE TO ESTABLISH OR MAINTAIN THESE RELATIONSHIPS AND COULD EXPERIENCE SUPPLY DISRUPTIONS OUTSIDE OF OUR CONTROL.

We currently rely on a worldwide network of third-party manufacturers to manufacture and distribute our drug candidates for clinical trials, and we expect that we will continue to do so to meet our commercial supply needs for these drugs, including telaprevir, if they are approved for sale. As a result of our reliance on these third-party manufacturers and suppliers, including sole source suppliers of certain components of our drug candidates, we may be subject to significant supply disruptions outside of our control. Our supply chain for sourcing raw materials and manufacturing drug product ready for distribution is a multi-step international endeavor in which we rely on third-party contract manufacturers in Asia, for the supply of raw materials, and in the European Union and the United States for the application of specific manufacturing processes for the conversion of raw materials into drug substance and drug substance into final dosage form. Establishing and managing this global supply chain requires significant financial commitments, experienced personnel and the creation or expansion of numerous third-party contractual relationships. There can be no assurance that we will be able to establish and maintain commercial supply chains on commercially reasonable terms, or at all, in order to support a timely launch of telaprevir or any of our other drug candidates.

We currently require for our own use, and are responsible to Janssen and Mitsubishi Tanabe for, a supply of telaprevir for clinical trials in North America, the European Union and the Far East, respectively. We will require a supply of telaprevir for sale in North America if we are successful in obtaining marketing approval. We are in the process of transferring technical information regarding the manufacture of telaprevir to Janssen so that Janssen will be able to manufacture telaprevir, if approved, for sale in Janssen's territories and as a secondary supply source of drug substance for us. While we believe there are multiple third parties capable of providing most of the materials and services we need in order to manufacture and distribute telaprevir, and supply of materials which cannot be second-sourced can be managed with inventory planning, there is a risk that we may underestimate or overestimate demand, and the manufacturing capacity, for which we planned and contracted with third-party manufacturers, may not be sufficient or may result in more inventory than is necessary. In addition, because of the significant lead times involved in our supply chain for telaprevir, we may have less flexibility to adjust our supply in response to changes in demand than if we had shorter lead times.

We currently require a supply of VX-770 for clinical trials in North America and Europe, and will require a supply of VX-770 for sale in North America and Europe, if we are successful in obtaining marketing approval. We are manufacturing VX-770 through our third-party manufacturer network to meet our clinical supply needs and are focused on completing the technical development work and commercial formulation of VX-770. Over the next several years, we will need to expand our relationships with the third-party manufacturers that comprise our supply chain for telaprevir or establish new relationships with third-party manufacturers in order to establish a supply chain for VX-770 and support the potential commercial launch and subsequent commercial supply of VX-770.

Even if we successfully establish arrangements with third-party manufacturers, supply disruptions may result from a number of factors including shortages in product raw materials, labor or technical difficulties, regulatory inspections or restrictions, shipping or customs delays or any other performance failure by any third-party manufacturer on which we rely.

Any supply disruptions could impact the timing of our clinical trials and the commercial launch of any approved pharmaceutical drugs. Furthermore, we may be required to modify our production methods to permit us to economically manufacture our drugs for commercial launch and sale. These

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modifications may require us to re-evaluate our resources and the resources of our third-party manufacturers, which could result in abrupt changes in our production methods and supplies. Upon approval of a pharmaceutical drug for sale, if any, we similarly may be at risk of supply chain disruption for our commercial drug supply. In the course of its services, a contract manufacturer may develop process technology related to the manufacture of our drug candidates that the manufacturer owns, either independently or jointly with us. This would increase our reliance on that manufacturer or require us to obtain a license from that manufacturer in order to have our products manufactured by other suppliers utilizing the same process.

WE RELY ON THIRD PARTIES TO CONDUCT OUR CLINICAL TRIALS, AND THOSE THIRD PARTIES MAY NOT PERFORM SATISFACTORILY, INCLUDING FAILING TO MEET ESTABLISHED DEADLINES FOR THE COMPLETION OF SUCH TRIALS.

We do not have the ability to independently conduct clinical trials for our drug candidates, and we rely on third parties such as contract research organizations, to help manage our clinical trial process and on medical institutions and clinical investigators to enroll qualified patients and conduct our clinical trials. Our reliance on these third parties for clinical development activities reduces our control over these activities. Accordingly, these third-party contractors may not complete activities on schedule, or may not conduct our clinical trials in accordance with regulatory requirements or our trial design. If these third parties do not successfully carry out their contractual duties or meet expected deadlines, we may be required to replace them. Although we believe that there are a number of other third-party contractors we could engage to continue these activities, it may result in a delay of the affected trial. If clinical trials are not conducted in accordance with our contractual expectations or regulatory requirements, action by regulatory authorities might significantly and adversely affect the conduct or progress of these trials. Accordingly, our efforts to obtain regulatory approvals for and commercialize our drug candidates could be delayed.

RISKS ASSOCIATED WITH OUR INTERNATIONAL BUSINESS RELATIONSHIPS COULD MATERIALLY ADVERSELY AFFECT OUR BUSINESS.

We have manufacturing, collaborative and clinical trial relationships, and we and our collaborators are seeking approval for our drug candidates, outside the United States. In addition, we expect that if telaprevir is approved for commercial sale, a significant portion of our commercial supply chain, including sourcing of raw materials and manufacturing, will be located in Asia and the European Union. Consequently, we are, and will continue to be, subject to risks related to operating in foreign countries. Risks associated with conducting operations in foreign countries include:

- differing regulatory requirements for drug approvals in foreign countries;
- unexpected changes in tariffs, trade barriers and regulatory requirements;
- economic weakness, including inflation, or political instability in particular foreign economies and markets;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;
- foreign taxes, including withholding of payroll taxes;
- foreign currency fluctuations, which could result in increased operating expenses or reduced revenues, and other obligations incident to doing business or operating a subsidiary in another country;
- workforce uncertainty in countries where labor unrest is more common than in the United States;

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production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad; and

business interruptions resulting from geo-political actions, including war and terrorism.

These and other risks associated with our international operations could materially adversely affect our business.

IF WE ARE UNABLE TO REALIZE THE EXPECTED BENEFITS OF OUR DRUG DISCOVERY CAPABILITIES AND OTHER TECHNOLOGIES, WE MAY NOT BE ABLE TO COMPETE IN THE MARKETPLACE.

The pharmaceutical research field is characterized by rapid technological progress and intense competition. As a result, we may not realize the expected benefits from our integrated drug discovery capabilities and technologies. For example, a large pharmaceutical company, with significantly more resources than we have, could pursue a systematic approach to the discovery of drugs based on gene families, using proprietary drug targets, compound libraries, novel chemical approaches, structural protein analysis and information technologies. Such a company might identify broadly applicable compound classes faster and more effectively than we do. 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, or at all, our business could be adversely affected.

IF WE FAIL TO EXPAND OUR HUMAN RESOURCES AND MANAGE OUR GROWTH EFFECTIVELY, OUR BUSINESS MAY SUFFER.

We expect that if our clinical drug 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. For example, the number of our full-time employees increased by 16% in 2008, and we expect to experience additional growth in 2009. Because our drug discovery and development activities are highly technical in nature, we require the services of highly qualified and trained scientists who have the skills necessary to conduct these activities. In addition, as we attempt to grow our capabilities with respect to clinical development, regulatory affairs, quality control and sales and marketing, we need to attract and retain employees with experience in these fields. We face intense competition for our personnel from our competitors, our collaborators and other companies throughout our industry. Moreover, the growth of local biotechnology companies and the expansion of major pharmaceutical companies into the Boston area have 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 to these areas. Our ability to commercialize our drug candidates, 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 to hire qualified personnel or manage our growth effectively, there could be a material adverse effect on our business.